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Abstracts

XXXI International Congress of the IAP and 28th Congress of the ESP

Oral Free Paper Sessions

Monday, 26 September 2016, 08.30–12.00, Conference Room 5
OFP-01 Digestive Diseases Pathology - GI

OFP-01-001
Comparison of KRAS, NRAS and PIK3CA mutational status in Poorly Differentiated Clusters (PDC) and corresponding main tumour mass of colon cancer
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Objective: To assess and compare the mutational status of KRAS, NRAS and PIK3CA in poorly differentiated clusters (PDC) of neoplastic cells and corresponding main tumour tissue in colon cancer (CC).
Method: Twenty-five CCs with KRAS mutation and at least 10 PDC in a 20× microscopic field were considered. Tumour cells forming PDC and main tumour mass were separated by laser microdissection and KRAS, NRAS and PIK3CA mutational status was analyzed in each of the two components by using mass spectrometry.
Results: In 20 cases PDC had the same biomolecular profile as the main tumour, but in 2 cases they had WT KRAS and in 3 cases they had additional PIK3CA mutations not observed in the main tumour. Cases with PIK3CA mutations in PDC but not in the main tumour had higher frequency of nodal metastases ($P = 0{,}07$), high pTNM stage ($P = 0{,}07$) and LVI ($P = 0{,}07$), although statistical significance was not reached.
Conclusion: Intra-tumour heterogeneity in biomolecular profile of CC may depend upon different histological aspects. Since PDC reflect epithelial mesenchymal transition and they are likely to produce metastatic disease, their molecular status, if different from that of the main tumour, may be relevant for prediction of response to targeted therapies.

OFP-01-002
Characterization of MEK1 and DIAPH3 expressions in colorectal mucinous and non-mucinous carcinomas with relation to clinicopathological parameters and prognosis
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Objective: The exact role of MEK1 and DIAPH3 in colorectal carcinogenesis is not yet well known. This study aims to investigate expression of MEK1 and DIAPH3 in colorectal mucinous adenocarcinoma (MA) and non-mucinous adenocarcinoma (NMA), and their relation to clinicopathological and survival data.
Method: Tumour tissue specimens from 75 patients with colorectal MA and 75 NMA were included in the study. All clinicopathological data of these 150 cases were revised with re-examination of all their slides. Three high density manual tissue microarrays were constructed and immunohistochemistry for MEK1 and DIAPH3 was done.
Results: Cytoplasmic MEK1 and DIAPH3 were overexpressed in 74 and 73 CRC cases (49.3 and 48.6 % respectively). NMA showed significantly higher MEK1, but not DIAPH3, expression than MA. MEK1 overexpression was significantly associated with positive lymphovascular emboli in the NMA group and with old age in MA group. DIAPH3 overexpression was not significantly associated with any of the tested variables. MEK1 overexpression was associated with better overall survival.
Conclusion: MEK1 and DIAPH3 have a significant interrelated role in colorectal carcinogenesis, especially in the non-mucinous type. Unlike DIAPH3, MEK1 overexpression is associated with better survival. Patients with non-mucinous carcinomas, and not mucinous ones, can benefit from MEK1 and DIAPH3 targeted therapies.

OFP-01-003
Combining digital image analysis with ngTMA construction: Lessons from a study analyzing CDX1 and CDX2 in colorectal cancer
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Objective: Immunohistochemical biomarker evaluation on TMAs is a standard technique. Until now, few attempts have been made to retrieve the maximum information from digital pathology during construction of TMAs and their subsequent analysis. As CDX2 (and CDX1) may have potential predictive power as colorectal cancer biomarkers, we aim to assess their robustness in terms of pre-analytics, tumour heterogeneity and effects of different intensity-percentage combinations on patient selection and prognosis.
Method: Next-generation tissue microarrays (ngTMA) of 636 colorectal cancer patients with cores covering tumour center and invasive front were immunostained for CDX1 and CDX2, scanned and analysed using Tissue Studio software (Definiens) Pre-analytical variables analysed included storage and fixation times. Three different types of heterogeneity were defined and investigated; prognostic relevance was determined.
Results: A complete ngTMA-DIA workflow can optimize on-target punching and leads to less core-loss. Pre-analytically both biomarkers were stable. Over 7 million epithelial cells of finally 612 accessible patients were labelled. Tumour heterogeneity was only slightly detectable as a mosaic, but excluded for the targeted differences between center and front as well as for occurrence of haphazard hot/cold spots. CDX1 and CDX2 protein loss are independent biomarkers of worse prognosis in multivariate analysis. Two-dimensioned intensity-percentage graphs can highlight the differences in cohort stratification and patient selection.
Conclusion: Tumour heterogeneity of CDX1 and CDX2 is minimal and protein expression is stable over different fixation and storage times. Both markers are prognostically relevant. However, we recommend that CDX2 loss be evaluated as percentaged complete negativity. New standards for digital image analysis are needed.

OFP-01-004

Does histopathological scoring system predict complications in pediatric patients with Crohn's diesease?

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Objective: In pediatric Crohn's disease (PCD), the benefit of microscopy in disease activity assessment and prediction of clinical outcome is, due to the focality of the inflammation, disputable. We investigated whether histopathological scoring system predicts complications in PCD and correlates with endoscopical and clinical scores.
Method: We performed a retrospective study on 63 patients. Endoscopy was evaluated using the Simple Endoscopic Score (SES), histopathology with the Global Histology Activity Score (GHAS). Pediatric Crohn's Disease Activity Index (PCDAI) was also calculated retrospectively. The patients were grouped according to the presence or absence of defined complications (intraabdominal abscess or fistula, perianal fistulizing disease, stricture with prestenotic dilatation or anti-TNF treatment). Associations were tested with Cox regression analysis.
Results: SES was higher in patients with complications. However, in case of GHAS and PCDAI we did not find any significant correlation. SES above 15 points was revealed as an independent risk factor for development of complications in PCD, in contrary to GHAS and PCDAI.
Conclusion: We did not prove any significant value of GHAS for predicting of complication development in pediatric Crohn's disease.

OFP-01-005

SOX2 loss predicts adverse survival of esophageal adenocarcinoma patients

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Objective: The prognosis of EAC remains poor, but highly variable amongst patients. SOX2 is a transcription factor involved in various gastrointestinal carcinomas. Here we aimed to test if SOX2 could improve prediction of prognosis of EAC patients.
Method: Two large independent cohorts of surgically treated EAC patients with known follow-up and clinicopathological characteristics were studied: the Rotterdam cohort (336 patients) and the Oesophageal Cancer Clinical and Molecular Stratification Study (OCCAMS) cohort (420 patients). Protein expression of SOX2 was evaluated using immunohistochemistry on tissue microarrays.
Results: SOX2 was significantly predictive for overall survival in both univariate and multivariate Cox regression analysis. Loss of SOX2 was predictive for adverse overall survival in both cohorts (Rotterdam: HR = 1.54, 95 % CI 1.16–2.04, $p = 0.003$; OCCAMS: HR = 1.58, 95 % CI 1.12–2.22, $p = 0.009$). In the multivariate analysis stratified for both cohorts, loss of SOX2 remained a significant prognostic factor with HR = 1.43 (95 % CI 1.15–1.78, $p = 0.002$). The most significant effect of SOX2 was identified within stage I patients (pT1 tumours: HR = 3.53, 95 % CI 1.24–10.08, $p = 0.018$; pN0 tumours: HR = 1.61, 95 % CI 1.38–1.89, $p < 0.001$).
Conclusion: The present study identified and validated SOX2 as a significant incremental factor for prognostication in EAC patients, specifically in the group of patients with pT1- and pN0-tumours.

OFP-01-006

Evolution to microscopic colitis-like change: Possible pattern of ulcerative colitis?

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Objective: To study frequency of ulcerative colitis (UC) patients subsequently evolving into microscopic colitis (MC).
Method: This prospective study included 53 eligible adult UC patients. 35 patients had active disease at baseline and were followed up for 8 weeks, whereas 18 patients were in remission and only baseline evaluation was done in them including colonoscopy with concurrent biopsy.
Results: Most patients had relapsing remitting disease (85.7 % in active disease and 83.3 % in remission group). Active disease group had longer disease duration than remission group. Progression to MC-like histologic change seen in 17/53 (32.1 %). Of which 88.2 % associated with CC and 11.8 % with LC. Five in active disease group had CC-like change at baseline biopsy, 3/5 (60 %) showed regression of thickness of collagen band on follow-up biopsy.
Conclusion: MC-like histologic changes in UC are common. UC subsequently developing into CC or LC suggesting MC could be a part of the spectrum of IBD. Prognostic implication of this histological transformation to MC in chronic UC patients is still unknown and has to be further evaluated with prospective studies. Until then it might be prudent to consider MC as a part of the natural history of IBD, at least in some cases.

OFP-01-007

Endoscopic nodular gastritis with Helicobacter pylori infection: An indicator of high-grade bacterial colonization and severe gastritis in children

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Objective: To assess the significance of Helicobacter pylori infection associated with endoscopic nodular gastritis (NG).
Method: This prospective study included 468 children in whom UGIE and antral biopsy was taken. 67 children were diagnosed as having NG. Demographics, clinical characteristics, endoscopic and pathologic findings were recorded.
Results: The prevalence of NG in children was 14.3 % (67/468) and consisted of 46.3 % male and 53.7 % female. Children age ranged from 3 to 18 years. The prevalence of NG increased gradually with age. H pylori infection was identified in 68/468 (14.5 %) children. Nodular gastritis had a poor accuracy rate to determine H. pylori infection (sensitivity, 40.3 %; positive predictive value, 39.7 %) and was observed in 27/68 (39.7 %) H pylori positive patients and in 40/400 (10 %) H pylori negative patients. There was a significant increase in grade of inflammation, activity, atrophy, number of lymphoid follicles and H pylori density on histologic evaluation in H pylori positive patients with NG than other groups.
Conclusion: Nodular gastritis has a poor prediction for H pylori infection in children. Gastric biopsies should always be obtained during endoscopy in children to establish the H pylori infection. H. pylori infection in children with NG identifies cases with severe gastritis and marked bacterial colonization.

OFP-01-008

The search for an epithelial-mesenchymal phenotype in colorectal cancer reveals a subset of cytokeratin-positive / vimentin-positive cells derived from the tumour

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Objective: It is hypothesized that tumour buds in colorectal cancer represent an epithelial-mesenchymal transition (EMT)-like phenotype. Here, we determine the existence and frequency of an epithelial/mesenchymal double-positive cell type and its origin in colorectal cancer.
Method: One tumour block from a patient with high-grade tumour budding was cut, immunostained for cytokeratin (CK) and scanned. Using digital pathology, regions of tumour buds, tumour center and normal stroma were annotated, aligned to the block and punched out. Punches were dissociated into single cell suspensions and fluorescently-labeled with CK and vimentin (VIM). Using DepArray technology, cells were sorted based on their single or double-positivity and analysed by NGS (Ion Torrent 50-gene cancer panel).
Results: Tumour and stromal fractions contained only CK+ or VIM+ cells, respectively. In the budding fraction, 10 (2.9 %) CK+/VIM+ double-positive cells were identified. Sequencing revealed that CK+ tumour cells carried mutations in BRAF and TP53 and a deletion in PTEN. The exact same mutational profile was seen in the CK+/VIM+ cells. VIM+ stromal cells were negative.
Conclusion: CK+/VIM+ double-positive cells exist at the invasion front of colorectal cancer, albeit in low number. These cells originate from the tumour. Whether this is evidence of EMT in colorectal cancer requires further elaboration.

OFP-01-009
Histological and immunological characteristics of colitis associated with anti-CTLA-4 antibody therapy

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Objective: Treatment of neoplasias with ipilimumab, a monoclonal antibody against CTLA-4, has been associated with the development of immune-mediated colitis. Aim of this study was the evaluation of histological and immunological characteristics of ipilimumab-associated colitis (IAC) in 9 patients with severe diarrhea after treatment for metastatic melanoma.
Method: The histological features of IAC were evaluated in 9 colonic biopsies. The mucosal immunophenotype was assessed by examination of the inflammatory infiltrate, including semi-quantitative immunohistochemical characterization of lymphocytic subsets and by measuring the relative mRNA expression for lymphocyte-lineage specific transcription factors and cytokines.
Results: Histological characteristics were non-specific, highly resembling Crohn's disease or ulcerative colitis exhibiting a predominance of either plasma cells or CD4+ T-cells with high CD4/CD8 ratios. Neutrophils and crypts with mucin depleted flat epithelium were almost constantly present. IAC was related to significant upregulation of Th1 and Th17 immunological effector pathways, with high elevations of IFN-γ (>10-fold increase over baseline) and IL-17A (>5-fold increase). In addition, elevation of the regulatory T cell markers Foxp3 and IL-10, and the TNF-like cytokine TL1A/TNFSF15 was observed.
Conclusion: Ipilimumab administration usually results in IBD-like colitis probably ascribed to increased influx of effector lymphocytes and enrichment of the mucosa milieu with pro-inflammatory mediators.

OFP-01-010
High grade dysplasia and large size as predictors of mismatch repair deficiency in Lynch Syndrome-associated colorectal adenomas

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Objective: The prevalence of loss of protein expression by immunohistochemistry (IHC) in Lynch syndrome (LS) polyps remains poorly studied. We aimed at describing the prevalence of loss of MMR protein expression in LS-associated polyps and to identify independent predictors of MMR deficiency.
Method: 171 colorectal polyps (121 adenomas, 50 serrated lesions) from 53 LS patients (18 MLH1,22 MSH2,10 MSH6,3 PMS2) were IHC stained with MLH1, MSH2, MSH6 and PMS2 proteins. Clinicopathological variables associated to pathological IHC were assessed.
Results: The median size of adenomas was 5,2 mm;19 (15,7 %) > 10 mm;11 (9,1 %) were villous and 15 (12,4 %) showed high-grade dysplasia (HGD). IHC was pathological in 69 (57 %) adenomas. In univariate analysis, variables associated with pathologic IHC staining were: female genre ($p = 0,04$), rectal location ($p = 0,02$), MLH1 mutation ($p = 0,03$), HGD ($p < 0,001$) and size >5 mm ($p = 0,001$). PMS2 mutation was inversely associated to protein loss ($p = 0,03$). In multivariate analysis, independent predictors were: HGD ($p = 0,02$), PMS2 mutation ($p = 0,03$) and size >5 mm ($p = 0,03$). Serrated lesions retained protein expression.
Conclusion: In LS patients, large adenomas and those with HGD were associated with loss by IHC. Adenomas with PMS2 germline mutations and serrated lesions tended to retain protein expression. Normal IHC in colorectal polyps should not discard a LS diagnosis.

OFP-01-011
Gastric microbiota and carcinogenesis: The role of non-helicobacter pylori bacteria. A systematic review

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Objective: H.pylori is the strongest risk factor for gastric cancer (GC); recent advances in DNA sequencing technology have unraveled a complex gastric microbial community that may participate in gastric carcinogenesis. We aim to review scientific evidence regarding the role of non-H.pylori bacteria in gastric carcinogenesis.
Method: A systematic review of original articles published in PubMed in the last 10 years related to gastric microbiota and GC was performed.
Results: 13 original articles were included. The constitution of gastric microbiota appears to be significantly affected by GC and premalignant lesions as well as by H.pylori. A gradual shift in the gastric microbiota profile from non-atrophic gastritis to intestinal metaplasia, and then to intestinal type cancer appears to exist. Gastric carcinogenesis can be associated with an increase in many bacteria (such as Acinetobacter baumannii or Klebsiella pneumoniae and Lactobacillus coleohominis) as well a decrease in others (such as Porphyromonas spp, Prevotella pallens, Neisseria spp or Streptococcus sinensis). However, no conclusive data suggest if these changes in microbiota are cause or consequence of the carcinogenesis process.
Conclusion: GC may be the result of a complex cross-talk between gastric microbiota and H.pylori. Gastric microbiota appears to play an important role in gastric carcinogenesis, beyond the well-known influence of H.pylori.

OFP-01-012
Gastric carcinoma with lymphoid stroma: A study of Epstein-Barr virus, microsatellite instability, tumour immune microenvironment and PD-L1 expression

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Objective: To analyse Epstein-Barr virus (EBV) status, microsatellite instability (MSI), tumour immune microenvironment and PD-L1 expression in gastric carcinoma with lymphoid stroma (GCLS).
Method: Twenty-four GCLSs were analysed by: RNA in situ hybridisation for EBV, PCR/fragment analysis for MSI status,

immunohistochemistry for cytokeratin (CK) AE1/AE3, CD68, CD3, CD8 and PD-L1, and double immunofluorescence for CK/PD-L1 and CD68/PD-L1. CD3+, CD8+ T cell densities and CD8/CD3 ratio (CD8/CD3R) were calculated both in the tumour centre (TC) and at the invasive front (IF).
Results: Regarding EBV and MSI status, 3 groups were identified: EBV+/MSS ($n = 15$), EBV-/MSI-high ($n = 4$), and EBV-/MSS ($n = 5$). Overall, CD8/CD3R in the TC exceeded CD8/CD3R at the IF ($p = 0.048$). CD8/CD3R in the TC was significantly higher ($p = 0.032$) in EBV+ ($n = 15$) than in EBV- ($n = 9$) cases. PD-L1 overexpression in neoplastic cells (≥50 %) was observed at the cell membrane in EBV+ (4/15; 23 %) and MSI-high (2/4; 50 %) GCLSs. Whole-Genome-Sequencing of one PD-L1+ case revealed PD-L1 amplification. Five-year survival rate was high (60 %) and not influenced by PD-L1 expression.
Conclusion: GCLSs are characterized by EBV infection (63 %), MSS status (83 %), high CD8/CD3R in TC and PD-L1 overexpression (25 %). PD-L1 overexpression was restricted to EBV+ and MSI-high cases, reinforcing its role in these molecular subtypes of GCLS.

OFP-01-013
Expression of the histone methyltransferase EZH2 in colorectal cancer
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Objective: Immunohistochemical characterization of histone methyltransferase EZH2 expression in a series of colorectal cancer (CRC) patients, and correlation with clinicopathological features.
Method: CRC patients primarily submitted to surgery at Portuguese Oncology Institute-Porto (2003–2006) were selected; one representative slide/block per case and relevant clinicopathological data were retrieved. Assessment of EZH2 nuclear expression (median percentage ± interquartile range) in normal mucosa and CRC using a semi-automated software system.
Results: A total of 199 cases were selected: median age: 70 years; 111(55.8 %) male; 141(71.0 %) left colon tumours. All cases were adenocarcinomas (5 mucinous; 194 tubular, 183 low-grade); 16 (8,0 %) presented lymphatic invasion; 33 (16.6 %) were stage I, 77 (39.0 %) had lymph node metastases and 21 (11.0 %) displayed distant metastases. EZH2 was overexpressed in CRC (36.70 ± 30.9) compared to normal colon (5.90 ± 7.40). EZH2 expression was significantly higher in right colon tumours ($p = 0.022$) and in CRCs with regional lymph node metastases ($p = 0.047$). Age, gender, histological pattern, tumour grade, lymphatic invasion, tumour extent and presence of distant metastasis at diagnosis were not associated with EZH2 expression. A trend for higher EZH2 expression in stage III/IV tumours compared to stage I/II tumours was depicted ($p = 0.065$).
Conclusion: EZH2 may play a role in cell growth and invasion in colorectal carcinogenesis. Quantitative EZH2 immunoexpression might be a promising biomarker for assessing CRC clinical aggressiveness. Survival analysis (ongoing) will determine if this biomarker might be of prognostic relevance.

OFP-01-014
The role of the central pathology lab in SPECTAcolor
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Objective: The objective of SPECTAcolor (Screening Patients for Efficient Clinical Trial Access) is to build a quality assured, clinically annotated colorectal cancer biobank for molecular tumour profiling for optimized trial access and for biomarker discovery and validation.
Method: After informed consent, clinicopathological data are captured and FFPE tumour material is collected in SPECTAcolor central biobank. Only patients with sample deemed adequate by the central pathologist are enrolled. Samples are analysed for MSI and with targeted exon-NGS. QA/QC criteria are pre-defined and applied from biobank selection to NGS data reporting. Quality performance is monitored also via participation in proficiency testing programs.
Results: SPECTAcolor recruited 900+ patients with ~900 centralized samples: 15 % biopsy and 85 % surgical specimens. 3.6 % of them were rejected due to low tumour cellularity (<30 %). Block failure rate for DNA extraction was 4.5 % (3.6 % surgical vs. 11 % biopsy samples). DNA from ~800 blocks was sequenced: 524 passed, 163 pending and 105 failed. ~450 NGS patient report was released via a secured web portal. NGS sample failure rate was highest during library preparation due to low amount of DNA (DNA < 100 ng: 34 % vs. DNA >200 ng: <2 %).
Conclusion: A logistically complex infrastructure including quality-controlled HBM collection and management for next generation trials in multinational setting is feasible.

OFP-01-015
The serrated neoplasia pathway of colorectal tumours: Identification of MUC5AC hypomethylation as an early marker of polyps with malignant potential
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Objective: The serrated neoplasia pathway accounts for 20 to 30 % of colorectal cancers (CRC), which are characterised by extensive methylation (CIMP), BRAF mutation and high microsatellite instability (MSI). We recently identified MUC5AC mucin gene hypomethylation as a specific marker of MSI CRC. The early identification of preneoplastic lesions among serrated polyps is currently challenging. Objective. We performed a detailed pathological and molecular analysis of a large series of serrated polyps and evaluated the usefulness of mucin genes MUC2 and MUC5AC to differentiate serrated polyps and to identify lesions with malignant potential.
Method: A series of 330 colorectal polyps including 218 serrated polyps (42 goblet cell-rich hyperplastic polyps (GCHP), 68 microvesicular hyperplastic polyps (MVHP), 100 sessile serrated adenoma (SSA), 8 traditional serrated adenoma (TSA)) and 112 conventional adenomas was analysed for BRAF/KRAS mutations, MSI, CIMP, MLH1, MGMT methylation, MUC2 and MUC5AC expression and methylation.
Results: MUC5AC hypomethylation is an early event in the serrated pathway, and specifically detects MVHP and SSA, arguing for a filiation between MVHP, SSA, and CIMP-H/MSI CRC. Moreover, MUC5AC hypomethylation specifically identified serrated lesions with BRAF mutation, CIMP-H or MSI, suggesting that it may be useful to identify serrated pathway-related precursors.
Conclusion: Our data suggest that MVHP may require particular attention.

Monday, 26 September 2016, 14.45–16.45, Conference Room 5
OFP-02 Digestive Diseases Pathology - Liver/Pancreas

OFP-02-001
The histopathologic changes of alcoholic steatohepatitis over time after glucocorticoid therapy
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Objective: To determine time course of histopathologic regression of severe alcoholic steatohepatitis under steroid treatment and alcohol abstinence in patients with chronic liver disease and superimposed alcoholic steatohepatitis.

Method: 110 paired liver biopsies from presentation (days 0) and then intervals of 10, 30 or 90 days after treatment were assessed for alcoholic steatohepatitis features (steatosis, lobular neutrophil, ballooning degeneration, Mallory bodies, megamitochondria, and cholestasis) and fibrosis.
Results: At 10 days, odds of reduced steatosis from presentation were 0.73. Mean ballooning degeneration/high power field (HPF) were increased ($p = 0.017$); mean neutrophils/HPF showed no significant change. At 30 days, odds of reduced steatosis increased to 1.62; megamitochondria were not seen at intervals of 30 days or more. Mean neutrophils/HPF remained unchanged; mean ballooning degeneration/HPF were decreased ($p = 0.006$). At 90 days, odds of reduced steatosis were 5.2; there was significant reduction in odds of Mallory bodies from baseline, odds ratio (95%CI): 0.05 (0.01,0.40). Odds of improvement in Laennec fibrosis score remained unchanged ($p = 0.119$).
Conclusion: We observed a different time course regression (from day 0 to day 90) of the histologic features in treated alcoholic steatohepatitis. These data increase the confidence of the interpretation of delayed liver biopsies in the setting of treated alcoholic steatohepatitis.

OFP-02-002
The short bowel syndrome is a major risk factor of liver disease in adults with intestinal failure and parenteral nutrition
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Objective: The intestinal failure-associated liver disease (IF-ALD) is rare in adults and multifactorial. The aims of the study were (1) to describe IF-ALD diagnosed on biopsy in adults receiving parenteral nutrition (PN) for irreversible IF, (2) to characterize the risk factors of IF-ALD, (3) to analyze the impact on survival.
Method: During a follow-up of 118 months, 32 patients (mean age 46 years, receiving a 4 year-PPN mean duration) had a liver biopsy performed for abnormal hepatic tests and an intestinal transplantation project.
Results: 18 of the 32 patients (56 %) presented IF-ALD defined as an advanced hepatic fibrosis (≥ F2: 4 stage F2, 10 F3, 4 F4). Steatohepatitis and cholestasis prevailed in 72 and 9 % of patients respectively. In multivariate analysis, short bowel syndrome and especially ultra-short bowel (<15 cm of small bowel) were highly associated with IF-ALD ($p < .004$). PN modality, quantity or duration, sepsis episodes, excluded intestine, alcohol consumption and diabetes were not significantly associated with IF-ALD. During follow-up, 11 of the 32 patients died, 9 had IF-ALD; IF-ALD predicted a bad overall survival ($p = 0.028$).
Conclusion: The short bowel syndrome was the major risk factor of IF-ALD in adults requiring prolonged PN. The prevalence of steatohepatitis lesions needs further studies for mechanistic explanation.

OFP-02-003
Prognostic role of c-myc amplification in pancreatic acinar cell carcinomas
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Objective: The molecular alterations of pancreatic acinar cell carcinomas (ACCs) are not completely understood and the possible role of c-myc amplification in tumour development, progression, and prognosis has been poorly investigated. In the present study we evaluated the prognostic role of c-myc amplification and its nuclear protein expression in a series of 48 well characterized pancreatic ACCs.
Method: Gene amplification was investigated using interphasic FISH analysis simultaneously hybridizing c-myc and the centromere of chromosome 8 probes (Dako, Carpinteria, CA, USA). Protein expression was investigated with immunohistochemistry using a specific rabbit monoclonal anti-c-myc antibody (Abcam, Cambridge, UK).
Results: 6/48 (12.5 %) ACCs showed c-myc amplification and six (12.5 %) showed c-myc nuclear immunoreactivity. However, only 3 cases showed simultaneous c-myc amplification and nuclear protein expression. C-myc immunoreactivity was not associated with patient's prognosis, while c-myc amplification was statistically associated with worse prognosis (p: 0.04).
Conclusion: c-myc amplification is present in about 12 % of pancreatic ACCs and identifies a subset of more aggressive neoplasms.

OFP-02-004
Programmed cell death and immune response by modulated electro-hyperthermia in colorectal cancer allografts
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Objective: Modulated electro-hyperthermia (mEHT) using radiofrequency and the concomitant heat (<42oC), can selectively target malignancies due to their elevated glycolysis, ion concentration and conductivity compared to normal tissues. mEHT treatment, which can be used as a complementary to radiation- or chemotherapy of human cancer, can provoke apoptosis and immune cell infiltration in HT29 colorectal cancer xenografted into immunocompromised mice.
Method: Here we tested the mEHT related damage, stress and immune response in CT26 colorectal cancer symmetrical allografts of immunocompetent mice.
Results: mEHT caused significant tumour damage in treated right-leg tumours, accompanied by elevation of activated caspase-3 levels and cytochrome-c release from mitochondria indicating apoptosis, confirmed also by DNA fragmentation TUNEL test. After mEHT treatment, the release of damage-associated molecular pattern (DAMP) signals involving hsp70, calreticulin and HMGB1 proteins, along with elevated number of S100+ antigen presenting cells and CD3+ T-cells were also observed. In addition, mEHT supplemented with a chlorogenic acid rich, T-cell promoting agent induced damage also in the untreated left-leg tumours suggesting a systemic effect.
Conclusion: In conclusion, mEHT can induce caspase-dependent apoptosis in CT26 colorectal cancer allografts and the release of stress associated DAMP proteins, which may support a dendritic cell and T-cell mediated immunogenic tumour cell death response.

OFP-02-005
Hepatic progenitor cells: A potent survivor in metastatic carcinomas: Preliminary results
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Objective: Hepatic progenitor cells (HPC) are activated in a variety of liver diseases but their behavior in carcinomatous environment is still unknown. Aim of the study is the investigation of HPC reaction in carcinoma metastatic foci (MF).
Method: The presence of HPC was examined in 10 cases of liver metastasectomies for colorectal adenocarcinoma, within and at the periphery of MF. Immunohistochemical investigation included keratin (K) 20, K7, CDX2, HPC (K19, CD56) and stem cell (CD44) markers. Double immunostaining CDX2/K7 was also applied while p63/K7 was performed in an additional case of metastatic anal squamous cell carcinoma (SCC).
Results: HPC usually forming ductular structures (K7, K19, CD56, CD44 positive, K20 negative) were encountered at the MF periphery in contact with neoplastic tissue (K20 diffusely, CD44 rarely positive) and adjacent liver parenchyma. Additionally, HPC

incorporation in carcinoma tubules created structures of mixed cellular composition. The intratumoural presence and identity of HPC cells was proven by the absence of CDX2 and p63 expression in contrast to nuclear positivity of metastatic adenocarcinoma and SCC cells, respectively.
Conclusion: Our findings provide indications that HPC, possibly due to stemness, are supplied with adjustment and survival potential in an ominous environment associated with metastatic carcinoma.

OFP-02-006
Characterization of pancreatic stellate cells in pancreatic ductal adenocarcinoma and cases of chronic pancreatitis of various etiologies
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Objective: An abundant stromal reaction is a hallmark of pancreatic ductal adenocarcinoma (PDAC) and chronic pancreatitis (CP). Pancreatic stellate cells (PSCs) are mainly responsible for the stromal reaction. Despite their crucial role, PSCs are not well characterized. However, PSCs share numerous characteristics with the elaborately described hepatic stellate cells (HSCs). The aim of this study was a detailed immunophenotypical analysis of PSCs in PDAC and CP.
Method: The stroma of PDAC ($n = 10$) and CP ($n = 12$) tissue sections was characterized using Movat's stain. Sections were then stained for PSC markers (α-SMA, CD34, desmin, NGFR, SPARC and tenascin C) and HSC markers (α-crystallin B, CD56, NGF, NT-3, synaptophysin and TrkC). PSCs isolated from PDAC and CP tissue samples were evaluated by immunofluorescence.
Results: PSCs expressed all tested markers. In PDAC, perilesional staining patterns were observed for all markers, while staining patterns in CP were more varying. Staining patterns were heterogeneous in PDAC and CP cases. α-SMA and SPARC staining was correlated with collagen-rich fibrosis, while NT-3 staining was correlated with stroma remodeling.
Conclusion: The close similarities between PSCs and HSCs were confirmed. Heterogeneous expression patterns of the tested markers might reflect different activation or differentiation levels of PSCs or even multiple PSC subpopulations. An active role of the stroma in PDAC and CP is strongly suggested.

OFP-02-007
Ampullary carcinoma: Analysis of RAS-pathway gene mutation status
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Objective: Currently there is a priority for searching of new selective cellular-target anticancer drugs for ampullary carcinoma (AC). Targeting therapy requires information about mutational status of cellular target. Aim: To compare two methods of KRAS-gene mutational status analysis in DNA samples from tumour tissue.
Method: We analyse specimens of 24 patients with ampullary carcinoma. Molecular investigation was provided in samples containing at least 80 % of tumour tissue. Analysis was performed using two methods: Sanger sequencing (2nd exon) and digital droplet PCR (ddPCR) (p.G12D ир.G12V).
Results: In 87.5 % of cases tumour was presented as moderately-differentiated adenocarcinoma; in 12,5 % cases—as well-differentiated adenocarcinoma. Results of Sanger sequencing revealed KRAS-gene mutation in 33.3 % of cases (8 of 24): five of them had p.G12D and three—p.G12V. Analysis of ddPCR results revealed 10 additional mutations in an amount of 0,1–2,82 % of mutated allele. Thus, there were 75 % (18 of 24) cases with KRAS-gene mutation: 12 cases had p.G12D, 3 cases—p.G12V and 3 cases—both p.G12D and p.G12V.
Conclusion: Comparative analysis of two methods of molecular-genetic investigation showed high sensitivity of ddPCR method, which could be recommended for practice in clinical oncology for analysis of mutational status of RAS-family genes in patients with ampullary carcinoma.

OFP-02-008
Epithelium-mesenchyme transformation in pancreas duct adenocarcinoma
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Objective: Most researches are currently focused on epithelium-stroma relationship that plays an important role in epithelial tumour progression towards to de-differentiated phenotype.
Method: 100 patients with PDAC. Molecular analysis was performed in 21 cases. IHC—p63, aSMA, PanCK, CK 7, vimentin, E-cadherin, and EMA (Dako, Lab Vision Flex). Evaluation of changes in genes ZEB1, ZEB2, CDH1,VIM using real-time PCR on frozen sections previously prepared in the lysis buffer.
Results: In 21 % (21/100) cases of PDAC along with glandular structures we revealed anaplastic component with minimal stromal component. The volume of anaplastic component was ranged from 5 to 20 %. In the cells of anaplastic component IHC revealed: SMA, vim, p63. At the same time in separate anaplastic cells marked loss of expression of panCK and CK 7, EMA. In all cases there were negative membrane and cytoplasmic expression of the protein E-cadherin in AC. Molecular analysis showed that AC was characterized by coordinated changes in expression levels of genes with increasing of ZEB1, ZEB2, VIM and significant decreasing of CDH1.
Conclusion: Heterogeneity of PDAC is manifested by appearance of anaplastic (sarcoma like) component, in which epithelial tumour cells acquire properties of mesenchymal cells, and don't require presence of stroma and have an aggressive malignant potential impacting on survival of patients.

OFP-02-009
Survey of hepatocellular adenoma in Japan
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Objective: Hepatocellular adenoma (HCA) has been estimated to have a lower prevalence in Japan than in Western countries, though definitive data are as yet lacking. We endeavored to ascertain the HCA prevalence in Japan.
Method: We sent a questionnaire survey to Japanese University Hospitals, National Hospital Organizations, Japan Red Cross Hospitals and other flagship hospitals, 394 in total, conducting large numbers of liver operations.
Results: The response rate was 80 %. The average number of hospital beds was 585. During periods of 5 to 30 years, there were 157 HCA cases. The male/female ratio was approximately 3/2. The age range was 14–87 (mean 39.3) years. Approximate complication rates of were: glycogen storage disease, 9 %; DM, 7 %; obesity, 10 %; hyperlipidemia, 5 %; HBsAg-positive, 0.6 %; anti-HCV-positive, 0 %; history of alcohol intake, 6.5 %; oral contraceptives or steroid use, 17.6 %. Forty-six cases were analyzed immunohistologically for HCA subtype: HNF1α-inactivated, Beta-catenin activated, Inflammatory and Unclassified HCAs comprised 38.6, 4.5, 40.9 and 16 %, respectively.
Conclusion: Characteristically, elderly and male were not rare among Japanese HCA cases, and there were fewer drug-related cases than in Western countries, while prevalences of the 4 subtypes tended to be similar in the Japan and the West. Acknowledgement: We appreciate the participated hospitals.

OFP-02-010

TXNIP overexpression promotes aggressive phenotpe in HCC cell lines

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Objective: Thioredoxin interacting protein (TXNIP) regulates cellular responses under stress conditions, such as hypoxia, serum starvation. The over-expression of TXNIP results activation of oxidative stress and apoptosis. In breast cancer and hepatocellular carcinoma (HCC) models TXNIP is considered as a tumour suppressor gene. However, its role in the development, progression of HCC and the mechanisms behind it warrant further investigation.
Method: In this study the expression levels of TXNIP were examined in 12 HCC cell lines by RT-PCR and Western blotting (WB). Expression of TXNIP was examined in 16 non-HCC and 79 HCC ($n = 26$ well, $n = 53$ moderate & poorly differentiated) tissue samples by immunohistochemical staining (IHC).
Results: TXNIP expression was significantly high in poorly-differentiated cell lines such as SNU-182, SNU-387 and SNU-423 than the well-differentiated HCC cell lines such as HuH-7, HepG2 and PLC/PRF/5. Immunohistochemical TXNIP positivity was observed in 40 % of well differentiated and 80 % of poor differentiated HCC tissues. However, no strong TXNIP positivity was observed in non-HCC tissues. To investigate whether TXNIP might be involved in biological responses such as cell adhesion, proliferation, motility and invasion, we used transient overexpression. The adhesion and proliferation were investigated with real-time cell analysis. Overexpression of TXNIP minimally inhibited adhesion and proliferation, whereas Boyden-chamber motility and invasion assay showed that the invasiveness of HCC cells was increased.
Conclusion: Our findings suggest that TXNIP expression is increased in HCC and TXNIP over-expression is important for invasive phenotype during hepatocarcinogenesis.

OFP-02-011

Histological tumour stroma negative mesopancreatic resection margin correlates with patients outcome and can be predicted by preoperative radiologic parameters

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Objective: Pancreatic ductal adenocarcinoma (PDAC) is characterized by a dense desmoplastic stroma. Peritumoural fibrosis is often evident during surgery. The aim of this study was to investigate the role of peritumoural stroma as a criterion for radical resection.
Method: Tumour stromal status (S-Status) was defined as the presence or absence (S+/S0) of fibrotic/desmoplastic tissue at the mesopancreatic resection margin. Detailed retrospective clinico-pathologic re-evaluation of margin status and preoperative cross-sectional imaging was performed in a cohort of 91 patients.
Results: Conventionally margin positive resection (R+) was significantly associated with reduced median survival. S-Status further divided the negative margin group into patients with median survival of 14 months (S+) versus 31 months. Median survival in patients without lymph node metastasis and S0 resection was significantly increased. Multivariate, S-Status constituted the only significant predictor of survival after resection among all standard clinico-pathological parameters. A panel of preoperative radiological parameters characterizing mesopancreatic tissue achieved an 82 % correct prediction of S-Status.
Conclusion: Complete removal of tumour cells and concomittant fibrotic stroma seems to be a determinant of curative resection in PDAC. Additionally, preoperative prediction of non-curative resection by cross-sectional imaging is possible, hence a redefinition of borderline resectable PDAC advocating neoadjuvant therapy might be discussed.

OFP-02-012

Histopathological tumour invasion of the mesenterico-portal vein is characterized by aggressive biology and stromal fibroblast activation

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Objective: Mesentericoportal vein resection (PVR) during pancreatoduodenectomy for pancreatic head cancer is a routine procedure in specialized centers. Current large-scale retrospective cohort studies report controversial results concerning survival benefit of PVR. Portal vein invasion has been shown to be predictive of poor prognosis after PVR. The aim of this study was to examine the relationship between PVI and features of aggressive tumour biology.
Method: Patients treated by pancreatoduodenectomy with en-bloc PVR for pancreatic ductal adenocarcinoma of the pancreatic head were identified from a prospectively maintained database. Immunohistochemical staining of tumour tissue was performed for the markers of epithelial-mesenchymal transition (EMT) E-Cadherin, Vimentin and beta-Catenin. Morphology of cancer-associated fibroblasts (CAFs) was assessed as inactive or activated.
Results: In total, 41 patients could be included. Median overall survival was 25 months. PVI was found in 17 patients (41 %) and was significantly associated with loss of membranous E-Cadherin in tumour buds ($p = 0.020$), increased Vimentin expression ($p = 0.03$), activated CAF morphology ($p = 0.046$) and margin positive resection ($p = 0.005$).
Conclusion: Our findings suggest that PVI is associated with aggressive tumour biology and disseminated growth less amenable to margin-negative resection.

Monday, 26 September 2016, 17.15–19.15, Conference Room 5
OFP-03 Cytopathology

OFP-03-001

Medical simulation training in fine needle aspiration cytology using phantoms: University teaching experience

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Objective: Fine needle aspiration cytology (FNAC) is a minimally invasive and extremely useful procedure. The characteristics of pathology practices, together with limited equipment, make teaching this technique difficult. We therefore have introduced phantoms designed to perform FNAC in the educational program in our hospital.
Method: Phantoms are two life-sized hand-made reproductions of a head-&-neck and a trunk (utility-models ES1140059/ES1149563), coated with silicone simulating skin and with inserted tumour areas. They allow performing the whole FNAC process (palpation/puncture/aspiration/placement-of-material-on-slide/smear-preparation) and, furthermore, are reusable. The practice was running during 3 academic years (2013–2016) and each student performed the procedure individually, in a clinical context with subsequent cytological correlation.
Results: 178 medical students, in their third year, from the 178 third-year medical students (University of Murcia, Spain) took part in the FNAC practice (28 groups: 105women/73men). The success rate in the first attempt (puncture/aspiration-of-material/placing/extending-on-slides) was 97.2 %. Furthermore, 13 students from 10 other universities (national/international) also took part, not having such a program in their medical schools. The practice was considered to be valuable in an anonymous survey.
Conclusion: FNAC training is easily implementable in the undergraduate curriculum and also in the Objective-Structured-Clinical-Examination (OSCE) evaluation format. There is no proper standardization in practices among different universities. FNAC simulation provides students with greater knowledge and appreciation of our specialty.

OFP-03-002

On-site cytology for patient derived three dimensional organoid cultures: A pilot study

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Objective: Development of patient derived three-dimensional (3D) organoid cultures is an emerging technique in the field of precision medicine (PM). We aimed at integrating on-site cytologic adequacy evaluation into the organoid development workflow to ensure precise characterization and growth of these cultures.
Method: Cytology smears were prepared on-site in real time from fresh tumour tissue collected from consented patients prior to tissue submission for whole-exome/RNA sequencing and organoid development.
Results: Cytology preparations were made from 45 different tumour samples and evaluated prior to tissue submission for organoid development. In 36 (80 %) of those tumour samples, the cytology preparation was sufficient for diagnosis, thus providing adequate lesional material for organoid development (Figure 1).
Conclusion: Characterizing the tissue in real time, prior to submission for organoid development is feasible and ensures submission of lesional tissue only. Furthermore, it is a cost effective method to help document the diagnosis also for medico-legal reasons since the tissue submitted for organoids is subsequently lost for clinical diagnosis. In addition, cytologic evaluation of the organoid cultures few weeks into development ensures growth of pure tumour organoids only and not contaminants. Our findings in this pilot study led to the implementation of on-site cytologic evaluation in the organoid development workflow at the Institute for Precision Medicine.

OFP-03-003

Reparative, neoplastic and cancer epithelial-mesenchimal structures with stem cell markers and their role in uterine cervical cancerogenesis

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Objective: to investigate spheroid epithelial-mesenchymal structure (SEMS) in HPV associated uterine cervical precancer and cancer.
Method: Samples of 61 patients with cervical pathologies were obtained. Immunohistochemistry of p53, C-Myc, HIF1-alpha, VEGF, Oct-4, Aldh1A1, CD34, Vimintin and p16/Ki-67 was done.
Results: Three types of Oct4 positive SEMS were found: Reparative SEMS distributed frequently among chronic cervicitis and L-SIL samples with expression of p53, CD34, low expression of C-MYC, HIF1-alpha, VEGF, ALDH, Vimintin; Neoplastic SEMS—among the samples of L-SIL and H-SIL, with cellular atypical, low expression of p53 and high expression of p16, C-MYC, HIF1-alpha, VEGF, ALDH, Vimintin; Cancer SEMS—among carcinoma samples with distinguishable atypical polymorphic nucleus and high expression of p53, p16, C-MYC, HIF1-alpha, VEGF, ALDH, CD34, Vimentin.
Conclusion: development of HPV-associated squamous cell cervical cancer is associated with arising of cancer stem cell in Oct4-positive neoplastic and cancer SEMS.

OFP-03-004

Triage of ASC cytology using biomarkers: A comparative study of SurePath, ThinPrep and CellSolutions platforms

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Objective: The objective of this study was to assess and compare the predictability of novel biomarkers, MCM/Top2A, HPV E6E7 mRNA and HPV DNA in women with ASC (atypical squamous cell) cytology in ThinPrep, SurePath and CellSolutions liquid based cytology (LBC) platforms.
Method: Study population consisted of patients referred for colposcopy in 5 of the 10 Canadian provinces. Two separate cytology samples from each patient were collected ($n = 1821$); the first sample was collected in ThinPrep with the second collected in SurePath. ThinPrep specimens were tested for HPV DNA and E6/E7 mRNA while those collected in SurePath tested for MCM/Top2A. From the residual SurePath sample, a CellSolutions slide was prepared and stained. Histology confirmed CIN2+ served as the disease end point. Binary logistic regression models were performed to examine the usefulness of biomarker profiles for each of the LBC platforms.
Results: Of 1821 patients, 392 (21.5 %), 251 (13.8 %), and 69 (20.8 %) patients were identified having ASC cytology by ThinPrep, SurePath, and CellSolutions platforms, respectively. The frequency of CIN 2+ in ThinPrep, SurePath, and CellSolutions cohorts were 20.9 % (82/392), 22.3 % (56/251), and 17.4 % (12/69). No statistically significant difference was found between the odds ratio in each model between the three platforms.
Conclusion: Our findings show that combining biomarkers are useful in identifying high grade dysplasia in patients with ASC cytology. Although no statistically significant difference was found between the odds ratio in each model between the three LBC platforms, the ThinPrep group showed a stronger predictability than the two cohorts by measure of the higher odds ratios.

OFP-03-005

Breast cytology continues to be relevant in a large academic medical center

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Objective: Fine needle aspiration (FNA) is efficient, accurate, and cost-effective for diagnosis of palpable breast lesions, but is increasingly being supplanted by core biopsy. In our institution, breast surgeons continue to rely on breast FNA. Diagnostic accuracy of breast FNA and its utility for biomarker testing was evaluated in a large cohort.
Method: 1654 breast FNAs were performed at our institution from 2009 to 2015. Eighteen percent of samples ($N = 300$) included cell block material. ER, PR, HER2 immunohistochemistry (IHC) and fluorescent in-situ hybridization (FISH) were performed in malignant cases. Statistical analysis utilized SPSS20 software.
Results: Positive predictive value for malignant cytology diagnosis was 100 % ($N = 275$). Negative predictive value of benign cytology diagnosis was 97.4 % (kappa = 0.93, $N = 1183$). Non-diagnostic rate was 4.8 %. Cell block and surgical specimen agreement was excellent for ER IHC (kappa = 0.95, $N = 58$), and substantial for HER2 FISH (kappa = 0.79, $N = 47$), with no false positive detection of HER2 amplification using cell block material.
Conclusion: Review of consecutive breast FNAs in a large cohort with clinical follow up confirmed the high accuracy of this biopsy technique for breast cancer diagnosis and biomarker evaluation. Breast FNA is particularly suited to settings where core biopsy is not desirable or available, and in low resource regions.

OFP-03-006

Assisting the neurologist in diagnosis of CNS malignancies. Current possibilities and limits of cerebrospinal fluid cytology and immunocytochemistry

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Objective: In tumourous impairment of CNS, identification of neoplastic cells in cerebrospinal fluid (CSF) frequently requires

ancillary techniques. Immunocytochemical examination can contribute.
Method: During the years 2010 to 2015 altogether 31,448 samples of CSF were examined in our laboratory in a complex setting including biochemical, immunological, microbiological, molecular-genetic, and cytological investigations.
Results: There were 721 patients with hematologic malignancies and 1272 patients with tumourous infiltration of CNS of non-hematologic origin. Only a minor part (tens of cases increasing recently) of malignant meningeal infiltration cases were verified with immunocytochemistry. Working algorithms for three clinically different situations of recent, past, and hidden malignancy were elaborated.
Conclusion: Diagnostic laboratory providing nonstop service, broad spectrum of methods, and an experienced team, and co-operating clinicians supplying sufficient amount of good quality sample and comprehensive patient's data represent the basis for quick and accurate diagnosis, enabling appropriate treatment in patients with neoplastic involvement of intracranial space.

OFP-03-007
Accuracy of cytology in typing of non-small cell lung cancer
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Objective: Non-small cell lung cancer (NSCLC) nowadays indicates further classifying in cytological and small biopsy material taken during bronchoscopy because of the improvement of cancer therapy and the fact that most of the cancers are diagnosed in advanced clinical stages. We investigated the accuracy of cytology in typing of NSCLC.
Method: One year retrospective study included 323 cytological samples May-Gruenwald-Giemsa stained of brush and transbronchial needle aspiration (TBNA) of suspicious lesions of 260 patients, 26,5 %(69/260) women and 73,5 %(191/260) men, age between 44 and 80, average 64,49 ± 7,93 diagnosed NSCLC. A standard for diagnosis comparison was histopathological small biopsies' material stained by hematoxylin-eosin. Material was diagnosed using morphological criteria and immunohistochemistry on small biopsies in poorly differentiated cancers. Data was statistically analyzed using descriptive methods and Kendal tau correlation (statistical significance level $p < 0,05$).
Results: Cytologically diagnosed NSCLC cases, 161 brush and 162 TBNA, were typed:18,1 % (47/260)adenocarcinoma, 22,3 %(58/260) squamous cell carcinoma and 59,6 %(155/260) NSCLC not otherwise specified (NOS). Histologically diagnoses: NSCLC NOS 11,9 %(31/260), adenocarcinomas 55 %(143/260) and squamous 33,1 %(86/260). There's no statistically significant difference between cytological-histological diagnosis ($p = 0,369$).
Conclusion: Cytology is sensitive and accurate procedure for typing NSCLC for further diagnostic and treatment. In poorly differentiated doubtful cases, ancillary techniques (immunohistochemistry) improve diagnostic yield.

OFP-03-008
Neutrophil extracellular DNA networks to limit the peripheral tumour cell proliferation
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Objective: The objective of the study is to assess the viability and functional status of neutrophil granulocytes in contact with tumour cells in vitro.
Method: Due to the co-incubation of pure fraction of neutrophilic granulocytes and cell lines of tumour cells HEp-2 (human laryngeal epidermoid carcinoma) and RD (human rhabdomyosarcoma) at 37 °C for 30–60 min, oxygen-dependent metabolism was revealed to enhance greatly (NST-test) in neutrophils in 30 min, and the absence of neutrophilic granulocytes was recorded in an hour, only light green DNA neutrophils threads were visualized by staining of native preparation with methylene blue Evans Sytox Green fluorescent dyes, at the same time the morphology of the tumour cells did not change and there was a significant oxygen-dependent metabolism of tumour cells (NST-test).
Results: Microscopy has shown monolayer of tumour cells, neutrophils were not visualized; alsoa monolayer of tumour cells was noted to belimited to the strands of DNA neutrophils, some peripheral tumour cells were completely wrapped with strands of nuclear matter.
Conclusion: Thus, the experiment proved the neutrophils trapping the tumour cells to be activated and die, forming networks of DNA strands, which are likely to limit the peripheral and tumour cell proliferation.

OFP-03-009
Neoplastic mucinous cysts of the pancreas: Cytology grading adds value to risk stratification
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Objective: A multimodal clinicopathological approach to diagnosis of neoplastic mucinous cysts (NMCs) is optimal. Those with high grade features or malignancy on cytology require resection. Our aim is to establish the accuracy of cytological grading and KRAS mutational status in predicting high grade (HG) or malignant NMCs.
Method: Cytological grade and KRAS mutational status of NMCs diagnosed between 2011 and 2016 were compared with histological grade and presence of invasion at resection. Cases diagnosed as HG (including suspicious) and malignant on cytology were reclassified as high risk (HR), and all others as low risk (LR).
Results: There were 54 LR and 26 HR NMCs on cytology. Cytology-histology correlation was available for 38 resected cases. The positive predictive value and sensitivity of HR cytology for HGNMCs with and without malignancy was 82.35 and 77.78 %; and LR cytology for LGNMCs was 80.95 and 85 % respectively. KRAS was mutant in 20 NMCs; 14/45 LR and 6/11 HR cytology and was not discriminatory. Twenty-eight of 42 non-resected cases had clinical follow-up; 16(57 %) with LR cytology were stable NMCs, 4(14 %) with LR cytology developed HR features, while 8(29 %) with HR cytology were malignant in behavior on follow-up.
Conclusion: 1. The 2-tiered grading system shows a high level of accuracy in predicting carcinoma, HGNMCs, and LGNMCs. 2. KRAS mutation is specific for a diagnosis of NMC but not discriminatory in risk stratification.

OFP-03-010
Adequacy of cytology specimens for molecular testing in lung adenocarcinoma
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Objective: Molecular testing of lung adenocarcinoma helps select patients for therapy with epidermal growth factor (EGFR) and anaplastic lymphoma kinase (ALK) inhibitors. Although cytology samples are considered acceptable specimens for molecular testing, most studies have focused on biopsy samples. Herein we summarize the results of 2 years of EGFR/ALK testing, based on cytology specimens, carried out at our Institution.
Method: The database of the Institution was retrospectively queried for EGFR/ALK testing performed in cytology specimens of lung adenocarcinomas, during 2014–2015.
Results: A total of 57 cases were analyzed for EGFR mutation status and ALK translocation, when relevant. Forty-five cases

correspond to FNA samples and 12 were exfoliative specimens. Quality DNA for EGFR status evaluation was obtained in 89 % ($n = 40$) of FNA smears (8/40 (20 %) mutated) and in 67 % ($n = 8$) of exfoliative smears (5/8 (63 %) mutated). Quality DNA for ALK translocation analysis was obtained in 28 % ($n = 9$) of FNA smears (1/9 (11 %) translocated).
Conclusion: The low percentage of insufficient samples for EGFR evaluation (11 % for FNA and 33 % for exfoliative specimens) and the rates of EGFR mutation and ALK translocation, that are only slightly higher than the literature for FNA specimens, support the adequacy of cytology smears for molecular testing in lung adenocarcinoma.

OFP-03-011
Antibody specificity, epitope retrieval, and detection method sensitivity as important determinants in the immunohistochemical detection of programmed death ligand 1
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Objective: Nivolumab, an anti-programmed death 1 (PD-1) antibody, is approved in the US and EU for advanced melanoma, non-small cell lung cancer, and renal cell carcinoma. PD-ligand 1 (PD-L1) is a biomarker that correlates with magnitude of response to nivolumab and other PD 1/PD-L1 inhibitors in certain tumour types. Multiple antibodies and immunohistochemistry (IHC) assays to detect tumour PD-L1 expression are available. This study compared the specificity/sensitivity of two PD-L1 antibodies and performance of their respective IHC assays in detecting cell-surface PD-L1 expression.
Method: Rabbit monoclonal anti-PD-L1 antibodies clone 28-8 (Bristol-Myers Squibb and Dako) and E1L3N (Cell Signaling Technology) were compared. Target specificity was assessed using PD-L1 genetic deletion tumour cell lines (L2987 and ES-2). Sensitivity was compared in tumour and immune cells using the same IHC detection method for both antibodies and the manufacturer-recommended method specific for each antibody.
Results: Using L2987 and ES-2 cell lines, both antibodies demonstrated PD-L1−target-specificity (E1L3N, only at the plasma membrane). E1L3N sensitivity was slightly higher than 28-8 when identical procedures for retrieval and detection were used. Detection significantly improved with 28-8 versus E1L3N using the specific manufacturer-recommended procedures.
Conclusion: Epitope retrieval and sensitive detection reagents are important in achieving maximal target specificity/sensitivity.

OFP-03-012
Tuberculous pleural effusion: Cytologic review of 52 patients with corresponding histopathological diagnoses
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Objective: The aim of this study was to investigate the role of cytology pleural effusion examination in an attempt to diagnose Tuberculous infection.
Method: Fifty two pleural effusion cases from Hasan Sadikin General Hospital Bandung were reviewed in this study. All cases were sputum AFB positive and histopathologically showed typical Tuberculosis appearance on pleural biopsy.
Results: The mean age of the patient were 39.2 years and 35 (67 %) were male. Almost all (92 %) effusions were Rivalta positive, with mean level of Lactic dehidrogenase and Glucose were 1598.4 U/L and 84.7 mg/dL consecutively. The cytological finding showed moderate to high cellularity but 3 cases (5.8 %) were hypocellular. Lymphocyte predominance was observed in 43 (82.7 %) cases. Six (11.5 %) cases were polymorphonuclear cells predominance. All cases showed scanty mesothelial cells. Proteinaceous background was found in 23 (44.2 %) cases. There were no epitheloid cells observed in all cases.
Conclusion: Lymphocytes predominance and absence or scanty mesothelial cells were highly suggestive for Tuberculous pleural effusion. Cytology examination alone cannot confirm the diagnosis of Tuberculous infection.

Tuesday, 27 September 2016, 14.45–16.45, Conference Room 5
OFP-04 Joint Session: Neuropathology / Nephropathology / Ophthalmic Pathology

OFP-04-001
BAP1 mutations are associated with metastasis in polyploid uveal melanoma
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Objective: This study attempts to gain insight in polyploidy in Uveal melanoma (UM) and supplement old data with current knowledge on mutations in UM specific genes.
Method: In 202 patients the ploidy status of the UM was determined using cytogenetic analysis, FISH, MLPA and/or SNP array analysis. Immunohistochemistry was used to determine the BAP1 expression and mutation analyses of BAP1 (coding regions) or the hotspots for the SF3B1, EIF1AX, GNAQ and GNA11 genes was carried out using Sanger Sequencing or Whole-Exome Sequencing.
Results: Twenty-three patients had a polyploid UM (11.4 %). Polyploid tumours were larger (15.61 mm versus 13.13 mm, $P = 0.004$), and more often showed loss of heterozygosity of chromosome 3 ($P = 0.003$). No difference in occurrence of mutations between polyploid and diploid tumours was observed. Polyploidy did not affect survival ($P = 0.143$). BAP1 mutation was the only significant independent prognostic predictor for patients with polyploid tumours, with a 16 fold increased hazard ratio (HR 15.90, $P = 0.009$).
Conclusion: Patients with polyploid UM do not differ from diploid UM based on prevalence of mutations in the UM related genes. Similar to patients with diploid UM, BAP1 mutation is the most significant prognostic predictor of metastasis in patients with polyploid UM.

OFP-04-002
SF3B1 and EIF1AX mutations in uveal melanoma
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Objective: To investigate the prevalence and prognostic value of SF3B1 and EIF1AX mutations in uveal melanoma (UM) patients.
Method: SF3B1 and EIF1AX mutations in primary tumours were investigated using whole-exome sequencing and Sanger sequencing ($n = 133$). For the detection of BAP1 mutations, BAP1 sequencing or immunohistochemistry was performed.
Results: Patients with tumours harboring EIF1AX mutations rarely demonstrated metastases and overall had a longer disease-free survival (DFS; 190.1 vs. 100.2 months; $P < 0.001$). Within the tumours with disomy 3, UM patients with an SF3B1 mutation had an increased risk for late metastases (median, 8.2 years; range, 23–145 months) compared with those without an SF3B1 mutation resulting in a shorter DFS (132.8 vs. 174.4 months; $P = 0.008$). Patients with UM and loss of BAP1 expression had a significantly decreased survival (DFS, 69.0 vs. 147.9 months; $P < 0.001$).

Conclusion: According to our data, patients with UM can be classified into 3 groups: EIF1AX-mutated tumours and tumours without BAP1, SF3B1, or EIF1AX mutations are associated with prolonged survival and low metastatic risk, SF3B1-mutated tumours are associated with late metastasis, and tumours with an aberrant BAP1 are associated with an early metastatic risk and rapid decline in patient DFS.

OFP-04-003

A correlation of ultrastructural microvascular features with endothelial cell transcripts in renal transplant biopsies

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Objective: In antibody-mediated rejection both ultrastructural changes to endothelial cells and increased expression of endothelial transcripts have been described. Our study compares these two features in biopsies from patients with de novo donor specific antibody (DSA) with surveillance biopsies.
Method: Ultrastructural features of glomerular and peritubular capillaries were examined in 37 biopsies, 13 1-year surveillance biopsies from DSA-negative patients, and 24 biopsies from patients with de novo DSA. Real-Time-PCR was used to analyse 3 endothelial-associated transcripts (vwf, pecam and DARC) and the z-scores for these were summed to obtain a transcript sum score (TSS). Spearman's rank correlation coefficient was applied using GraphPad Prism 6.
Results: There was no statistically significant correlation between the endothelial TSS and mean endothelial swelling per glomerular loop, percentage of loops with severe endothelial swelling, mean endothelial crenellation per loop, mean loss of fenestration per loop, or mean subendothelial rarefaction per loop. However in peritubular capillaries a significant correlation was observed between endothelial TSS and percentage of peritubular capillaries with severe endothelial cell swelling (Spearman's rank coefficient $r = 0.35$ (0.02–0.61), $p = 0.03$).
Conclusion: These initial results correlate changes in endothelial cell transcripts with peritubular capillary endothelial features.

OFP-04-004

Bile cast nephropathy in cirrhotic patients: Effects of chronic hyperbilirubinemia

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Objective: Bile cast nephropathy (BCN) is a frequently under-recognized renal complication of liver failure usually occurring at serum bilirubin (sBili) levels above 20 mg/dL. Our goals were to determine the prevalence of BCN in cirrhotic patients at autopsy, and find an algorithm for better recognition of bile casts in renal parenchyma.
Method: Renal pathology of 114 autopsy cases of cirrhosis were assessed for the presence of bile casts using H&E, Trichrome, PAS, and Hall stains. Bile casts were correlated with the etiology of cirrhosis, serum creatinine/BUN, eGFR, sBili and urinalysis.
Results: Bile casts were identified in 55.3 % of cirrhotic cases. The most common etiologies of cirrhosis were HCV-related (52.1 %), combined HCV/alcohol-related (33.0 %), and alcohol-related (5.3 %). Serum creatinine ($p = 0.02$) and BUN ($p = 0.01$) were significantly higher in the Hall-positive group. Conjugated sBili levels were <20 mg/dL in 90 % and <10 mg/dL in 80 % of Hall-positive cases.
Conclusion: This is the largest study of BCN in human subjects. We demonstrate that in the face of chronic hyperbilirubinemia, bile casts form at much lower sBili levels than previously thought and the sBili cut-off of 20 mg/dL should not be used for diagnosis of BCN when dealing with cirrhotic patients. An algorithm is proposed to increase the sensitivity of Hall stain for tissue diagnosis of BCN.

OFP-04-005

Pattern of IgA and C3 staining in 76 biopsies with staphylococcus infection associated glomerulonephritis

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Objective: IgA-dominant immune complex deposits (along with C3) are considered key diagnostic features in Staphylococcus infection-associated glomerulonephritis (SAGN). However recent articles have reported that Staphylococcal endocarditis associated GN may show pauci-immune pattern and positive ANCA serology, causing diagnostic overlap with ANCA-associated GN. This has important implications in regards to choice of antibiotics or immunosuppressives. Immunosuppressive therapy is essential in ANCA GN, but can be detrimental in endocarditis-associated GN.
Method: We studied the immune complex pattern in detail and also presence or absence ANCA serology in our single-center cohort of 76 patients with SAGN from January 2004 to January 2016. All 76 patients had culture proven Staphylococcal infection.
Results: Out of the 76 biopsies with SAGN, 27 (36 %) had focal crescents or segmental necrotizing lesions. Pauci-immune pattern on immunofluorescence (trace to weak IgA, IgG and C3 staining) with scant to absent electron dense immune-type deposits was seen in 11/76 (14 %) of the biopsies and 7 of these 11 biopsies also had crescents. Trace/scant staining for IgA was seen in up to 26 % of the biopsies. Even C3 staining was trace/scant in up to 14 % of the biopsies. One patient had all three features—focal crescents, positive ANCA serology and a pauci-immune pattern on immunofluorescence staining and ultrastructural examination. On electron microscopic examination, only 24 out of 76 (32 %) biopsies showed subepithelial humps.
Conclusion: Weak to absent IgA does not preclude the diagnosis. C3 is usually present. Pauci-immune pattern of deposits and positive ANCA serology although infrequent, are potential diagnostic pitfalls in SAGN. Subepithelial humps are seen infrequently in SAGN.

OFP-04-006

Targeting of the MAPK and AKT pathways in conjunctival melanoma shows potential synergy

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Objective: Similar to cutaneous melanoma, CM frequently carries activating mutations in BRAF and NRAS. We studied whether CM as well as conjunctival benign and premalignant melanocytic lesions express targets in the MAP kinase (MAPK) and AKT pathways, and whether specific inhibitors affect CM growth in vitro.
Method: 132 conjunctival lesions were collected from 128 patients. BRAF V600E mutation and the level of phospho-ERK and phospho-AKT was assessed by immunohistochemistry. We studied cell proliferation, phosphorylation, cell cycling and apoptosis in CM cell lines using BRAF inhibitors (Vemurafenib and Dabrafenib), MEK inhibitor (MEK162) and AKT inhibitor (MK2206).
Results: BRAF V600E mutation was observed in 19 % of nevi and 26 % of melanomas, but not in primary acquired melanosis with or without atypia. Nuclear and cytoplasmic p-ERK and p-AKT were identified in all conjunctival lesions. BRAF inhibitors inhibited the cell growth of two BRAF-mutant CM cell lines, while MEK162 and MK2206 suppressed cell proliferation of all cell lines in a dose-dependent manner. Synergistic growth inhibition and increased cell death were observed in all three cell lines when MEK162 and MK2206 were combined.
Conclusion: ERK and AKT are constitutively activated in conjunctival melanocytic lesions. The co-inhibitory effect of combination treatments may benefit patients suffering from metastatic conjunctival melanoma.

OFP-04-007

Is chronic curcumin supplementation neuroprotective against ischemia for antioxidant activity, neurologic deficit score, or neuronal apoptosis in an experimental stroke model?

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Objective: We investigated the neuroprotective effect of chronic curcumin supplementation on the rat forebrain prior to ischemia and reperfusion.
Method: Forebrain ischemia was induced by bilateral common carotid artery occlusion for 1 h, followed by reperfusion for 72 h. Older rats were divided into five groups: I, 300 mg/kg oral curcumin for 21 days before ischemia and 300 mg/kg intraperitoneal curcumin after ischemia; II, 300 mg/kg intraperitoneal curcumin after ischemia; III, 300 mg/kg oral curcumin for 21 days before ischemia; IV, only ischemia; V:, sham-operated.
Results: In forebrain tissue, enzyme activities of superoxide dismutase, glutathione peroxidase, and catalase were significantly higher in Group I than Groups II or III ($p < 0.05$ while xanthine dehydrogenase and malondialdehyde enzyme activities and concentrations of interleukin-6 and TNF-alpha were significantly lower in Group I compared to Groups II and III ($p < 0.05$). A significant reduction in neurological score was observed after 24 and 72 h in the curcumin-treated groups compared with the ischemic group. We also found a marked reduction in apoptotic index after 72 h in the groups receiving curcumin. Significantly more TUNEL-positive cells were observed in the ischemic group compared to those treated with curcumin.
Conclusion: We demonstrated the neuroprotective effect of chronic curcumin supplement following ischemia and reperfusion.

OFP-04-008

Analysis of the status of O6-methylguanine-DNA methyltransferase (MGMT) gene promoter methylation in different topographical samples, as well as during progression ad recurrence of glioblastoma

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Objective: To analyze whether the status of O6-methylguanine-DNA methyltransferase (MGMT) gene promoter methylation in glioblastoma (GBM) varies in different topographical portions, or during progression or recurrence.
Method: Status of MGMT gene promoter methylation was analyzed in different topographical samples of 24 GBM, as well as in their eventual preceding low grade astrocytoma (LGA) and recurrences by Real Time PCR with AlphaReal MGMT kit. Data on immunohistochemical expression of isocitrate dehydrogenase-1 mutated protein (IDH1-R132H), p53 and Ki-67, overall survival and post-surgical treatment were available in all the cases.
Results: MGMT gene promoter was homogeneously unmethylated in 13 GBMs and methylated in 8. 3/24 GBMs were heterogeneous, with MGMT promoter methylated in the inner portion of the tumour and unmethylated in the intermediate and outer portions. Conversion from unmethylated to methylated MGMT status was seen in 2/2 GBMs originated from progression of LGA. Methylation status changed in 3/12 (25 %) GBMs at recurrence. Overall survival was longer than 36 months in all patients with MGMT methylated and IDH1 mutated GBM.
Conclusion: MGMT methylation status may be heterogeneous through GBM samples, and between GBM and its recurrence. Methylation may be acquired during progression from LGA and it is prognostically significant in tumours with IDH1 mutation.

OFP-04-009

Adenomas of the pituitary gland: Size matters - experience of a neuropathology referral center

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Objective: To assess the prognostic value of histological and non-histological characteristics of Pituitary Gland Adenomas (PGA).
Method: All cases of PGA over a 10 year period were revised. Tumour size, invasion on Magnetic Resonance Imaging (MIR), histologic type, cytological atypia and follow-up of patients were analyzed. Logistic regression model was used to estimate the relative risk of tumour relapse and need for subsequent surgery.
Results: Among the 188 PGA identified, 165 cases were evaluated. Average tumour size was 21 mm, with 30 cases classifying as microadenomas (<10 mm) and 50 presenting with invasion. Only 10 cases showed cytological atypia. Average follow-up period was 39 months, with 103 cases presenting with residual tumour after surgery. Tumour relapse with subsequent surgical procedure occurred in 19 cases. Presence of invasion and tumour relapse was significantly associated with larger tumours when compared with smaller ones ($p < 0{,}001$ and $p = 0{,}015$ respectively) Tumour size proved to be an independent prognostic factor in predicting tumour relapse (Odds Ratio = 2,53, 95 % confidence interval = 1,09–5,82).
Conclusion: These findings corroborate the results published in literature. Although presence of cytological atypia and invasion on MRI are related with residual tumour and relapse, tumour size was the most important factor in predicting the outcome of these patients.

OFP-04-011

CNS germinomas are characterized by global demethylation, chromosomal instability and mutational activation of the Kit-, Ras/Raf/Erk- and Akt-pathways

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Objective: CNS germinomas represent a unique germ cell tumour entity. Only limited information is available on their underlying genomic, epigenetic and biological alterations.
Method: We performed a genome-wide analysis of genomic copy number alterations and allelic imbalances in 49 CNS germinomas by molecular inversion profiling. CpG dinucleotide methylation was studied by immunohistochemistry. Mutational analysis was performed by sequencing of candidate genes including KIT and RAS family members. Ras/Erk and Akt pathway activation was analyzed by immunostaining for phospho-Erk, phosho-Akt, phospho-mTOR and phospho-S6.
Results: All germinomas showed extensive global demethylation of nuclear DNA. Predominant genomic instability was found in all tumours with a high frequency of regional alterations including gene amplifications. Activating mutations of KIT exons 11, 13, and 17 or KIT amplification and mutations of RAS gene family members indicated mutational activation of crucial signaling pathways. Coactivation of Ras/Erk and Akt pathways was demonstrated by immunohistochemistry of phosphorylated signaling components in 83 % of germinomas.
Conclusion: CNS germinoma cells display a demethylated nuclear DNA similar to primordial germ cells in early development. This finding is associated with extensive genomic instability. Mutational activation of Kit-, Ras/Raf/Erk- and Akt- pathways indicates the biological importance of these pathways and their components as potential targets for therapy.

OFP-04-012

Gradual brain involvement in fetal TSC

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Objective: CNS Tuberosclerosis (TSC) a systemic, autosomal dominant genetic disorder is characterized by brain lesions where balloon cells can be considered as histopathological hallmarks. We purpose here the development shedule of TS lésions constitution.
Method: We analysed 12 fetal and perinatal brains (from 21 GW until 3 days after birth) with TSC lesions. For each patient we considered: 1) the type of cell lesion 2) their nature (using both glial and neuronal markers) 3) their cytoarchitectural and 3) spatial organization.
Results: We identified 3 types of TSC Cells (b cells, balloon cells (BC) and dysplastic giant neurons (DN) and 3 types of cytoarchitectonics (A and B cocards, cortical tubers). Cells were characterized using neuronal and glial markers. While b cells were exclusively neuronal, balloon cells could be both, the glial ones being proeminent and appearing earlier during pregnancy. DN and cortical tubers are respectively observed are observed after 25GW and 30GW. Type A cocard remained located on periventricular area while type B cocarde evolved with age and progressively occupied more superficial white matter areas. Both contained glial and neuronal BC. Cortical BC are firstly observed at 25GW on layer I, and were present in all layers after 30GW.
Conclusion: Our study demonstrates that in fetal brain TSC lesions evolved progressively following distinct patterns according to their location or the TSC cell nature.

Tuesday, 27 September 2016, 17.15–19.15, Congress-Saal 1
OFP-05 Uropathology

OFP-05-001
Disease-specific survival of patients with invasive cribriform and intraductal prostate cancer at diagnostic biopsy
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Objective: To determine the prognostic value of invasive cribriform and intraductal carcinoma in pre-treatment biopsies on time to disease-specific death.
Method: We pathologically revised the diagnostic biopsies of 1031 patients from the first screening round of the European Randomized Study of Screening for Prostate Cancer 1993–2000). The median follow-up was 13 years. Patients who either had invasive cribriform growth pattern or intraductal carcinoma were categorized as CR/IDC+. The outcome was disease-specific survival. Relationships with outcome were analyzed using multivariable Cox regression and log-rank analysis.
Results: In total, 486 patients had Gleason score 6 (47 %) and 545 had ≥7 (53 %). The 15-year disease-specific-survival probabilities were 99 % in Gleason score 6 ($n = 486$), 94 % in CR/IDC- Gleason score ≥7 ($n = 356$) and 67 % in CR/IDC+ Gleason score ≥7 ($n = 189$). CR/IDC- Gleason score 3 + 4 = 7 patients did not have statistically different survival probabilities from those with Gleason score 6 ($P = .30$), while CR/IDC+ Gleason score 3 + 4 = 7 patients did ($P < .001$). In multivariable analysis CR/IDC+ status was independently associated with a poorer disease-specific survival (HR 2.6, 95 % CI 1.4–4.8, P = .002). We conclude that CR/IDC+ status in prostate cancer biopsies is associated with a worse disease-specific survival.
Conclusion: Our findings indicate that men with biopsy CR/IDC- Gleason score 3 + 4 = 7 prostate cancer could be candidates for active surveillance, as these patients had similar survival probabilities to those with Gleason score 6.

OFP-05-002
Gleason Grade 4 prostate adenocarcinoma patterns: An inter-observer agreement study among genitourinary pathologists
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Objective: To assess the inter-observer reproducibility of individual Gleason grade 4 growth patterns.
Method: Twenty-three genitourinary pathologists participated in the evaluation of 60 selected high-magnification photographs. The selection included 10 cases of Gleason grade 3, 40 Gleason grade 4 (10 per growth pattern) and 10 Gleason grade 5. Participants were asked to select a single predominant Gleason grade per case (3, 4, 5) and to indicate the predominant Gleason grade 4 growth pattern if present. "Consensus" was defined as at least 80 % agreement and "favoured" as 60–80 % agreement.
Results: Consensus on Gleason grading was reached in 47/60 (78 %) cases, 35 of which were assigned a grade 4. In the 13 non-consensus cases, ill-formed (6/13, 46 %) and fused (7/13, 54 %) patterns were involved in disagreement. Among the 20 cases where at least 1 pathologist assigned the ill-formed growth pattern none (0 %, 0/20) reached consensus. Consensus for fused, cribriform and glomeruloid glands was reached in 2, 23, and 38 %, respectively. In 9/35 (26 %) consensus Gleason grade 4 cases, participants disagreed on growth pattern. Six of these were characterized by large epithelial proliferations with delicate intervening fibro-vascular cores, which were alternately given fused or cribriform growth pattern ("complex fused").
Conclusion: Consensus on Gleason grade 4 growth pattern was predominantly reached on cribriform and glomeruloid patterns, but rarely on ill-formed and fused glands. The complex fused glands seem to be a borderline pattern of unknown prognostic significance on which a consensus could not be reached.

OFP-05-003
Histopathological analyses of renal tumours in Birt-Hogg-Dube syndrome
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Objective: Birt-Hogg-Dube syndrome (BHD) is a familial disorder caused by genetic mutations of FLCN. Affected patients have increased risks for developing renal cell carcinomas (RCCs). Most of RCCs in BHD are histopathologically chromophobe RCCs and hybrid oncocytic/chromophobe tumours (HOCT). Differences between BHD-associated RCCs and sporadic counterparts are incompletely understood.
Method: We investigated cytogenetics, FLCN mutations and histopathology of 58 BHD-associated RCCs. Copy number variation, FLCN sequencing, Western blotting and immunostaining were performed.
Results: Most of BHD-associated RCCs lacked FLCN expression at the protein level regardless of the status of somatic mutation and loss of heterozygosity (LOH) of FLCN. They showed balanced genomic profiles with genome-wide LOHs. These LOHs existed as uniparental disomy. Similar immunostaining patterns were observed between BHD-associated RCCs and their sporadic counterparts; however, FISH/CISH analysis of the centromeric region of chromosomes 2, 6 and 17 revealed that most of BHD-associated RCCs were disomic whereas the majority of sporadic chromophobe RCCs were monosomic.
Conclusion: The data indicate that BHDS-associated RCCs are distinctively different in cytogenetics and molecular abnormalities from those of sporadic histological counterparts. Although current WHO classification does not specialize BHD-associated RCCs, these features will be informative for correct diagnosis of previously overlooked BHD patients.

OFP-05-004

Metabolomics analysis reveals distinct profiles of non-muscle invasive and muscle-invasive bladder cancer

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Objective: Bladder Cancer affects >70,000 patients annually in the United States. Despite its high incidence, therapeutic options are limited in early or late stage. We wanted to identify key metabolic pathways that were altered in bladder cancer development and progression.
Method: We performed global metabolomics profiling of benign urothelium, high-grade non-muscle invasive bladder cancer (NMIBC) and advanced, muscle-invasive bladder cancer (MIBC) using GC-MS and LC-MS platforms.
Results: Categorical pathways globally dysregulated in cancer relative to benign urothelium included glucose, TCA cycle, lipid, amino acid and nucleotide pathways. Bladder cancers demonstrated Warburg metabolism, with elevated glucose utilization to drive glycolysis and sorbitol pathway intermediates. Elevated late TCA cycle intermediates, coupled with higher levels of amino acids and dipeptides, suggest the possibility of anaplerotic activity in bladder cancer as a mechanism to sustain energy production. Medium and long chain fatty acids were produced at the expense of dicarboxylic fatty acids. MIBCs showed enhanced use of cycloxygenase (COX) and lipoxygenase (LOX) pathways and a possible role for inflammation in regulating NAD+ synthesis in MIBC.
Conclusion: This study identifies multiple parallel metabolomics changes unique to NMIBC and MIBC that can be used to justify testing novel therapeutics targeting metabolic pathways in bladder cancer.

OFP-05-005

Relation of percentage Gleason grade 4 and cribriform/ intraductal growth in Gleason score 3 + 4 = 7 prostate cancer biopsies

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Objective: Histopathology and clinical outcome of Gleason score 7 prostate cancer is heterogeneous. Relative increase of Gleason grade 4 (%GG4) pattern, and presence of invasive cribriform and/or intraductal carcinoma (CR/IDC) have been associated with adverse outcome of Gleason score 7 tumours. The objective of this study is to investigate the relation of %GG4 and CR/IDC in Gleason score 3 + 4 = 7 prostate cancer biopsies.
Method: We reviewed 1031 diagnostic prostate cancer biopsies from the first round of the European Randomized Study of Screening for Prostate Cancer (1993–2000). A total of 370 men had revised Gleason score 3 + 4 = 7.
Results: The mean %GG4 was 16 % in men without and 28 % in men with CR/IDC ($P < .001$). CR/IDC occurred in 6 % of patients with 1–10 %, 22 % with 10–25 %, and 44 % with 25–50 % GG4 ($P < .001$). In bivariate Cox regression analysis, CR/IDC (HR 3.3; 95 % CI 1.4–8.0; $P = .008$) was an independent parameter for disease-specific death, while %GG4 (HR 1.5; 95 % CI 1.0–2.4; $P = .06$) did not reach statistical significance.
Conclusion: Increasing %GG4 was associated with CR/IDC in prostate biopsies. While biopsy CR/IDC was an independent parameter for disease-specific death, %GG4 was not. Biopsy CR/IDC is a promising parameter for therapeutic stratification of Gleason score 3 + 4 = 7 prostate cancer patients.

OFP-05-006

Assigning Composite Grade Groups (CGG) in prostate adenocarcinoma: Concordance between needle biopsy and prostatectomy, and factors associated with upgrade and downgrade

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Objective: Composite Grade Groups (CGG) were evaluated on biopsy and prostatectomy in a large contemporary prostate carcinoma cohort.
Method: CGG on biopsy and prostatectomy were correlated in 2529 patients from single institution. CGG upgrades and downgrades were evaluated overall and for individual CGG. Factors associated with GG1 upgrade and GG2 downgrade were analysed by multivariable logistic regression.
Results: The final CGG was identical with the biopsy CGG in 59.3 % cases overall. In CGG 1–5, identical grades were found in: (1) 47.6 %, (2) 73.5 %, (3) 52.8 %, (4) 21.4 % and (5) 68.3 %, respectively. Final CGG was upgraded in 32.3 % cases [CGG1-4: (1) 52.4 %, (2) 19 %, (3) 16.4 % and (4) 32.9 %]. Final CGG downgrade was found in 8.4 % of cases [CGG2-5: (2) 7.4 %. (3) 30.8 %, (4) 42.9 % and (5) 31.7 %]. Upgrade of biopsy CGG1 was associated with: age ≥60y, PSA density ≥0.3 ng/ml and ≥5 % core involvement. Downgrade of biopsy CGG2 was associated with: age <60y ($p = .019$), PSA <10 ng/mL ($p = .029$) and 1 positive core.
Conclusion: In 59.3 % cases, we found identical CGG on biopsy and prostatectomy. The concordance was lowest for CGG4, with most frequent upgrades occurring in biopsy CGG1 to CGG2. Considering factors associated with CGG1upgrade and CGG2 downgrade may play a role in clinical decision making.

OFP-05-007

Warthin-like papillary renal cell carcinoma with prominent lymphocytic infiltrate: Morphological and immunohistochemical study

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Objective: Papillary renal cell carcinoma (PRCC) represents up to 18 % of renal cell carcinomas (RCC). Besides the traditionally recognized type 1 and type 2, more variants were recently described. We analyzed a cohort of PRCC with prominent lymphocytic infiltrate, reminiscent of Warthin's tumour morphology.
Method: Eleven cases of PRCC with prominent intratumoural lymphocytic infiltrate were selected. The tumours were analyzed for multiple clinical, pathological, and immunohistochemical (IHC) parameters. Intratumoural lymphocytes and mismatch repair protein (MMR) expression were analyzed by IHC.
Results: The patients were predominantly male (78 %), with average age of 64 years. Half of the tumours were at pT1 stage. Tumours showed papillary growth pattern with oncocytic cells, and ISUP grade 2 nuclei. The lymphocytic infiltrate was mostly CD5 and CD3 positive. Tumours were positive for AMACR (91 %), PAX-8 (100 %), vimentin (91 %) and OSCAR (100 %); variable for CK7 (27 %), EMA (45 %) and CD10 (54 %), and negative for CANH9, c-kit, CK20. MMR proteins MLH1 and PMS2 were positive in all of the cases, except MSH2 and MSH6 in one case.
Conclusion: Warthin-like PRCC may be one of the several variants within a heterogeneous PRCC group, with predominant oncocytic morphology and lymphocytic (T-cell) tumour infiltrate. It appears not to be associated with microsatellite instability.

OFP-05-008

Clinicopathologic findings of patients without biochemical recurrence more than 8 years following radical prostatectomy: How many patients might have been suitable for active surveillance instead of definitive treatment?

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Objective: Detect patients without biochemical recurrence (BR) more than 8 years following radical prostatectomy (RP) with criteria for low-risk cancer (LRC) who might have been suitable for active surveillance (AS) instead of surgery.

Method: BR was considered as PSA >0.2 ng/mL. LRC was considered as being clinical stage T1c, stage pT2, needle and pathologic Gleason score <6, and preoperative PSA <10 ng/mL.
Results: From a cohort of 506 consecutive RPs, 62/506 (12.3 %) patients were free of BR more than 8 years after RP (mean 10 years, range 8–14 years). From these 62 patients, 14/62 (22.6 %) had criteria for LRC. Comparing our criteria for LRC with Epstein's, the only significant discrepancy was related to PSA density. From the total of 14 patients with criteria for LRC, 9/14 (64.3 %) had PSA density >0.15.
Conclusion: From a total of 62 patients without BR more than 8 years following RP, 14/62 (22.6 %) patients had criteria for LRC. These patients might have been suitable for AS instead of RP. Comparing our criteria of LRC with Epstein's criteria, a significant discrepancy was related to PSA density. The majority of patients had PSA density >0.15 and would not be enrolled for AS.

OFP-05-009
DeltaNp63 is critical for progression of high grade non-muscle invasive bladder cancer through deregulation of specific genetic pathways
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Objective: We have previously reported the significance of ΔNp63 as a protective individual marker of high grade non-muscle invasive bladder cancer (HG-NMIBC) tumour progression. The main goal of this project was to study the mechanisms by which ΔNp63 loss triggers tumour progression to muscle invasive disease.
Method: We generated specific ΔNp63 Knock-down cell lines (shΔ) in RT112 and BFTC NMIBC lines and gene expression and in vitro and in vivo functional experiments were performed.
Results: We observed that RT112_shΔ and BFTC_shΔ cells showed higher proliferation rate both in vitro and in vivo as well as increased colony formation activity when compared to parental cells. Furthermore, they displayed superior invasion capacity in vitro, which correlated with higher local tumour initiation and metastatic potential in the in vivo bladder orthotopic mouse model. Gene expression analyses revealed that there were nine commonly upregulated (AGR2, CAPS, CHD2, GCHFR, HOXC6, HRK, LRRC26, SORBS2 and S100A4) and four commonly downregulated (EPDR1, PPARG, SCML1 and SPOCK1) genes amongst both experimental cell lines. Functional studies to assess which genetic pathways are critical for tumour progression subsequent to ΔNp63 loss are further being pursued.
Conclusion: Our findings may be able to identify high-risk patients who could benefit from early radical cystectomy to prevent tumour progression, as well as low-risk patients who could benefit from more spaced follow-up visits. Also, they may unlock the opportunity of identifying new therapeutic strategies to target previously understudied pathways in HG-NMIBC, therefore avoiding progression to more aggressive disease.

OFP-05-010
Tertiary grade assessed on radical prostatectomies: Effect on prognosis using the 2016 ISUP grade group system
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Objective: In 2016, the International Society of Urologic Pathology (ISUP) proposed a revision of the ISUP / Gleason grading system using 5 grade groups (GG), validated based on follow-up biochemical recurrence (BCR). The role of tertiary pattern was incompletely addressed. This study examined GG score, with and without tertiary grading, with odds of BCR and distant metastasis (MET).
Method: Patients were enrolled in a prospective, longitudinal cohort study over 23 years. 1505 untreated carcinomas were retrospectively graded on radical prostatectomies (RP) using the 2016 ISUP GG system, with and without consideration of tertiary pattern (modified grade).
Results: There were 283 BCR (19 %) and 36 MET (2.4 %) events, at a mean of 36 and 80 months post-RP, respectively. Most patients had GG2 tumours (58 %), but few had GG3 tumours (3.5 %). No GG1 patient developed MET. Two percent of unmodified GG2 and GG3 tumours, and 0.5 % of modified GG2 and GG3 developed MET ($p = 0.02$). GG5 tumours had a significantly higher risk for BCR ($p < 0.0001$), but there was no difference in unmodified GG1- GG4. Modified GG1-2, GG3-4, and GG5 separated clearly into 3 worsening prognostic groups ($p < 0.0001$).
Conclusion: As a predictor of MET and BCR, the use of the tertiary pattern is superior to GG grading without tertiary pattern.

OFP-05-011
Prognostic impact of p63 and Beta-catenin coexpression in urothelial bladder cancer
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Objective: To investigate the expression of p63 and β-catenin in urothelial bladder cancer (UBC), assess the significance of their coexpression, and evaluate their prognostic value.
Method: We analyzed the expression of β-catenin and p63 by double staining immunohistochemistry in 633 cases of UBC included in tissue-microarrays. Expression status was correlated with clinicopathological and follow-up data.
Results: Low p63 expression, observed in 255 (40.3 %) tumours, was significantly associated with high grade, and pathologic stage ($p < 0.001$, respectively). In pT1 UBC ($N = 292$), p63 correlated with variant differentiation ($p = 0.048$). Reduced/absent β-catenin immunoreactivity (82.3 %) correlated to high grade and stage ($p < 0.001$, $p = 0.006$, respectively), and strongly correlated with impaired p63 staining ($p < 0.001$). Loss of both markers was linked to cancer specific death ($p < 0.001$, $p = 0.003$, respectively). High p63 was associated with better overall survival ($P < 0.001$), while preserved β-catenin correlated with longer recurrence-free survival ($p = 0.017$). Simultaneous decrease/loss of immunoreactivity of both markers was a strong predictor of poor survival ($p < 0.001$). In Cox regression analysis decrease of β-catenin was independent predictor of recurrence.
Conclusion: Coexpression of β-catenin and p63 in UBC predicts better survival of the patients and may serve as potential prognostic tool for improvement of risk stratification and therapy decision-making in UBC, especially in early invasive bladder cancer.

OFP-05-012
Predictive impact of angiogenesis and hypoxia related markers in urothelial bladder cancer
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Objective: To determine immunohistochemical markers helpfull in follow-up of unpredictable urothelial bladder cancer patients. Hypoxia-inducible factor1 alpha (HIF1-alpha) is an important trigger of the angiogenic VEGF activity. In bladder cancer, presence of cytoplasmic vascular endothelial growth factor receptor 1 (VEGFR1) can delay the angiogenesis, limiting VEGF availability for genuine receptors in VEGF signaling.
Method: The immunohistochemical expressions of HIF1-alpha, VEGF, and VEGFR1 were evaluated in 647 bladder cancer samples, incorporated in tissue microarrays. HIF1-alpha was assessed through nuclear

staining, while the angiogenic profile was estimated by cytoplasmic positivity of the VEGF and VEGFR1.
Results: After a mean follow-up of 60 months, in 647 patients diagnosed with urothelial bladder cancer, we found nuclear HIF1-alpha expression to be an independent prognostic factor for both recurrence-free survival ($p < 0.001$) and overall survival ($p < 0.01$). HIF1-alpha was significantly associated with low histological grade ($p < 0.001$), and low pathologic stage ($p < 0.01$). Patients with positive VEGFR1 had longer disease-free ($p < 0.01$) and overall survival ($p < 0.01$), while VEGF did not have significant impact to survival rate and further outcome.
Conclusion: Estimation of HIF1-alpha and VEGFR1 expression could be diagnostic supplement, selecting the urothelial bladder cancer patients that could require more attentive follow-up.

Tuesday, 27 September 2016, 17.15–19.15, Conference Room 1–2
OFP-06 Paediatric and Placental Pathology

OFP-06-001
Expression of miR-146a & miR-155 in placenta tissue in cases of early- and late-onset pre-eclampsia
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Objective: The aim of the study was to evaluate expression and localization miR-146a and miR-155 in cases of early- (EPE) and late—onset (LPE) of preeclampsia.
Method: Groups with PE included 5 women with EPE and 5—with LPE. Control groups included 4 women with physiological pregnancy (PP), 38–39 gestation weeks, 4—with preterm labor (PL) of 26–30 weeks. By hybridization in situ (Exicon, USA) was performed on 18 formalin-fixed paraffin-embedded placenta tissue specimens after cesarean section. Moreover, previously we performed histological study (hem&eosin).
Results: MiR-146a was determined in syncytiotrophoblast, stroma cells of villi, syncytial knots, major, minor subset of decidual cells, amnion in control group. EPE miR-146a was absence in syncytium, syncytial knots, decidual cells, but in cases of preeclampsia mIR-146a was almost completely absent in placenta samples. MiR-155 expression in amnion, syncytium, syncytial knots in PL, but moreover, in PP we observed week staining in stroma cells of placenta villi and decidual cells. In cases of preeclampsia miR-155 was evaluated predominantly in syncytium, syncytial knots.
Conclusion: In control groups we observe balance between anti-inflammatory (miR-146a) and pro-inflammatory (miR-155) in placenta tissue. In preeclampsia miR-146a was negative, but miR-155 expression was present. Thus, both EPE&LPE are associated with pro-inflammatory immune response.

OFP-06-002
Are there differences in expression of corticotropin releasing hormone in placentas from pregnant women with hypertensive syndrome?
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Objective: To evaluate the expression of corticotropin releasing hormone (CRH) in decidua and chorionic villi from human placentas with hypertensive disorders of pregnancy (HDP).
Method: A hundred and sixteen biopsies from placentas (54 preterm, 62 term) between 2013 and 2014 were analyzed as follows: (A) control group (C): 12 cases; (B) gestational hypertension (GH): 23 cases; (C) pre-eclampsia / eclampsia (PE): 30 cases; (D) chronic hypertension (CH) 25 cases and (E) hypertension superimposed on PE (SPE): 26 cases. The expression of CRH was assessed by immunohistochemistry; positive areas were expressed in percentage of area per field. ANOVA (F) followed by the Tukey test was used; $p < 0.05$.
Results: Decidua and chorionic villi in PE, GH, CH and SPE showed higher expression of CRH, compared to C ($p < 0.0001$) in the term group. In the preterm group, the expression was higher in cases associated with PE and SPE in both evaluated structures.
Conclusion: These data demonstrate that placental stress was higher in preterm cases associated with PE and SPE, justifying the high frequency of maternal and fetal complications usually observed in preterm pregnancies with these types of HDP.

OFP-06-003
TGF-beta 1 and TGF-beta 3 evaluation in kidney during experimental renal failure progression in a fetal reprogramming model
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Objective: This study evaluates if TGF-β1 and TGF-β3, cytokines with important role in tissue repair, are altered during acute kidney injury in cases of fetal programming.
Method: Diabetic dams' offspring were divided into CC (offspring of controls, receiving vehicle); DC (offspring of diabetics, receiving vehicle); CA (offspring of controls receiving Folic Acid, 250 mg/kg); and DA (offspring of diabetics receiving Folic Acid) at age of 2 and 5 months old. Renal TGF-β1 and TGF-β3 were analyzed by immunohistochemistry.
Results: Immunoexpression of TGF-β3 was higher in DA compared to DC and CA at age of 2 months-old. At age of 5 months-old, TGF-β3 was higher in CA when compared with CC and higher in DA when compared with DC. TGF-β1 immunoexpression was lower in DA when compared with CA only at age of 5 months-old (All results, $p < 0.05$).
Conclusion: This study showed, in face of induction of renal failure, the offspring of 5 months-old, which suffered fetal reprogramming, had a lower capacity to synthesize TGF-β1. But both groups that suffered renal failure showed increased TGF-β3, regardless of fetal reprogramming. As demonstrated in other studies, there is possibly an early upregulation of TGFβ3, followed by TGFβ1. However, our data demonstrate modification of kidney response regarding damage in reprogrammed subjects.

OFP-06-004
When is a post-mortem skeletal survey of the fetus indicated, and when not?
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Objective: Radiography after fetal or perinatal death has become a routine part of post-mortem diagnostics. However, only a selected subset of these babygrams or fetal post-mortem skeletal surveys (FPSSs) provides useful information. We investigated the indication for a FPSS.
Method: Inclusion consisted of the routinely made FPSS (2002–2012) in our university hospital in cases of fetal or perinatal death up to 7 days after birth. We categorized the diagnostic value of the FPSS as no, minor, major or pathognomonic. Regression analysis was used to determine the selection criteria for a useful FPSS.

Results: 337 FPSS were included. 305 (91 %) FPSS showed no or minor skeletal malformations. 14 (4.2 %) FPSS had major skeletal malformations. In 18 (5.3 %) cases the diagnosis was based on the pathognomonic skeletal malformations on the FPSS. Two cases were false positive after major birth trauma. The presence of multiple skeletal malformations on prenatal ultrasound or at post-mortem external inspection was highly indicative of a diagnostic FPSS ($p < 0.001$).
Conclusion: The majority of the babygrams/FPSS has no contribution to the diagnostic process. Multiple skeletal malformations on prenatal ultrasound or post-mortem external inspection are indicative for a diagnostic FPSS, and this should be the main selection criterion.

OFP-06-005
Morphology and next-gen sequencing of six cases of lethal malignancies in giant congenital melanocytic nevi / neurocutaneous melanocytosis
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Objective: Giant Congenital Melanocytic Nevi (GCMN) or neurocutaneous melanocytosis (NCM) show NRAS or BRAF mutations, and ≈4 % risk of malignant transformation, which is poorly understood. Aim: to describe novel pathology and genetics in six lethal GCMN/NCM patients.
Method: Six NCM/GCMN patients, prospectively collected or de-identified, who died from malignancies. Nevi/tumours were studied histologically, immunohistochemically and by Ion AmpliSeq Cancer Panel. NRAS and BRAF mutation-negative samples were analyzed by ARMS PCR (1 % sensitivity).
Results: 4/5 melanoma patients had CNS primaries (one multimetastatic; one V-P shunt peritoneal dissemination) and 1/5 had subcutaneous nodular melanoma. The 6th patient had a brain sarcoma. 5/6 cases showed NRAS codon 61 mutation. In 2 cases, high percentage of mutant NRAS in the tumour suggested somatic homozygosity. One patient with NRASp. Q61K mutated brain primary melanoma showed MLH1 mutation (MLH1p.R385C). The cancer panel also found mutations and SNV of uncertain significance in KIT, KDR, TP53 and ATM genes.
Conclusion: These are novel findings regarding GCMN/NCM malignant transformation, showing 3 cases with either amplification or homozygosity of mutated NRAS. Others genes involved in potentially relevant pathways like mismatch repair, control of cell proliferation, melanocytic signaling and angiogenesis could also contribute to malignant transformation of NRAS mutated GCMN.

OFP-06-006
MiR-100, Mir-195 and MiR-770 are associated with astrocytomas, ependymomas and medulloblastoma in childhood central nervous system malignancies
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Objective: CNS are common tumours in childhood. Recently modern microRNAs measuring technology has enabled sensitive detection of distinct miRNAs and can distinguish between different types of CNS cancers. Most studies are in adults, we decide to compare the expression levels of different miRNAs in astrocytoma, ependymoma, medulloblastomas, and non-neoplastic brain in pediatric patients.
Method: We used low density arrays to evaluate 756 miRNAs in CNS tumours and non-neoplastic brain. We calculate the expression of each miRNAs and we choose the ones that showed a difference, more than 5 times up or low, with control brain. This was corroborate with RT-qPCR.
Results: Of 756 miRNAs, 51 % were expressed in astrocytomas and ependymomas, 37 % in non-neoplastic brain. We selected miR-100, miR-195 and miR-770. In astrocytomas and ependymomas, the levels of expression of miR-100 and -195 was higher than non neoplastic brain. In medulloblastomas miR-195 showed a lower expression ($p = 0.049$). In all the tumours the expression of miR-770 was lower ($p < 0.001$).
Conclusion: Analysis of miRNAs could be a promising contribution to clinical practice, guide diagnosis of different brain cancer types and be helpful predicting progression and therapy response, adding tools for treatment of patient with CNS tumours.

OFP-06-007
Comparison of ultrastructural features between pediatric Mammary Analogue Secretory Carcinoma (MASC) of the salivary glands and pediatric Secretory Breast Carcinoma (SBC) reveals similar pathological features
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Objective: To describe the electron microscopic (EM) features of the mammary analogue secretory carcinoma (MASC) and to compare it with the secretory breast carcinoma (SBC) and acinic cell carcinoma (ACC).
Method: One case each of MASC and SBC (13 and 3 years old) and 12 ACC cases were selected from the pathology archive (1965–2016) of a pediatric hospital. PCR was used to detect ETV6-NTRK3 fusion in both MASC and SBC cases. EM was performed on both tumours and most of the ACC cases for this study.
Results: EM of the ACCs showed classical acinic differentiation with electron-dense zymogen granules and surface microvilli. MASC lacked the electron dense cytoplasmic bodies, but had multiple vacuoles filled with electron-neutral uniform material consistent with mucin/lipid globules. The vacuoles accumulated near the apical cell membranes. Abundant smooth endoplasmic reticulum and surface microvilli were present. SBC had additional secretory granules, fewer mucin/lipid globules and increased extracellular mucin.
Conclusion: In these rare epithelial glandular malignancies in distinct anatomical sites (MASC and SBC), ETV6-NTRK3 fusion results in the transformation of secretory glandular tissue and differentiation to mucin/lipid globule-producing glands. These findings support the common pathogenesis of MASC and SBC in contrast to ACC which lacks this translocation.

OFP-06-008
Fetal postmortem MRI: How can it help the pathologist?
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Objective: With the decreasing numbers of fetal autopsy, probably as a result of the public reluctance of invasive procedures, non-invasive diagnostic procedures are increasing. Postmortem fetal and neonatal MRI (PM-MRI) have shown to have a very high diagnostic value for neurological and thoraco-abdominal malformations. How can PM-MRI be useful to the pathologist?
Method: We investigated our cohort of 200 PM-MRI cases and compared to autopsy results, especially for completeness and differences in findings.
Results: Of 200 PM-MRI cases, only 80 cases had body autopsy and 65 cases skull autopsy; in the other cases (skull) autopsy was refused because of religious or emotional reasons. PM-MRI had a very high diagnostic performance. Neurological abnormalities were diagnosed more often with PM-MRI, whereas cardiac abnormalities were diagnosed more often in autopsy.

Conclusion: PM-MRI has a higher acceptance rate than autopsy and has a very good diagnostic value and performs especially good in neurological anomalies. Autopsy was especially better in cardiac anomalies. Therefore, the alliance of PM-MRI and autopsy should be pursued to have the highest diagnostic value. We advise pathologists and radiologists to work together in postmortem diagnostic centers.

OFP-06-009

Distinctive histopathological findings in liver biopsies from 10 children with lysosomal acid lipase deficiency

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Objective: The purpose of this work is to describe the liver biopsy findings of a group of children with Lysosomal Acid Lipase Deficiency (LALD); partial or total deficiency of lysosomal acid lipase leads to lysosomal cholesterol accumulation mainly in hepatocytes and macrophages. Clinical presentation of LALD varies widely and may be underdiagnosed.
Method: Liver biopsies of children diagnosed as cholesterol ester storage disease in a 10 year period, were obtained, light and electron microscopy (EM), were reviewed and clinical data collected. Immunohistochemistry for LIMP2, LAMP1, and Catepsin-D were performed.
Results: Seven patients were male, aged 30 to 60 months; all presented hepato-splenomegaly, increased ALT and LDL, and decreased HDL; LAL activity was under 0.01 mMol in all patients. Microvesicular steatosis and cholesterol crystals were observed in the cytoplasm of hepatocytes, Kupffer cells, and portal macrophages, as well as moderate to severe liver fibrosis. Lysosomal deposits of lipids and cholesterol were demonstrated under EM, and immunohistochemistry in all liver biopsies.
Conclusion: Microvesicular steatosis and cholesterol crystals storaged in the lysosomes of hepatocytes and macrophages are distinctive of LADL; those liver changes may help to differentiate it from other diseases, and can also have prognostic implications.

OFP-06-010

Expression of miR-221, miR-29b and miR-29c in alveolar rhabdomyosarcoma with pax3/foxo1 and pax7/foxo1 translocations

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Objective: Alveolar rhabdomyosarcoma (ARMS) has two unique translocations with clinical implications. PAX3/FOXO1 has a lower survival and frequently metastasis at diagnosis. MicroRNAs plays an essential role in muscle differentiation. We review the correlation between miRNAs expressed in myogenic differentiation and ARMS with or without translocations.
Method: We review the histology of ARMS cases and search fusion status by RT-PCR, look for alteration on expression levels in miR-221, miR-29b and miR-29c, all involved in muscle maturation.
Results: We study 42 ARMS, 27 (64 %) PAX3/FOXO1, 2 (5 %) PAX7/FOXO1 and 13 (31 %) fusion negative. We found lower expression levels in miR-29b and miR-29c in ARMS with both translocations compared with non-neoplastic muscle. In PAX3/FOXO1 the expression of miR-29b/c decreased compared with control ($P < 0.05$). The fusion negative tumours had higher levels than ARMS with positive fusion status. Mir-221 has no statistical significance.
Conclusion: New molecular technics permit the understanding of cancer steps. MiRNAs in ARMS and other tumours could promote molecular and morphological differentiation, cell cycle exit and apoptosis, and impede invasiveness. Reexpression of specific miRNAs may have therapeutic anticancer value.

OFP-06-011

Composite Neuroblastoma: Unique tumours with morphologically and genetically defined intratumoural heterogeneity

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Objective: Peripheral neuroblastic tumours make one of the most common paediatric neoplasms, and are characterized by clinical and biological heterogeneity. Intratumoural heterogeneity is well documented in Ganglioneuroblastoma, nodular category. However little is known about "Composite Neuroblastoma" with intratumoural heterogeneity in Neuroblastoma category.
Method: First, a series of 12 neuroblastomas showing morphological heterogeneity were identified by the International Neuroblastoma Pathology Committee. All of those tumours were composed of 2 clearly distinct histology areas. Then genetic intratumoural heterogeneity was analyzed by the fluorescence in situ hybridization (FISH) method FISH performed in this study tested (1) MYCN genomic status using a MYCN probe in 2p24 and a reference DNA probe Laf (2q11), and (2) Gene rearrangements (gain) using a Dual Fusion Probe containing a mixture of two probes for PML gene (15q22) and RARA gene (17q21.1).
Results: The first FISH analysis with MYCN and Laf probes demonstrated genetic difference between the two morphologically distinct components for 10 of 12 cases: namely one component showed disomy and the other had polysomy/gain. None of 24 components in this series had amplified MYCN. The second FISH analysis also demonstrated difference of 17q21.1 status between the two components for 11 of 12 cases. Overall, the two morphologically distinct areas (components) of all the 12 tumours demonstrated different genetic characteristics by the FISH tests.
Conclusion: This study verified the intratumoural heterogeneity; i.e., presence of different clones, in "Composite Neuroblastoma". Those different clones in the individual tumours were first identified morphologically and then completely confirmed genetically.

Tuesday, 27 September 2016, 17.15–19.15, Conference Room 5
OFP-07 Gynaecological Pathology

OFP-07-001

Exploring chromosomal abnormalities and genetic changes in uterine smooth muscle tumours

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Objective: The aim of the study was to investigate a well-characterized group of challenging uterine smooth muscle tumours.
Method: 20 leiomyomas (LM), 13 leiomyoma with bizarre nuclei (LBN) and 14 leiomyosarcomas (LMS) were investigated for copy number alterations (CNA), MED12 mutations and FH deletions to search for potential diagnostically useful surrogate markers.
Results: MED 12 mutations were detected in 47, 15 and 25 % of LM, LBN and LMS, respectively. MED 12 mutations in LBN were detected outside the hot spot region. FH-deletions were seen in 27, 30,8 and 25 % of LM, LBN and LMS, respectively. By using CNA profiling a clear separation of LM, LBN and LMS could not be observed. CNA revealed clear genetic similarities between LBN and LMS.

Conclusion: This study demonstrates that known FH-deletions, a recurrent molecular change in LM, occur in morphologically challenging variants of LMs, LBN and LMS. MED12 mutations are common in LM, however, occur infrequently in LBN and LMS. The genetic similarities between LBN and LMS suggest that uterine LBN and LMS are closely related and challenge the traditional concept that LBN is a tumour with just marked "degenerative" cellular changes. Our findings support the hypothesis that tumour progression within uterine smooth muscle tumours might occur.

OFP-07-002

Identifying novel targetable chromosomal alterations using germline copy number variation association analysis of ovarian carcinoma

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Objective: To identify germline CNVs that may be associated with risk for different subtypes of ovarian carcinoma.
Method: We analyzed 132 germline DNA samples of non-familial ovarian carcinoma from ethnically homogeneous women between the ages of 15–94 years (mean = 49.8 years) presented with different pathological subtypes. Germline CNV data generated from DNA by using Affymetrix genome wide human SNP 6.0 arrays using Golden Helix (SVS7) software. Validation of resulting top hits using TaqMan quantitative-PCR and NanoString Copy Number analysis system were carried out to assess DNA products quality.
Results: In the CNVs overlapping the EYA2 (20q13.12) and WNK1 (12p13.33) genes are the top hits with significant p-value (<0.05). Deletion is more frequent in normal samples and in some low grade carcinomas. The ovarian carcinoma samples are mostly copy neutral (CN2) or have copy number gains (CN3). Amplification at these locations is associated with high grade cases which have worse overall survival. Copy number gain of WNK1 gene is associated with higher expression.
Conclusion: Each subtype of ovarian cancer has its own characteristic CNVs that may lead to better understanding the pathogenesis of ovarian carcinoma for development of early screening tools. WNK1 and EYA2 may serve as prognostic markers for ovarian carcinoma with possible oncogenic activity.

OFP-07-003

Insight in intratumour genetic heterogeneity in endometrial cancer

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Objective: Individual prediction of tumour behaviour based on genetic characteristics may refine adjuvant treatment decision in endometrial cancer (EC) patients. Intratumour heterogeneity may hamper clinical implementation of prognostic markers; therefore, we aimed to examine intratumour heterogeneity of promising prognostic markers in EC.
Method: 49 ECs were selected to include equal numbers of patients with alterations in: POLE (n = 10), CTNNB1 (n = 8), p53 (n = 10), mismatch-repair (n = 11) and L1CAM (n = 10). Twelve ECs contained >1 alteration. Three tumour blocks of each EC were analysed for POLE and CTNNB1 hotspot mutations after DNA extraction from microdissected tumour tissue. P53, mismatch-repair and L1CAM expression were analysed by immunohistochemistry. Scoring was performed blinded.
Results: Concordance between the three tumour blocks for POLE- and CTNNB1-mutation status and p53, mismatch-repair and L1CAM protein expression was found in 100 % (48/48), 95.8 % (46/48), 91.8 % (45/49), 91.8 % (45/49), and 89.8 % (44/49) of tumours, respectively. In 10 out of 15 discrepant cases, one block showed an alteration, whereas no alteration was found in the two remaining blocks.
Conclusion: Intratumour heterogeneity is uncommon but requires further research to determine how to approach these situations. However, to facilitate rapid clinical implementation, testing one block is sufficient to ensure correct molecular classification in >90 % of ECs.

OFP-07-004

Comprehensive analysis of microsatellite instability and mismatch repair protein expression in nearly 700 endometrial cancers

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Objective: Microsatellite instability (MSI) testing is increasingly recommended for all endometrial cancer (EC) patients, as it identifies Lynch syndrome, and is emerging as prognostic classifier to guide adjuvant treatment. We aimed to define the optimal approach and clarify discrepancies between MSI and mismatch-repair protein expression (MMR-IHC).
Method: 696 ECs were analysed for MSI (five-marker NCI panel) and MMR-IHC (MLH1, PMS2, MSH2, MSH6). MLH1 promoter hypermethylation and somatic MMR and POLE gene mutations (next-generation sequencing) were analysed in discordant cases.
Results: A PMS2- and MSH6-antibody MMR-IHC panel detected all cases with MMR deficiencies. Discrepancies between MMR-IHC and MSI were observed in 40/696 cases and included heterogeneous MMR-IHC (n = 18), MSS/MSI-low cases with loss of MMR-IHC (n = 19), and MSI-low/MSI-high cases with retained MMR-IHC (n = 3). Heterogeneous MLH1-PMS2-IHC corresponded with MLH1 promoter hypermethylation and heterogeneous MSI. MSS/MSI-low cases with loss of MLH1-PMS2-IHC showed MLH1 promoter hypermethylation, whereas cases with loss of PMS2- or MSH6-IHC carried somatic MMR gene mutations. MSI-high cases with retained MMR expression carried a POLE mutation.
Conclusion: MMR-IHC and MSI analysis are highly concordant in ECs, also in cases with heterogeneous MMR-IHC, therefore, a two-antibody approach is sufficient for MSI testing. Discrepant MMR proficient/MSI-high cases (<1 %), may be explained by POLE mutations.

OFP-07-005

Diagnostic challenges of metastatic malignancies to the ovary: Emphasis on variability of clinical and pathological features

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Objective: To characterize the clinicopathological features of ovarian metastases (OM) presenting as an ovarian mass and compare them with their corresponding primary tumours.
Method: Retrospective review (2000–2014) of clinical/histological material of 120 patients diagnosed with OM.
Results: OM represented 25.8 % of all malignant ovarian tumours; 50.8 % OM were diagnosed either before or synchronously to primary tumours. Most originated from gastrointestinal tract (73.3 %), followed by breast (12.5 %) and gynecological tract (10.0 %). Not uncommonly were unilateral (40.0 %) and ≥13 cm (47.1 %). Gross features varied with primary tumour site, gastrointestinal OM being larger, appendiceal metastases mainly cystic (93.8 %) and gastric/breast metastases predominantly solid (95.5/86.7 %). There were significant histological differences between OM and corresponding primary tumours. Histological pattern was discordant in 44.1 % cases, mainly due to OM cystic change. Other OM showed a predominant component present focally in corresponding primary tumour. OM showed significantly more edema, necrosis and hemorrhage, but less lymphovascular invasion and inflammatory infiltrate than corresponding primary tumours.
Conclusion: OM have variable clinicopathological features, constituting a challenging diagnosis. They frequently differ from their corresponding primary tumours and should always be considered in the differential diagnosis of an ovarian mass.

OFP-07-006

Blinded in-depth characterisation reveals distinct features associated with POLE proofreading domain mutations in endometrial cancer, facilitating clinical implementation

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Objective: POLE exonuclease domain mutations (EDMs) identify a subset of endometrial cancer (EC) patients with an excellent prognosis. Implementation of this biomarker has been suggested for risk refinement. To make this implementation more accessible and cost-effective, we aimed to identify histopathological characteristics to aid detection of POLE EDMs.
Method: Seventy POLE mutated, 20 microsatellite unstable (MSI) endometrioid-type, 17 microsatellite stable (MSS) endometrioid-type and 19 serous ECs were selected (total N = 126). Two gynaecopathologists, blinded for molecular features, evaluated each case (≥3 slides) for 15 histological characteristics.
Results: POLE EDMs were associated with high grade ($P < 0.01$), but not with serous-like features ($P = 0.336$). Tumour giant cells and peritumoural lymphocytes strongly associated with POLE EDMs compared to combined MSI and MSS ECs (both $P < 0.01$). Compared to serous cancers, POLE EDMs contained more lymphocytes ($P < 0.001$) but fewer tumour giant cells ($P = 0.034$). A trend for POLE-mutant ECs was seen towards a pushing border invasion-type ($P = 0.056$).
Conclusion: POLE-mutant ECs distinguish themselves from other molecular subgroups and serous cancers by a combination of endometrioid morphology, high grade, tumour giant cells and prominent immune infiltrate. Use of these histopathological features will assist pre-screening of POLE EDMs, facilitating implementation of this prognostic marker in routine pathology.

OFP-07-007

Cytomorphological patterns of cervical smears of Sudanese infertile women: A case control study

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Objective: To identify the cytomorpholgical changes of cervical smears from infertile Sudanese women.
Method: A case control study conducted in four maternity and infertility centers in Khartoum State, Sudan. Cervical smears were stained with Pap stain and the results were reported using the revised Bethesda System.
Results: Out of 230 cervical smears (165 from infertile and 165 from fertile women aged 15–45 years), 22(13.33 %) of the infertile and 16 (9.69 %) of the fertile women showed abnormal epithelial changes: low grade squamous intraepithelial lesions (9/22), high grade squamous intraepithelial lesions (HSIL) (7/22), atypical squamous cell of undetermined significance (3/22), atypical glandular cells (2/22), and squamous cell carcinoma (1/22), while in the control group these types were 9, 1, 2, 3 and 1, respectively. The cervical smears from the studied infertile and fertile women showed significantly different results ($P = 0.013 < 0.05$).
Conclusion: Cervical smears from infertile women are significantly associated with cytomorphlogical changes particularly of HSIL. The study recommends integration of cervical cancer screening programme in primary health care services. The findings in the cohort of infertile women suggest this group as a potential risk group for HSIL but this needs verification in large scale studies.

OFP-07-008

Identification of POLE exonuclease domain mutations in precursor lesions in endometrial cancer

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Objective: Endometrial cancers (ECs) carrying POLE exonuclease domain mutations (EDMs) define an ultramutated, highly immunogenic subset of ECs with an excellent prognosis. Because it is unknown whether POLE EDMs are initiating carcinogenesis, we analysed endometrial intraepithelial neoplasias (EINs) adjacent to POLE-mutant ECs.
Method: ECs with proven POLE EDMs (n = 70) were evaluated for the presence of adjacent EIN. Four EINs were identified by two independent pathologists. Of one patient, also a positive lymph node was available. DNA was isolated by microdissection and subjected to Sanger sequencing to detect the POLE mutation. One EIN was screened for CTNNB1 mutations using Sanger sequencing as this was identified in the corresponding carcinoma. Slides were immunohistochemically stained for CD8.
Results: Three EINs carried the same heterozygous somatic POLE EDM as the corresponding carcinomas. In one case, the POLE EDM was also present in a positive lymph node. For one cancer containing a CTNNB1 mutation, the EIN was CTNNB1-wildtype. Both EINs and carcinomas demonstrated pronounced CD8+ lymphocytic infiltrates.
Conclusion: POLE EDMs are found in precursor- and in metastatic lesions in EC. Its occurrence prior to another frequently mutated oncogene suggests POLE EDM as an early and perhaps initiating event in carcinogenesis.

OFP-07-009

Molecular classification of grade 3 endometrioid endometrial carcinomas: A retrospective study

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Objective: To classify grade 3 endometrioid endometrial carcinomas (G3-EEC) according to the molecular categories proposed at the light of The Cancer Genome Atlas (TCGA) results.
Method: A retrospective cohort of 50 cases with primary G3-EEC diagnosed between 1997 and 2011 with at least 5 years follow-up was collected. Pathology reports, clinical history and HE stained slides were reviewed. Mismatch repair (MMR) protein and p53 immunohistochemistry and POLE mutational analysis were performed on a selected paraffin-embedded block for each case.
Results: 7/50 cases (14 %) were classified as POLE mutant, 6/50 (12 %) as abnormal p53 (copy number high), 16/50 (32 %) as abnormal MMR and 21/50 (42 %) as copy number low. All patients in the POLE mutant subset had no recurrence and were alive. In the abnormal p53 subset, 4/6 had no evidence of disease (NED) and 2/6 died due to unrelated causes (DUC). In the abnormal MMR group, 4/16 died because of disease (DOD), 2/16 DUC and 10/16 had NED. In the copy number low group, 6/21 DOD, 2/21 DUC, 1/21 was alive with disease, 11/21 NED and 1/21 was lost.
Conclusion: G3-EEC is an heterogeneous group of tumours that includes the four categories proposed by TCGA. This approach has a prognostic value.

OFP-07-010

URI1, BRCA1/BRCA2 and CCNE1 as potential drivers of a poor: Prognosis subset of High-grade Serous Ovarian Cancer (HGSOC)

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Objective: CCNE1 amplification occurs in about 20 % of HGSOC cases, correlates with platinum resistance and is mutually exclusive of BRCA1/2 mutation. CCNE1 codes for cyclin E1 protein and is co-located on 19q12 with URI1, a pro-survival gene. We aim to investigate the interaction between CCNE1 and URI1 in HGSOC.

Method: 222 HGSOC sections with known germline BRCA status were stained by in situ hybridization using a DNP-19q12 probe containing both CCNE1 and URI1, and immunohistochemistry for cyclin E1 and URI1.
Results: 19q12 was amplified in 18.5 % of cases, of which 53.7 % highly expressed both cyclin E1 and URI1. There was significant correlation between 19q12 amplification and cyclin E1 ($p < 0.0001$) and URI ($p < 0.006$) expression; and between cyclin E1 and URI1 ($p < 0.0001$). 19q12 amplification, high cyclin E1 or URI1 high expression were each associated with poor overall survival ($p = 0.028$, $p = 0.021$, $p = 0.039$, respectively) and were mutually exclusive of germline BRCA1 mutations ($p = 0.035$, $p = 0.031$, $p < 0.0001$ respectively.
Conclusion: The frequent co-occurrence of 19q12 amplification, cyclin E1 and URI1 high expression and their mutual exclusivity with BRCA1 mutations suggest that cells giving rise to this tumour type require a cooperation of a proliferative signal (cyclin E1) and a pro-survival factor (URI1) and an intact DNA repair mechanism (BRCA) in tumourigenesis.

OFP-07-011

Inflammatory cell infiltrates in vulvar low/high grade intraepithelial neoplasia and invasive squamous cell carcinoma: Differences, prognostic value and relationship to HPV

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Objective: (1)Describe and compare inflammatory cell infiltrates (ICI) in vulvar low and high grade intraepithelial neoplasia (LVIN/HVIN) and invasive squamous cell carcinoma (SCC); (2)evaluate their prognostic value as biomarkers; (3)assess eventual differences of ICI in HPV-related SCC.
Method: LVIN(21), HVIN(45) and SCC(44) retrospective cases from AC-Camargo-Cancer-Center, Brazil, between 1980 and 2013. H&E slides were reviewed by expert pathologists. Peri/intratumoural hotspots were evaluated. ICI characterization was accomplished by morphology and immunohistochemistry (anti-CD3/SP7, CD4/EPR685, CD8/EP1150Y, CD20/EP459Y and FOXP3/Poly). HPV was assessed by linear array. Quantification by HSCORE of ICI was performed by APERIO® system. Statistics data were calculated considering $p < 0.05$. Kaplan-Meier curves were based on Log-Rank test.
Results: Most ICI showed moderate/intense plasmocytes/lymphocytes count (P2L13/21-LVIN, P9L35/45-HVIN, P18L44/44-SCC). ICI showed progressively increased expression of CD3, CD8 and FOXP3 in peritumoural ICI in SCC>HVIN>LVIN ($p < 0.0001$). CD4 show reduced expression in SCC<HVIN<LVIN ($p < 0.0001$). ICI showed reduction in peri/intratumoural CD4 expression ($p = 0.007/p = 0.048$) and increase in intratumoural CD8 expression ($p = 0.035$).
Conclusion: (1)ICI showed total plasmocytes and T lymphocytes count, CD8+/CD4+ ratio and FOXP3 expression progressively increased in SCC>HVIN>LVIN; (2)patients with SCC associated to intratumoural T lymphocytes and peritumoural T lymphocytes expressing FOXP3 had prolonged disease-free survival; (3)there was association between HPV and increased CD8+/CD4+ ratio intratumoural T lymphocytes in HPV-related SCC.

OFP-07-012

Uterine serous carcinomas frequently metastasize to the fallopian tube and can mimic serous tubal intraepithelial carcinoma

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Objective: To study frequency, histopathological and immunohistochemical characteristics of tubal involvement in uterine serous carcinoma (USC) and to clarify the relationship between serous tubal intraepithelial carcinoma (STIC) and USC.
Method: Cases of USC with complete tubal examination were prospectively collected and reviewed for presence of tubal involvement. Immunohistochemistry for p53 and WT1 was performed on endometrial and tubal components in cases with tubal involvement.
Results: Of 161 USC cases, 32 (19.9 %) showed tubal involvement (unilateral: $n = 19$, bilateral: $n = 13$). Patients with tubal manifestations were older, and there were higher rates of deep myometrial and lymphovascular invasion (LVI) compared to cases without. Tubal fimbriae were involved in 16/32 cases. Tubal tumours were mucosal in 28/32, mural in 14/32, serosal in 3/32, invasive in 22/32 cases, and showed LVI in 15/32. STIC-like features were seen in 16/32 cases. Immunostaining showed complete concordance of p53 and WT1 between endometrial and tubal tumours in 23/28 cases, the majority being WT1 negative or only focally positive (19/23), and all being p53 mutant.
Conclusion: Tubal involvement is detected in one-fifth of USC. Although STIC-like features might suggest tubal origin in half of these, our study shows that tubal manifestations represent intramucosal metastasis from USC in most cases.

Wednesday, 28 September 2016, 08.30–12.00, Conference Room 1–2
OFP-08 Breast Pathology

OFP-08-001

Continuous quantification of HER2 expression by microfluidic precision immunofluorescence estimates HER2 gene amplification in breast cancer

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Objective: Immunofluorescence (IF) has recently gained attention as been more suitable than chromogenic stainings to quantify antigen expression. We introduce a microfluidic precision IF technique, which accurately quantifies the target expression level in a continuous scale based on microfluidic IF stainings of standard tissue sections and automated image analysis.
Method: FFPE breast carcinoma samples were obtained from the Institute of Pathology. Microfluidic IF staining was performed using rabbit anti-human c-erbB-2 oncoprotein (Dako) and mouse anti-human cytokeratin (CK) (clone AE1/AE3, Dako). AF 594 goat anti-rabbit IgG (Life Technologies) and AF 647 goat anti-mouse IgG (Life Technologies) secondary antibodies were used. The signals from the CK and DAPI channels were used to identify epithelial cells. Average values for CK and HER2 were assigned to each case and then used to obtain the final score.
Results: Microfluidic-based double stainings were achieved successfully. Low antibody incubation times of 2 min resulted in a proportional relationship between the IF signal and the corresponding antigen concentration. The continuous scoring, established for the complete cohort of 25 cases, linearly correlated with the HER2 gene copy number as assessed by FISH analysis.
Conclusion: Microfluidic precision IF proved to be very powerful in terms of quantifying antigen expression in breast carcinoma cases. The generated quantitative data can be used as a scoring aid to pathologists to increase success of treatment response prediction and prognosis. In the future, larger clinical studies for several markers will be required to further validate and prove the impact of microfluidic precision IF technology in cancer diagnosis.

OFP-08-002

Prognostic significance of CD9 expression in tumour cells and stromal lymphocytes of invasive breast carcinoma

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Objective: The aim of this study is to examine the prognostic significance of CD9 expression in invasive breast cancer.
Method: We evaluated CD9 expression in cancer cells (E-CD9) and stromal tumour-infiltrating lymphocytes (TILs) (S-CD9) of 1357 invasive breast cancer samples using immunohistochemistry on tissue microarrays. Correlations of CD9 expression with clinicopathological factors and disease-free survival (DFS) were investigated.
Results: High E-CD9 expression was observed in 736 (54.2 %) cases, and S-CD9 expression in 852 (62.8 %) cases. E-CD9 expression was associated with lymph node metastasis ($P < 0.001$), high histological grade ($P = 0.001$), lymphovascular invasion ($P < 0.001$), and HER2 positivity ($P < 0.001$). S-CD9 expression showed an association with large tumour size ($P = 0.006$), lymph node metastasis ($P = 0.05$), high histological grade ($P < 0.001$), negative hormone receptors ($P < 0.001$), HER2 positivity ($P < 0.001$), and abundant TILs ($P < 0.001$). Patients with high E-CD9 expression showed worse DFS than those with low expression of CD9 ($P = 0.001$). In contrast, expression of S-CD9 was a positive prognostic factor for DFS ($P = 0.031$). High expression of E-CD9 was found to be an independent prognostic factor in multivariate analysis.
Conclusion: CD9 expression should be evaluated in tumour cells and stromal TILs, separately, and E-CD9 expression could be a promising prognostic marker in patients with invasive breast cancer.

OFP-08-003

Comparison of risk classification between EndoPredict and Mammaprint scores in ER+/HER2- invasive breast cancer

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Objective: The prognostic performance of the EndoPredict (EP) assay on 40 estrogen-receptor positive/HER2-negative early breast carcinomas (BC) was compared with the MammaPrint (MP) scores obtained for the same samples.
Method: Formalin-fixed, paraffin embedded invasive BC tissues were analyzed by the EP assay, a second generation gene expression test that combines expression of 8 genes (EP score) with the two clinicopathological factors tumour size and nodal status to the EPclin score. The same tumour blocks were previously analyzed with MP (20 high-risk and 20 low-risk tumours), a first generation gene expression test that includes gene expression only.
Results: The EP score classified 15 patients as low-risk and 25 patients as high-risk. EPClin re-classified 5 of the 25 EP high-risk patients into low-risk, resulting in a total of 20 high-risk and 20 low-risk tumours. Discrepancies between both tests occurred in 10 cases: 5 low-risk MP were classified as high-risk and 5 high-risk MP were classified as low-risk by EPClin.
Conclusion: This study demonstrates a moderate concordance between MP and EndoPredict. Differences in results could be explained by the inclusion of different gene sets in each platform and the consideration of independent clinical risk factors such as tumour size and nodal status in the EndoPredict test result.

OFP-08-004

PD-L1 expression in breast carcinoma

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Objective: The PD1/PD-L1 pathway participates in the immune system's response to cancer. The pathway is targeted by immunotherapeutic agents, employing PD-L1 expression as a predictive marker, in non-small cell lung carcinoma. We investigated the expression of PD-L1 in a series of breast carcinomas, where this pathway has not been adequately examined.
Method: PD-L1 expression was examined by immunohistochemistry in whole tissue sections of 71 consecutive breast carcinomas and separately assessed in the tumour cells (T) and the tumour infiltrating lymphocytic/dendritic cells (L/D), using the Allred score. The results were compared with the clinicopathological features of the tumours. Statistical analysis was performed with the Mann-Whitney and Kruskal Wallis tests.
Results: L/D and T PD-L1 expression was associated with molecular subtype surrogate groups ($p = 0.008$ and $p = 0.042$, respectively), with higher expression in HER2+/triple negative breast carcinomas versus luminal tumours ($p = 0.004$ and 0.007, respectively). L/D PD-L1 expression was associated with grade ($p = 0.002$) and T PD-L1 expression with Ki-67 ($p = 0.049$). No association was observed with tumour type, size, lymph node or distant metastases.
Conclusion: Higher PD-L1 expression in higher grade, HER2+ and triple negative breast carcinomas suggests a possible participation of the PD1/PD-L1 pathway in these subtypes, which if proven, might be exploited therapeutically.

OFP-08-007

HER-France - A real-world national database for HER2 results by IHC-ISH in breast cancer. Impact of 2013 ASCO/CAP guidelines

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Objective: Pathologists are at the front line for HER2 determination in breast cancer. HER-France aims to provide French pathology labs with statistics on their own data compared with the national data (aggregation of data of all participants) to detect possible deviations from reference conditions and amend their practice if necessary.
Method: It was developed by AFAQAP (French quality control association in pathology). Collected data include type of sample, tumour type, HER2 score and HER2 amplification status. From October 2011 to April 2016, 125 public and private labs voluntarily joined HER-France and more than 127 000 specimens were registered. To avoid possible bias due to adverse pre-analytical conditions, focus was made on core-needle biopsies (CNB).
Results: Among 53 156 CNB on untreated primary tumours, percentage of HER2 scored 0, 1+, 2+ and 3+ was 50.4, 24.9, 14.5 and 10.2 %, respectively. Among score 2+ cases, and for two periods clearly separated by 2013 ASCO/CAP guidelines publication (before and 1 year after), ISH "equivocal" rate rose from 2.3 to 10.7 % ($p < 0.001$). For the same periods, HER2 positivity (3+ and 2+ amplified) was equivalent: 12.30 % (IC95% [11.82–12.78]) and 11.77 % (IC95% [11.35–12.19]) ($p = 0.478$), respectively.
Conclusion: HER-France is considered by French pathologists as an essential tool providing good practice indicators.

OFP-08-008

Morphological characteristics of breast cancer in association with the levels of DNA methyltransferases and histone deacetylase

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Objective: The role of epigenetic modifications in stimulating initiation and progression of breast cancer is widely discussed. The aim of our study is to analyze specific changes in the levels of enzymes in nuclear extracts associated with breast cancer.

Method: The levels of DNMT1, DNMT3a (DNA methyltransferases) and H3K(4) (histone deacetylase) were measured in nuclear extracts of white blood cells of 21 breast cancer patients and 10 healthy controls using ELISA based DNMTs assay kits (Abcam). Histological grade and phenotype were assessed independently by three pathologists.
Results: The level of DNMT1 was higher in control group in comparison to the study group. Neither of the methyltransferases correlated with the size of the tumours. The level of DNMT3a increased with the higher grade and with higher proliferative activity of the tumours. H3K(4) level was higher in smaller tumours and in tumours with lower histological grade. Neither of the enzymes correlated with the degree of hormonal receptor positivity.
Conclusion: This primary study showed that the level of enzymes, regulating epigenetic modifications may be altered in blood cells of patients with breast cancer and this needs further evaluation including comparison with precise epigenetic patterns, analyzing the changes in tumour cells along with the blood cells.

OFP-08-009
Quantification of immune cells in triple negative and non-triple negative of breast cancer

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Objective: To investigate and compare the tumour microenvironment of triple negative and non-triple negative breast cancer.
Method: A total of 104 breast cancer tissue were analyzed in the study. Clinico pathological parameter of breast cancer patients were investigated for age, tumour size, tumour grade and lymph node status. Special stains (giemsa and toluidine blue) and immunohistochemistry technique were performed using α-ER, α-PgR, α-Her-2, α-CD3 and α-CD20 antibodies. Quantification of immune cells/mm2 was performed. Data were entered and analyzed using SPSS version 16. Correlation of immune cell densities with various tumour sub-types was investigated using paired t-test and Chi square test. A p-value of <0.05 was considered as significant.
Results: Our data showed out of 104 patients mean age was 47 years. 27 (25 %) patients were triple negative and 77 (74 %) were non-triple negative. 100 (96 %) were IDC, where as 4 (0.03 %) showed special subtypes. Moreover there was increased infiltration of immune cells in triple negative breast cancer. Moreover there was significantly high infiltration T-lymphocytes (p-value = 0.013) and B-lymphocytes (p-value = 0.01) were recorded as compare to non-triple negative breast cancers. In addition, there was no significant difference (p-value > 0.05) demonstrated in number of macrophages, mast cells and neutrophils in triple negative and non-triple negative breast cancer cases.
Conclusion: Lymphocytes are densely infiltrating in triple negative breast cancer cases as compare to non triple negative cases which indicates that presence in significant number, they may play some role in tumouriogenesis in triple negative breast cancer.

OFP-08-010
Estrogen receptor negative breast cancers show quasi-mesenchymal phenotype

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Objective: Epithelial-to-mesenchymal transition (EMT) is considered an important mechanism for tumour progression and metastasis. Mesenchymal gene upregulation has been described as a quasi-mesenchymal phenotype and prognostic marker in other cancer types. We wish to characterize mesenchymal gene expression (M-high) in human breast cancer.
Method: Ninety-four estrogen receptor negative (ER-) and 130 ER+ clinically annotated breast cancer samples from female patients were evaluated by colorimetric in-situ hybridization (View RNA, Affymetrix, CA) on formalin-fixed paraffin-embedded tissue microarrays. The mesenchymal gene expression profile included FN1, CDH2, and SERPINE1 and was semiquantitatively assessed as M-low (0/1) or M-high(2/3). MedCalc V16.2.0 was used for statistical analysis.
Results: Of 34 M-high cases, 76.5 % (N = 26) were ER- and 23.5 % (N = 8) ER+. Of 159 M-low cases, 35 % (N = 55) were ER- and 65 % (N = 104) were ER+. Quasi-mesenchymal phenotype M-high was associated with ER status and histologic grade ($p < 0.0001$ by chi square) but not with HER2 amplification, lymph node stage or tumour size. Grade, lymph node stage and tumour size ($p < 0.0001$) were predictive of disease free survival by Kaplan Meier analysis.
Conclusion: Quasi-mesenchymal phenotype M-high associated with ER negative and high grade breast cancers may contribute to their biologically aggressive behavior. Additional samples are being investigated to confirm associations with outcome.

OFP-08-012
Optimal Ki67 cut-off for ER+/HER2- breast cancer prognostic evaluation: A large case series study with a long-term follow-up

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Objective: Different Ki67% cut-offs have been proposed to select treatment for estrogen receptor positive (ER+) breast cancer (BC) patients. The aims of the present study were: (i) to establish the optimal Ki67 cut-offs for stratifying prognosis; (ii) to create a comprehensive prognostic index for clinical applications.
Method: Clinical, histological and follow-up data of a mono-institutional cohort of 1577 ER+/HER2- BC patients (operated between 1994 and 2001) were collected. Ki67 cut-offs of 14 and 20 % were correlated to disease free interval (DFI) and disease specific survival (DSS). Independent variables selected by univariate and multivariate analyses were used to create a comprehensive prognostic index (CPI).
Results: Patients with tumours having Ki67 > 20 % showed the poorest prognosis considering both DFI and DSS. Ki67 expression, tumour size and nodal status were then scored and used to create the CPI. Patients with a CPI ≥ 3 had an increased risk of relapse (HR = 4.74) and death (HR = 5.03) and showed a DSS disadvantage if treated with hormone therapy alone.
Conclusion: We confirm that 20 % of Ki67 expression is the best cut-off to stratify luminal BC patients, and could be integrated with other parameters to better stratify patients outcomes and drive therapeutic strategies.

OFP-08-013
One-day diagnosis on core biopsies of suspected breast lesions: Comparison with routinely processed surgical samples

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Objective: To evaluate the preservation of morphology and antigenicity of tumours, the reliability of predictive/prognostic factors determination, and the nucleic acids integrity in rapidly processed breast biopsies, diagnosed on the same day of sampling.
Method: 301 patients underwent breast "Core needle biopsy-one day diagnosis" between 2013 and 2015 and were classified according to NHSBSP2006. One-day tissue processing is based on preheating of reagents at 50 °C. Immunohistochemistry (IHC) and in situ hybridization (ISH) were performed. PCR amplification of 4 housekeeping-genes (AF4/PLZF/RAG1/TBXAS1) was carried out from formalin-fixed paraffin-embedded tissue of 15 infiltrating carcinomas to evaluate the gDNA quality.
Results: Out of 301 cases, 191 (63.5 %) were infiltrating carcinomas (B5), 58 (19,3 %) were benign lesions (B2), all confirmed on surgical

samples. Twelve percent of infiltrating carcinomas showed HER2 2+ score by IHC, half of which demonstrated amplification of HER2 by SISH. 52 cases (of which 9 were operated elsewhere) were classified as B1/B3/B4, accordingly. At surgery, out of the remaining 43 cases, 7 B4 were all infiltrating carcinomas; 27 B3 were non-malignant lesions (n.22 = 81,5 %), in situ carcinomas (n.4 = 14,8 %) and infiltrating carcinoma (n.1 = 3,7 %); 9 B1 were non-malignant lesions (n.8 = 88,9 %) and infiltrating carcinoma (n.1 = 11,1 %). PCR products showed clear bands of 100, 200, 300, 400 bp in all 15 samples when compared with paired non-rapidly processed series.
Conclusion: One-day diagnosis allows a good preservation of the cellular details and the confident use of IHC, ISH and molecular techniques. It is also important to decrease patients' stress due to the diagnosis await.

OFP-08-015
Determining the expression profiles of stem cell markers (CD44, CD24, and ALDH1) in breast carcinoma subtypes and investigating their relationship with prognostic factors
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Objective: To determine the stem cell marker (CD44, CD24, and ALDH1) expression profiles in breast carcinoma subtypes and to investigate their relation with prognostic factors.
Method: 167 breast carcinoma subtypes from the pathology archive between 2007 and 2015 were selected. Each case is scored based on ALDH1 and CD24/44 staining. Correlation with patients' age and tumoural prognostic factors (size, grade, stage, hormone receptor profile, HER2 status, lymph node metastasis, distant metastasis) were studied.
Results: ALDH1+ and CD24-/CD44+ cases were younger patients. ALDH1 expression was positively correlated with increasing tumour size and grade. Cases included in the study are divided into two groups based on their histological subtypes. ALDH1+ and CD24-/CD44+ phenotype were found to be more common within invasive ductal carcinoma subtype. Among other subtypes, metaplastic carcinoma was the leading one to express ALDH1+ and CD24-/CD44+ profile. As a molecular subtype, basal-like phenotype was the most frequent carcinoma expressing that profile. CD24-/CD44+ phenotype among hormone-receptor-negative cases was 5 times higher than that of hormone-receptor-positive cases.
Conclusion: In this study, we determine the expression profiles of CD24, CD44, and ALDH1 among the histological and molecular subtypes of breast carcinomas using immunohistochemistry and showed the relationship of these stem cell markers with the well-known prognostic factors.

Wednesday, 28 September 2016, 08.30–12.00, Conference Room 4
OFP-09 Other Topics

OFP-09-001
The role of the technicians in the digital pathology implementation: Searching optimization
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Objective: Scanning is a crucial element in the process of digitization of Pathology Departments. Scanning time and the high size of the files are still considered suboptimal for full implementation. In order to optimize, a comparative study has been carried out.
Method: 25 endoscopic samples were selected in order to compare different parameters: scanning time (ST), error rate (ER) and hard-disk storage (HDS), between the original glass slides (group A (A): 2 slides/case, 50 preparations) and new sections, with levels grouped into a single slide (group B (B): 1 slide/case, 25 preparations). They were scanned at 20x magnification in routine way using the Ventana iScan Coreo scanner.
Results: The average ST was 5 h 40 min (13m36s/case) (A) and 5 h 10 min (12m24s/case) (B). The ER was 6 % (A) and 4 % (B). The HDS was 11.87 GB (A) and 9.6 GB (B) (475 MB/case vs 385 MB/case, respectively). The average number of tissue sections/case was 7 (A) and 8 (B).
Conclusion: There is a clear benefit of standardizing and optimizing the number of cuts/slide in terms of storage (saving 19 %), biopsy sampling (14 % more tissue) and ER (33 % less), including a not negligible decrease in the ST (9 %) in the study conducted.

OFP-09-002
A comparison of ultrastructural glomerular features in biopsies from patients with de novo donor specific antibodies with surveillance biopsies
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Objective: Patients with de novo donor specific anti-HLA antibody (de novo DSA) are at increased risk of antibody-mediated rejection and our aim is to compare biopsies from such patients with surveillance biopsies, to identify the effect of DSA on ultrastructural features of glomeruli.
Method: Ultrastructural features in 40 biopsies: 15 1-year surveillance biopsies from DSA-negative patients and 25 biopsies from patients with de novo DSA were recorded. Unpaired t tests were applied (Mann-Whitney) using GraphPad Prism 6.
Results: There was a statistically significant difference between de novo DSA biopsies and surveillance biopsies for: mean loss of endothelial fenestration per loop ($p = 0.0001$), mean endothelial swelling per loop ($p = 0.03$), mean endothelial crenellation per loop ($p = 0.02$), percentage of loops with new basement membrane ($p = 0.02$), percentage of loops with double contours ($p = 0.006$), and percentage of loops with extensive foot process effacement ($p = 0.02$).
Conclusion: Ultrastructural glomerular features are significantly different between biopsies from patients with de novo DSA and surveillance biopsies. Further investigations will be carried out on a wider range of biopsies, to validate the diagnostic value of these features.

OFP-09-003
The impact of daily surgical pathology huddles on quality, safety culture and team engagement
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Objective: Timeouts (team huddles) at the start of surgical procedures have become the standard of care because of their positive impact on patient safety. The aim of this study is to describe the implementation and impact of such a huddle in surgical pathology at a major academic medical center.
Method: Results of a patient culture survey and additional collected data were used to develop specific and focused quality improvement (QI) projects. This included implementation of a daily surgical pathology huddle. The impact of this on different quality metrics, safety culture and team engagement was assessed.
Results: The entire team for the day participates in the huddle, including technologists, trainees and pathologists. Main items communicated in this 5–10 min session are highlights of the operating room schedule including predicted intraoperative consultations, key volume metrics for the previous day, staffing coverage, expected slide delivery times and debriefing of

previous day work issues. The impact of this huddle and other associated high reliability practices included (1) reduction of major frozen section (FS) discrepancy rates, (2) improved FS TAT, (3) increased QI projects across the lab, (4) increased staff engagement and (5) improvement in safety culture, manifested by improvements in 9/12 dimensions measured in a repeat survey, including 5 % improvement in overall perception of safety.
Conclusion: Huddles provide a constructive, blame-free environment for respectful personal interaction that allows for dissemination of information and brief discussion, create a nidus for generating additional improvements and result in improved outcomes and increased engagement and mindfulness of the entire team.

OFP-09-004
Billroth's specimen of the first gastrectomy: A modern histological and molecular analysis
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Objective: Christian Albert Theodor Billroth (1829–1894) was a Prussian-born surgeon and is regarded as the father of modern visceral surgery. On January 29, 1881, Billroth performed the first gastrectomy on pyloric cancer. Billroth resected the pyloric cancer of Therese Heller, a 43-year-old woman who complained weight loss, nausea, vomiting and melena due to this cancer. The specimen of Billroth's operation was analysed at the department of Richard Heschl (1824–1881) and was stored in formalin up to now. We investigated this specimen and that of the remaining stomach of the autopsy.
Method: We took biopsies and processed by routine techniques of pathohistology. In addition, we tried to extract DNA from those samples using usual procedures.
Results: Grossly, we found the distal part of the stomach measuring 13 cm in length with a tumour of 8 cm that narrowed the gastric lumen significantly. Histology revealed a mucinous adenocarcinoma. DNA could be extracted and first attempts are on the way to identify potential mutations.
Conclusion: In conclusion, the surprisingly well-preserved exhibits, which have been on display for 135 years, are accessible to modern histopathology and even to molecular analysis. Such examinations allow us to assess the occurrence of diseases and tumours in the sociocultural environment of the 19th century.

OFP-09-005
The contribution of neuropathological post-mortem examinations to the coronial service
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Objective: Neuropathological post-mortem (PM) examinations can be requested as part of death investigations however, some question their value. This project provides a snap-shot of the coronial service provided by the neuropathological department at King's College Hospital, and attempts to semi-quantify the contribution of this specialist service.
Method: A retrospective review of all reports issued to the coroner for neuropathological PM examinations undertaken at King's College Hospital between 1.1.2014 and 20.10.2015 was undertaken. The contribution of specialist neuropathology examination was scored on a scale of 0 (no contribution) to 3 (significant contribution) by an independent reviewer. It was also noted if neuropathological opinion was sought for potentially medico-legal, rather than clinical, reasons.
Results: 127 neuropathological PM examinations were performed, with 51 % receiving neurological imaging prior to death. Mostly cases were referred due to histories of epilepsy, trauma, or uncharacterised brain lesions. The contribution of neuropathological PM examinations was characterised as follows: no contribution 0, minor 8 %, moderate 13 %, and significant 79 %. It was deemed medico-legally prudent in 18 % of cases.
Conclusion: Despite approximately half of cases receiving neurological imaging prior to death, the contribution of neuropathological PM examination is significant and/or medico-legally prudent in 84 % of cases.

OFP-09-006
Concerns about falling autopsy rates have given rise to new autopsy legislation in Norway
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Objective: The Norwegian health authorities have long been concerned about falling autopsy rates. A total of 7 % of the deceased in Norway were examined post mortem in 2012, including both forensic and medical cases. Medical autopsies have traditionally been performed on patients dying in hospitals. As nearly 70 % of deaths in Norway now occur outside hospitals, the monitoring of medical diagnostics and treatment through post mortem quality control is under threat. Furthermore, the implications for cause of death statistics are serious.
Method: To improve autopsy practice, a new law has been implemented from January 2016.
Results: The preamble lists accuracy in cause of death, quality assurance, teaching, achievement of new knowledge and better statistics as valid reasons for autopsies. Doctors who fill out the death certificates are now obliged to consider the need for autopsy in every case, regardless of place of death, and are required to file the result of their considerations in the patient's clinical records. The accepted practice of oral consent from next of kin has been continued. Due to the possibility of work overload, the departments of pathology have been given the right to refuse autopsy requests if necessary.
Conclusion: Norwegian politicians recognize the importance of post mortem quality control and have, through the enactment of a new law, strongly signalized the need for autopsies as good medical practice.

OFP-09-007
How accurate is the postmortem CT scan?
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Objective: Postmortem diagnosis is an important condition to monitor the quality of care. Conventional autopsy (CA)rates have decreased worldwide to <10 % nowadays, which seems to be caused by objections to the invasiveness. Therefore, non-invasive techniques are being investigated such as postmortem CT (PMCT). The aim of this study is to investigate the diagnostic performance of PMCT in identifying the causes of death (CoD) compared to CA.
Method: 79 deceased patients (46M, 33F,mean 58 years) underwent PMCT before CA. PMCT consisted of cerebro-thoraco-abdominal images. CA consisted of thoraco-abdominal with/without skull autopsy. The radiologist and pathologist were blinded for each other's results. % Agreement and sensitivity of CoD on PMCT were calculated, with CA as the reference standard.
Results: CA found 89 % CoD, and PMCT diagnosed 51 % of these correctly. PMCT sensitivity was 51 % (95%CI 39–64 %). PMCT performed relatively good in cases of hemorrhage and dissection; however poor in cases of myocardial infarction. PMCT correctly diagnosed the organ of the CoD in 73 %.
Conclusion: The diagnostic performance of PMCT is not sufficient to replace CA. However, PMCT performs good in pointing out the site of the pathology. Therefore, PMCT as a screening tool prior to (mini-)autopsy should be investigated further.

OFP-09-008

Moulages: Art in the history of medicine

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Objective: A brief history about a Dermatological Moulage Museum in our School of Medicine to avoid oblivion of old teaching methods in Dermatology.
Method: The specimens of the Dermatological Moulage Museum that were purchase from the Hospital Saint Louis of Paris in 1922 by an argentine dermatologist were classified according to the pathological diseases and evaluated regarding the conservation of the specimen.
Results: Total number of specimens in the Moulage Museum at the School of Medicine, is as follows: 358. 100 French manufacturing and 258 by local specialized artisans. Diseases Classification: Infectious skin diseases 143: syphilis, leprae, mycosis, skin tuberculosis. Skin cancer 47: spinocellular epithelioma, lymphoma, Bowen's disease. Other dermatitis 73: erythema multiform, lichen. Benign tumours 16: hemangiomas, sebaceous adenomas. Autoimmune diseases 33: pemphigus vulgaris, lupus erythematosus. Several etiologies 26: milium, mal de Pinto, neurofibromatosis. Unclassified skin diseases: 2. Not tagged: 18.
Conclusion: Most famous Dermatological Museums are in Paris and Zurich, exclusively dedicated to medicine, such as in the hereby presented collection, therefore, history, art and science could still teach new generations.

OFP-09-009

Fetal akinesia deformation sequence

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Objective: Fetal akinesia deformation sequence (FADS) is a rare condition characterized fetal akinesia, IUGR, facial anomalies, arthrogryposis, pulmonary hypoplasia and other developmental abnormalities. we present 3 cases of Fetal akinesia deformation sequence, 2 of them with molecular confirmation and our goal is to demonstrate the specific characteristics that may be present or not and help with future diagnosis of this often underdiagnosed sequence.
Method: We report and summarize 3 cases from non-consanguineous healthy couples who showed specific alterations in the US and in which fetal autopsy helped recognizing FADS.
Results: After identification of these characteristics by fetal autopsy we performed whole exome sequence that revealed a pathogenic variant in homozigoty in the gene RYR1 in the 1st case and Trusight one disease exome in the 2nd case that revealed a pathogenic variant in homozigoty in the gene RAPSN. The study of the 3rd case is in progress.
Conclusion: Lack of fetal movement produces a recognizable sequence of deformations; prenatal US diagnosis is possible, as early as 12 weeks. Most cases die in utero, at birth, or in new born period. Advances in embryo/fetal pathology have led to the improvement of recognition allowing more accurate genetic counseling and early detection in future pregnancies.

OFP-09-010

Primary ciliary dyskinesia: An update with molecular correlation

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Objective: Historically, Transmission Electron Microscopy (TEM) played a key role in the diagnosis of Primary Ciliary Dyskinesia (PCD), but currently newer diagnostic modalities including genetic testing are available. In light of these developments, it is of interest to correlate the results obtained from TEM and molecular genetics, in the same patients. The aim of this study is to present the results obtained in the Cyprus PCD cohort and highlight the diagnostic role of EM in the era of molecular medicine.
Method: The diagnostic records of PCD patients were reviewed and data on TEM were compared with the emerging results from the recent molecular genetic tests performed in our department.
Results: 30 PCD patients have been diagnosed in our centre since 1998. TEM analysis revealed a combined ODA and IDA defect in 43 % and an ODA defect in 10 % of the patients. Normal ultrastructure (NU) was identified in 34 % of the patients while the remaining presented other defects. Sixty percent of patients with NU carried a mutated DNAH11 gene and all patients with an ODA defect carried a mutated DNAH5 gene.
Conclusion: Among the 30 PCD genes, only mutations in DNAH11 are associated with a NU. Mutation in other genes, such as RSPH4A (radial spokes) and CCDC164 (nexin links), cause subtle morphological defects that may missed by TEM. However, TEM remains a useful tool for PCD diagnosis as it can guide genetic testing through the identification of specific ultrastructural defects.

OFP-09-011

The inclusion of pathologists in monitoring inpatient deaths significantly improves the notification procedures in cases of unnatural deaths due to medical malpractice or errors

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Objective: Follow up of deaths by unnatural causes, especially if due to medical malpractice, is important for medical teaching and maintenance of patient safety. Doctors who certify deaths in Norway are under legal duty to report deaths due to unnatural causes to the police. In cases of medical malpractice, the health authorities must also to be notified. Notification may be difficult for clinicians, who often are in the situation of reporting themselves or their colleagues.
Method: Since 2008, reporting procedures at our institution have been improved by engaging pathologists in the monitoring. The pathologists do not report to the authorities, but notify the clinician and the Quality Department.
Results: A review of 1519 deaths from 2012 to 2013 showed that 60 % of the reports due to malpractice were initiated by pathologists. Pathologist are most likely to notify cases of surgical complications, whereas clinicians more frequently report cases of treatment delay, intoxication and sudden deaths. The autopsy rate in cases of malpractice was higher if notified by clinicians (77 vs 58 %).
Conclusion: The inclusion of pathologists in monitoring inpatient deaths has increased the number of reported deaths due to unnatural causes. Pathologists and clinicians complement each other in the types of cases they notify.

OFP-09-012

Grading of oligodendroglioma based on Ki-67 labeling index assessment performed manually and automatically in hot-spot fields

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Objective: Concordance analysis of oligodendrogliomas grading based on Ki-67 labeling index assessment performed manually in light microscope and automatically in whole slide images (WSI) by designed software.
Method: Eighteen WHO GII and 12 GIII oligodendrogliomas were stained with Dako FLEX Ki-67/MIB-1 antibody. The manual quantitation of staining was performed on light microscope in ten high-power-fields with highest Ki-67 LI (hot-spots). Next, WSIs were acquired on 3DHistech Pannoramic II Flash scanner under the 200x magnification. Selection of 20 hot-spots on WSIs was done automatically with the

gradual extinction scheme and quantified by computed-based system. The statistical analysis of results was performed with the Spearman, Wilcoxon and Chi-square tests.
Results: Correlation analysis of the manually and automatically estimated Ki-67 LI showed good accordance of both methods with $R = 0.9293$ ($p < 0.000005$). Ki-67 LI evaluated manually and automaticaly correlated well with tumour grade with $p = 0.000041$ and $p = 0.00002$, respectively. For 8 % Ki-67 LI cut-off in tumour grading, Chi-square test gived $p < 0.0001$ for both evaluation methods.
Conclusion: The presented results showed good accordance of manual and automatic Ki-67 LI examination in oligodendrogliomas. Computed-based Ki-67 LI assessment can help in grading of oligodendroglial neoplasms. This study was supported by the National Centre for Research and Development, Poland (grant PBS2/A9/21/2013).

OFP-09-013
Colo-rectal adenocarcinoma: 100 years after
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Objective: "Colo-rectal Adenocarcinoma" is a common malignant neoplasia of the industrialized countries, with relevant morbidity and mortality, whether sporadic or genetically inherited. The authors intended to evaluate the tissue quality/viability of 100 years-old colorectal tumour non-formalin fixed specimens of a Pathology Museum.
Method: The XIIIth century Coimbra University was classified World Heritage by UNESCO in 2013 and within it, the Medical School Pathology Museum. FMUC's Pathology Museum dates from the XIXth century; occupies a 500 m2 area and gathers 3000 pieces (namely fixed pathological specimens). The authors procured tissue samples from 5 colo-rectal specimens, prepared them using routine anatomo-pathological technique, stained with hematoxylin-eosin (HE) and immunomarked with cytokeratin (CK20) and vimentin. Every step, from the museum shelf to the stained/marked glass-slide, was photographed. Microscopic examination was done by 2 independent observers.
Results: All the specimens stained well with HE, allowing microscopic diagnosis of adenocarcinoma [2 well differentiated/3 moderately differentiated (one with mucinous areas)]. Tumoural and normal epithelial structures were CK20+. Tumoural stroma and normal connective tissue structures were Vimentin+.
Conclusion: These results are of major relevance, since they proved tissue quality/viability preservation, opening doors for further investigation using recent technologies/equipments, namely molecular. "Old material may contribute to new science!".

OFP-09-014
A robust algorythm for nucleus detection on whole slide images
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Objective: In the era of targeted therapy pathology reports are supplemented with prognostic and predictive factors. As therapy relies on these data, reliable quantitative and qualitative evaluation is needed, for which purpose image analysis modules might help pathological work. Hereby, we describe a robust nucleus detection algorythm for whole slide imaging purposes on Hematoxilin-Eosin, Immunohistochemically-stained and FISH slides.
Method: Our algorythm works on RGB (HE and IHC) or grayscale images (FISH-slides). After extracting chanel nuclei an adaptive tresholding is performed. A Hole filling method is also introduced to deal with histological variants of the appereance of cell nuclei. Maxima finding, Segment labeling, Watershed object cut and Label smoothing/filtering makes the algorythm robust. Differently stained slides were analysed by human eyes and later by the automated algorythm.
Results: Nuclei were defined as True Positive when found both manually and automatically, False Positive when found only by software and False Negative when found only manually. We found excellent correlation between manual and automatic nucleus-detection ($r = 0,99052$). Precision rate/Positive Predictive Value was $90,23 \pm 4,29$ %, while Recall rate/Sensitivity was $88,23 \pm 4,84$ % of the algorithm.
Conclusion: We succeded to develop and validate a robust nucleus detection algorythm independent from staining with a very high correlation, Precision Rate and Recall rate when compared with manual nucleus finding. This method is capable to use in real time setting and with a subsequently used immunostain detection method it will help our precise quantification of predictive and prognostic markers in diagnostic pathology.

OFP-09-015
Prepared to scale: Experiences with building a department-wide digital pathology infrastructure
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Objective: At Brussels Free University (VUB), we wanted to build a core digital pathology infrastructure to support a range of different use cases. Various images platforms needed to be accessible through a single access point, while still supporting different user profiles. We wanted a scalable solution that would allow interaction between equipment from different research groups intra- and extra-muros.
Method: A combination of commercial hardware, commercial software, and open source software was used to get this accomplished. Custom coding to connect interfaces was used where needed.
Results: We built a centralized infrastructure that integrates a variety of imaging platforms (brightfield, fluorescence, z-stacking), and we now have an interconnected network of heterogeneous and scalable information silos.
Conclusion: Image analysis and data/image mining projects can remain stuck in micro-environments due to limits artificially imposed by vendor-specific solutions. We have shown this need not be the case, and have integrated five different imaging platforms onto one architecture. We are storing data from all modalities in a single storage facility, and can manage it through a single access point. We support 40+ users, working on different use cases, including education, biobanking, and telepathology.

Wednesday, 28 September 2016, 14.45–16.45, Conference Room 1–2
OFP-10 Joint Session: Soft Tissue and Bone Pathology / Infectious Diseases Pathology

OFP-10-001
Worse survival in elderly patients with extremity soft-tissue sarcoma
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Objective: Nearly half of soft-tissue sarcoma (STS) patients are over the age of 65 and the behavior of cancer in these elderly patients is poorly understood. Aim of this study was to assess the impact of age, sarcoma histotype, grade, stage and treatment modalities on survival of extremity STS (ESTS) patients.
Method: Patients ≥18 years, diagnosed with ESTS between 1989 and 2008, were selected from the Netherlands Cancer Registry. Survival rates and patient and treatment characteristics were analyzed for all patients. Relative survival and Relative Excess Risks

of death were estimated for young (<65 years) and older (>65 years) patients.
Results: Overall, 3066 patients were included in this study. Histotype was different between young (<65 years) and elderly (>65 years) patients ($p < 0.001$). Patients over the age of 65 years were more often diagnosed with high-stage ESTS and an increasing proportion of high-grade ESTS ($p < 0.001$). The proportion of patients who received no treatment increased with age and the elderly received fewer combined modality treatments. Age was significantly associated with relative 5-year survival (72.7 % for younger patients and 43.8 % for the oldest elderly (>85 years)). In multivariable analysis, age still remained a significant prognostic factor.
Conclusion: Different distribution of sarcoma histotypes, more high-stage and high-grade sarcomas at diagnosis, less aggressive treatment and worse survival rates urge the need for optimizing sarcoma research and care of the elderly.

OFP-10-002
Evident epigenetic regulation of SMARCB1 by miR-206, -381 and -671-5p in SMARCB1 immunonegative soft tissue sarcomas. miR-765 appears to be specific for epithelioid sarcoma
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Objective: Complete/partial loss of SMARCB1 nuclear-immunopositivity is characteristic of a certain subset of soft tissue sarcomas.
Method: Using quantitative PCR, we conducted a miRNA study of 51 ESs, 20 rhabdoid tumours, 20 synovial sarcomas, 15 malignant peripheral nerve sheath tumours, 11 myoepithelial carcinomas, and 10 extraskeletal myxoid chondrosarcomas with complete/partial loss of SMARCB1 nuclear immunostain, in contrast to controls of 96 STSs, 13 melanomas and 10 sarcomatoid carcinomas.
Results: A subset of ESs (5/51) showed biallelic deletion of SMARCB1 with no overexpression of any miRNA, suggesting these tumours could be the counterpart of pediatric RT, at least genetically. Another subset (5/51) was genetically either intact or monoallelic deleted with at least threefold overexpression of one of miR-206,-381,-671-5p, suggesting epigenetic regulation only. 39/51 ESs had biallelic deletion (>20 % by FISH and/or by MLPA) but with overexpressed miR-206,-381, and 671-5p, suggesting intratumoural heterogeneity, i.e., both genetic and epigenetic regulation. At least threefold overexpression of one of miR-206,-381, and 671-5p was detected in all MPNSTs, EMCSs, SSs and 7 MCs. Except for ESs, four SSs and one MPNST, there was no event above threefold overexpression of miR-765 among all 195 tested tumours. Our ongoing permanent transfection experiments with miR-206 seems to support the above mentioned results.
Conclusion: Our results suggest a general role of miR-206,-381, and 671-5p in SMARCB1 gene silencing. miR-765 could possibly be a diagnostic tool for ES because of its 97 % specificity and 80 % sensitivity.

OFP-10-003
An autopsy-based study of Trypanosoma cruzi persistence in chronic chagasic patients
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Objective: Chagas' disease is caused by infection with the protozoan Trypanosoma cruzi. We evaluated the persistence of parasites in organs of chronic chagasic patients, from where they can disseminate, generating new pathological lesions, and contaminate recipients through organ transplantation.
Method: Necropsy samples of the heart, lung, liver, kidney, pancreas, adrenal gland, oesophagus and gastrointestinal tract of 21 patients with chronic Chagas' disease were fixed in formalin and paraffin-embedded. Parasite persistence was investigated through histology, immunohistochemistry for T. cruzi antigens, conventional and real-time PCR for T .cruzi DNA.
Results: We succeeded to obtain DNA from 121/166 (72.9 %) samples. Parasite persistence was detected in 12/21 (57.1 %) heart samples, mainly through PCR-based assays. Additionally, T. cruzi parasites were detected by histology and immunohistochemistry in one single smooth muscle cell of the central vein from 1/21 (4.8 %) adrenal gland samples. No fragments of lung, liver, kidney, pancreas, oesophagus or gastrointestinal tract presented parasites by histology, immunohistochemistry or tested positive for T. cruzi DNA.
Conclusion: The heart is a major reservoir of T. cruzi in chronic chagasic patients, but the parasites can also hide in the central vein of adrenal glands. Apart from the heart, the other solid organs of T. cruzi-infected donors can be considered for transplantation.

OFP-10-004
Is SATB2 expression a useful tool for differentiating osteogenic from non-osteogenic bone and soft tissue sarcomas?
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Objective: Osteosarcoma diagnosis may be difficult when no malignant osteoid matrix is identified. SATB2 specificity for osteosarcoma diagnosis is controversial. We aimed to analyze SATB2 expression in osteosarcomas and non-osteogenic bone and soft tissue sarcomas.
Method: Our immunohistochemistry (IHC) study comprised: 42 osteosarcomas, 31 conventional chondrosarcomas, 371 genetically-confirmed Ewing sarcomas (ES) and 131 soft tissue tumours (25 undifferentiated pleomorphic sarcomas (UPS), 79 synovial sarcomas (SS), 4 angiosarcomas, 10 rhabdomyosarcomas, 2 malignant rhabdoid tumours (MRT) and 11 myxoid extraskeletal chondrosarcomas/MECh).
Results: SATB2 was positive in 90.4 % of osteosarcomas, 46.6 % of chondrosarcomas, and 1.3 % of ESFT. Regarding chondrosarcoma, SATB2 immunoexpression was more frequent and intense in high-grade chondrosarcoma (Grade III) and uncommon in chondrosarcoma Grade I. Strong positive SATB2 expression was also observed in 4/25 UPS (16 %), 8/79 SS (10.2 %), 3/4 angiosarcomas (75 %), 1 MRT (50 %), 2/10 rhabdomyosarcomas (20 %) and 6/11 (54.6 %) MECh. In osteosarcoma, SATB2 sensitivity was 90.4 % and specificity 91.1 %.
Conclusion: SATB2 expression is useful in differentiating osteosarcoma and small cell osteosarcoma from ES. It does not differentiate chondroblastic osteosarcoma from high/grade chondrosarcoma. SATB2 is not definitely specific for osteosarcoma diagnosis, it is also expressed in several non-osteogenic bone and soft tissue sarcomas. This study was supported by grants of the 6th FP of the EC: EuroBoNeT Network, contract number: 018814, and from the Fundación Instituto Valenciano de Oncología (FIVO), Valencia, Spain.

OFP-10-005
PDL1 expression is significantly associated with shorter patients survival and grading in soft tissue tumours
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Objective: The cell surface receptor programmed death-1 (PD1) and its ligand (PDL1) have been detected in various cancer types. However, the expression has never been studied in soft tissue tumours in a large well characterized cohort.
Method: We examined PDL1 and PD1 expression in 240 soft tissue tumours and correlated expression levels with clinicopathological parameters including long term survival.
Results: Expression of PDL1 was observed in 81 undifferentiated pleomorphic sarcomas (UPS) in 22 %, 48 leiomyosarcomas in 13 %, 28

synovial sarcomas in 4 %, 45 dedifferentiated liposarcomas in 13 %, 5 angiosarcomas in 60 %, 10 MPNSTs in 0 % and 23 mixed sarcomas in 23 %. Expression of PDL1 showed a significant correlation with shorter patients 5-year survival ($p < 0.05$), higher grading (G2 vs G3, $p < 0.03$) and PD1 positive tumour infiltrating lymphocytes (TILs, $p < 0.001$). Furthermore high PD1 in TILs (more than 3) also showed a significant correlation with shorter patients survival in high grade tumours. In RNA-Seq data high PDL1 expression of leiomyosarcomas correlated significantly with poorer patients survival ($p < 0.005$).
Conclusion: PDL1 expression is significantly associated with shorter patients survival, grading and PD1 positive TILs. PDL1 expression might guide the use of PDL1 inhibitors in immunotherapy in soft tissue sarcomas.

OFP-10-006
Intrasynovial versus extrasynovial autografts for anterior cruciate ligament reconstruction: An experimental study in rabbits
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Objective: In the last decades there has been an increase of anterior cruciate ligament (ACL) ruptures. Unfortunately ACL reconstruction using extrasynovial tendon autografts is inadequate due to poor integration. Our hypothesis is that intrasynovial tendon grafts might be more suitable in ACL reconstruction.
Method: This preliminary study included 10 adult male New Zealand white rabbits, divided into two groups of 5 animals (A and B). In both groups there was an ACL reconstruction using an autologous tendon graft; extrasynovial for group A (extensors digitorum of the foot) and intrasynovial for group B (flexor digitorum profundus). The animals were sacrificed 6 weeks postoperatively and specimens from the knee were obtained for histopathological examination. The specimens were fixed in formalin, decalcified in nitrous oxide and embedded in paraffin.
Results: H/E sections showed that there was better integration in group B than in group A. The integration of the graft was evaluated through the presence of incipient calcification of the tendon and the absence of necrosis or foreign-body reaction at the graft-cartilage junction. Furthermore, during the sacrifice the intrasynovial graft had better hue than the extrasynovial graft.
Conclusion: Intrasynovial autografts seem to be promising for ACL reconstruction, though further research is needed.

OFP-10-007
Are postmortem studies necessary in lethal cases of influenza?
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Objective: During the epidemics strains of influenza A virus (2009–2016 predominantly H1N1 swine) cause numerous lethal outcomes. The attention is focused upon the properties of the pathogens, epidemiological and clinical aspects. Pathological studies are rare and limited to description of lung lesions.
Method: Detailed histopathological analysis of more than 300 lethal cases in children and adults during the epidemics in70th–90th, 2009, 2011, 2016 with comparison with virological data (PCR and serology) has been provided.
Results: In 70th–90th with predominating H3N2 virus typical were the deaths in infants with generalized infection and in adults with destructive staphylococcal pneumonias. In 2009–2011 lethal outcomes were only in adults 18–50 years usually with obesity, mostly dyed due to diffuse alveolar damage (DAD). More severe course was in pregnant women. In 2016 we noted that majority of lethal outcomes were in adults in the age 50–80 years with obesity and chronical cardiovascular diseases. Nearby virus induced changes in lungs (cytopathic and cytoproliferative) and DAD in more than a half were bacterial superinfection and endothelium damage.
Conclusion: 1) In different epidemics the age prevalence and immediate courses of death are variable. 2) Histopathological analysis is useful while discussing single patients and for understanding pathogenesis of influenza.

OFP-10-008
Clinico-pathological parallels in occult viral Hepatitis B
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Objective: Chronic viral hepatitis B (CVHB) in cirrhotic stage remains an important cause of death and invalidity allover the world. It has been accepted that in patients with CVHB HBsAg may constantly or occasionally not be detected in blood. Such variant of the disease was designated as occult hepatitis. In spite numerous publications concerning clinical, epidemiological and virological aspects of the problem many questions related to histopathology remain unclear.
Method: In 28 autopsy cases of occult hepatitis nearby analysis of usual clinical, laboratory, macroscopical and histopathological data has been provided immunohistochemical (IHC) study with sera against HBsAg and HBcAg.
Results: All the patients had typical for CVHB clinical and biochemical symptoms. Macroscopical and microscopical picture was characteristic for HVHB in cirrhotic stage. Among the histopathological findings we paid special attention to nuclear polymorphism and inclusions which are considered to typical for HVHB. In 10 cases was positive reaction with sera against HBsAg and in 5 of them HBcAg was revealed as well. In additional 7 cases we have found slightly expressed (+/−) reaction with HBsAg.
Conclusion: 1) Absence of HBsAg in blood doesn't exclude death threaten course of CHVB. 2) Morphological picture of occult hepatitis is comparable with classic one. 3) Pathogenic mechanisms of the disease needs further complex studies.

OFP-10-009
Characterisation of Epstein-Barr virus associated gastric carcinomas in Portugal
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Objective: Epstein-Barr virus (EBV) has been detected in different subtypes of gastric carcinoma (GC) and EBV-associated gastric carcinomas (EBVaGC) are thought to account for 10 % of all cases. We intended to characterize the clinicopathological features of EBVaGCs and evaluate its impact as prognostic marker. This is the first study to characterize EBVaGC in Portugal.
Method: 133 consecutive patients (81M&52F; mean age 64) submitted to gastrectomy during 2011 at IPO-Porto were evaluated. EBV presence was tested with in situ hybridization (ISH) targeting EBV-encoded small RNA (EBER-ISH). Statistical analysis was performed according to clinicopathological data.
Results: EBVaGCs represent 6.8 % of all GC cases. EBV was present in 7.2 %(5/69) of tubular adenocarcinomas, 11.1 %(2/18) of mixed type and 100 %(2/2) of medullary carcinomas; EBV was absent in poorly cohesive carcinomas. EBVaGC are more frequent in gastric body and antrum. Patients with infiltrative carcinomas, lymphovascular and perineural invasion had significantly reduced survival ($p < 0.001$); EBVaGC patients had better survival.
Conclusion: 6.8 % of GC cases are EBV-associated. Despite some similarities, our study showed different clinicopathological features when

compared with previous studies, mainly the absence of EBV in poorly cohesive carcinomas. The tumour infiltrative growth pattern and the presence of lymphovascular and perineural invasion are independent predictor factors of poor survival in GC patients.

OFP-10-010

EWS/FLI expression impairs adhesion and promotes motility of Ewing sarcoma cells

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Objective: Ewing sarcoma (ES) is characterized by oncogenic fusions of the EWS gene with ETS transcription factor family genes, with EWS/FLI rearrangements representing the most common fusion (85 % of cases). ES shows early metastatic dissemination, and generalized disease is associated with poor prognosis in ES patients. It has previously been shown that expression of the EWS/FLI oncogene is associated with dysregulated actin reorganization in ES cells; however, the impact of EWS/FLI on ES cell adhesion and migration as a prerequisite for metastasis has so far not been investigated.
Method: Various ES cell lines including a stably transfected EWS/FLI knock-down line were used to investigate the impact of EWS/FLI expression on cell morphology and kinase signalling in ES cells by immunofluorescence microscopy and western immunoblotting. Cell adhesion and migration assays were performed in real-time using the xCelligence platform.
Results: EWS/FLI expression decreases filopodial outgrowth and cell adhesion and enhances motility of ES cells. EWS/FLI knockdown decreases mitogen-associated protein (MAP) and p70S6 Kinase signalling that have both been shown to regulate focal adhesion kinase (FAK) activity as well as protein composition of focal adhesion complexes.
Conclusion: Our results indicate that EWS/FLI enhances invasive properties of ES cells via dysregulation of MAPK and p70S6K signalling, leading to altered composition and activity of focal adhesion complexes. Since both pathways are possible targets for inhibitors that are already in clinical use, the results point towards a possible role for kinase inhibitors to prevent metastatic dissemination of ES cells.

OFP-10-011

Label-free imaging of infectious agents in routine histology and cytology by fluorescence lifetime Imaging (FLIM)

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Objective: After stimulation by photons, fluorophores will remain for a short period "excited", called lifetime, and then drop to their ground state emitting fluorescence. Lifetime can be used to create virtual fluorescence lifetime imaging (FLIM) pictures, where the contrast is created by artificial colours attributed to different lifetime ranges. The aim of the study was to apply this technique to the detection of infectious agents in human material.
Method: Fresh material or unstained cytologic or histologic preparations were examined from 30 patients with infections by toxoplasma, trypanosoma, aspergilllus, cryptococcus, enterobius, giárdia, strongyloides or schistosoma species. FLIM images were created by a confocal microscope using a pulsed laser at 405 nm, and a time-correlated single-photon counting equipment.
Results: This technique showed precisely morphologic details, generally superior to that seen in usual special stains. Lifetimes of infectious agents were often different from those of human tissues thus enabeling their rapid and easy detection. Signal intensity was usually higher in fresh or formalin-fixed material than in histologic sections, due to the loss of intracytoplasmatic fluophores during the embedding process.
Conclusion: The FLIM technique permits rapid and efficient screening of unstained material and reveals new insights into the histology.

OFP-10-012

Clinicopathological and genomic features of a series of 30 SMARCA4-deficient thoracic sarcomas

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Objective: We sought to characterize the clinicopathological features of SMARCA4-deficient thoracic sarcomas (SMARCA4-DTS), a sarcoma subtype recently identified through combined next generation and pathological screenings.
Method: We retrieved 49 cases of thoracic malignancies from our consultation cases suspicious for SMARCA4-DTS (including 12 cases of the initial paper). Pathological review was performed by pathologists experts in soft tissue and thoracic pathology fields. Genomic profiling (oncoscan, Affymetrix platform) and SMARCA4 sequencing (Illumina, Miseq platform) were performed when material was available.
Results: Thirty cases were finally classified as SMARCA4-deficient thoracic sarcomas. Patient's median age and survival were respectively of 42 years old and 8 months. Tumours were located in mediastinum (n = 13), mediastinopulmonary (n = 7), pleura (n = 10). Morphologically, tumours were composed of sheets of epithelioid cells dotted with vesicular monomorphic nuclei. By immunohistochemistry, they expressed consistently CD34, AE1/E3 and/or EMA and SOX2. SMARCA4 and SMARCA2 were lost in all cases. All cases displayed complex genetic profiles and SMARCA4 inactivating mutations. Differential diagnoses included SMARCA4-inactivated lung carcinoma (n = 5), midline NUT carcinoma (n = 3), SMARCB1-deficient rhabdoid tumour (n = 3), Ewing-like sarcomas with CIC rearrangement (n = 3) rhabdomyosarcoma (n = 1) and unclassified sarcoma (n = 2).
Conclusion: This first clinicopathological series of SMARCA4-DTS highlights these tumours can be reliably diagnosed in routine practice. They represent aggressive malignancies which should be recognized as patients are therapeutically benefit from EZH2 inhibitors.

Wednesday, 28 September 2016, 17.15–19.15, Conference Room 1–2
OFP-11 Joint Session: Endocrine Pathology / Head and Neck Pathology

OFP-11-001

Mutation profiling of BRAF, RAS and TERT on thyroid liquid-based fine needle aspirations improves diagnostic accuracy

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Objective: Liquid-based fine needle aspiration (LB-FNA) is widely recognized as a reliable diagnostic method to evaluate thyroid nodules. Use of molecular biomarkers has been proposed to improve pathologic accuracy. Recently TERT promoter mutations were associated with aggressive thyroid cancers.
Method: We evaluated feasibility and performance of mutation profiling of BRAF, NRAS, HRAS and TERT on residual material from LB-FNA in a prospective cohort of 649 cases including 245 atypia of undetermined significance (AUS), 219 follicular neoplasms (FN), 97 suspicious for malignancy (SM), and 88 malignant (M).
Results: Overall 159 cases (24.5 %) were mutated: 92 BRAF, 50 NRAS, 16 HRAS and 9 TERT mutations. Surgical samples were available for 319 cases. In the AUS category, 10/18 malignant cases were mutated vs

9/42 benign cases (p = 0.014). In the FN category, 5/16 malignant cases were mutated vs 8/104 benign cases (p = 0.016). In the SM group, 28/61 malignant samples were mutated versus 0/11 benign cases (p = 0.005). Finally in the M group, all samples were malignant with 52/67 mutated cases. Importantly TERT mutations were present in 8 cases (2 FN, 1 SM and 5 M) all confirmed to be malignant (p = 0.008).
Conclusion: Mutation profiling can be successfully performed on residual material of thyroid LB-FNA and may help to improve the diagnostic accuracy of FNA. TERT mutation is rare but associated with malignancy, and as so should be systematically tested.

OFP-11-002
High risk Human Papillomavirus (HPV) infection is actively involved in the etiopathogenesis of a significant subset of sinonasal carcinomas: A clinicopathological study with detection of E6/E7 mRNA transcripts
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Objective: To investigate prevalence of high risk human papillomavirus (HR-HPV) infection in sinonasal carcinomas.
Method: Immunohistochemistry, in situ hybridization, and polymerase chain reaction, detecting p16 expression and presence of HPV DNA and HPV E6/E7 mRNA, were used.
Results: The study comprised 47 males and 26 females, aged 23–83 years (median 62 years). Fifty-three percent tumours arose in nasal cavity, 42 % in maxillary sinus, and 5 % within ethmoid complex. Forty-nine tumours were squamous cell carcinomas (SCCs). Follow-up period ranged 1–241 months (median 19 months). A total of 18/73 (25 %) tumours were HPV-positive (17 SCCs and 1 small cell neuroendocrine carcinoma). Types HPV16, HPV18, and HPV35 were detected. There was strong correlation between HPV status and p16 expression (p < 0.005). HPV-positive SCCs occurred more frequently in smokers (p = 0.04), were more frequently p16-positive (p < 0.0001), and were non-keratinizing (p = 0.02), the latter occurring more commonly in nasal cavity (p = 0.03). Median survival for HPV-positive SCC patients was 30 months, while for HPV-negative SCC patients was 14 months (p = 0.23).
Conclusion: HR-HPV are actively involved in etiopathogenesis of a subset of sinonasal SCCs. p16 may be used as surrogate marker for determination of HPV status in sinonasal carcinomas.

OFP-11-003
FGFR1 is a potential prognostic biomarker and therapeutic target in head and neck Squamous Cell Carcinoma (SCC)
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Objective: Targeting FGFR1 (fibroblast growth factor receptor 1) has shown to be of great therapeutic value in preclinical models of various solid tumours. In this study we have investigated the prognostic value of FGFR1 expression in HNSCC and the therapeutic relevance of targeting FGFR with AZD4547.
Method: Immunohistochemistry was applied on tissue microarrays to investigate FGFR1 protein expression in 452 HNSCC. Sensitivity of HNSCC cell lines to AZD4547, either as single or combination treatment with EGFR-inhibitor gefitinib, was assessed using long-term colony formation assays, short-term viability assays, and biochemical analysis.
Results: FGFR1 protein was overexpressed in 82 % of HPV-positive and 75 % of HPV-negative HNSCC. Overexpression was related to poor survival in HPV-negative HNSCC (HR: 3.07; 95 % CI: 1.74–6.90; P = 0.001). Treatment of high FGFR1 expressing cell line CCL30 with AZD4547 reduced cell proliferation and FGFR signaling. Cell lines SCC147 and BICR16 were resistant to AZD4547 treatment due to EGFR signaling. Combined AZD4547 and gefitinib treatment synergistically inhibited proliferation of resistant cell lines.
Conclusion: Here we identify high FGFR1 expression as a candidate prognostic biomarker in HPV-negative HNSCC. Furthermore, we provide a rationale for treating FGFR1-expressing HNSCC with FGFR inhibitor AZD4547 and for combining AZD4547 and gefitinib in FGFR inhibitor resistant HNSCC.

OFP-11-004
Molecular profile of nasopharyngeal carcinoma: Analyzing tumour suppressor gene promotor hypermethylation by multiplex ligation-dependent probe amplification
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Objective: Assessing promoter hypermethylation of tumour suppressor genes in nasopharyngeal carcinomas (NPC) in relation to clinicopathological features.
Method: Methylation status of 23 tumour suppressor genes were assessed in 108 NPCs using methylation-specific multiplex ligation-dependent probe amplification. Correlation between methylation, clinicopathological features and survival were examined.
Results: Hypermethylation of RASSF1A and ESR1 was significantly more frequent in EBV positive NPC, while hypermethylation of DAPK1 was more frequent in EBV negative NPC. In logistic regression RASSF1 (p = 0.049), with RASSF1 being more frequent in EBV positive NPC, remained significant. In EBV positive NPC, RASSF1A (p = 0.035) predicted worse overall survival (OS) (HR 3.044, 95 % CI 1.022–9.068, p = 0.046). In EBV negative NPCs, APC predicted worse disease-free survival (DFS) (HR 6.868, 95 % CI 2.142–22.022, p = 0.001).
Conclusion: Important epigenetic differences exist between EBV negative and EBV positive NPC, with EBV negative NPCs having a more similar hypermethylation profile to other HNSCC than EBV positive NPCs. Hypermethylation of RASSF1A seems to be an independent predictor of worse OS in EBV positive NPC, and may be important in the pathogenesis of EBV infected NPC. Hypermethylation of APC may be an independent predictor of worse DFS in EBV negative NPCs.

OFP-11-005
Papillary thyroid carcinomas—adverse prognostic factors
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Objective: Papillary thyroid carcinomas (PTC) are known to have an excellent survival rate. However, it remains difficult to predict which patients need to be monitored more closely due to an increased risk of tumour relapse.
Method: PTCs of 125 patients including 57 patients with an adverse outcome were immunohistochemically stained for PTEN, VEGF-A, p27, Galectin-3, HBME-1, Thyroglobulin and the Androgen Receptor. Forty-four of those tumours underwent miRNA profiling and the results were examined in the light of tall cell morphology, a phenotype known for its more aggressive behavior.
Results: Univariate analysis showed a signification correlation between relapse free survival and an altered expressions for PTEN, p27, Galcetin-3, VEGF-A and Thyroglobulin. In multivariate analysis including tall cells as a confounder, only reduced expression of PTEN and an increased expression of VEGF-A correlated significantly with a shorter relapse free survival. MiR-362-3p and miR-155-5p were identified as targets for

VEGF-A and miR-222-3p and miR-17-5p for PTEN. Three of these four miRNAs harbor significant prognostic patient information as well.
Conclusion: PTEN and VEGF-A can predict patient outcome independent from tall cell morphology, age, stage and gender. Several identified miRNAs may be responsible for this observation.

OFP-11-006
Multinodular goiter and well differentiated thyroid carcinoma in a child with embryonal rhabdomyosarcoma of the cervix: Another example of a DICER1 syndrome
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Objective: Carriers of germline DICER1 mutations are predisposed to a rare cancer syndrome. Botryoid-type embryonal rhabdomyosarcoma (bERMS), multinodular goiter (MNG) and thyroid carcinoma (TC) are emerging phenotypes. We report a case of a 12-year-old girl with the aforementioned conditions.
Method: The patient underwent total thyroidectomy for bilateral, multiple nodules, detected by routine ultrasound examination. She had a bERMS of the cervix at the age of 7, treated by surgery and adjuvant chemotherapy. There was a family history of thyroid pathology.
Results: FNAB of two nodules revealed a colloid nodule (Bethesda II) and a follicular neoplasm (Bethesda IV). The thyroid gland was enlarged and multinodular (61 g). Besides numerous encapsulated nodules with variable degrees of cellularity and brisk mitotic activity (maximum 18/10 HPF) there was one, larger than the others (2.1 cm), displaying capsular and vascular invasion. This tumour showed nuclei of the "intermediate type" and was thus classified as Well Differentiated TC, not otherwise specified. Molecular testing for BRAF, NRAS and TERT promoter did not reveal any mutation.
Conclusion: This case demonstrates the malignant potential of MNG in the setting of DICER1 syndrome and highlights the need to understand this peculiar carcinogenic process that does not fit with the classic division in papillary and follicular TC.

OFP-11-007
Detailed genomic characterization identifies high heterogeneity and histotype-specific genomic profiles in adrenocortical carcinomas
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Objective: To correlate the mutational profile with clinical and pathological characteristics in adrenocortical carcinoma (ACC).
Method: Targeted next-generation sequencing and copy number variation (CNV) analyses for 18 genes most frequently altered in ACC were performed in a series of 62 cases (including 10 with matched primary and metastatic/recurrence samples) and correlated with major clinical and pathological characteristics of tumours.
Results: A total of 433 somatic deleterious genetic alterations (328 gene mutations and 105 CNV) were identified in 57/62 cases, the remaining five being wild-type for all genes tested. TERT, CDK4, ZNRF3 and RB1 were altered in more than 30 % of cases. The genotype was significantly different among histological variants, with the lowest mutation burden in the oncocytic one ($p = 0.006$) and the highest prevalence of RB1 ($p = 0.001$) and CDK4 ($p = 0.002$) in the conventional and myxoid ones, respectively. None of the 10 cases with matched samples showed a stable genotype along tumour progression. Among individual genes, TP53 mutations were associated with high Ki-67 index, high tumour stage and aggressive disease status (all $p < 0.02$).
Conclusion: The genomic signature in ACC is unstable along tumour progression and differs among histological variants; moreover, TP53 mutations represent the most relevant prognostic molecular marker.

OFP-11-008
High miR-100a expression is associated with aggressive features and decreased response to mTOR inhibitors in lung carcinoids
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Objective: To analyze in vitro and in vivo the expression and the functional role of miR-100a in lung carcinoids, as an alternative mechanism targeting mTOR pathway.
Method: miR-100a expression was analyzed by means of real-time PCR in 92 lung carcinoids and compared with mTOR mRNA expression, as well as with major clinical and pathological parameters. In vivo, the effect of miR-100a silencing on the responsiveness to mTOR inhibitors was assessed in typical carcinoid H727 cells.
Results: miR-100a was inversely correlated with mTOR mRNA expression ($p < 0.0001$), supporting its effect in the negative regulation of mTOR pathway in lung carcinoids, in vivo. Moreover, high miR-100a expression was associated with aggressive features (atypical histotype, high clinical stage, vascular invasion and aggressive disease status; all $p < 0.05$) and with shorter survival at univariate analysis (HR 4.5, $p = 0.013$). Silencing of miR-100a in H727 cells significantly increased mTOR mRNA expression and sensitivity to mTOR inhibitors, in vitro.
Conclusion: miR-100a actively participates to the regulation of mTOR expression in vivo and in vitro, and represents a novel candidate prognostic biomarker in lung carcinoids; moreover, repression of its expression is associated to increased responsiveness to mTOR inhibitors and might represent a novel tool to sensitize lung carcinoid cells to these target agents.

OFP-11-009
Validation of the prognostic role of the Helsinki score in 225 cases of adrenocortical carcinoma
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Objective: The present study aimed to validate the prognostic role of the newly proposed Helsinki Score for adrenocortical carcinoma.
Method: 225 adrenocortical carcinomas were reclassified using Weiss Score and Helsinki Score (3× mitotic count + 5× necrosis + Ki-67).
Results: At univariate analysis, statistically significant prognostic values were observed at the log-rank test for mitotic count (cut off values: <6 and ≥55; $p < 0.0001$), Ki-67 (cut off values: <20 and ≥50; $p < 0.0001$), Weiss Score (cut off values: <5 and ≥8; $p < 0.0001$), Helsinki Score (cut off values: <13 and ≥19; $p < 0.0001$), histological variant (conventional vs oncocytic; $p = 0.009$), necrosis ($p = 0.001$) and stage ($p = 0.005$). Cox multivariate analysis using a backward stepwise selection method retained Helsinki Score and Weiss Score, only, as predictors of poor prognosis ($p < 0.0001$ and $p = 0.0005$, respectively). The best and equivalent areas under the curve (AUC) to predict the occurrence of disease-related deaths, determined using ROC statistics, were found for Helsinki Score (with a threshold of 28,5 points; AUC = 0.729, 95 % confidence interval = 0.66–0.79) and Ki-67 (with a threshold of 20,5 %; AUC = 0.727, 95 % confidence interval = 0.66–0.79).
Conclusion: The Helsinki Score is a valuable system to predict prognosis in adrenocortical carcinoma, outperforming the currently established prognostic parameters.

OFP-11-010
Granulation tissue-like spindle cell squamous carcinoma (SCSC) of the larynx. A clinicopathologic study of five cases
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Objective: The diagnosis of spindle cell squamous carcinoma (SCSC) of the larynx is challenging, because the conventional SCSC component, may be limited and difficult to recognize. Infact lesions with a prominent inflammatory infiltrate and reactive vessels, may have a granulation tissue-like appearance, like post-intubation granulomas or inflammatory pseudotumours. We analysed the clinico-pathological features of a group of laryngeal SCSC with granulation tissue-like appearance.
Method: All cases of SCSC between 1996 and 2015 were reviewed and tumours with a inflammatory infiltrate and abundant capillary vessels were selected. Immunohistochemistry for cytokeratins AE1/AE3, CAM5.2 and 5/6, as well as for p63, p40 and ALK1 were performed. Ten cases of true granulation tissue were controls.
Results: Five cases of granulation tissue-like SCSC were identified. Patients were males, 57–65 years. All lesions consisted of a ulcerated polypoid proliferation of atypical spindle cells, with a minor component of conventional invasive or in situ squamous carcinoma. The spindle cells expressed AE1/AE3 or CAM5.2, while cytokeratin 5/6, p63 and p40 were positive only in the conventional squamous component. ALK1 was negative.
Conclusion: The diagnosis of granulation tissue-like SCSC is challenging due to the clinical and histological overlap with benign conditions. The use of an immunohistochemical panel is recommended.

OFP-11-011
Epithelioid osteosarcoma of the maxilla: Review of a rare and agressive variant
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Objective: To analyse clinical, histologic and immunohistochemical features of epithelioid osteosarcoma which develops in the maxilla.
Method: 434 patients were diagnosed with osteosarcoma from 1966 to 2015 in Hospital La Paz. Only five were epithelioid variant, three of which were located in the jaw. The two remaining cases were in the humerus and femur. Data regarding the objective were obtained from medical and pathological records.
Results: All patients were female with a mean age of 36 years (range, 21–56). Microscopically, the tumour was composed of large epithelioid cells with prominent nucleolus and scattered giant multinucleated cells. The predominant growth pattern was sheet-like. Cord, rosette-like structures and hemangiopericitoid pattern were also observed. Osteoid was found. Cytokeratins were negative. Despite treatment with systemic chemotherapy and surgery the disease progressed and the patients died.
Conclusion: Epithelioid osteosarcoma is a rare aggressive variant. Differential diagnosis includes small cell-type osteosarcoma, metastatic neuroblastoma, PNET, metastatic carcinoma and malignant neoplasias with epithelioid characteristics. The osteoid formation by neoplastic cells is the most important key. The usual treatment consists in preoperative chemotherapy followed by surgery. It has been predominantly reported in the long bones of young people and only few cases have been reported in the jawbones, therefore more studies are required.

OFP-11-012
Human papillomavirus-related carcinoma with adenoid cystic-like features: Characterization of the Danish material
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Objective: Human papillomavirus-associated carcinoma with adenoid cystic-like features (HPV-related ACC-like carcinoma) is a recently described entity of the sinonasal tract. Only 9 cases have been reported worldwide, and information on the clinicopathologic features and prognosis are warranted. We set out to investigate the prevalence, clinicopathologic features, and outcome of these patients in the Danish national material.
Method: Morphological mimics of HPV-related ACC-like carcinoma from the sinonasal tract were collected from Danish pathology departments from 1990 to 2015 and histopathologically reviewed. HPV screening was performed with PCR using GP5+/6+ primers. Positive cases were genotyped by sequencing and in situ hybridization. Immunohistochemistry was used for evaluating p16 status and morphological characterization.
Results: Seven HPV-related ACC-like carcinoma cases were identified: 5 in the nasal cavity, 2 in the paranasal sinuses. Four were female and 3 were male. One case was treated 20 years previously and experienced a local recurrence after 11 years. This patient has now remained recurrence-free for 9 years. All remaining cases were diagnosed in 2012 or later with no recurrences. One case harbored HPV-16, 2 cases HPV-33, 2 cases HPV-35, 1 case HPV-56 and 1 case HPV-68.
Conclusion: We present a large material of this newly described, rare tumour of the sinonasal tract. The incidence seems to have risen dramatically through recent years, paralleling what is seen for HPV-positive oropharyngeal SCC. Only one case had long-term follow-up, and this patient experienced a local recurrence. However, the prognosis seems more favorable than for other sinonasal malignancies.

Wednesday, 28 September 2016, 17.15–19.15, Conference Room 4
OFP-12 Haematopathology

OFP-12-001
Tumour initiating cells of the follicular lymphoma
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Objective: Follicular lymphoma (FL) is an indolent lymphoma but rather frequently recurs. It is very important to know its tumour initiating cells (TIC) and we sought to find the TIC of FL.
Method: We examined immunohistology, response to anti-cancer drugs, transplantablity.
Results: TRA-1-60 positive cells were found in non-neoplastic germinal centers, which may be related to reprogamming by AID. TIC of FL recognized by TRA-1-60 were located mainly at interfollicular area, and stayed next to vessels"Niche". They were positive for CD20 and with t(14;18) and negative for Ki67. In surgically resected samples, TRA-1-60 positive cells increased in number at the recurrence after chemo-therapy with rituximab. Unexpectedly, TRA-1-60-positive population was increased in number resistant to rituximab-treatment. TRA-1-60-positive cells showed high level of drug resistant gene. TRA-1-60 positive tumour initiating cells highly frequently form transplantable tumours in NOD-SCID mice, and the size of the transplanted cells was much larger than TRA-negative population.
Conclusion: We strongly believe TRA-1-60-positive cells of FL are tumour-initiating cells, which is crucial to get the best therapeutic way. As far as I know, this is the first report of TIC of FL.

OFP-12-002
Diagnostics of splenic diffuse red pulp B-cell lymphoma
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Objective: Splenic diffuse red pulp B-cell lymphoma (SDRPL)- rare and insufficiently studied entity with challenging diagnostic criteria. During 2013–2015 the splenectomy specimens was analyzed compare with preoperational BMB in 87 pts who were under observation with massive splenomegaly and receiving treatment at NRCH.
Method: BMB and splenectomy specimens were formalin fixed and paraffin embedded. IHC study was performed using antibodies to CD3,

CD5, CD20, CD23, CD25, CD27, CD76 (DBA.44), CD103, CD123, TRaP, Annexin1, cyclin D1. Mutational analysis of BRAF (exon 11 and 15), MAP2K1 (exons 2–3, 11), NOTCH1 was performed by Sanger sequencing. Tumour DNA was obtained from frozen tissues.
Results: Splenic B-cell lymphoma was diagnosed in 71/87 (81,6 %) pts, predominantly SMZL (70 %). 5/71 cases (ratio m:f 1:1.5; median age 55 years, normal or high level leukocytosis) were characterized by similar splenic morphology and heterogeneous expression of CD11c, TRaP, CD103, CD123 without expression CD25, CD27, Cyclin D1, Annexin1. In 4/5 cases predominantly intravascular CD20+ lymphoid infiltrates in BMB were revealed. Using cytology nucleoli were invisible, the number of villous lymphocytes ranged 12–60 %. MutBRAF V600E or NOTCH1 were not found. Sequencing MAP2K1 showed the presence of activating mutations of the gene G128D MAP2K1 in one patients
Conclusion: SDRPL was diagnosed in 7 % of splenic B-cell lymphomas (2013–2015). Using molecular study for BRAF, MAP2K1, NOTCH sustainable mutations have not been identified.

OFP-12-003
Functional single nucleotide polymorphisms in IL2 and IL10 alter predisposition to mantle cell lymphoma, as well as its progression and imune antitumour response
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Objective: To assess mantle cell lymphoma (MCL) tumour-host interaction dependent on IL2 and IL10 by genotyping functional single nucleotide polymorphisms (SNPs) to evaluate risk for tumour onset, prognosis and cellular microenvironment composition.
Method: We selected 100 consecutive patients with MCL and 151 blood donors as controls. Genotyping for rs2069762, rs6822844 (IL2), rs1800872, rs1800890 and rs3024491 (IL10) was performed using Taqman® Openarray® technology. Paraffin-embedded tumour tissue was submitted to immunohistochemistry (IHC) for CD68, CD163, iNOS, FOXP3, IL2 and IL10. Slides were analyzed using the Aperio® system.
Results: A higher frequency of IL10 AGA haplotype was found in MCL patients as compared to controls ($p = 0.06$ after correction for multiple comparisons). AA genotypes of both rs2069762 and rs3024491 were independently associated with unfavorable overall ($p < 0.01$ and $p < 0.001$, respectively) and event-free survivals ($p = 0.03$ and $p = 0.06$, respectively). Patients carrying rs3024491 AA genotype showed increased levels of FOXP3 ($p = 0.06$) and iNOS-positive macrophages ($p = 0.01$) in tumour biopsies. Neither IL2 nor IL10 expression seemed modulated by the respective SNPs.
Conclusion: Our data suggest that a 3-SNP haplotype in IL10 might predispose to MCL. Moreover, the AA genotype of rs3024491 may increase T-reg lymphocyte and cytotoxic macrophage levels in MCL. Finally, both rs3024491 and rs6822844 are independently associated with unfavorable prognosis in this lymphoma.

OFP-12-004
AIDS related Non Hodgkins lymphomas: A report on 320 cases from single institution addressing gray zones in diagnosis
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Objective: AIDS related lymphomas (ARL) form a unique and interesting spectrum of tumours. Not many papers have highlighted the gray zones in diagnosis given the uncommon nature of the disease.
Method: This study on 320 ARL focused on evaluating these tumours using a wide panel of antibodies and attempting to segregate the clear from unclear tumours or gray zone areas.
Results: Of the 320, 122 were diffuse large B cell lymphoma(DLBL), 152 Plasmablastic lymphoma(PL) and 46 Burkitt lymphoma. There were no T cell lymphomas during the study period. In 308 cases detailed immunohistochemistry could be performed after which there were 102 DLBL, 129 PL, 42 BL and 35 tumours were gray zone cases. The gray zone areas included a gray zone between DLBL/BL(4), tumours that expressed markers like plasmablastic lymphoma but morphologically were Burkitt's lymphoma (Blastic BL/PL. 7), large B cell lymphomas that expressed markers like PL but were morphologically DLBL(14), and unclassifiable lymphomas that expressed only LCA(10). When stratified by original diagnosis PL Showed poor OAS/ overall survival but using the revised definition a significant better survival of PL as compared to the gray zone cases was seen(p - 0.013). Amongst other factors affecting OAS were CD4 counts (p - 0.0001), site of disease(p - 0.006)), HAART therapy (0.0001) and type of chemotherapy.
Conclusion: Gray zones exists in ARL and there is tendency to overcall PL and the gray zone entities need to be weeded out for better patient management.

OFP-12-005
Stathmin-1, a marker of problematic cases in folicular lymphoma
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Objective: The aim of this study was to assess stathmin-1 status, its correlation with clinicopathological parameters and with 1p36 gene rearrangement, and its role as a diagnostic marker in follicular lymphoma.
Method: This study included 81 follicular lymphoma cases. Stathmin 1 was evaluated by immunohistochemistry on tumour tissue macroarrays. Besides, 1p36, bcl-2, bcl-6, IgH gene rearrangement by FISH analysis was performed.
Results: Stathmin 1 expression was detected in 88,9 % of cases. There was a positive correlation between the histologic grade and Stathmin 1 positivity ($p = 0.001$, Chi-Square test). All BCL2- cases ($n = 13$) were positive for Stathmin 1 whereas, 8/9 of CD10- cases were positively stained. FISH analyses are pending.
Conclusion: We showed that Stathmin 1 was helpful in detecting BCL2- and CD10- follicular lymphomas, and it could be a novel diagnostic marker for those problematic cases.

OFP-12-006
The incidence & prognostic impact of ASXL1 mutations/protein expression in myeloid stem cell diseases with concurrent bone marrow fibrosis and concordance between Sanger sequencing & immunohistochemistry
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Objective: The aim of the study is to determine the incidence& prognostic impact of ASXL1 mutations and protein expression in myeloid stem cell diseases with concurrent bone marrow fibrosis.
Method: The bone marrow aspirations&biopsies of 84 adult patients diagnosed as MDS-F, MDS/MPN-F and PMF-SF at Cerrahpasa Faculty of Medicine, Pathology Department between the years 2008–2013 were included in the study. Patients were evaluated according to clinicomorphological parameters& ASXL1 mutations/protein expression and their prognostic value were investigated.
Results: Immunohistochemistry(IHC) was found to be concordant with sequencing in terms of detecting nonsense mutations (100%sensitivity&specifity). ASXL1 mutations/protein expression shorten the OS and were significantly associated with male gender, anemia, high blast count, dysplasia in ≥2 lineages, increase in stromal plasma cells and leukemic transformation, but not correlated with fibrosis. This is the first study investigating the associations between ASXL1 mutations/

protein expression and morphological parameters and comparing the ASXL1 mutational status and protein expression. Two nonsense, 5 missense unannotated mutations and 2 novel genetic alterations on 3'UTR have been discovered.
Conclusion: The algorithm to be chosen to detect the ASXL1 mutational status could be screening the protein expression by IHC and if score 2/3 staining is observed, molecular method could be performed to define the specific mutation.

OFP-12-007
MicroRNA expression in enteropathy associated T-cell lymphoma type 1
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Objective: Enteropathy-associated T-cell lymphoma type 1 (EATL) is a leading cause of mortality in adult-onset coeliac disease. While miRNA expression has been investigated in other T-cell lymphomas, the objective of this pilot study is to elucidate the miRNA signature of EATL.
Method: A search of the laboratory information system of two university-affiliated hospitals was carried out to identify cases of EATL over a 14-year period (2000–2014). Available histological and molecular features were reviewed by two histopathologists. An extensive meta-analysis of miRNA associated with T-cell lymphoma and T-cell function was carried out and a shortlist of 95 miRNAs was created. RNA was extracted and quantified from 20 paraffin-embedded samples (10 EATL and 10 controls, comprising 5 samples of small bowel without enteropathy and 5 samples with coeliac disease), and assays were run, using customised TLDA cards. Statistically significant miRs were identified, using a t-test on R bio conductor software.
Results: Findings included identifying an increase in the expression of vertebrate-specific miRNAs, miR-196a and miR196b. An eight-fold increase in the expression of miR-127, known to be associated with the regulation of genes involved in apoptosis, was identified. An eight-fold reduction in the expression of miR-141 was identified.
Conclusion: This pilot study has identified candidate miRNAs potentially involved in the pathogenesis of EATL.

OFP-12-008
Label-free imaging of routine bone marrow smears by autofluorescence permits identification of erythroid precursors in human bone marrow
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Objective: Fluorescence lifetime imaging (FLIM) creates images by measuring the delay of the fluorescence photon emission at each image pixel reflecting differences in molecular structures and their physicochemical environment. We investigated the utility of this technique for diagnosis in routine bone marrow (BM) smears.
Method: We used unstained BM smears: 13 normal, 10 acute myeloid leukemias, 5 megaloblastic anemias, 3 acute erythroid leukemias and 2 sideroblastic anemias. Images were captured with a confocal microscope and a HPM-100-40-Hybrid detector, with an excitation at 405 nm (diode laser,80 MHz). Images were compared with May-Grünwald-Giemsa (MGG) stained smears.
Results: We obtained highly contrasted FLIM images. Different cell types could be easily recognized by their similarity with MGG images. Erythrocytes exhibited short lifetimes (hemoglobin component) with similar values in all groups except for those with sideroblastic anemia. Nuclear lifetimes were higher than those of cytoplasm, which showed intermediate values, similar to the protein background. Nuclei and cytoplasm of granulopoetic precursors had values considerably higher than those of erythroblasts.
Conclusion: The FLIM technique was easily applicable on routine smears without stain. The images had good quality permitting cell identification. FLIM values allowed to distinguish different lineages of cells thus suggesting relevant physicochemical differences of the nuclear and cytoplasmic organization.

OFP-12-009
Bone marrow histopathology in patients with myelofibrosis following allogeneic stem cell transplantation: Single institution experience
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Objective: To assess hematopoietic reconstitution and regression of bone marrow (BM) fibrosis in patients with myelofibrisis (MF) following allogeneic stem cell transplantation (alloHSCT).
Method: At our institution 12 pts were treated with alloHSCT for MF between 2012 and 2015, in 7 cases BM trephines at diagnosis and at follow-up (days +40 ± 10 and +100 ± 10) were available. These pts were aged 36–57 years. 5 pts had primary MF, 1 - post-PV MF, 1 -post-ET MF. 3/6 were JAK-2+, 1/2 were CALR+. 6 pts are alive in remission at the present time with median follow-up 13 months, one patient died from graft failure and infectious complications. Bone marrow samples were fixed in 10 % buffered formalin, decalcified in EDTA and processed routinely. H&E, Giemsa and Gomori stains were done.
Results: At diagnosis all pts showed features of corresponding myeloproliferative neoplasm with severe MF, consistent with grade 2–3 according to European consensus approach. At day +40 MF was reduced by 1 grade, and at day +100 5 of 7 pts showed MF grade 0–1 with restoration of normal BM architecture.
Conclusion: AlloHSCT is an effective treatment modality for myelofibrosis. By day +100 we observed restoration of normal BM architecture with MF0-1 in 5 of 7 pts included in the study.

OFP-12-010
Myeloid sarcoma: Clinicopathological evaluation of 40 cases
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Objective: Myeloid sarcoma (MS) is a tumour mass consisting of myeloid blasts presenting at an anatomical site other than the bone marrow (BM). It can be seen de novo or in association with acute myeloid leukemia (AML), myeloproliferative neoplasias (MPN), or myelodysplastic syndrome (MDS). The aim of this study was to evaluate the presenting features, morphological and immunohistochemical features of MS cases diagnosed in our institution, in view of the literature.
Method: We searched the medical records of our institution for the patients diagnosed as MS between 1999 and 2015. Fourty cases were found and reevaluated.
Results: Median age was 37.9 years (range: 5 months–84 years); 26 were male, 14 were female. The most commonly involved sites were the lymph nodes, soft tissue, bone, and skin. Immunohistochemically, CD68-KP1 was the most commonly expressed marker (31/34; 91 %), followed by CD33 (7/9; 77.7 %), MPO (25/36; 69.4 %), CD117 (18/28; 64 %), lysozyme (18/29; 62 %), CD68-PGM1 (2/4, 50 %), and CD34 (12/33; 36.3 %). BM examination revealed AML in 13 cases (only five cases manifested with preceding or coincidental AML); MPN or MDS in 11 cases, and none were found in 9 cases. Four cases showed central nervous system involvement in cerebrospinal fluid. Three cases manifested in multiple sites.
Conclusion: MS is a rare extra-medullary tumour mass composed of immature myeloid cells. It may present with variable morphological and phenotypic features in addition to pathological diagnostic challenges. Extensive immunohistochemical panel may be necessary for accurate differential diagnosis which is critical for appropriate therapy.

OFP-12-011

Flow cytometry and fine needle aspiration cytology in the screening of lymphoproliferative diseases: Ten years experience

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Objective: To determine the accuracy of fine needle aspiration cytology (FNAC) complemented by flow cytometry (FC) for the diagnosis of lymphoid lesions.
Method: Consecutive 252 FNACs of lymphoid lesions studied with complementary FC, over a period of 10 years, were retrieved from our files and correlated with histology and/or clinical follow-up if available. FC was performed with the following antibodies in a panel: CD45, CD19, CD3, CD4, CD8, CD5, CD10, CD23, FMC-7, Kappa and Lambda chains.
Results: 198/252 (78,6 %) FNACs were diagnosed as reactive, 32/252 (12,7 %) as aberrant phenotypic trait (suspicious), 20/252 (7,9 %) as malignant and 2/252 (0,8 %) as inconclusive. The results of histological examination were available in 18/20 malignant lesions, in 23/32 suspicious cases, in the 2 inconclusive cases and in 28/198 reactive cases. 16/18 (88,9 %) malignant lesions, the 2 (100 %) inconclusive cases and 10/23 (43,5 %) suspicious cases were diagnosed as malignant. In 23/28 (82,1 %) reactive cytological cases, a benign process was diagnosed by histology. Correlation with histology showed a sensitivity of 86 % and a specificity of 90 %.
Conclusion: FC is an important additional tool in the cytological diagnosis of lymphoproliferative disorders, being the combined approach a useful technique for distinguishing reactive lymphoid proliferations from malignant lymphomas.

Thursday, 29 September 2016, 08.30–12.00, Conference Room 5
OFP-13 Thoracic Pathology

OFP-13-001

Preoperative detection of circulating epithelial cells in non-neoplastic pulmonary pathology. Pitfalls and limits of the CellSearch method

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Objective: The detection of circulating "tumour" cells (CTCs) by the CellSearch (CS) system is the only method approved by the FDA for the follow-up of patients with metastatic breast, prostate or colon cancer. The CS assay uses anti-EpCAM ferrofluid magnetic particles to capture and anti-CK8/18/19 to visualize CTCs. This approach entails potentially false negatives given the epithelial-mesenchymal transition in some CTCs. The absence of cytopathological criteria on isolated cells does not assert their tumour nature. We evaluated the CS specificity in patients with non-neoplastic lung disease.
Method: The CS analysis was performed in 37 patients before surgery for non-tumoural thoracic pathology: infectious diseases [tuberculosis (n = 6); actinomycosis (n = 1), aspergillosis (n = 2), abscess (n = 3); bronchopneumonia (n = 2)], inflammatory and degenerative diseases (n = 15); and various other thoracic non-tumoural diseases (n = 8).
Results: 5/36 (14 %) patients had at least 2 epithelial cells detected by the CS method. One patient had prior history cancer but progression was not observed. No patient developed cancer pathology after 6 years of clinical follow-up.
Conclusion: CS technique can detect non-tumoural epithelial cells and gives false positive results of CTCs. "CTCs" terminology may seem overused when reporting results. The lack of precise cytomorphological criteria with the CS method is a strong limit to this technology.

OFP-13-002

Sphingosine kinase 1 and epithelial-mesenchymal transition in lung adenocarcinoma

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Objective: To uncover copy-number deregulated genes that drive phenotypes in lung cancer.
Method: An integrated analysis of copy-number aberrations and gene expression profiles in 105 lung adenocarcinomas was used to uncover genes associated with coordinated gene expression profiles. Gene expression levels were validated by qPCR. Gene products were localized by Immunolabeling in tumour tissues.
Results: Sphingosine-kinase 1 (SphK1) was overexpressed in cases with gains of 17q compared to cases with diploid 17q ($p < 0.05$). SphK1 overexpression correlated with a signature that overlapped with the epithelial-mesenchymal transition (EMT) hallmark signature (q value 1 E-67, GSEA, Broad Institute). Genes in the SphK1-associated signature included EMT inducers (SNAI1, SNAI2 and TWIST1), many collagens and fibroblast activation genes (FAP, POSTN). Using monoclonal antibodies that reacted specifically with SphK1 or SNAI2—the EMT inducer that most strongly correlated with SPHK1 expression -, we could localize the proteins to tumour cells. These results were confirmed by showing the localization of SphK1 or SNAI2 to cells overexpressing TP53.
Conclusion: Deregulated SphK1 in tumour cells was associated with 17q gains and an EMT signature in lung adenocarcinomas. This suggests that overexpression of SphK1 in tumour cells can contribute to an EMT in lung cancers.

OFP-13-003

PD-L1 expression in primary tumour and circulating tumour cells in patients with advanced non-small cell lung cancer

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Objective: Expression of PD-L1 in tumour and immune-cells has demonstrated predictive value to atezolizumab treatment in NSCLC patients1, and emerged as a promising biomarker for the selection of patients to cancer immunotherapies. Given the difficulty in obtaining tissue for biomarker assessment in NSCLC, we investigated the utility of circulating tumour cells (CTCs) as a non-invasive method to evaluate PD-L1 status in advanced NSCLC patients.
Method: CTCs were enriched from peripheral blood samples from 80 NSCLC patients (ISET platform, Rarecells). PD-L1 expression in CTCs and matched-tumour-tissue was evaluated by IHC (SP142, Ventana), and quantified in tumour and white blood cells.
Results: CTCs ranged from 2 to 268 CTCs/4 ml, with median 65 CTCs/4 ml. 6 patients (7.5 %) showed ≥1 PDL-1 positive CTC, and 16 patients (20 %) showed >1 % PDL-1 positive tumour cells in tissue with 93 % concordance between tissue and CTCs. 46 patients (58 %) showed >1 % PDL-1 positive immune infiltrates in tissue, and 39 patients (49 %) showed >1 % PDL-1 positive in circulating WBC, with 80 % concordance between blood and tissue.
Conclusion: PD-L1 status in CTCs and WBCs correlated well with PD-L1 status in tissue, revealing the potential of CTCs as a non-invasive real-time biopsy to evaluate PDL-1 expression in NSCLC.

OFP-13-004

Prognostic value of Fibroblast Growth Factor Receptor (FGFR) 1 gene amplification and FGFR2/FGFR3 driver-mutations in patients with Squamous Cell Carcinoma (SCC) of the lung

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Objective: ΔNp63/p40-positive resected SCC of the lung (n = 101) were analyzed for FGFR1 gene amplification and driver-mutations in FGFR2/3 genes to investigate their prognostic value.
Method: FISH-analysis was performed on formalin-fixed paraffin embedded tissues. For the detection of K660N/K660E (FGFR2) and R248C/S249C (FGFR3) mutations, tumour DNA was sequenced by Sanger sequencing.
Results: Twenty-two of 101 (22 %) samples were amplification positive based on a FGFR1/CEN8 ratio 2.0 or higher. In advanced stages (III–IV), patients carrying the amplification showed significantly longer overall survival (p = 0,006). Among women, amplification was significantly associated with longer overall survival (p = 0,023). The FGFR1 gene amplification status was associated with younger patient age (65 versus 69 years, p = 0,046); there was no association with gender, tumour stage, histologic subtype, tumour grade or ΔNp63/p40-immunoreactivity. In one out of 101 cases (1 %) the S249C mutation was identified, there was no indication that it influences overall survival; the K600N, K660E or R248C mutations were not identified.
Conclusion: In SCC of the lung, FGFR1 gene amplification is a frequent genetic alteration whereas K660N/K660E (FGFR2) and R249C/S249C (FGFR3) are rare events. In SCC of the lung, FGFR1 gene amplification appears not to be a negative but rather a favorable prognostic factor for women and particularly for patients with advanced tumours.

OFP-13-005

End-stage sarcoidosis: Radiologic-pathologic correlation

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Objective: To correlate radiologic and pathologic findings in patients who received lung allografts for a clinical diagnosis of end-stage sarcoidosis.
Method: From 2001 to 2016, 20 patients (4 % of our total) were transplanted for presumed end-stage pulmonary sarcoidosis. Pre-transplant high-resolution computed tomography (HRCT) images of the chest were reviewed by a thoracic radiologist. The explants were reviewed for the type of fibrosis and the presence of granulomas.
Results: The HRCT opinions were as follows: likely sarcoidosis, likely usual interstitial pneumonia (UIP), and other. The "likely sarcoidosis" HRCT category (15 cases) histologically corresponded to sarcoid type fibrosis with granulomas in 11 cases and without granulomas in 4 cases. The "likely UIP" HRCT category (4 cases) histologically corresponded to UIP pattern in 3 cases and sarcoid type fibrosis with granulomas in 1 case. Multidisciplinary discussion concerning these latter cases resulted in a diagnosis of idiopathic pulmonary fibrosis (IPF) in 3 cases and sarcoidosis in 1 case, respectively. Finally, "other" HRCT findings (1 case) represented sarcoidosis-related pulmonary veno-occlusive disease histologically.
Conclusion: (1) End-stage sarcoidosis may lack granulomas. (2) Patients presumed to have end-stage sarcoidosis may show UIP pattern. This may be due to the development of IPF in a patient with a clinical history of sarcoidosis.

OFP-13-006

Morphological and functional features of pulmonary embolism

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Objective: To study morphological features of pulmonary embolism.
Method: Autopsy examination.
Results: 2926 autopsies served as the material for the analysis (1568 men—48.1 %, 1358 women—51.9 %), which were obtained from postmortem studies in Moscow and Ryazan. Among the sources of all thromboembolic complications by frequency of occurrence in the first place are the veins (venous sinuses) of crus and thigh (femoral popliteal-iliac-segment) (50.1 % of both men and women), in the second—the right heart cavity (18.7 %). Other separate systems of vena cava inferior (pelvic, hemorrhoidal, hepatic veins and vena cava inferior itself) were the source of thrombosis in 9.8 %. With genetically determined factors the state of thrombophilia is associated, clinical implementation of which is induced by external influences. Acquired factors predisposing to thrombosis are many conditions that can be grouped by the pathogenetic principle: activation of coagulation factors and fibrinolysis violation; pathology of platelets; deceleration and/or blood flow disturbance; changes in blood rheology; damage to the endothelium and vascular wall; drug therapy. For example, thrombin increases the expression of cell adhesion molecules. Also, we can indicate that the thromboembolic process is associated with the expression of cell adhesion molecules such as P-selectin, ICAM-1 (CD54) and VCAM-1 (CD106).
Conclusion: At this level of study leading factor in this pathology is mechanical obstruction of the pulmonary arterial system. Pathologic picture of death by pulmonary embolism is made by complex of pathological changes. The main of them is the presence of thromboembolism in the gaps of pulmonary trunk system, the second—the source of thromboembolism, the third—the macro and / or microscopic reactive changes.

OFP-13-007

Association of Type V collagen regulated genes and isoforms chains with systemic sclerosis-related pulmonary fibrosis

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Objective: Type V collagen (COLV) can be a possible trigger involved in the pathogenesis in early stages of systemic sclerosis (SSc). This study aimed to analyze morphological and molecular features of α1(V) and α2(V) chains and the role of COL5A1, COL5A2 gene expression in fibrillogenesis in a cohort of patients with early SSc-related pulmonary fibrosis.
Method: Pulmonary biopsies were obtained from 7 patients with SSc-related fibrosis and 7 healthy controls. Morphometry, immunofluorescence and qPCR were performed to characterize microscopic changes of α1(V) and α2(V) protein and levels of RNA COL5A1, COL5A2.
Results: Lung immunofluorescence and qPCR data distinguished patients with SSc-related pulmonary fibrosis from healthy controls. In lungs of patients with SSc-related fibrosis who had abnormal histoarchitecture, immunofluorescence confirmed increased markers of α1(V) protein around the alveolar septa and capillaries resulting in a fine net pattern on collapsed areas and overexpression of α2(V) in capillaries and vessels. qPCR revealed increased COL5A1 and COL5A2.
Conclusion: These results highlight major pathogenic pathways relevant to lung in SSc-related fibrosis suggesting that a post-translational modification of α1(V) chain and up-regulated expression of COL5A1-regulated gene can interfering with the normal extracellular matrix lung parenchyma. Further studies on the inhibition of α1(V) chain are necessary to test if gene therapy can attenuate effects of this disease.

OFP-13-008

Micropapillary carcinoma has the worst prognosis among stage Ia lung adenocarcinomas

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Objective: In view of the new WHO classification of lung neoplasms, we analyzed the survival of resected stage Ia adenocarcinomas according to their histological type.
Method: Between 2004 and 2013, 183 stage Ia adenocarcinomas were resected from 72 men and 111 women (mean age: 62.3 years). The subtypes of the adenocarcinomas were as follows: in situ adenocarcinoma 11 (6 %), minimally invasive 9 (5 %), lepidic 31 (17 %), acinar 45 (24 %), papillary 29 (16 %), solid 47 (26 %) and micropapillary carcinoma 11 (6 %). The subtypes of adenocarcinomas and the overal survival were compared between the low grade (in situ, minimally invasive, lepidic), intermediate grade (acinar, papillary) and the high grade (solid and micropapillary) adenocarcinoma groups.
Results: The 5-year Kaplan-Meier estimates of overall survival were as follows: in situ (100 %), minimally invasive (88.9 %), lepidic (87.7 %), acinar (89.6 %), papillary (85.8 %), solid (65.5 %) and micropapillary (27.3 %) with a significant difference between the low+intermediate and high grade (55.6 %) groups ($p = 0.001$), and inside the high grade group between solid and micropapillary carcinomas ($p = 0.001$).
Conclusion: Micropapillary adenocarcinoma had the worst survival among the different subtypes of stage Ia adenocarcinomas, therefore adjuvant treatment should be considered even in stage Ia.

OFP-13-009

Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia syndrome versus carcinoid tumours with/without neuroendocrine cell hyperplasia: A clinicopathologic, imaging and immunomolecular comparison study

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Objective: To evaluate similarities and differences between diffuse idiopathic pulmonary neuroendocrine cell hyperplasia syndrome (DIPNECH) and carcinoid tumours with/without NECH.
Method: Clinical and imaging data (gender, age, symptoms, respiratory function, smoking habit, computed-tomography/CT pattern), pathologic features (histotype, tumour size, and stage, mitotic rate, necrosis, central/peripheral site), immunohistochemical findings (TTF-1, hormonal receptors, CD10, chromogranin, synaptophysin, CD56, p40, napsin, GRP/bombesin, ACTH, p70S6K, mTOR, SSTR2, Rb, ALK) and molecular gene mutations (EGFR, KRAS, c-KIT, PDGFRs) were collected from 19 DIPNECH and 132 pulmonary carcinoids.
Results: Overall, there were 77 females and 74 males with a median age of 57 years. Fifty-eight percent were non-smokers, 49 % were symptomatic. One-hundred forty-one were typical carcinoids (93.4 %), 110 in stage IA and 82 showed a central/peri-hilar location. Neither molecular alterations nor ALK expression were detected. Patients with DIPNECH significantly differed in terms of gender (all females, $p < 0.0001$), smoke (non-smokers, $p = 0.021$), presence of symptoms, obstructive/mixed respiratory function, peripheral location and air-trapping with histology-confirmed constrictive bronchiolitis ($p < 0.0001$). Among immunohistochemical markers, DIPNECH was statistically correlated with higher expression of TTF-1, CD10 and GRP/bombesin-like peptide ($p < 0.0001$).
Conclusion: No single biomarker may distinguish DIPNECH from carcinoids with/without NECH, but patients with DIPNECH syndrome are significantly associated with symptomatic small airway alterations.

OFP-13-010

Epidermal growth receptor mutations and TTF-1 status in Turkish non-small cell lung carcinoma cases

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Objective: To investigate the incidence of Epidermal Growth Factor Receptor (EGFR) mutations in Turkish non-small cell lung carcinoma (NSCLC) patients and to evaluate the associated pathological and immunohistochemical features.
Method: 600 primary and metastatic therapy-naive NSCLC cases (biopsy, cytology, resection specimens) were evaluated for EGFR mutation by Sanger sequencing. H&E and immunohistochemical sections were examined; available cases were stained for TTF-1 and NapsinA by forming a tissue array.
Results: Sequencing was successful in 532 (88.6 %) cases. A total of 74 mutations were detected in 70 patients (13.1 %) (61.4 % woman, 38.6 % man). The distribution of mutations was 6.8, 51.3, 8.2 and 33.7 %; in exons 18, 19, 20 and 21 respectively. All EGFR mutant cases, except for one case was positive for TTF-1. All mutant cases were also positive for Napsin A, except for two cases.
Conclusion: EGFR mutation rate is lower than that of Asia Pacific in Turkish NSCLC cases. Mutation rate and distribution are similar to other European countries. TTF-1 negativity is a good predictor of a wild type EGFR. We think that, TTF-1 status could be incorporated in molecular algorithm of NSCLC cases in resource poor countries.

OFP-13-011

What pathologies have we found in the mediastinum these past 25 years?

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Objective: To report, for the first time in Lebanon, the descriptive epidemiology of pathologies diagnosed in the mediastinum.
Method: All 1039 patients with a mediastinal pathology exam at Hôtel-Dieu de France University Hospital from January 1991 to December 2015 were included.
Results: 628 (60.4 %) had a mediastinal neoplasm. Most cases were lymphomas (33.3 %) with a mean age of 34.0 years, or metastases (32.3 %) with a mean age of 59.8 years. Those were followed by thymic neoplasms (17.5 %), ectopic tumours (8.0 %), mesenchymal tumours (5.9 %), germ cell tumours (1.6 % with a mean age of 29.6 years), and other rare tumours (1.4 %). A striking male predominance was found for metastases and mesenchymal tumours (Male/Female sex ratios of 1.9 and 2.1 respectively). Within thymic neoplasms, thymomas represented 71.8 %. Of the 411 non-tumoural patients (39.6 %), 42.1 % had a granulomatous reaction, 9.0 % a thymic hyperplasia or cyst, and 4.4 % a cyst (bronchogenic/pericardic/enteric). The remaining 44.5 % cases had no specific diagnosis (mostly lymph nodes and thymectomies). The mean age of patients with a granulomatous reaction was 46.4 years, compared to 31.1 years for the cysts.
Conclusion: Reporting the descriptive epidemiology of mediastinal pathologies establishes the basis for further investigations. The adopted diagnostic procedures efficacy can now be evaluated.

OFP-13-012

Blood sample-based New Generation Sequencing detects circulating free MicroRNA from chronic thromboembolism pulmonary hypertension (liquid biopsy)

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Objective: Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by thrombus organization, pulmonary remodeling and increased pulmonary vascular resistance. Our aims was to determinate a plasma circulating microRNA profile as a diagnostic and prognostic biomarker of CTEPH.
Method: 12 CTEPH patients, 10 patients with pulmonary hypertension of other causes and 10 healthy volunteers were sequentially studied in

2016. All relevant clinical data from medical records, the V/Qscan and/or angiotomography, and right heart catheterization results were analyzed. An optimized protocol for RNA extraction from plasma samples by Qiagen mirneasy serum/plasma kit in combination with the Vac-Man® Vacuum Manifold were used. The Illumina TruSeq Small RNA-Seq Sample Prep Kit was used to generate small RNA library directly from total RNA. Clustering and sequencing was accomplished using the Illumina NextSeq500. Further databases and software used for analysis were the Diana software.
Results: The New York Heart Association Functional Classification and the levels of N-terminal-pro-brain-type natriuretic peptide did not differ between pulmonary hypertension groups. High-quality RNA were extracted. Circulating microRNAs were differentially expressed and associated with prognostic outcome ($p < 0.05$).
Conclusion: The MicroRNA profile might reflect pathogenesis of CTEPH, providing some clue for biomarker screening, however it still needed to be validated to clinical practice.

OFP-13-013
Inflammatory cell characterization and localization in malignant pleural mesothelioma
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Objective: Malignant pleural mesothelioma is a pleural tumour associated with asbestos exposure and subsequent chronic inflammation. Epithelioid mesothelioma is associated with a better patient prognosis compared with sarcomatoid/biphasic subtypes. The aim of this study was to characterize inflammatory cell infiltrates in mesothelioma samples and to correlate morphological features with clinical data.
Method: Peritumoural and intratumoural inflammatory cells were characterized by Immunohistochemistry and quantified in 34 mesotheliomas (17 epthelioid and 17 sarcomatoid/biphasic) and expressed as percentage of neoplastic area. Overall (OS) and progression free survival (PFS) after standard first-line platinum/pemetrexed were also evaluated.
Results: Higher inflammation percentages were seen in epithelioid mesotheliomas both in intra and peritumoural areas ($p = 0.03$ and $p = 0.05$). B lymphocytes were mainly detected in peritumoural area, while T lymphocytes and macrophages were present both at the intra and peritumoural level. Epithelioid mesotheliomas seem to be characterized by higher values of peritumoural B lymphocytes, while sarcomatoid/bipahasic samples showed higher percentages of intratumoural T lymphocytes and macrophages. A significant correlation was found between total inflammation and PFS ($p = 0.03$) and between intratumoural macrophage infiltration and OS ($p = 0.05$).
Conclusion: Epithelioid and sarcomatoid/biphasic mesotheliomas are characterized by different inflammation patterns that might impact survival. A confirmatory study on a larger sample size and correlation with asbestos exposure is currently ongoing.

OFP-13-014
Next Generation Sequencing of lung adenocarcinoma of smokers with and without Chronic Obstructive Pulmonary Disease (COPD)
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Objective: Few recent works report some different morphological features of lung cancer in smokers with and without COPD. To date it is unknown if COPD-associated lung cancer has a different molecular profile. We aimed to analyze gene mutations in adenocarcinoma samples from smokers with COPD versus smokers without COPD by using next generation sequencing (NGS).
Method: 27 surgical specimens of lung adenocarcinoma (8 COPD and 19 non-COPD) were analyzed using a 30-gene NGS panel on MiSeq platform.
Results: COPD and non-COPD smokers showed a median value of 1.5 and 2 mutations for each patient. When considering only mutations with well known pathogenetic role, at least one gene was altered in 75 % of COPD, 79 % of non-COPD smokers, and the most affected genes were KRAS (48 %), PTEN (19 %), P53 (19 %), EGFR (11 %) with no significant differences among the groups. Sporadic mutations in MET, STK11 and PIK3CA were detected only in non-COPD smokers. Adenocarcinoma of non-COPD smokers showed a higher prevalence of solid/papillary pattern and proliferation index.
Conclusion: NGS analysis revealed a partially different molecular profile in lung adenocarcinoma of smokers with and without COPD. The significance of sporadic mutations detected in non COPD smokers and their influence on the different histological pattern of adenocarcinoma should be confirmed by larger scale studies.

OFP-13-015
An expression signature as an aid to the histologic classification of non-small cell lung cancer
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Objective: Most non-small cell lung cancers (NSCLCs) are diagnosed from small specimens, and classification using standard pathology methods can be difficult. This is important as many therapies and clinical trials are histology-dependent. Our objective was to develop an RNA signature as an adjunct test for histo-pathological classification of NSCLCs.
Method: A microarray dataset of resected adenocarcinomas (ADCs) and squamous cell carcinomas (SCCs) was used to develop an ADC-SCC classifier. Another dataset of ADCs and non-malignant lung was used for a Tumour vs Nonmalignant classifier. Sample classification was determined by a nearest distance approach.
Results: We developed a 62-gene expression signature that contains many genes used in immunostains for NSCLC typing. It includes 42 genes that distinguish ADC from SCC and 20 genes differentiating non-malignant lung from lung cancer. Testing of the TCGA and other public datasets resulted in high prediction accuracies (93–95 %). A prediction score was derived that correlates both with histologic grading and prognosis. Using the HTG EdgeSeq technology (HTG Molecular Diagnostics, Inc. (HTG)) the classifier can be applied to FFPE specimens and core-needle biopsies, demonstrating the potential for deployment in standard clinical practice.
Conclusion: Our classifier provides an objective, quantitative method for the pathological classification of NSCLC.

Thursday, 29 September 2016, 14.00–16.00, Congress-Saal 2
OFP-14 Molecular Pathology

OFP-14-001
H3K27me3 immunohistochemistry highlights the inactivated X chromosome (Xi) and predicts sex in nonneoplastic tissues
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Objective: Histone 3 trimethylation at lysine 27 (H3K27me3), a crucial epigenetic silencing mark, is detectable by immunohistochemistry (IHC). In mammalian female cells, dosage compensation is achieved by transcriptional silencing of one X chromosome (Xi) by complex epigenetic modifications including H3K27me3. The aim of this study was to evaluate H3K27me3 IHC in nonneoplastic tissues for the detection of the Xi.

Method: Tissue samples (lymph node, bone marrow, liver, kidney, lung, colon, skin, and breast) from 14 female and 14 male patients, 2 patients with Turner syndrome (45,X), and one with Klinefelter syndrome (47,XXY) were stained using a monoclonal anti-H3K27me3 antibody.
Results: H3K27me3 IHC highlighted the Xi as an eccentric intranuclear dot in all karyotypically normal female but none of the male patients. Interestingly, the Xi was detected in hematopoietic cells in bone marrow from a male patient who had received a female bone marrow transplant 2 years before. Xi was detected in 47,XXY but not in 45,X patients.
Conclusion: H3K27me3 IHC detects the Xi with high sensitivity and specificity. With prior knowledge of patient sex, this may be useful for detecting extent of mosaicism in Turner syndrome, clarifying sample identity, and possibly also assessing chimerism after gender mismatched transplant.

OFP-14-002
Impact of Kras mutant subtypes on PD-L1 expression in lung adenocarcinoma

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Objective: Clinical responses to immunotherapy by anti-PD-1/PD-L1 antibodies in NSCLC may be associated with PD-L1 expression. We investigated the activation of Kras-mutant subtypes as a mechanism of PD-L1 regulation in lung adenocarcinoma (LUAD).
Method: PD-L1 expression was evaluated by IHC (SP142 clone, Ventana) on 117 LUAD (KrasWT, n = 51; Krasmut, n = 66). Stable cell lines were generated by transfection of Kras-G12D, G12V, G12C and WT plasmids into Beas2B bronchial cells.
Results: IHC analysis showed higher expression of PD-L1 in both tumour and immune cells in Kras-mutant LUAD compared with KrasWT tumours (37 vs. 18 %; P = 0.005). Kras-mutant PD-L1+ tumours had increased CD66b+neutrophil infiltrates and lower CD8+ T-cell content than PD-L1 − tumours. In vitro, mutant Kras led to significantly higher cell-surface PD-L1 expression and PD-L1 transcripts, notably in KrasG12C and KrasG12V cells, suggesting PD-L1 transcriptional regulation. There was differential activation of NF-kB, ERK and Pi3k/Akt pathways between Kras-mutant subtypes. PD-L1 was upregulated 3-fold by stimulation with IFNγ, independently of the Kras codon subtypes. Instead, hypoxia significantly increased PD-L1 expression in KrasG12C and KrasG12D cells only.
Conclusion: PD-L1 may be a therapeutic target in Kras-mutant LUAD. According to the Kras mutation subtype, potential drugs targeting the NF-kB, ERK or Pi3k/Akt pathways may increase the antitumour adaptive immune responses.

OFP-14-003
Liquid biopsy testing in routine clinical management of advanced non-small cell lung cancer: Clinical validation in a single biopathology laboratory

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Objective: We carried out clinical validation of liquid biopsy/ctDNA testing in patients with advanced NSCLC in ISO15189-accredited biopathology laboratory.
Method: We performed (i) ctDNA analytic validation in 170 NSCLC patients; and (ii) real-time evaluation of EGFR mutations before anti-EGFR treatment in 16 patients, and resistance mutations in 34 refractory patients under treatment. EDTA and BCT tubes (Streck) were used for blood collection. Mutation status was assessed by (i) EGFR RGQ kit (Qiagen), and (ii) NGS assay with Oncomine panel (>1800 mutations; 22 genes) on Ion PGM sequencer (ThermoFisher).
Results: The analytic validation demonstrated 70 % sensitivity and 98 % specificity for the ctDNA assays (limit-of-detection <5 %). ctDNA yield was not affected by storage in BCT tubes for up to 3 days. Real-time longitudinal ctDNA analysis showed that among 18 % of initially EGFR mutated patients, 33 % acquire T790M resistance mutation during treatment. 74 % of patients had at least one somatic alteration detected by NGS assay, with druggable alterations in various genes (e.g. MET, FGFR3). Mean turnaround time was 13 [4–22] days for tumour tissue and 6 [1–11] days for ctDNA analyses.
Conclusion: Rigorously validated ctDNA assays is an alternative approach for tumour tissue molecular analysis and may enable longitudinal examination of molecular profiling in NSCLC patients.

OFP-14-004
Molecular oncology: Structural and functional impact of mutations in RAS gene family

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Objective: Structural and functional impacts of mutations on RAS genes encoded protein namely KRAS, HRAS and NRAS.
Method: Full length molecular models of wild type RAS proteins were constructed using iterative threading alignment. The models were refined for the structural parameters and thermodynamic parameters. Subsequently, cavity analysis and molecular docking was conducted between GTP/GDP and RAS proteins.
Results: Superimposition of RAS proteins with its mutants at tertiary structure level did not show any considerable differences with RMSD deviation ranging from 0.06 to 0.10 Å. However, mutant residues superimposition showed noticeable differences in the spatial orientation. For example in KRAS, K5E, K5N, G10GG, G13D, Q22E, I36M, Q61H, Y71H, K117N, K147E, F156I and F156L showed considerable change in the orientation of residues. Similarly, wildtype GTP/GDP binding cavity holds volume and surface area as 680.64 Å3 and 1062.48 Å2. Where volume of G10GG, Y71H and K117N are 1123.71 Å3, 974.59 Å3 and 954.37 Å3 respectively. Similarly, surface area of the GTP/GDP binding region increased to substantial scale compared to wildtype. Subsequent molecular docking analyses verified this notion.
Conclusion: The present data report for the first time the molecular impact ensued by the structural perturbation due to mutations in RAS proteins.

OFP-14-005
Therapeutic implications of PDL1 (CD274) copy number alterations: Definition of core regions, correlations with gene expression and mutational loads across 22 major cancers

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Objective: Targeting the PDL1 (CD274)—PD-1 axis prevents evasion of tumour cells from the host's immune response. While PDL1 immunohistochemistry was introduced as a predictive biomarker with variable power, data on PDL1 copy number changes (CNVs) are limited.
Method: Employing The Cancer Genome Atlas (TCGA) datasets, we comprehensively analyzed 22 major cancer types for PDL1 CNVs including core amplified and deleted regions and relations to mutational loads as well as gene expression.
Results: PDL1 deletions were more prevalent than gains, and CNVs were differentially distributed across cancer types. Moreover, we observed significant correlations between PDL1 CNVs and mRNA expression levels for many cancer types. Tumours with PDL1 gains were associated with significantly higher mutational loads compared to normal cases. Core

amplified and deleted regions shared by more than 80 % of the cancer cases contained many genes with biological implications: e.g. CDKN2A, JAK2, KDM4C, class I interferons, IL33, among others. Our analysis indicates indicates different natures of PDL1 expression, i.e. 'adaptive' vs. 'oncogenic', and demonstrates that PDL1 CNVs are frequent across major cancer types, are associated with higher mutational loads, and influence PD-L1 expression levels.
Conclusion: In conclusion, PDL1 CNVs might be suitable predictive biomarkers for immunotherapy regimens across cancer types.

OFP-14-006
The importance of NFATc1 in the pathogenesis and survival of B cell lymphomas
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Objective: To examine the functional role of NFATc1 in the pathogenesis and survival of B cell lymphomas (BCLs).
Method: An Eμ-Myc transgenic mouse cell line was crossed with a mouse cell line harboring conditional deletion of NFATc1 to create a cell line in which B cells have Myc over expression and NFATc1 gene deletion. The immunophenotype of Eμ-Myc BCLs was analysed by Flow cytometer. The nuclear localization of NFATc1 was assessed by western blotting and confocal microscopy. Analysis of RNA was performed in MYC induced BCLs.
Results: The B cell lymphomas developed in Eμ-Myc mice showed an immature B-cell phenotype with constitutive nuclear localization of NFATc1. NFATc1 was also overexpressed and localized in the nuclei of human BCL cell lines. These findings suggest that NFATc1 expression is of importance in the pathogenesis of BCLs. Increased apoptosis in tumour cells with abolished NFATc1 indicates that NFATc1 is essential for the survival of tumour cells. In MYC induced BCLs, NFATc1 protein expression is regulated by post-transcriptional and post-translational levels.
Conclusion: NFATc1 has an important role in the pathogenesis and survival of BCL. Our findings showed that this component of the CN-dependent Ca2+/NFAT signalling pathway may be a promising target in therapeutic strategies of B cell lymphomas.

OFP-14-007
Comparing PD-L1 expression using mRNA in situ hybridization assay (RNAscope) and immunohistochemistry in squamous cell lung cancer
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Objective: Evaluation of PD-L1 expression by immunohistochemistry (IHC), a new predictive factor for therapies targeting PD1 and PD-L1, relies on several assays and semi-quantitative assessment by pathologists. We evaluated in situ hybridization at the mRNA level (RNAscope) as a new method to assess more quantitatively PD-L1 expression and compared results with IHC in a series of squamous cell lung cancer (SQCC).
Method: 181 cases of resected SQCC were collected on tissue microarrays. In situ mRNA detection of PD-L1 in tumour cells was performed using a chromogenic RNAscope assay (Advanced Cell Diagnostics) combined with image analysis (Spot Studio software). PD-L1 IHC was performed with E1L3N and SP263 clones.
Results: PD-L1 expression in IHC was highly concordant with the 2 antibodies used. PD-L1 mRNA expression was detected at various levels (average number of spots per cell: 0.741, range 0.01–9.61) and strongly correlated with immunohistochemistry (Spearman's rank correlation coefficient: 0.803).
Conclusion: In situ hybridization (RNAscope) is feasible to evaluate PD-L1 expression in tumour cells using formalin fixed paraffin embedded tissue samples, and strongly correlates with IHC. It may provide a quantitative and standardized assessment of PD-L1 expression in tumour cells using FFPE samples. Clinical relevance of this approach remains to be evaluated.

OFP-14-008
Comparative analysis of lung adenocarcinoma cases tested for ALK Immunohistochemistry (IHC) and Fluorescent in situ Hybridization (FISH)
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Objective: To compare ALK IHC test with ALK FISH test in 200 lung adenocarcinoma specimens.
Method: One hundred lung adenocarcinoma Formalin fixed paraffin embedded (FFPE) specimens were tested to validate ALK IHC test (Validation arm) and 200 were tested post validation (Test arm). The ALK IHC test was performed using anti-ALK (D5F3) primary antibody with OptiView detection system (Ventana). The ALK FISH results were available for all validation specimens and all ALK IHC positive cases of test arm. The ALK IHC performance was compared with ALK FISH.
Results: The validation arm revealed 96.4 % sensitivity, 94.4 % specificity and 95 % accuracy. Five specimens (5 %) were discordant; four of these were ALK IHC positive FISH negative and the fifth was IHC negative FISH positive. The test arm revealed 16 % ALK IHC expression. Four specimens were discordant with ALK IHC positive but ALK FISH negative. All ALK IHC negative specimens were also negative for ALK FISH . There was 100 % Sensitivity, 90 % Specificity and 93.75 % accuracy.
Conclusion: Thus ALK IHC negative results were concordant with ALK FISH results whereas ALK IHC positive results may be subjected to ALK FISH test. The observed discordance could represent wider range of detection by ALK IHC.

OFP-14-009
Detection of somatic mutations in plasma allows for non-invasive real time therapy response monitoring of lung cancer patients
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Objective: The aim of this study was to establish a comprehensive strategy for the detection of clinically relevant somatic mutations in plasma of lung cancer patients both at diagnosis and during disease follow-up.
Method: Plasma samples from controls were used to optimize the experimental approach. To evaluate our strategy, plasma samples obtained at different stages of disease were collected from 100 lung cancer patients. Different enrichment strategies where tested. All amplified products were used to prepare libraries and sequenced using Ion Torrent systems. Digital PCR was used to confirm results.
Results: In plasma isolated from lung cancer patients, tumour derived genetic mutations could be identified in as little as 10 ng of cfDNA. Mutations identified in cfDNA mirrored mutations identified in tumour biopsies. Mutations with VAF <0.1 % could be detected in cfDNA and confirmed using Digital PCR. Response to therapy could be observed by tracking specific mutations in cfDNA and detection of tumour relapse could be anticipated up to 2 months when compared to standard methodologies.
Conclusion: In conclusion, the comprehensiveness and speed of the NGS methodology, combined with the high sensitivity of detection, delivered a protocol for detection of somatic mutations in cfDNA for non-invasive real time therapy response monitoring of cancer patients.

OFP-14-010

Liquid biopsies in lung and skin cancer—a comparison of digital PCR and NGS methodologies

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Objective: Tumours release mutated DNA into the blood, which can be analyzed by sensitive molecular methods. This "liquid biopsies" are interesting in lung cancer pathology, for follow-up and monitoring of patients under TKI. There is not yet a gold standard for mutation testing of liquid biopsies. We have compared the Biorad QX200 droplet digital PCR and the Ion Torrent Semiconductor sequencing for analyzing mutations in liquid biopsies of lung and skin cancer patients.
Method: DNA was extracted from blood samples of patients suffering from lung or skin cancer using the Qiagen QIAamp circulating nucleic acid extraction kit. Mutation analysis was performed with the Biorad QX200 and the Ion Torrent Proton sequencer (Ion Ampliseq Colon/Lung; Cancer-Hotspot panel).
Results: The Ion Ampliseq panel analysis was able to detect a range of hotspot mutations in a single sample. Noise ratio of the sequencing approach was 0,5 % in formalin fixed samples and 0,1 % in liquid biopsies. Digital PCR had a lower noise ratio and slightly higher sensitivity. It was able to determine the reliability of the measurement in each analysis by counting molecules. However, only single mutations can be detected per PCR reaction.
Conclusion: Both approaches are valid methods to detect mutations in circulating tumour DNA. The additional sensitivity of digital PCR comes at the cost of using nearly all available DNA for a single hotspot analysis. NGS is sensitive enough to detect biologically relevant levels of mutated DNA offering the advantage of analyzing a range of mutations in parallel. This data suggests Ion Torrent Ampliseq as the most suitable methodology for the plasma analysis of multiple tumour markers.

OFP-14-011

Complete workflow for detection of somatic mutations at 0.1 % frequency from cell-free DNA using Ion Torrent platform

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Objective: To demonstrate a research use only workflow that includes blood collection, cfDNA isolation, library preparation, sequencing, and data analysis to enable detection of rare DNA variants in blood plasma samples. Such workflow provides a non-invasive approach to monitor cancer status and evaluate cancer evolution in the future.
Method: Blood samples were collected using EDTA tubes followed by plasma preparation and cfDNA isolation using MagMAX cfDNA Isolation Kit. Library preparation was performed using Lung cfDNA Assay. Barcoded libraries were pooled and sequenced on Ion Torrent sequencing platform. For data analysis, we developed an analysis algorithm that models errors accumulated during amplification and sequencing, and accurately reconstructs sequence of original DNA molecules based on tagged next generation sequencing reads. Analysis enables sensitive and specific detection of somatic mutations to 0.1 % allele ratio. We demonstrated the analysis in control and archived cfDNA research samples where 157 biomarkers relevant to non-small cell lung cancer were interrogated simultaneously.
Results: We achieved ~90 % detection sensitivity at 0.1 % frequency or 100 % sensitivity at 0.5 % frequency using engineered cfDNA samples. We validated the workflow on a set of research samples from matched tumour FFPE and blood plasma collected from research subjects with NSCLC. Results indicate high sensitivity of the workflow and high concordance between variants detected in the two types of research samples.
Conclusion: We demonstrated a highly sensitive and reliable research workflow to detect rare somatic mutations in circulating cfDNA samples. Significant overlapping of mutations discovered in FFPE tumour and cfDNA samples suggests that this workflow may be used to monitor tumour dynamics in NSCLC and potentially other tumours in the future.

OFP-14-012

Expression of programmed death ligand (PD-L1) in different tumours: Comparison of several current available antibody clones

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Objective: PD-L1 is a surface molecule of cancer cells, which contacts with PD1 molecule of T cells and inhibits the cytotoxic effect of lymphocytes against tumour cells. The modern target therapy uses this interaction to inhibit the PD-1 molecule of T cells to facilitate tumour cell death. The immunohistochemical stain against PD-L1 seems to be important for stratification of patients for these check-point therapies. The aim of this study was to evaluate different primary antibodies against PD-L1 next to lymphocyte characterization, PD1 and PD-L2 expression and PD-L1 amplification.
Method: Frequent types of carcinoma next to mesothelioma were selected and stained by immunohistochemistry, immunofluorescence and fluorescence in-situ hybridization. For primary antibodies, current available antibodies against PD-L1 (DAKO, Cell Signaling, Ventana, Biolegend, Abcam, Zeta), PD-L2 and PD1 were established and analyzed by light/fluorescence microscopy and polyspectral microscopy (Perkin Elmer Vectra). In addition, stains to detect intratumoural lymphocytes (CD3, CD20, CD8, CD57) were used.
Conclusion: Concurrent detection of all this markers on one section with different color signals helps to understand the different staining characteristics of a broad spectrum of PD-L1 antibodies, next to evaluation of additional, possibly therapy relevant expression patterns.

Thursday, 29 September 2016, 14.00–16.00, Conference Room 5
OFP-15 Dermatopathology

OFP-15-001

Expression of histone deacetylase 2 in Spitz tumours

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Objective: The lack of clear histological criteria and reliable immunohistochemical markers prevents clear determination of atypical Spitz nevi (ASN) toward Spitz nevus (SN) or Spitzoid melanoma (SM). Expression of histone deacetylase 2 (HDAC2) in Spitz tumours has not been studied so far.
Method: We evaluated HDAC2 expression in 78 cases of Spitz tumours (SN, ASN and SM) using immunohistochemistry. The percentage of positive was analyzed in epidermal, superficial and deep dermal parts and compared with clinical (sex and age of patients, localization and tumour size) and histological characteristics (histological type, thickness and depth of invasion of SM and mitotic count).
Results: High expression of HDAC2 was observed in all tumour parts (82.9 ± 12.60, 79.8 ± 15.33, 74.1 ± 15.31). HDAC2 expression was not associated with different clinical parameters. Moderate positive correlation of HDAC2 expression in different tumour parts was found. No difference in the HDAC2 expression was found between histological types of Spitz tumours. Huge variations in HDAC2 expression were found in SM, but no association with thickness, depth of invasion and mitotic count was found.
Conclusion: The expression of HDAC2 in Spitz tumours is high and homogeneous throughout, and it could be present from the early stages of their development.

OFP-15-002

Expression of HMGA2 in actinic keratosis, Bowen's disease and invasive Squamous Cell Carcinoma (SCC) of the skin

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Objective: High mobility group protein A2 (HMGA2) is architectural transcription factor which plays important role in cell differentiation and stem cell maintenance. Its expression in actinic keratosis (AK). Bowen's disease (BD) and invasive squamous cell carcinoma (SCC) has not been studied so far.
Method: We examined 78 AK, 48 BD and 173 SCC using immunohistochemistry. The level of HMGA2 expression was evaluated semiquantitatively as low (≤30 % of positive cells) and high (>30 % of positive cells). Distribution of positive cells was evaluated as non-diffuse and diffuse.
Results: Low expression was frequent in AK (80.8 %) and BD (68.8 %) compared to SCC (36.4 %) (p 0.001). Diffuse distribution was often seen in SCC (70.1 %), while non-diffuse was frequent in AK (80 %) and BD (51.5 %) (p 0.001). The level of HMGA2 expression wasn't associated with SCC grade, diameter or thickness. Diffuse distribution was often present in moderately (74.5 %) and poorly differentiated SCC (89.1 %) compared to well differentiated SCC (53.7 %) (p 0.001).
Conclusion: The increase in HMGA2 expression could play significant role in the development of invasive SCC of the skin, but the role in its progression could be less important.

OFP-15-003

Optimisation of tissue and plasma assessment of BRAF mutational status in metastatic malignant melanoma by the IDYLLA system

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Objective: The objective of this study was to evaluate the feasibility and analytical performance of the Idylla™ (Biocartis) system for i) characterization of V600 BRAF mutations at diagnosis and ii) minimal residual disease monitoring.
Method: FFPE sections and cfDNA from plasma of 20 patients with metastatic malignant melanoma was tested for V600 BRAF mutations, before and after targeted or systemic treatment, using the fully integrated real-time PCR-based platform (Idylla™, Biocartis, Mechelen, Belgium). Results were compared to pyrosequencing mutation analysis (Qiagen, Hilden, Germany) and BRAFV600E immunohistochemistry (VE1 clone, Ventana, Tucson, AZ) on tumour tissue from the ISO15189-accredited laboratory.
Results: The analysis on tumour tissue with the ISO15189-reference method yielded 90 % agreement. The concordance rate between tumour tissue and plasma cfDNA was 70 % before treatment. None of the patients showed residual BRAF mutation after Vemurafenib treatment. Overall, the turnaround time was quick (<90 min).
Conclusion: The Idylla™ system is a highly reliable, rapid and sensitive platform for detection of V600 BRAF mutations both in tissue and plasma samples, providing an efficient alternative to conventional diagnostic methods, particularly for routine diagnostics laboratories with limited experience in molecular pathology.

OFP-15-005

Nodular superficial thrombophlebitis: A study of clinical and histopathology spectrum of 34 cases

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Objective: To determine clinical manifestations and histopathology spectrum of nodular superficial thrombophlebitis (ST).
Method: Retrospectively review of 34 skin biopsies diagnosed as ST. Clinical manifestations and histopathology features were described.
Results: All 34 cases of ST, The most presention was multiple generalized bilateral leg nodules (32 patients). Ulceration, group arrangement and linear pattern were found in few patients. Histopathlogy revealed mostly septal panniculitis with inflammatory cell infiltration in muscular wall of vein and thrombosis in the lumen. We found predominantly granulomatous phlebitis (35 %), predominantly lymphocytic phlebitis (32.5 %), predominantly neutrophilic phlebitis (26.5 %) and mixture of neutrophil and granulomatous phlebitis (6 %). Small-vesseled vasculitis was found (11.7 %). One showed aneurysmal change. Immunofluorescence demonstrates superficial vessel wall deposition of IgM and /or complement (53 %).
Conclusion: Cutaneous manifestations and inflammatory response of nodular ST were similar to cutaneous polyarteritis nodosa (c-PAN). Although, vasculitis was present, this was not indicated of c-PAN.

OFP-15-006

Unusual distribution of Type V collagen isoforms determines the cutaneous fibrosis in scleroderma

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Objective: Our goal was to analyze morphological, ultrastructural and molecular features of α1(V) and α2(V) chains and COL5A1, COL5A2 gene expression in fibrillogenesis from patients with early systemic sclerosis (SSc)-related cutaneous fibrosis in order to understand the protein and molecular pathways implicated in cutaneous disease.
Method: Skin biopsies were obtained from 5 consecutive patients with SSc-related fibrosis and treatment-naïve, and 5 healthy controls. Immunofluorescence and immune electron microscopy were performed to characterize microscopic and submicroscopic changes of α1(V) and α2(V) chains. COL5A1 and COL5A2 mRNA was evaluated by qPCR.
Results: In skin of patients immunofluorescence and immunoelectron microscopy confirmed increased markers of α1(V) and α2(V) chains in reticular dermis, in addition to marked loss of α1(V) in the papillary dermis and overexpression of α2(V) in capillaries and vessels. COL5A1 and COL5A2 mRNA expression was increased, nevertheless relative level of α1(V) expression was significantly reduced in cutaneous fibroblasts. Interestingly, inhibition of COL5A2 gene was associated with increased expression of COL5A1 gene.
Conclusion: These results highlight major pathogenic pathways relevant to skin in SSc-related fibrosis: a post-translational modification of α1(V) chain, thus interfering with the normal extracellular matrix formation in papillary dermis. Further studies on the inhibition of α1(V) chain are necessary to test if gene therapy can attenuate effects of this disease.

OFP-15-007

Expression of a long non-coding RNA NEAT1 is significantly higher in MCPyV-positive Merkel cell carcinomas than MCPyV-negative ones

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Objective: Merkel cell polyomavirus (MCPyV) is monoclonally integrated into about 80 % of Merkel cell carcinoma (MCC), an aggressive neuroendocrine skin cancer. In this study, we investigated the involvement of NEAT1, a nuclear long noncoding RNA participating in the immune-regulation upon viral infection, in the MCC.
Method: In 15 MCPyV-positive and 12 MCPyV-negative MCCs, expression level of NEAT1 was determined by RT-qPCR. Pasraspeckles were visualized by RNA-FISH. Expression profiles of MCPyV-related or NEAT1-regulated genes were compared based on public microarray data.

Results: We firstly quantified expression of NEAT1 and SFPQ, a transcript factor, in MCPyV-positive and -negative MCCs. NEAT1 expression level was upregulated at almost two times in MCPyV-positive MCC comparing with MCPyV-negative ones ($P < 0.05$). Paraspeckle numbers of MCPyV-positive and -negative MCCs were approximately 2:1. 15 genes including immune-related genes overlapped among two profiles of gene expressions we sited.
Conclusion: Our findings suggest that NEAT1 regulates some genes including immune-related genes in MCPyV-positive MCCs by forming more number of paraspeckle. This is the first report of NEAT1 expression which may play as an actual regulator of genes in MCC.

OFP-15-008
BRAF V600E inter- and intra-tumour heterogeneity in primary melanoma and corresponding metastases
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Objective: To examine the extent of inter-and intra-tumoural heterogeneity of BRAF V600E in primary tumours and their corresponding metastases.
Method: Using BRAF V600E immunohistochemistry and Hematoxylin-Eosin stained slides inter-tumoural heterogeneity were studied in 255 samples from 56 patients (56 primary melanomas and 199 correspondingmetastatic samples) and intra-tumoural heterogeneity were studied in 482 samples from 224 patients.
Results: Complete BRAF V600E inter-tumoural homogeneity was found between the primary tumour and their corresponding metastases in all 56 examined patients. We found BRAF V600E intra-tumoural heterogeneity in 17 cases: 3 with a positive clone in a negative tumour, 5 with a negative clone in a positive tumour, 9 with focal areas staining with other intensities than the majority of the tumour. All of the found nevus remnants ($n = 9$) had a positive BRAF V600E expression and so had their corresponding primary melanoma. In one case we incidentally found a BRAF V600E positive nevus in close relation to a wild type primary melanoma.
Conclusion: Primary tumour tissue can be used just as safely as metastatic tissue for BRAF V600E mutation analysis since inter-tumoural heterogeneity does not exist. Intra-tumoural heterogeneity and coexisting nevi do exist in some cases and may influence BRAF inhibitor therapy response.

OFP-15-009
Fibril and network-forming collagen may influence crosslinked density of skin in diabetic rats
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Objective: Considering the poor healing of diabetic wound-repair process of diabetic our aim was to clarify whether the fibril and network-forming collagen may influence crosslinked density of skin in diabetic rats.
Method: Diabetes was induced in Wistar male rats, by streptozotocin inoculation. The animals were submitted to euthanasia at 7 ($n = 10$, DG7d) and 30 days ($n = 10$, DG30d). Matched control groups were inoculated with saline ($n = 10$, CG7d; $n = 10$, CG30d). The skin biopsies were analyzed by immunofluorescence and morphometry for fibril (I, III, V) and network (IV, VI) forming collagen.
Results: DG7d showed collagen type I relatively decreased, type V almost unchanged and types III, IV and VI highly expressed, compared to controls. In DG30d the expression of types I and V collagen decreased. Already types III and IV decreased slightly in relation to DG7d, but was more expressed that controls groups. However, type VI collagens were highly expressed in DG30d. Statistic value $p < 0.0001$.
Conclusion: The present study revealed significantly increase levels of types III, IV and VI collagen and decrease levels of types I and V in early stage of diabetic skin, thus suggesting decrease in the wound tensile strength. New approaches should be done to evaluate whether these collagen modulation provides a potential strategy for wound healing to ameliorate the ulceration in diabetic populations.

OFP-15-010
T cell landscape in primary melanoma predicts the survival of patients with metastatic disease after their treatment with dendritic cell vaccines
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Objective: Tumour infiltrating lymphocytes appear to be a predictor of survival in many cancers, including cutaneous melanoma. We applied automated multispectral imaging to determine whether density and distribution of T cells within primary cutaneous melanoma correlate with survival of metastatic melanoma patients after dendritic cell (DC) vaccination.
Method: CD3+ T cell infiltration in primary tumours from 77 metastatic melanoma patients treated with DC vaccination was quantified using the ratio of intratumoural versus peritumoural T cell densities (I/P ratio). To evaluate I/P ratio as a predictive biomarker, we also analyzed 19 chemotherapy-treated patients.
Results: Patients with longer survival after DC vaccination had stronger T cell infiltration than patients with shorter survival in a discovery cohort of 19 patients ($p = 0.000026$) and a validation cohort of 39 patients ($p = 0.000016$). I/P ratio was the strongest predictor of survival in a multivariate analysis including M substage and serum LDH level. Longer survival times of DC-vaccinated compared to chemotherapy treated patients was observed for high ($p = 0.000566$), but not low ($p = 0.154$) I/P ratios.
Conclusion: In conclusion, T cell infiltration into primary melanoma is a strong predictor of survival after DC vaccination in metastatic melanoma patients. The infiltration remains predictive even after adjustment for late-stage prognostic markers. Our findings suggest that the I/P ratio is a potential predictive biomarker for treatment selection.

OFP-15-011
Association between a synonymous EGFR polymorphism and EGFR expression in non melanoma skin cancer
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Objective: In non melanoma skin cancer (NMSC), as in several tumours, the epidermal growth factor receptor (EGFR) has been established as an important therapeutic target. However, the benefit from EGFR inhibitors appears to be limited to a subset of patients. It has been recently demonstrated that EGFR single nucleotide polymorphisms (SNP) are significantly associated with increased EGFR copy number and therapies response. Therefore, we aimed to evaluate genetic variations impact on EGFR expression in NMSC patients.
Method: This study enrolled 12 patients with NMSC subdivided in two groups according to EGFR gene polymorphism rs 1050171 mutation: six heterozygous for the mutation (G/A) and six homozygous for the mutation (A/A). The expression of EGFR protein was investigated by immunohistochemistry on formalin fixed paraffin embedded sections using monoclonal antibody (NCL-EGFR-384, Novocastra). Scoring took into account the percentage of stained tumour cells and the staining intensity.
Results: The results showed that all sections had membranous staining. Over expression of EGFR was found in all patients with GA genotype and in 3 of 6 patients with AA genotype.

Conclusion: This observation suggests that a simple SNP analysis might result in a an improvement in the selection of patients amenable to anti-EGFR therapy. Further studies are necessary to validate our findings in larger cohorts.

OFP-15-012

A clinicopathological features and treatment outcome of cutaneous polyarteritis nodosa in Thailand

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Objective: To evaluate clinicopathological features and treatment outcome of cutaneous polyarteritis nodosa (cPAN).
Method: Twenty-five cases of cPAN were retrospectively reviewed of clinical presentation and treatment outcome. Histopathologic finding were evaluated by consensus of two dermatopathologists.
Results: Seven men and 18 women were included with the average age of 34 years (14–52 years). Majority of cases presented with multiple nodules on both legs (92 %). Antinuclear antibody (ANA) was detected in 4 cases (4 %) and none of the cases showed systemic autoimmune/connective diseases. Histopathologically, detection of internal elastic lamina using Verhoeff-Van Gieson (VVG) elastic stain was the most common key features found in our study (68 %) followed by fibrinoid necrosis of muscular walls (56 %) and small-vessel vasculitis (32 %). Concentric continuous smooth muscle pattern was the supportive feature for diagnosis of arterial involvement in cPAN, however; we found one case of discontinuous wreath pattern of muscular wall despite the present of internal elastic lamina. Most cases were treated with oral anti-inflammatory agent as colchicine (81 %), NSAIDs (68 %) and prednisolone (36 %). None of the cases developed systemic PAN. Fifty-six percent of cases showed clinical improvement during follow-up period.
Conclusion: Cutaneous polyarteritis nodosa shows benign clinical course with favorable treatment outcome. The presence of vasculitis involving medium-sized arteries remains the key feature for histological diagnosis of this entity.

Poster Sessions

Monday, 26 September 2016, 09.30–10.30, Hall 11.3
PS-01 Breast Pathology

PS-01-001

Role of Galectin-3 in breast carcinoma chemoresistance

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Objective: Breast carcinoma is the most common malignant neoplasm and the second cause of cancer death in women worldwide. Galectin-3 is a member of the beta-galactoside-binding family that plays a role in cell proliferation, adhesion, and migration. A prospective study was done to determine the role of galectin-3 in breast cancer chemoresistance with the aim of establishing galectin-3 expression as a biomarker for drug resistance.
Method: In total, 75 cases of breast carcinoma treated with neo-adjuvant therapy were collected and tissue samples from pre-neo-adjuvant therapy as well as tissues from post-neo-adjuvant therapy of those cases were collected and stained with immunohistochemistry.
Results: Almost one quarter of the cases show complete pathological response with complete disappearance of the tumour following neoadjuvant therapy, while three quarters of the cases show incomplete pathological response. Approximately, 70 % of cases with complete response show no expression of galectin -3 in breast cancer cells in pre-neo-adjuvant biopsies and 61 % of residual cancer cells show high expression of galectin-3.
Conclusion: There is a significant correlation between the expression of Galectin-3 by breast carcinoma cells and resistance to chemotherapy.

PS-01-002

Clinicopathological profile and receptor status in breast carcinoma: Single institutional North Indian experience

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Objective: To evaluate the clinicopathological prognostic parameters and correlate them with estrogen receptor (ER), progesterone receptor (PR) and Her 2neu receptor status in females diagnosed with breast cancer. Breast cancer incidence has increased in India, but the prognosis is still poor with high mortality. Majority of the patients present at higher stage, possibly due to inadequate awareness and screening programmes. The analysis of receptor status is still not being done in all cases especially the cases being diagnosed and treated at periphery. We aim to present the Indian breast cancer scenario emphasizing upon the importance of receptor status evaluation in all cases.
Method: The 3 year study (2012–2015) included all cases of breast cancer diagnosed on histopathology in department of pathology of our medical college & hospital, situated in North India and catering to the urban, sub-urban as well as rural population. The clinicopathological data of all cases was collected. Receptor status for ER, PR and Her 2neu was done using immunohistochemistry.
Results: Breast carcinoma in our population presented at a younger age then western countries. Invasive ductal carcinoma- Not otherwise specified, grade III and triple negative (ER-, PR-, Her 2neu-) were the commonest histological type, grade and receptor status respectively.
Conclusion: The breast carcinoma profile in north indian population has a histologically aggressive phenotype with possible lower responsiveness to conventional hormonal and targeted antibody treatment. However, there is a need for receptor analysis in all cases so as to identify the cases with better therapeutic response.

PS-01-003

Analysis of BMI and the molecular profile of the primary tumour in patients with invasive Breast Carcinomas (BC)

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Objective: The aim of this study is to assess the association between patient's BMI and molecular profile of the primary invasive BC.
Method: We retrospectively reviewed the invasive BC (2012–2015). Molecular profile included the assessment of the ER, PR, Ki 67 and HER2 status. Patients were divided into normal weight (NW), overweight (OW) and obesity (OB) group based on the WHO criteria.
Results: 173 consecutive patients: 55 (31.79 %) NW, 60 (34.68 %) OW and 58 (33.52 %) OB. Out of the 173 cases, 58 were Luminal A-type (51.72 % OW and 27.58 % OB), 66 were Luminal B-Her 2 negative-type (28.78 % OW and 36.36 % OB), 21 were of Luminal B-Her2 positive-type (23.8 % OW and 42.85 % OB), 5 were of Her2 positive-type (none in the OW group and 20 % OB) and 23 were of triple negative-type (26.08 OW and 34.78 OB). OW/OB patients presented significantly higher ER expression (but NSS) and OW were more likely of Luminal A-type of breast cancer ($p = 0.035$), while NW patients were more frequently of Luminal B-Her2 negative-type.
Conclusion: In contrast to previous studies, in our series the OW groups was strongly associated with Luminal A-type of tumours, while OW/OB patients were ER-positive, which might have a better prognosis, with good response to anti-hormonal treatment.

PS-01-004

Androgen Receptor (AR) expression in invasive Male Breast Carcinoma (MBC): An international multi-institutional review of 168 cases

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Objective: This study aims to evaluate the expression of AR in invasive MBC in correlation with clinical-pathological parameters and molecular biomarkers in order to identify the potential use of AR as a therapeutical target.
Method: 168 cases (1999–2015) were identified and prevalence of AR positivity was assessed in correlation with: age, clinical and pathological stage, histological tumour type and grade, molecular biomarkers (ER, PR, Ki67, HER2).
Results: Mean age of patients was 62 (range: 30–85). Most of the cases were of NST histological type (83 %), G2 histological grade (52 %), Luminal B molecular subtype (52 %) and T2N2M0 stage (75 %). AR was the most frequently expressed among molecular biomarkers with positivity in 94 %, followed by ER 91 %, PR 86,3 %, HER2 11.3 % of cases. A high Ki-67 proliferation index was present in 67 % of cases. Out of the 168 tumours evaluated 5 (2,9 %) were TN (ER-, PR-. HER2-), 3 (1.7 %) were QN (ER-, PR-, AR-, HER2-), while 135 (80 %) were + for ER, PR, AR, 13 (7.7 %) were QP (ER+, PR+, AR+, HER2+) and 22 cases (13 %) were TP (ER+, PR+, HER2+). All TN cases were AR positive.
Conclusion: We strongly support the routine assessment of AR in all MBC as they may benefit from anti-androgen therapy.

PS-01-005

Is radiation essential to breast conserving therapy? Twelve year follow-up results with a systematic shaved margin assessment

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Objective: The aim of this cohort study is to demonstrate that true local recurrence is rare even though radiation is omitted, if a systematic assessment of the tangential shaved margins guarantees complete removal of carcinoma.
Method: A precision method of margin assessment was developed for wide local excision using an adjustable mold to prevent the three dimensional specimen from distorting during fixation. We prospectively studied consecutive 108 wide local excisions of breast carcinomas (Stage 0 = 13, Stage I = 56, Stage IIA = 29, Stage IIB = 8, Stage IIIA = 2) examined by this method during a 2-year period between June 2003 and May 2005.
Results: Cases with negative shaved margin (Group A, n = 80, 74.1 %) were followed up without radiation treatment; those with positive shaved margin (Group B, n = 28, 25.9 %) were treated with a combination of various treatments including surgery, radiation and pharmacotherapy. To date 5 cases (4 %) of Group A and 6 cases (21.3 %) of Group B developed ILR (log-rank test, $p < 0.01$). Based on the histopathologic, topological and molecular analysis, 4 ILR cases of Group A were considered as new primary breast carcinomas and one patient with ILR of Group A was considered due to lymphatic spread. All 6 ILR cases of Group B were true recurrences from remaining carcinoma. With regard to distant metastasis (cancer-related death), Group A developed 4 (2) and Group B 2 (1) such cases, respectively (the difference not statistically significant).
Conclusion: The patients showed very much lower recurrence rates after breast conservation surgery alone without radiation therapy if the negative margin is assured by a systematic and precision margin assessment.

PS-01-006

Immunohistochemical profile of male breast cancer in Nigerians

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Objective: There are no known published literature on the immunohistochemical profile of male breast cancer in Nigerians. This objective of this pilot study was to characterise the histologic and immunohistochemical profile of male breast cancer (MBC) seen over a 10-year period in a Nigerian tertiary healthcare institution.
Method: The formalin fixed, paraffin embedded MBC tissue received between 2003 and 2013 were retrieved and stained with routine Hematoxylin and Eosin (H&E). Subsequently Oestrogen receptor (ER), Progesterone receptor (PR) and HER2 immunohistochemistry was done. The immunohistochemistry stains were interpreted using the Allred score.
Results: There were 25 cases of MBC diagnosed between 2003 and 2013. This comprised 1.6 % of the total number of breast cancer diagnosis in the institution during this period. Eighteen blocks were suitable for analysis. Age ranged from 44 to 78 years with peak incidence between 61 and 70 years. 16 (88.9 %) of the cases were invasive ductal carcinoma (not otherwise specified), with one case each of intracystic papillary carcinoma and mucinous carcinoma. 17 (94.4 %) cases were positive for ER and negative for PR, 16(88.9 %) cases were positive for ER and PR, while all the cases were HER2 negative. There was a solitary case of triple negative carcinoma.
Conclusion: MBCs in African men are largely hormone receptor positive and will benefit from hormonal therapy. Triple negative phenotypes are not as prevalent as those seen in Nigerian female breast cancers.

PS-01-007

Apocrine carcinoma as triple-negative breast cancer: Novel definition of apocrine-type carcinoma as estrogen / progesterone receptor-negative and androgen receptor-positive invasive ductal carcinoma

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Objective: Apocrine breast carcinoma expresses androgen receptor, but often lacks estrogen receptor and progesterone receptor. In this study, the authors analyzed the significance of apocrine-type carcinoma as triple-negative breast cancer.
Method: We collected 38 triple-negative invasive ductal carcinomas from 420 cases of breast cancers sampled in the period from January 2008 and December 2011. There 38 carcinomas, using tissue microarrays, were immunostained for androgen receptor, CK5/6, EGFR, C-kit, p53 and Ki-67.
Results: Invasive ductal carcinomas in the triple-negative breast cancer (TNBC) (n = 38) were divided into androgen receptor-positive (apocrine-type carcinoma, n = 3, 13 %) and quadruple-negative (non-apocrine-type carcinoma, n = 35, 87 %). Basal-like phenotype was observed in apocrine-type (2/3 = 66 %) and in non-apocrine-type (26/35 = 74 %). P53 overexpression was more often seen in the apocrine-type TNBC (3/3 = 100 %) than in non-apocrine-type TNBC (27/35 = 77 %). Ki-67 labeling was higher in the non-apocrine-type (15/35 = 42 %) than in the apocrine-type (1/33 = 33 %).
Conclusion: Androgen receptor should be added to immunohistochemical panels, since apocrine-type invasive ductal carcinoma, resembling basal-like phenotype, should be distinguished from the basal-like TNBC because of their favorable prognosis.

PS-01-008

Breast infiltration by haematological malignancie: Report of four cases

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Objective: Breast haematological malignancies (BHM) are rare. Most lymphomas involving the breast are of B-cell lineage, T-cell phenotype is rare. Breast multiple myeloma is exceptional. Our aim is to highlight the clinical and the pathological features of this rare entity.
Method: We report four cases of BHM occurring in four women, in the period from 2003 to 2015.
Results: Mean age of patients was 54 years (range 36–80 years). One among the four women was known to have chronic lymphocytic leukemia treated with chemotherapy; the second woman was known to have T-cell lymphoma involving lymph nodes and pancreas while the two other cases had no previous medical history. Clinical presentation was a unilateral breast mass in three cases with an inflammatory skin appearance in one case; in the fourth case, the patient presented with swelling and hardening of her both breasts. Histological and immunohistochemical examination revealed breast involvement with diffuse large B-cell lymphoma in two cases; T-cell lymphoma and multiple myeloma in the other cases.
Conclusion: BHM demonstrate a variable clinical presentation and radiological features similar to those of carcinoma. Diagnosis is based on histological and immunohistochemical findings. Treatment includes chemotherapy and radiation. Prognosis is dependent on histological type and staging of the disease.

PS-01-009
Triple negative invasive breast carcinomas with comedo necrosis have a better prognosis than the majority of other triple negative tumours

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Objective: Triple negative invasive breast carcinomas are a group of tumours with different microscopic appearances. A characteristic microscopic feature of a sub-group of these tumours is the presence of comedo-type necrosis. This study aimed at comparing the demographic features and prognosis of this subgroup of tumours with the rest of triple negative carcinomas.
Method: The study included 65 triple negative invasive breast carcinomas which were divided into 2 groups: those with comedo necrosis (23) and those without (42). Cases were compared as regards the immunohistochemical expression of cytokeratin (CK) 5, CD10, Maspin and Claudin 1, 3 and 4, as well as patients' ages, size of tumours, axillary lymph node status and incidence of recurrences.
Results: There was no statistically significant difference as regards age, tumours size or the expression of CK 5, CD10, Maspin or Claudin 3 and 4. Claudin 1 was significantly less expressed in tumours with comedo necrosis (13 vs 26 % for tumours with no comedo necrosis) and also showed a significantly less incidence of axillary lymph node metastasis (13 vs 52 %) and recurrences (14 vs 27 %).
Conclusion: Triple negative invasive breast carcinomas with comedo necrosis have a better prognosis than the majority of other triple negative tumours.

PS-01-011
Assessment of discordance of immunohistochemistry and in SITU hybridization HER2 testing results in breast cancer specimens: A regional slide-exchange ring study

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Objective: A regional slide-exchange ring study with four testing rounds was designed in order to assess immunohistochemistry (IHC) and in situ hybridization (ISH) interlaboratory consensus of HER2-testing in breast cancer among four experienced testing centers.
Method: In each round, one center selected and sent to the other centers two specimen sets (one for IHC, and one for ISH) consisting of four breast cancers. Institutions could participate irrespective of the staining methods, protocols, and antibodies used for IHC or ISH testing of HER2 status. Results were analyzed by an independent coordinator.
Results: After the IHC testing complete consensus among the four institutions was achieved for 7 (43.8 %) of the 16 specimens. Retesting by ISH of the 8 specimens scored as equivocal by at least one laboratory, increased the concordance rate to 68.8 % (11/16), while a diagnostic discordance was found in two cases. A complete concordance between testing centers for ISH was found for 9 (56.3 %) of the 16 specimens. The group of discordant findings consisted of 4 cases having borderline HER2-positivity determined by at least one center, and one case with diagnostic discordance.
Conclusion: The current regional ring study in which the level of consensus among the testing centers for HER2 testing by both IHC and ISH was similar to already reported in previous studies, in spite of the unstandardized conditions, highlights the usefulness of implementing such slide-exchange programs as an additional instrument for external quality control.

PS-01-013
TTF-1 expressing primary Small Cell Carcinoma (SCC) of the breast, present initially as a lymph node metastasis

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Objective: Thyroid transcription factor 1 (TTF-1) 1 expression in breast small cell carcinoma has been reported only rarely. This reported case is unique because of the first diagnosed in the axillary lymph node metastasis of unknown primary.
Method: A 60-year old women presented with a palpable mass in the right axillary region. A PET/CT Scan revealed a markedly FDG avid right axillary lymph nodes. PET/CT Scan showed no other malignancy other than axillary lymph nodes. As no origin for the tumour was found, a lymph node biopsy was performed.
Results: Microscopic investigation showed typical appearance of a small cell carcinoma with sheeds, irregular nests and trabeculae of small to medium sized cells with minimal cytoplasm, hyperchromatic nuclei, and inconspicuous nucleoli. By immunohistrochemistry the invasive carcinoma cells were positive for neuroendocrine markers: synaptophysin and CD56, were positive for TTF-1, E-cadherin, CK5/6. The carcinoma cells were positive for estrogen receptor, but negative for progesterone receptor, GCDPF-15, HER2/neu. As a result, the initial investigations of the biopsy gave suspicion of metastasis from breast cancer. The patient underwent a right radical mastectomy. In the upper iner quadrant there was multple firm irregularly shaped small nodules with largest diammeter 15 mm. Sixteen axillary lymph nodes examined were all involved by metastatic tumour.
Conclusion: We report a case of primary small cell carcinoma of the breast with coexisting carcinoma in situ in which the invasive and in situ component both showed a diffuse and strong positive reaction to TTF-1 and neuroendocrine markers.

PS-01-014
Lysyl oxidase (LOX) contribute to formation of intratumoural fibrotic focus (FF) by inflammation in invasive breast cancer

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Objective: LOX is an ECM enzyme that catalyzes the cross-linking of collagens. LOXs are related to tumour fibrosis and progression. FF was associated with poor prognosis in breast cancer. Inflammation precedes fibrosis and is related to tumourigenesis. Our hypothesis is that LOXs

contribute to the formation of FF, which is related to inflammation, and play a significant role in breast carcinogenesis.
Method: 291 invasive breast cancer TMAs were stained for LOX, LOX-like (LOXL)-1, -2 and -3. The FF, intratumoural (IT) and peritumoural (PT) lymphocytic infiltration were assessed. The clinicopathologic characteristics were evaluated from the medical records.
Results: The percentage of FF was 37.5 % and LOX was 49.1 %. LOXs were not associated with FF. FF was associated with IT and PT, stage, LN metastasis, high grade, larger size, and OSR. LOX was associated with IT and PT. LOXL-3 was associated with ER, PR, and molecular subtype. LOXL-1 and -2 show no correlation with clinicopathologic parameters.
Conclusion: FF and LOXs were associated with inflammation in breast cancer. However, there was no association between FF and LOXs. FF was associated with poor prognostic markers of breast cancer. Our results suggest that LOXs may contribute to the formation of a FF indirectly by inflammation in breast cancer.

PS-01-015
The diagnostic utility of cell block in fine needle aspiration cytology of palpable breast lesions in a Nigerian tertiary hospital
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Objective: The objective of this study was to determine the diagnostic utility of cell block preparations in FNAC of palpable breast lesions among female patients in Lagos University Teaching Hospital, Lagos, Nigeria.
Method: Cell blocks were prepared using 10 % neutral buffered formalin from the residual breast aspirates of 100 consecutive female patients attending the FNAC clinic of the Lagos University Teaching Hospital, Nigeria. The slides of the conventional smears, cell block preparations and excisional biopsies were examined and results were analysed using the Statistical Package for Social Sciences, version 20 (SPSS20).
Results: Cell block preparations had lesser equivocal cases. In all, a definitive diagnosis was achieved in 76 % of cases on conventional smears and 84 % of cases on cell blocks. Of the 100 patients that had FNAC, 44 (44 %) had excisional biopsy performed. All cases that were benign on cell block were confirmed to be benign on histology as compared to 95.2 % of cases on conventional smears. There is increased cellularity and additional yield of 13 % for malignancy on cell block, with the preservation of cellular architecture pattern even with excessive blood. Cell block preparations enhanced the sensitivity, specificity, positive and negative predictive values of breast FNAC from 76.5 to 100 %, 91.7 to 100 %, 86.7 to 100 % and 91.6 to 100 % respectively.
Conclusion: Cell block preparations remarkably improve the diagnostic accuracy of breast FNAC. We recommend that cell block techniques be incorporated in routine breast cytology examinations.

PS-01-016
Expression patterns of GATA3 and the androgen receptor are strongly correlated in patients with triple-negative breast cancer
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Objective: GATA3 is a diagnostically useful immunohistochemical marker of breast cancer, however, which has markedly reduced sensitivity in triple-negative breast cancer (TNBC). We evaluated GATA3 expression by TNBC subtype as defined by surrogate immunohistochemical markers.
Method: We constructed a tissue microarray using a large series of TNBCs. A total of 205 TNBCs were classified into 23 molecular apocrine types, 21 claudin-low types, 91 basal-like types, 62 mixed types, and 8 null types. The GATA3 scores (staining intensity × proportion) were categorized as negative (0), focally positive (1–10), or positive (11–300).
Results: The rate of focal positivity or positivity for GATA3 was significantly higher in the molecular apocrine type (73.9 %, 17/23) than in other types of TNBCs ($p = 0.001$). The mean GATA3 score of molecular apocrine type TNBC was significantly higher than that of the other types ($p = 0.001$) and differed significantly between AR- positive and -negative TNBCs ($p < 0.001$).
Conclusion: In conclusion, GATA3 expression was correlated strongly with AR- positive, molecular apocrine type TNBCs. Co-expression of AR and GATA3 is a specific feature of molecular apocrine type TNBC, which may serve as a diagnostic aid for cancer of unknown primary.

PS-01-017
Bilateral breast fibromatosis in context of classic familiar adenomatous polyposis and breast implants: Case report
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Objective: Breast fibromatosis is a benign fibroblastic proliferation accounting for 0.2 % of breast tumours. It presents sporadically, with breast implants representing a risk factor or as a manifestation of familial adenomatous polyposis (FAP). Fibromatosis in FAP may develop in patients with APC mutations anywhere through the gene, with an increased risk downstream codon 1400.
Method: We report a case of a 33 years old woman, with bilateral breast fibromatosis after breast implants, in a context of classic FAP.
Results: APC mutation (codon-935) was detected at 16 years of age. In the same year, a thyroidectomy for papillary carcinoma (pT1) was performed. Seven years later, a prophylactic total colectomy revealed more than 100 adenomas. At the age of 30 years she performed breast silicone implantation and, 1 year after, breast bilateral tumours were diagnosed in core biopsy as fibromatosis (nuclear β-catenin+, estrogen receptors-). Bilateral mastectomy was performed and fibromatosis relapsed in the right thoracic wall 1 year later.
Conclusion: This rare case illustrates a bilateral relapsed breast fibromatosis, very likely related to surgery and continuous implant trauma, in a FAP context. The increased risk of developing fibromatosis in patients with FAP should be considered in the decision to place breast implants.

PS-01-018
St. Gallen 2013 Consensus for molecular subtyping of breast carcinomas: Can pathologists (still) help to predict complete response to neoadjuvancy?
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Objective: Molecular classification is revolutionizing diagnosis and management of breast cancer. Our objective was to establish the correlation between the St. Gallen Consensus surrogate molecular classification of breast carcinomas and response to neoadjuvancy.
Method: Ninety four infiltrating breast carcinomas were immunohistochemically analyzed for the expression of hormone receptors, Her2 and ki67 and classified according to the 2013 St. Gallen guidelines (luminal A-B, Her2-enriched, basal-like). Neoadjuvancy consisted in hormone therapy for luminal A, taxanes +/− anthracyclin for luminal B, anthracycline+taxanes+Trastuzumab for Her2+ and anthracycline+taxanes for basal-like. Complete pathological response (CPR) was considered when no residual infiltrating carcinoma was detected.
Results: Forty cases (42 %) showed CPR and this occurred more frequently in Her2+ and basal-like carcinomas (11/17 = 64 %; 19/28 = 67 % respectively, Chi- square, $p < 0.00003$) and this significance increased

when luminal cases were grouped and compared with the rest: CPR in 10/49 (20 %) vs 30/45 (66 %) (Fisher's test, $p = 0.000008$). Moreover, Luminal B cases responded significantly more than Luminal A (28 % vs 0 %, Chi-square, $p < 0.05$).
Conclusion: Surrogate molecular subtyping correlates with response to neoadjuvancy, with less frequent CPR in luminal cancers, being useful as a predictive parameter and it is readily available in most institutions.

PS-01-019
Pathological complete response after cisplatin neoadjuvant therapy is associated with the downregulation of DNA repair genes in BRCA1-associated triple-negative breast cancers
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Objective: Pathologic complete response (pCR) after neoadjuvant chemotherapy is considered a suitable surrogate marker of treatment efficacy in patients with triple-negative breast cancers (TNBCs). However, the molecular mechanisms underlying pCR vs. pathological partial response (pPR) as a result of such treatment remain obscure.
Method: Using real-time PCR arrays, the expression levels of 120 genes involved in the main mechanisms of DNA damage repair were identified in pretreatment biopsies.
Results: Altogether, 25 genes were significantly differentially expressed between tumours exhibiting pCR and pPR, and these genes were downregulated in the pCR group compared to the pPR group. The NHEJ and NER pathways of DNA repair showed the most significant relevance. Expression profile of DNA repair genes associated with pCR was different in the node-positive and node-negative subgroups. PARP1 and PARP3 were upregulated in the node-positive subgroup with pPR.
Conclusion: Although BRCA1 germline mutations are the principal defects in BRCA1-associated TNBC, our results indicate that the additional downregulation of other genes engaged in major pathways of DNA repair may play a decisive role in the pathological response to cisplatin neo-chemotherapy. The results suggest that patients with node-positive BRCA1-associated TNBCs that do not exhibit pCR after cisplatin neoadjuvant chemotherapy may be candidates for subsequent therapy with PARP inhibitors.

PS-01-020
Triple negative breast carcinoma arising in Microglandular Adenosis (MGA)
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Objective: Microglandular adenosis (MGA) is a rare but important entity, which mimics well-differentiated carcinoma clinically and pathologically and carries a strong association with malignancy.
Method: A 65-year-old woman presented with a palpable S4 mass in the left breast, with a corresponding mammographic density. Ultrasonography revealed an ill-defined area with variable echogenicity(BIRADS 4).
Results: Core needle biopsy showed tubular glands lined by single layer of cells, lacking a myoepithelial cell layer, embedded in sclerotic stroma. ER and PR were negative. S100 was positive. The differential diagnosis included tubular carcinoma and MGA and on the basis of absent hormone receptor expression and S100 positivity, the latter was favoured. Subsequent wide local excision showed a 4 cm mass, demonstrating a spectrum of MGA and atypical MGA, merging with invasive carcinoma. Centrally, a 2 cm area showed unequivocal features of invasive ductal carcinoma grade 2, negative for ER, PR, Her2, CK5/6 and CK14 while positive for S100, Actin, AE1/3 and p53(weak). The sentinel node was negative for metastasis. Margins were extensively involved, necessitating subsequent mastectomy. The patient underwent systemic chemotherapy and remains well 3 years later.
Conclusion: Carcinoma arising in MGA appears to have a relatively favourable prognosis, despite often showing high grade features and a triple negative phenotype.

PS-01-021
Significance of cancer stem cell markers in mammary phyllodes tumour
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Objective: We determined immunohistochemical expression of cancer stem cells markers that influence the clinical outcome of phyllodes tumour of the breast.
Method: We retrospectively collected surgically treated phyllodes tumours from two institutions. We constructed tissue microarrays for immunohistochemical staining for CD44HIGHCD24-/LOW, GD2, and ALDH1. We analyzed the immunoreactivity that influenced clinical outcomes.
Results: A total of 190 phyllodes tumours were enrolled. The cancer stem cell markers were expressed in phyllodes tumour (3.2 to 11.1 %), and they were not significantly associated with tumour grade. Subsequent recurrence were occurred in 29 phyllodes tumours, and it was not significantly associated with cancer stem cell markers. CD44HIGHCD24-/LOW was the independent factors associated with recurrence-free interval in recurrent phyllodes tumour with previous history by univariate analysis, however not in the multivariate analysis. Metastasis and death were developed in only one patient, and her two phyllodes tumours was positive for CD44HIGHCD24-/LOW and tended to have higher grade ($p = 0.004$), more stromal overgrowth ($p = 0.018$), more mitotic count ($p = 0.002$), more CD44HIGHCD24-/LOW phenotype ($p = 0.012$) by Chi-square test for trend.
Conclusion: In this study, CD44HIGHCD24-/LOW immunoreaction were significant for clinical outcome of phyllodes tumour in particular clinical settings.

PS-01-022
Gene-protein assay for assessing breast cancer HER2 status
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Objective: The novel gene-protein assay (GPA) allows simultaneous demonstration of protein expression and gene status in a single slide combining immunohistochemistry (IHC) with dual bright-field in situ hybridization (ISH) technique.
Method: We reviewed recent publications dealing with validation of the GPA method and compared the results with the experience of one of our centers.
Results: The GPA results were concordant with fluorescence ISH results in 96.2 and 98 %, with chromogen ISH in 100 % and with silver ISH in 96 %, while the concordance with IHC alone was lower. In IHC2+ cases, the concordance between GPA and fluorescence ISH was 82 %. A TMA study including 589 cases found 95 % of IHC 3+, 60 % of 2+ and 0.6 % of 0/1+ cases being amplified in GPA slides. GPA used as diagnostic routine on whole slides generated similar results: 94 % (47/50) of the IHC3+ cases and 0.4 % (2/498) of the IHC0/1+ cases were amplified and the number of equivocal cases was low 1 % (6/567).
Conclusion: GPA is an elegant method of assessing HER2 status in breast carcinomas, with reliability equal to the other more established IHC and ISH techniques and with the advantage of a direct cell-to-cell comparison of protein expression and gene amplification status.

PS-01-023
Expression of p40 in different molecular subtypes of breast cancer and in metaplastic breast carcinomas
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Objective: p63 is used as an immunohistochemical marker of squamous, myoepithelial, prostate basal and urothelial cells in histopathology practice. p40 is reported to be superior to p63 as a squamous carcinoma marker in the differential diagnosis of lung cancer, and equal to p63 as a myoepithelial marker in breast lesions. We investigated the p40 expression of breast cancer tumour cells in molecular subtypes, and in metaplastic breast cancer subtypes reported to express p63 frequently.
Method: Breast carcinomas of each surrogate immunohistochemistry classified molecular subtypes and 20 metaplastic breast carcinomas were retrospectively evaluated for p40 expression by immunohistochemistry using a monoclonal antibody.
Results: p40 expression was detected in 5/37(14 %) of luminal A-like, 5/30(17 %) of luminal B-like, 7/33(21 %) of HER2-enriched and 40/52(76 %) of triple-negative cytokeratin 5 expressing carcinomas corresponding to basal-like breast cancer (BLBC). Positivity was weak and focal in all molecular subtypes. p40 expression in metaplastic breast cancer is less frequent (5/20;25 %), weaker and focal compared to p63 (9/20;45 %).
Conclusion: These results suggest that p40 expression is rare and focal in breast cancer cells, with BLBC being the most frequently positive. p40 is not an ideal BLBC marker. p40 is less sensitive marker of metaplastic squamous cell and spindle cell breast cancer compared to p63.

PS-01-027
Expression of microRNAs in molecular breast cancer subtypes
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Objective: The aim of the study was to determine differences in miRNAs expression levels of invasive breast carcinoma (BC) and normal tissue, as well as to analyze the variable of miRNAs expression in different BC molecular subtypes.
Method: We determined differences in mRNA expression in 35 tumour tissue biopsies and 35 biopsies of adjacent conventionally normal breast tissue by RT-PCR. Molecular subtype of BC was defined by IHC. We assessed the expression levels of miRNA-21, 221, 222, 155, 205, 20a, 125b and 200a.
Results: A significant increase in oncogenic miRNA-20a ($p < 0.0001$) and miRNA-221 ($p = 0.038$) expression levels in triple negative cancer in comparison to luminal A and luminal B HER2-negative BC subtypes was established. Assessment of the results significance was conducted using ROC analysis. For miRNA-221 AUC value was 0.772, for miRNA-20a—0.949.
Conclusion: The obtained results suggest the possibility of using the levels of miRNA-21, 155, 205, 125b expression in tumour tissue in order to assess a malignant potential of BC. The levels of oncogenic miRNA-221 and miRNA-20a expression are increased in TNBC compared to luminal A and luminal B HER2 -negative breast cancer subtypes.

PS-01-029
Breast cancer in young women: Data from the Epirus region of Greece
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Objective: The aim of the present study was the identification of the special clinicopathological characteristics (if present) of infiltrative breast carcinomas arising in women younger than 40-years-old.
Method: We thoroughly searched the electronic archival files of our Pathology laboratory, during the years 2007–2015 and downloaded all pathology reports of women younger than 40-years-old, who were diagnosed with breast cancer. In addition, we recorded the total number of pathology reports each year for breast cancer in women, irrespective of age.
Results: We found in total 104 breast cancer patients younger than 40-years of age, with mean age 35 years (range 20–40 year), three of which were pregnant at that time. Most carcinomas were invasive NST (86.5 %). The majority was grade 3 (47.5 %), 43.5 % were grade 2 and 9 % were grade 1. Ten of the carcinomas (9.6 %) were multifocal. The mean diameter was 2.8 cm (0.2–13 cm). Lymph node metastases were diagnosed in 58.2 % of patients. Ten of the carcinomas (9.6 %) were triple negative (ER-,PR-,HER2/neu-), while in 18 (17.3 %) there was overexpression of HER2/neu. Breast carcinomas on young women comprised yearly approximately 5–8.5 % of total breast carcinomas diagnosed in the Department of Pathology of the University Hospital of Ioannina, during the years 2007–2015, without increasing trend.
Conclusion: Breast cancer in young women attracts much attention, but does not differ substantially from carcinomas arising in older patients. In addition, at least in the area of Epirus, Greece, there is no recorded increase in incidence during recent years.

PS-01-030
The expression and significance of Ki-67 in the primary tumour and lymph nodes metastases in breast cancer patients
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Objective: To identify correlations between proliferation activity of tumour/metastatic lymph nodes and clinicopathologic features of breast cancer (BC).
Method: The analysis of clinical, pathological and immunohistochemical data of 30 patients with breast cancer with clinical stage T1-2N1-3M0 was performed. Ki-67 was determined in primary BC and metastatic lymph nodes by IHC using MIB-1 antibody. Integral pathological indices—Nottingham Prognostic Index (NPI) and Integrated Pathological Prognostic Index (IPPI)—were assessed. IPPI is the sum of micromorphological tumour parameters and can range from 6 to 20 points.
Results: The number of involved lymph nodes ranged from 1 to 14 (mean 3.77 ± 3.14). Mean of Ki67 expression level in primary tumour site was 16.93 ± 11.76 % (6÷53), in lymph node metastases—15.80 ± 9.68 % (4÷37). A statistically significant correlation was found between tumour grade and Ki-67 in primary BC ($p = 0.015$), but no such relationship was found in regional metastases ($p > 0.05$). There were no significant correlations between Ki-67 in primary BC and lymph node metastasis with the number of lymph nodes involved, HR expression levels, Her2-status, histological subtypes, patients' age ($p > 0.05$). There was a significant correlation between Ki67 level in lymph node metastases with IPPI and NPI ($p = 0{,}012$ и $p = 0{,}038$, respectively), unlike Ki67 in primary BC. It was also shown that Ki-67 index in lymph node metastasis is significantly higher in case of NPPI values ≥16 ($p < 0.05$).
Conclusion: Ki-67 in the regional metastases has more important prognostic value than in the primary BC lesion.

PS-01-031
Regulation of H-ras expression and caspase-3 apoptotic cell death in breast cancer epithelial MCF-7 cells by cadmium
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Objective: Identify the molecular pathway used by carcinogenic cadmium in tumour propagation through H-ras signaling in breast cancer.
Method: The effect of cadmium metal ion (Cd(II)) was investigated, in a concentration-dependent fashion, on cell viability, cell proliferation,caspase-3 mediated apoptosis and H-ras gene expression in human breast cancer epithelial MCF-7 cells transfected with the H-ras oncogene (wild type and G12V mutation).

Results: The findings show a significant modulation effect of cadmium on H-ras gene expression accompanied by up-regulation of caspase-3-related apoptosis in the concentration range of 100–1000 nM cadmium. Concurrently, there is a decrease in MCF-7 proliferation and up regulation in p21 protein expression.
Conclusion: Collectively, the results a) indicate an interplay of cadmium with H-ras (wt and G12V), with cadmium exhibiting a significant concentration-dependent effect on the modulation of H-ras expression, cell viability and proliferation, and b) project distinctly interwoven roles for both cadmium and H-ras in aberrant physiologies in cancer cells. As a consequence, ample insight is gained into the modulating interplay among cadmium, H-ras(wt)/H-ras(G12V) and cellular media in MCF-7 cells, that contribute considerably to our understanding of that metal ion's (bio)chemical potential toward tumourigenesis.

PS-01-032

Comparison of HER2 status determination methods: Fluorescent in Situ Hybridization (FISH) vs. dual silver enhanced in Situ Hybridization (SISH)

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Objective: HER2 amplification has been demonstrated in 15–25 % of invasive breast carcinomas and can be assessed using immunohistochemical and in situ hybridization methods. Here, we compared the accuracy of dual SISH to FISH in HER2 (2+) breast carcinoma and evaluated the feasibility of dual SISH method in routine practice.
Method: Sixty HER2 (2+) consecutive tumour samples diagnosed between January 2009 and February 2013 were selected. Demographic, histological and immunohistochemical features and FISH results were recruited from patient records and compared to dual SISH results.
Results: Nine (15 %) of 60 tumour samples were excluded from statistical analysis due to lack of interpretable SISH signals. HER2 staining percentages differed between 20 and 80 %. HER2 amplification was shown in 7 (13,7 %) and 8 (15,7 %) patients by FISH and SISH, respectively. Very good agreement was observed between FISH and SISH methods (kappa value: 0,92). Significant correlation was found between HER2 staining percentage and FISH positivity, in contrast to SISH positivity ($p = 0{,}012$ vs. $p = 0{,}069$).
Conclusion: Our results are consistent with previously reported literature, indicating SISH can be used to determine HER2 status. However, preanalytical problems may cause inadequate or uncountable signals, making interpretation impossible for the pathologist and highlighting the importance of standardization and quality control programs.

PS-01-034

Her2/neu expression in breast cancer patients who have a combination of low grade progesterone receptor with high grade estrogen receptor status

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Objective: The aim of the study was to establish correlation between Her2/neu status and the rate of expression progesterone and estrogen receptors.
Method: 136 patients with breast cancer who have been treated in the N.N. Blokhin Russian Cancer Research Center. The methods included ICH and FISH reaction (primary antibodies and detection system from DAKO and probe ON ERBB2, Her-2/Neu (17q12)/SE 17 (Kreatech)).
Results: The obtained results show that the Her2/neu amplification in 78 cases out of 136 (58 %) was associated with high level expression of estrogen reception and low level expression of progesterone receptors. In 23 cases (16 %) Her2/neu was not amplified but these patients showed polysomy of the chromosome 17. In 35 case (26 %) neither polysomy the chromosome 17, nor Her2/neu amplification were revealed.
Conclusion: The results of our study pursuit us to suppose that there is an inverse correlation between Her2/neu amplification and polysomy of the chromosome 17 with low level expression of progesterone receptors. These patients still show high level of estrogen receptors. Further study of the connetion between progesterone receptor and Her2/neu may lead to important correlations in the treatment of patients with breast carcinoma.

PS-01-035

Evidence for the association of Epstein - Barr virus in breast cancer in Indian patients using in-situ hybridization technique

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Objective: Epstein - Barr Virus (EBV) is etiologically linked to Burkitt lymphoma, nasopharyngeal carcinoma, post-transplant lymphomas, Hodgkin's disease, gastric carcinoma, etc. However, the association of oncogenic EBV with breast carcinoma (BC) is still controversial and a matter of debate. We aimed to study the presence of EBV genome in BC cases in Indian patients and its association with the clinicopathological features.
Method: Histologically proven 83 cases with primary invasive BC were studied for the presence of EBV by in-situ hybridization (ISH) technique using RISH Epstein Barr Encoded RNA (EBER) probe kit (Biocare, USA) with appropriate controls. Nuclear reactivity within the tumour cells was considered as positive result. Correlation of EBER-ISH positivity with clinicopathological features was performed using Fisher exact test and p value <0.05 was considered as significant.
Results: Eighty three BC cases were comprised of 47 (56.5 %) triple negative breast cancers (TNBC), 17 (20.5 %) hormone positive and 19 (22.9 %) HER2 positive cases. Frequency of EBER-ISH positivity was 30.1 % (25/83). EBER-ISH positivity was statistically associated with larger tumour size ($p = 0.014$) and with TNBCs ($p = 0.001$).
Conclusion: A possible causal association of EBV in BC cases in Indian patients is suggested by high frequency of EBER-ISH positivity noted in our study. This might have therapeutic significance because of the possible role of EBV specific cytotoxic T cells in targeting EBV associated tumour cells and can be considered as a potential targeted therapy.

PS-01-036

Microvascular proliferation is significantly associated with the HER2 positive, triple negative, and basal-like phenotypes in breast carcinoma

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Objective: Angiogenesis is important for tumour growth and metastasis. To quantify tumour angiogenesis, microvascular density (MVD) has been widely used. Here, we wanted to explore the prognostic significance of microvascular proliferation in a large series of breast carcinoma.
Method: A population-based cohort of 462 breast cancers was used as part of the prospective Norwegian Breast Cancer Screening Program (1996–2003). Microvascular proliferation was evaluated on full sections using dual immunohistochemical staining of Factor VIII and Ki-67 and estimated by vascular proliferation index (VPI); the ratio between the number of vessels containing proliferating endothelial cells and total number of tumour microvessels.
Results: High VPI was strongly associated with several aggressive features in breast cancer, such as high histologic grade ($P < 0.001$), negativity for estrogen and progesterone receptors ($P < 0.001$), positivity for HER2 status ($P < 0.001$), high tumour cell proliferation by Ki-67 ($P < 0.001$),

and a basal-like phenotype (P < 0.001). Among molecular subtypes, HER2 positive breast carcinomas showed the highest VPI (P < 0.001). High VPI was significantly associated with adverse outcome in univariate and multivariate survival analysis (P = 0.006, P = 0.004, respectively).
Conclusion: Microvascular proliferation is a novel marker of active angiogenesis and is highly associated with aggressive features in breast cancer.

PS-01-037
HER2/neu overexpressing Primary Breast Squamous cell Carcinoma: A case report of an
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Objective: Primary breast squamous cell carcinoma (B-SCC) is a subtype of metaplastic carcinoma and a rare (<0.1 % of all breast carcinomas) malignancy.
Nearly all B-SCC are "triple negative" for ER/PR receptors and HER2/neu and over-express high molecular weight cytokeratins:CK5/6,CK14,CK34βE12 and EGFR.
HER2/neu overexpressing B-SCC is extremely rare.
Method: An 89-year old woman presented with a right breast mass. Investigational CT showed no other lesions. Due to advanced age and co-morbidities a lumpectomy was performed.
Results: A circumscribed (10 × 8cm) friable grey tumour with little adjacent breast tissue and over-lying skin was received. Microscopically observed an intermediate-high grade invasive tumour composed entirely of squamous carcinoma cells. Stromal inflammation, abscesses, necrosis, perineural invasion and lymphovascular infiltration were observed also. Immunoprofile: CK5/6, CK14, CK34βE12, p63 and EGFR positivity. HER2/neu was evaluated, 3+ positive. Ki67: high ER/PR receptors: negative. Considering these findings and having ruled out other adjacent cutaneous or metastastic SCC, the diagnosis of HER2/neu overexpressing B-SCC was made. Four months post-operatively multiple lung, liver and lymph node metastasis were identified on CT.
Conclusion: HER2/neu overexpressing B-SCC is an extremely rare,aggressive, treatment refractory,frequently recurrent tumour with limited reports in the literature. Identification is important for appropriate patient management.

PS-01-038
Benign tumours of the breast in Kano, Northern Nigeria: A 10 year experience and review of literature
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Objective: Benign breast tumours are common worldwide and various reports suggest an increasing incidence in Nigeria which necessitates an urgent need to differentiate it from malignant tumours. The study was carried outto classify and determine the pattern, frequency, age and sex distribution of benign breast tumours seen in a tertiary hospital.
Method: This was a 10-year retrospective study of all benign breast tumours diagnosed at the pathology department of a teaching hospital from 1st January 2001 to 31st December 2010.
Results: A total of 1566 breast tumours were diagnosed during the study period, 1035 cases of benign breast tumours constituting 66.3 % of all breast tumours were seen. The female to male ratio was 72.9:1. The overall mean age for benign breast tumour was 29 years with a peak age occurrence in the third decade. Fibroadenoma was the commonest benign breast tumour followed by fibrocystic change and they accounted for 47.1 and 25.4 % of benign breast tumours with mean age of 24.7 and 33.4 years respectively. Fibroadenoma has a peak occurrence in the third decade while fibrocystic change has a peak occurrence in the fourth decade. Other major tumours encountered were tubular adenoma (6.0 %), lactating adenoma (5.6 %), benign phyllodes (4.8 %), sclerosing adenoma (3.3 %) and blunt duct adenoma (2.5 %). Gynaecomastia (1.4 %) was the only benign breast tumour seen in males.
Conclusion: Benign breast tumours are quite common, presenting mostly as fibroadenoma and fibrocystic change. The tumours are seen in both sexes with a striking female preponderance and occurred predominantly in young females with a peak in the third decade.

PS-01-039
Prevalence of different molecular subtypes of invasive breast cancer: Early experience in Armenia
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Objective: Classification of breast cancer into different molecular subtypes using immunohistochemistry is used in routine practice to provide important clinical information. The aim of this study was to have an insight into the pathological characteristics of invasive breast cancer in Armenian patients.
Method: We reviewed a histological and immunohistochemical results of 541 cases of invasive breast cancer, diagnosed between January 2013 and October 2015 in Davidyants laboratories.
Results: In our study group the average age of patients was 48 year. Luminal Type "B" cancer was the most prevalent type 45.28 %, followed by Luminal Type "A" 41.77 %. The HER2neu positive type was diagnosed in 16.26 %, and Triple negative type in 6.65 %. The peak incidence of Luminal Type "A" cancers was in age 41–50 years. (39.4 %). The most diagnosed subtypes of breast cancer in age 51–60 years. were HER2neu positive (34 %) and Luminal Type "B" (32.6 %). The highest incidence of Triple negative cancers was in patients with age more than 61 year.
Conclusion: Our data shows that the incidence of clinically more aggressive, Luminal "B" Type of breast cancer was higher in our patients group than Luminal Type "A", which could be a reflection of peculiar gene profile.

PS-01-041
The role of tenascin-C in triple-negative breast cancers
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Objective: Triple-negative breast cancers (TNBC) are a heterogeneous set of tumours characterized by absence of actionable therapeutic targets. Increased aggressiveness of TNBC, as well as a resistance to standard therapies, may be associated with the presence of cancer stem cell (CSC) populations within the tumour, the role of which and a prognostic value in TNBC is still debatable.
Method: We analised the relationships between CD44/CD24 CSC cell phenotype, expression of tenascin-C, described as an extracellular marker for CSC niche, parameters of tumour progression and a pathologic response to neoadjuvant chemotherapy. We evaluated TNBC specimens of 30 patients who received neoadjuvant chemotherapy with platinum agents. The protein expression of CD44, CD24 and tenascin-C was detected by immunohistochemistry.
Results: Our results didn't reveal any correlation between CSC markers and tumour characteristics, such as Ki-67, nodal status and distant metastasis. Tenascin-C was found to be highly associated with the CD44+/CD24-/low phenotype and a chemotherapy sensitivity. All tumour cases where CD44+/CD24-/low phenotype combined with a prominent tenascin-C expression had a poor pathologic response and exhibited the chemotherapy resistence. All other pattern combinations of CSCs markers didn't relate to negative response to chemotherapy.
Conclusion: Our results highlighted a potential prognostic role for CD44+/CD24-/low/ tenascin-C+ tumour phenotype in TNBC resistance to neoadjuvant chemotherapy with platinum agents.

PS-01-042

Radiation-induced angiosarcoma and atypical vascular lesion of the breast: Case report and meta-analysis of observational studies

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Objective: Angiosarcoma is a rare complication of radiation therapy (RT) for breast cancer. Knowledge of its epidemiology and natural history is useful for multi-disciplinary breast management teams, but not readily available in the literature. Aims: To present a case of radiation-induced angiosarcoma and synthesize evidence on incidence, relative risk (RR), number needed to harm (NNH), and prognosis of radiation-induced angiosarcomas and atypical vascular lesions (AVL) of the breast.
Method: A 10 year evidence search was conducted using DynaMed and MEDLINE.
Results: We present a case of breast angiosarcoma in a 77-year old woman 12 years after RT for invasive lobular carcinoma. The evidence search identified 119 references; 8 contained extractable numeric information at evidence level 3 (Oxford system). We calculated relative risk of post-radiation breast angiosarcoma of 3 to 6 and number needed to harm of 1500 to 3000, after a median latency of 7 years. The prevalence of radiation-induced breast angiosarcoma is 36/1000, compared to 6/1000 for primary breast angiosarcoma. The median survival for radiation-induced breast angiosarcoma is 35–49 months (5-year survival 38–54 %), compared to 48 months for primary angiosarcoma (5-year survival 46 %). Survival is not statistically different from post-radiation angiosarcoma (1 study). AVL: in one study of 30 patients diagnosed with AVL (median latency 48.5 months), 2 patients developed angiosarcoma.
Conclusion: RT for breast cancer carries an increased RR of angiosarcoma, but minimally increased absolute risk due to disease rarity. The prognosis of radiation induced breast angiosarcoma is not different from primary breast angiosarcome. Evidence on clinical course of AVL is very limited.

PS-01-044

Cancer stem cell and epithelial-mesenchymal transition interactions in Phyllodes Tumours: Outcome analysis in relation to clinical features and patient survival

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Objective: We evaluated immunohistochemical expression of EMT and CSC markers in PTs in relation to their expression to various clinicopathological parameters and survival outcomes.
Method: Immunohistochemistry was performed on 360 PTs using tissue microarray sections. The expression of molecules related to EMT (S100A4) and CSCs (ALDH1) was assessed in stromal cells of tumours. Biomarker expression was correlated with clinicopathological parameters and disease free survival (DFS) and overall survival (OS) calculated.
Results: 360 tumours were assessed. Of these 241 (67 %) tumours were benign, 87 (24.2 %) borderline and 32 (8.9 %) malignant. Stromal expression of ALDH1 and S100A4 was observed in 52.5 and 22.5 % of cases. Combined expression of both markers was seen in 13.3 % of tumours. Tumour grade, stromal cell atypia and increased stromal mitoses were associated with increased expression of ALDH1 and S100A4 ($p < 0.001$). Patients whose tumours expressed ALDH1disclosed a trend of poorer OS but this was not statistically significant ($p = 0.160$) whereas a near significant decrease in OS was noted in patients whose tumours co-expressed ALDH1 and S100A4 ($p = 0.065$).
Conclusion: Determination of EMT and CSC markers provides significant biological insights into breast PTs. These markers may promote new therapeutic paradigms in management, especially for malignant PTs.

PS-01-045

Bioinformatics analysis of multi-omics (transcriptome and proteomic) reveals molecular pathways that inhibit tumour growth after nicotinamide treatment in a triple negative breast cancer cell line model

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Objective: Triple negative breast cancer (TNBC), which is characterized by no specific molecular targeted agents. Nicotinamide has been proven to have protective effects in reducing the rate of skin cancer without toxicity.
Method: The Illumina sequencing (Hiseq 2500) and iTRAQ LC-MS/MS techniques were employed for transcriptomic and proteomic analyses, respectively, of TNBC cells treated with and without 25 mM nicotinamide. Obtained samples were utilized in network-based approaches to identify altered representative molecules of such pathways. In vitro functional tests were conducted to evaluate biologic functions in a cell.
Results: By KEGG enrichment analysis of the transcriptome, seven pathways, including those of chemokines, metabolism and growth factor binding sites, cell cycle, DNA repair, and apoptosis, showed significant differential expression of genes between the two groups. KEGG enrichment analysis showed that among the 5028 proteins identified, 346 and 168 genes showed altered expression and pathway network interactions were derived between the differentially expressed genes. In vitro functional experiments validated the results of the Omics analysis.
Conclusion: This study highlights the landscape of genetic and protein alterations after nicotinamide treatment in TNBCs by identifying alterations in numerous molecular pathways of nicotinamide and provides a rationale for identification of a therapeutic drug for TNBC.

PS-01-046

Next generation proteomic analysis reveals suppression of Bmi-1 mediates molecular pathways for inhibiting tumour progression in triple negative breast cancer

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Objective: Bmi-1 has been correlated with tumour aggressiveness. Clinical trials with Bmi-1 inhibitors are currently underway. However, much still remains unknown regarding the landscape of genomics and proteomic molecular pathways in triple negative breast cancer (TNBC), which is characterized by no specific molecular targeted agents.
Method: We conducted proteomics of TNBC cells treated with or without a Bmi-1 siRNA by using the iTRAQ LC-MS/MS technique to identify differentially expressed proteins between the two groups. Enrichment analysis was conducted and biological network analysis was performed Finally, the selected proteins were validated for their clinical significance in a TNBC tissue microarray ($n = 319$).
Results: Among the 7890 proteins identified, 722 differentially expressed proteins were obtained. By Panther analysis, 13 pathways, including those for kinases and the cell cycle, showed significant differential expression between the two groups. Pathway networks from functional interactions revealed tumour suppressive networks mediated by Bmi-1 suppression. Increased expression of Bmi-1 related proteins was related to aggressive clinical course.
Conclusion: These findings shed light on the complex mechanisms underlying Bmi-1 by using proteomic analysis and provide pilot data necessary to support the role of Bmi-1 in TNBC and the application of a Bmi-1 inhibitor as a potential therapeutic to target TNBC.

PS-01-047

Iron regulation in the breast carcinoma microenvironment

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Objective: To analyze particular 'iron-phenotypes' of stromal inflammatory cells and their possible role in the regulation of iron in the breast tumour microenvironment.
Method: Immunohistochemistry for hepcidin, ferroportin, transferrin receptor 1 and ferritin was performed in primary breast tissues and axillary lymph nodes to dissect the 'iron-profiles' of epithelial cells, lymphocytes and macrophages. Breast carcinoma core biopsies were subjected to imaging flow cytometry to confirm FPN1 expression in the cell types previously evaluated.
Results: We confirm previous results by showing that breast cancer epithelial cells present an 'iron-utilization phenotype'. On the other hand, lymphocytes and macrophages infiltrating primary tumours and from metastized lymph nodes display an 'iron-donor' phenotype, with increased expression of ferroportin and ferritin, concomitant with an activation profile reflected by a higher expression of transferrin receptor 1 and hepcidin. A higher percentage of breast carcinomas, compared to control mastectomy samples, present iron accumulation in stromal inflammatory cells, suggesting that these cells may constitute an effective tissue iron reservoir. The expression of iron-related proteins in epithelial cells, lymphocytes and macrophages is associated with clinicopathological markers of breast cancer prognosis and behavior.
Conclusion: These results reinforce the importance of analyzing the tumour microenvironment in breast cancer, extending the contribution of immune cells to local iron homeostasis.

PS-01-048

Tumour associated macrophages are strongly related to vascular invasion, non-luminal molecular subgroups and interval breast cancer

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Objective: Tumour-associated macrophages (TAMs) resemble M2 macrophages, promote tumour invasion and show strong expression of CD163 in breast cancer. The association between CD163-positive macrophages and vascular invasion, molecular subgroups, mode of detection, and outcome was investigated.
Method: A population-based retrospective study of invasive breast cancer was performed using data from the Norwegian Breast Cancer Screening Program, including 200 screen-detected and 82 interval cancers. The percentage of CD163-positive macrophages was quantified using immunohistochemistry and considered as high (upper quartile) and low expression. Lymphatic (LVI) and blood vessel invasion (BVI) were recorded by immunohistochemistry.
Results: High levels of CD163-positive TAMs were associated with BVI ($p < 0.001$), LVI ($p < 0.001$) and interval cancers ($p < 0.001$). Median levels of CD163-positive cells were 42 % (Luminal A), 42 % (Luminal B, Her2 neg.), 50 % (Luminal B, Her2 pos.), 59 % (Her2 pos.) and 62 % (triple-negative tumours) ($p < 0.001$). Survival analyses showed cases with high level of CD163-positive cells to be associated with reduced disease-specific survival ($p = 0.005$).
Conclusion: High levels of CD163-positive TAMs in breast cancer is strongly associated with blood and lymph vessel invasion, as well as screening interval presentation. Furthermore, high levels of these macrophages are associated with non-luminal molecular subgroups and poor prognosis.

PS-01-049

Clinicopathologic features of Triple Positive Breast Cancer (TPBC): An experience from Mexico

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Objective: Initially, an inverse association was described between HER-2 positivity and the presence of hormonal receptor (HR), but subsequently it was reported that 50 % of the patients with HER-2 positive tumours are also HR positive. (J Natl Cancer Inst 2003;95:142–153) The aim of the study was to investigate the frequency, clinical and pathological features of TPBC.
Method: Using our institutional data base, we retrospectively evaluated 1528 cases of primary breast cancer (2000–2009). Immunohistochemical studies for ER, PR and HER2/neu amplification by SISH testing were done to identify 302 (19.7 %) cases of triple positive carcinomas. Clinical information was retrieval from the records.
Results: Mean age was 62 years, and 5 % of patients were diagnosed at <40 years old. One hundred and two patients (33.7 %) were normal weight and 200 patients (66 %) were overweight (BMI ≥ 30). The mean tumour size was 4.9 cm. 10 % were T1, 46 % were T2, 32 % T3 while 12 % were T4. 82 % of the patients had axillary lymph node metastases. 267 (88 %) tumours were classified as invasive ductal carcinomas of no special type, and 35 (12 %) as micropapillary carcinomas.
Conclusion: We conclude that TPBC in a Mexican population harbor adverse pathobiological features and is mainly present in obese postmenopausal women.

PS-01-050

Are heterogeneity and cellularity important in behavior of phyllodes tumour - A comparative study of WHO classification with a modified WHO classification including heterogeneity - cellularity

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Objective: This retrospective study sought to evaluate various histologic features especially stromal heterogeneity and cellularity that may impact behavior of phyllodes tumour (PT).
Method: A total of 216 PTs were studied for histologic features impacting prognosis. As heterogeneity cellularity emerged significant in impacting behavior it was added to the WHO 2012 classification with a scoring system to divide PTs as benign, low grade and high grade malignant.
Results: Parameters were scored as: A) Tumour borders: circumscribed/partly infiltrating (0), infiltrative (1). B) Stromal overgrowth at 4X: absent (0), present (1). C) Stromal heterogeneity—cellularity: uniform/heterogeneous with low cellularity (0), heterogeneous with intermediate cellularity (1), uniform intermediate or high cellularity (2). D) Stromal nuclear grade: 1, 2, 3. E) Mitosis/10hpf: ≤5 (1), 6–9 (2), ≥10 (3). Final score for benign was ≤5, low grade malignant PT was 6–9 and ≥10 for high grade malignant PT. Both the WHO and modified system documented that after excluding incomplete excisions none of the benign PTs recurred. All 38 high grade PTs were equally classified by both systems, 7 PTs labeled as low grade by WHO were labeled as benign by modified system and two labeled as low grade by modified system were labeled as benign by WHO but none of discrepant cases had recurrence or death. A slightly better prediction of death was seen with modified system then traditional WHO classification.
Conclusion: Though the WHO classification predicts events accurately, our study indicates that prediction may improve with addition of scores and heterogeneity and cellularity.

PS-01-051

Breast metastasis from ovarian serous micropapillary carcinoma

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Objective: Metastases to the breast from extramammary neoplasms are uncommon, and metastatic ovarian carcinoma to the breast is rarely encountered.
Method: We presented a 33-year-old female with metastasis of ovarian serous micropapillary carcinoma to the breast occuring 10 months after the initial diagnosis of the ovarian tumour.

Results: Clinical examination revealed a palpable and firm mass in her left breast. Both tru-cut biopsy and fine needle aspiration cytology were performed. The cytological, histopathological and immunohistochemical examination revealed similar findings with the tumour of the ovary and it was consistent with invasive micropapillary carcinoma.
Conclusion: It is important to distinguish primary breast carcinoma from metastases because the treatment modality and the prognosis between them are different. Clinical history, histopathological features, such as the presence of micropapillary pattern, and using an appropriate immunohistochemical pannel would be helpful in establishing the accurate diagnosis.

PS-01-052
Review of columnar cell lesions in fibrocystic changes of the breast: A 10 year retrospective study
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Objective: The Objective was to estimate the occurrence of Columnar Cell Lesions (CCLs) in Nigerian women using Fibrocystic changes (FCC) as a surrogate lesion and to determine the range of CCLs found using standard histologic criteria.
Method: All consecutive breast biopsies that were diagnosed with FCC within a 10-year period at the department were reviewed by the authors.
Results: Thirty cases of CCLs were identified among the 559 cases of FCC found. The ages ranged from 16 to 63 years, the age group with the highest incidence was in the 5th decade (26.7 %), while the least incidence is in the 2nd decade of life (9.8 %). The commonest pattern was Columnar Cell Change(CCC) at 66.7 %, Columnar Cell Hyperplasia at 16.7 %, CCC and CCH occurring together at 16.7 %. No case of flat epithelial atypia (FEA) was found.
Conclusion: This study shows that CCLs occur among Nigerian. The absence of FEA in our cohort maybe because of the restriction of study material to fibrocystic changes. The age distribution of our patients was similar to those reported among Caucasian women. We recommend larger studies be carried out when mammography becomes widely available.

PS-01-053
Heterotypical Cell Cannibalism (CC) in breast cancer tumour cells
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Objective: Study a possibility of heterotypical CC in mammary gland cancer and also analyze internalized cells within «cannibal»-cells in heterotypical CC.
Method: Tests were conducted on samples of mammary gland cancer tissues, received from 23 females, aging from 36 to 85 years old,with confirmed morphological diagnosis of infiltrative ductal mammary gland cancer. In our study we used methods of light and fluorescence microscopy, scanning and transmission electron microscopy.
Results: In all examined sections we discovered cells that were inside of another cells. With the help of scanning electron microscope the localization of internalized cell within "cannibal"-cell in homotypical CC was proven. Entosis is defined by invasion of one tumour cell inside the other, with forming of vacuole in cytoplasm of the absorbing cell. Internalized cell has a round shape. Internalized cell localizes inside gigantic vacuole in cytoplasm of a host-cell. Nucleus of a host-cell has a crescent form and dislocated to the periphery of cytoplasm. Later cells dissapear by means of lysosomal degradation. In some cases internalized cells undergo cell division within cannibal cell or they can be released. Entosis is provoked by the loss of attachment to extra-cellular matrix(ECM), that leads to internalization of one sell within the other by means of actin-myosin contraction. Generally, the result of entosis is a lysosome-mediated degradation of internalized cell or,in some cases their release from the host-cell.
Conclusion: We have proved the posibility of «cell-in-cell» phenomenon in breast cancer.

PS-01-054
Features of cell adhesion molecules expression in primary breast cancer cells and its metastases
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Objective: Immunohistochemical analysis of expression features, distribution and interaction of E-cadherin and β-catenin proteins in primary tumours of mammary gland.
Method: Immunohistochemistry
Results: In our test group there were 32 (n = 32) matching cases(primary mammary gland tumours) and their metastases in lymphatic nodes (n = 4) and liver (n = 8). Expression of E-cadherin, β-catenin in mammary gland cancer cells was defined by of immunohistochemical method with specific antibodies usage. In our resaerch we discovered that reduction and total absence of E-cadherin expression more frequently occured in mammary gland cancer patients with developed in different periods metastases in liver (70 %) than patients without metastases (30 %) (p = 0,014). The increase of cytoplasmic immunoreactivity and nuclear translocation of β-catenin was found in more than 80 % mammary gland cancer cases, following the development of metastases.
Conclusion: These changes in E-cadherine and β-catenin expression in tumour cells can be considered as factors of unfavorable prognosis in mammary gland cancer. β-catenin expression appearance indicates signaling pathway activation, which is triggered by aberrant expression of epithelial cadherins, which leads to the increase of mobility and invasion of tumour cells.

PS-01-055
Expression of PD-L1 in triple-negative breast cancer based on different immunohistochemical antibodies
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Objective: The aim of this study was to evaluate the expression of PD-L1 by 3 different immunohistochemical antibodies in TNBC.
Method: Interpretation of all three PD-L1 antibodies showed good concordance among three readers (kappa value >0.610) in both cancer cells and immune cells. Using a tissue microarray (TMA) constructed from 218 cases of TNBC, we performed immunohistochemical staining using 3 the most popular commercially used PD-L1 monoclonal antibodies (clones 28-8, E1L3N, and SP142) in cancer cells and immune cells.
Results: Using various cut-off values of previous studies (1, 5, 10, and 50 %), the expression rates in cancer cells were: PD-L1 (E1L3N) (14.7, 14.7, 11.0, 2.3 %), PD-L1 (28-8) (13.3, 12.4, 10.1, 1.8 %), and PD-L1 (SP142) (11.5, 11.0, 6.9, 0.5 %), respectively. At the 5 % cut-off value, the discordance rate among the three antibodies was 6.0–10.6 % and was highest between PD-L1 (SP142) and the other two antibodies. The expression rates in immune cells were PD-L1 (E1L3N) (37.6 %), PD-L1 (28–8) (36.7 %), and PD-L1 (SP142) (19.3 %), and the discordance rate among the three antibodies ranged from 13.8 to 24.8 % and was also highest between PD-L1 (SP142) and the other two antibodies.
Conclusion: PD-L1 detection in cancer cells and immune cells varied by antibody clone. The concordance rate among monoclonal PD-L1 antibodies was higher between PD-L1 (28-8) and PD-L1 (E1L3N).

PS-01-056

Invasive carcinoma of no special type arising from an atypical microglandular adenosis of the breast: A case report and review of the literature

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Objective: Microglandular adenosis of the breast is a rare proliferative lesion that mimics invasive carcinoma. Herein, we report a case of invasive carcinoma arising from MGA with a review of the literature.
Results: Segmental mastectomy was performed in a woman aged 57 years. Histologically, it was a high-grade invasive carcinoma of no special type arising from microglandular adenosis. The patient also had metastases in 4 of 11 axillary lymph nodes. Immunohistochemically, all the epithelial cells of the microglandular adenosis and invasive tumour showed positivity for cytokeratins (LMWCK, CK 14, and focal CK 5), no reactivity with estrogen receptor, progesterone receptor, HER-2, p63, and smooth muscle actin (SMA). EGFR and p53 was absent in this invasive tumour. Reticulin and collagen-IV staining highlighted the basal membranes. Ki67 was found to increase with the severity of lesions to invasive carcinoma. Absence of S-100 expression, which is rare in invasive carcinomas arising from microglandular adenosis, was observed in the present case. There was no evidence of recurrence or distant metastasis after 96 months of clinical follow-up.
Conclusion: MGA remains to be solved in terms of pathogenesis and malignant potential, so more cases with long follow-up like our case are needed to clarify the uncertainties.

PS-01-057

Robustness of scoring stromal features in ductal carcinoma in SITU of the breast: An inter-observer variability study

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Objective: This study aims to determine a cut-off for assessment of stromal architecture in ductal carcinoma in situ (DCIS), based on inter-observer variability. Robustness of scoring myxoid stroma is compared with reliability of other histopathological features.
Method: Hematoxylin/eosin stained sections of 213 DCIS patients were retrieved from the Department of Pathology of Leuven University Hospital. The following features were independently assessed by two pathologists: nuclear atypia, intraductal calcifications, necrosis, DCIS architecture, stromal architecture and stromal inflammation. Stromal architecture and stromal inflammation were classified into four categories (0 %, 1–33 %, 33–66 % or >66 % myxoid stroma or stromal inflammation). Kappa values were determined to assess inter-observer variability.
Results: The kappa value for scoring stromal architecture was highest by dichotomization with a 33 % cut-off (k0,604), compared to k0,494 and k0,578 when using a 1 and 66 % cut-off, respectively. A similar analysis for stromal inflammation revealed that the highest kappa value (k0,731) was obtained by dichotomization as 'absent to mild' versus 'moderate to extensive' inflammation (33 % cut-off). Inter-observer variability for stromal features was similar to inter-observer variability for the other histopathological characteristics.
Conclusion: Adequate prognostic markers require robustness of assessment. This study demonstrates the robustness of dichotomous scoring of both stromal architecture and stromal inflammation.

PS-01-058

Breast cancer intratumour heterogeneity in routine practice

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Objective: Intratumour heterogeneity denotes the coexistence of subpopulations of tumour cells that differ in their characteristics within the primary tumour and metastasis. Cell clones evolving independently from each other leading to the spatial and temporal heterogeneity. of this study was to evaluate the inter- and intratumour heterogeneity of breast cancer (BC) using standard IHC characteristics (ER, PgR, Her2/neu and Ki67).
Method: We studied 20 primary BC, cT2N0 and 10 BC and metastasis cT2N1/2 using 7-punched core-biopsy. Tumour type, grade and immunostaining were analyzed by three pathologists.
Results: No heterogeneity of tumour type or grade was evaluated, concordance between experts was 100 %. Intraclass correlation coefficient between immunostaining measured by different pathologists were high (0, 94); the lowest (0,89) were obtained in Ki67 expression. Intratumour heterogeneity of ER-expression was observed in 8/30 primary cases (26 %) and in 2/10 (20 %) cT2N1/2 tumours, PgR-expression—in 12/30 (40 %) and 6/10 (60 %) respectively, were higher in percentage than in intensity for both markers. Intratumour heterogeneity of Ki67 expression was observed in 17/30 primary cases (56 %) and in 1/10 (10 %) of cT2N1/2; HER2—in 4/30 (13 %) and in 0/30 respectively.
Conclusion: Intratumour heterogeneity should be manshioned when BC is diagnosed, it is important to study optimal volume of tissue.

PS-01-059

Multiple subcutaneous papillomas of the chest caused by needle tract seeding from the breast

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Objective: Iatrogenic epithelial cell displacement in the breast is a recently described complication of needle procedures. However the fate of the tiny epithelial fragments displaced in the needle tract remains unknown. Here we describe a case of multiple subcutaneous papillomas of the chest presumably caused by needle tract seeding from recurrent mammary papillomas.
Method: Morphological, topological, immunohistochemical (CK5/6, ER, CD10, p63) and molecular (Mitochondria DNA D-loop direct sequence) features are compared between subcutaneous and mammary papillomas.
Results: After 4 needle manipulations during 16 months, the patient underwent wide local excision for the mass in the right breast. The resected tissue revealed a mammary papilloma measuring 19.5 mm (A) and two subcutaneous papillomas measuring 10.5 and 8.5 mm (B), which situated in the same straight line. Two year later, she underwent an excisional biopsy which contained a subcutaneous papilloma measuring 3 mm (C). These three papillomas (A,B,C) were identical in morphology, topology, immunohistochemistry and molecular features.
Conclusion: 1) Our results indicate that the subcutaneous papillomas develop from the needle tract seeding from the breast papilloma. Awareness of such a phenomenon is important in diagnosing papillomas in an unusual location because such lesions may lead to confusion about its malignant potential, histogenesis, terminology and treatment if the patients' past history of needle procedure is missed. 2) The cystic spaces that contain the papillomas are not necessarily the preexisting ducts or lobules but may be newly generated by the stem cells of papilloma. A mechanism analogous to "ductneogenesis" for ductal carcinoma in situ proposed by Tibor Tot (2007) may also work in papillary lesions of the breast.

PS-01-060

HER2 in situ hybridization analysis from 0 and 1+ immunohistochemistry in breast cancer

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Objective: HER2 analysis should be performed from all primary invasive breast carcinomas. Srong 3+ positive cases with immunohistochemistry (IHC) receive anti-HER2 therapy like trastuzumab. 2+ positive cases show less intense and fragmented staining and are retested by in situ hybridization (ISH). 0 or 1+ IHC are considered negative, and ISH is not obligatory.
Method: We analysed HER2 status from 750 consecutive breast cancer patients operated between 1.10.2014 and 31.5.2015 in Helsinki University Central Hospital Breast Unit. Both IHC and silver-enhanced in situ hybridization (SISH) analysis were performed.
Results: 400 tumours were 0 or 1+ in HER2 IHC. 398 of these were also negative in SISH, but two were positive. 279 tumours showed 2+ positivity in IHC. 242 out of these were negative in SISH and 37 were positive in SISH. 71 tumours were 3+ in IHC and 68 were also positive in SISH. Three cases were not amplified in SISH.
Conclusion: Our study showed that a small number of 0 or 1+ IHC positive breast tumours have also HER2 gene amplification. Similar numbers have been previously described in literature.

PS-01-061
Tumour-suppressive effects of oregano in N-methyl-N-nitrosourea-induced mammary carcinogenesis in female Sprague–Dawley rats
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Objective: Nowadays the anti-tumour effects of some natural plant foods are extensively studied. One of them, oregano is rich in phenolic compounds and monoterpenoids with high antioxidant capacity. The effects of lyophylized oregano were evaluated in N-methyl-N-nitrosourea-induced mammary carcinogenesis in female Sprague-Dawley rats.
Method: Animals were randomly divided into three experimental groups (n = 25 per group): 1/ control group without chemoprevention; 2/ group with chemoprevention with oregano at a concentration of 0.3 %; and 3/ at concentration of 3 %. The experiment was terminated after 14 weeks of carcinogen exposal. Various macroscopic (tumour-bearing animals, tumour frequency, incidence and latency, tumour volume), histological (tumour type, grade) and immunohistochemical parameters (caspase-3, Bax, Bcl-2, Ki67, VEGF, VEGFR and some cancers stem cell markers) were evaluated.
Results: In both treated groups histology was similar and demonstrated decrease in the ratio of high-/low-grade carcinomas compared to control group. In group with 0,3 % of oregano there was reduced tumour frequency by 55,5 %, tumour incidence by 44 %, and tumour volume by 44.5 % compared to control group. Immunohistochemistry confirmed in both treated groups decreased expression of VEGFR-2, CD24 and EpCAM and increased positivity of caspase-3. Moreover, the lower dose group had decreased proliferative activity and the group with 3 % of oregano had increased latency by 12.5 days and decreased expression of Bcl-2.
Conclusion: Results our study show a distinct tumour-suppressive effects of oregano in the breast cancer model characterized by antineoplastic impact on tumour stem cells, as well as pro-apoptotic, antiangiogenic and antiproliferative activity in breast cancer.

PS-01-063
The effect of heavy metals accumulation on morphological and immunohistochemical features of breast cancer
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Objective: The chemical composition determination of neoplastic breast tissue, study of prognostic-important receptors expression in the breast cancer cells, establishing linkages between all the derived indicators.
Method: We used the following methods: studying of the chemical composition of breast cancer tissue (94 cases) by atomic absorption spectrophotometry and energy-dispersion spectrometer; immunohistochemical study of ER, PR, HER2/neu, p53, Ki-67, E-cadherin, MMP1, VEGF, OPN, hsp90 and MGMT receptors; statistical analysis of the results.
Results: The total number of heavy metals (zinc, iron, copper, chromium, nickel and lead) in breast cancer tissue ranged from 51.21 to 84.86 mkg/g (average 72.44 mkg/g). There is an interrelation between the accumulation of the above elements with the degree of cancer malignancy. Their number was higher in the parenchymal component of tumour tissue. The growth of heavy metals in neoplastic tissue is accompanied with the increase of HER2/neu, p53, Ki-67, MGMT, MMP1, VEGF, OPN, hsp90 expression and decrease of ER, PR and E-cadherin expression ($p < 0.05$).
Conclusion: The heavy metals stimulate tumour anaplasia, inhibit the expression of prognostically-favorable receptors and activate negative intracellular proteins, which negatively affects the morphogenesis of neoplastic process in the breast and reduces its sensitivity to treatment.

PS-01-065
Increased CD4+ and CD8+ lymphocytic infiltration in patients with triple negative breast cancer suggests susceptibility to immune therapy
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Objective: To investigate tumour-associated immune cell densities in TNBC patients.
Method: Samples from 104 breast cancer patients were investigated by IHC using antibodies against ER, PgR and Her-2, CD3, CD20, CD4 and CD8. Immune cell densities were quantified as cell/mm2 using the CAP guidelines. Correlation of immune cell densities with tumour sub-types was undertaken using paired t-test, ANOVA and Chi square.
Results: A total of 27(25 %) patients had TNBC and 77(74 %) were non-TNBC patients. Patients with TNBC showed significantly increased infiltration of lymphocytes (T and B cells) compared to the patients with non-TNBC, while myelocytic infiltration was not significantly different. Within the TNBC group, infiltration of T-lymphocytes was significantly higher compared to B-lymphocytes. However, CD4 and CD8 infiltration was not significantly different within the TNBC group.
Conclusion: Patients with TNBC show increased lymphocytic (both T and B lymphocytes) infiltration compared to the patients with non-TNBC. Moreover, TNBC are heavily infiltrated with T lymphocytes compared to the B lymphocytes. This suggests higher immunogenicity of TNBCs and may indicate a higher responsiveness of these cancers to immunotherapy.

PS-01-066
Breast adenoid cystic carcinoma: A case report
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Objective: Report a case of an adenoid cystic carcinoma (ACC) of the breast. Present a brief review of its different characteristics in light of existing literature.
Method: A 50-year-old postmenopausal woman, with no significant medical history, presented with a palpable right breast lump. The physical examination found a 1 cm sized, irregular shaped, and firm lump at her left breast. Mammography and breast ultrasonography showed an ill-defined 8 × 7mm sized lump with irregular borders at the upper quadrants of right breast. A core biopsy was performed and identified an ACC. The patient underwent lumpectomy with axillary lymph node dissection.
Results: The pathological examination showed a 6,2 × 3 × 1,5 cm sized, irregular shaped lesion Microscopic examination revealed small basaloid

cells arranged in variable architecture with cribriform, trabecular and tubular patterns. The SBR grade was I. Tumour cells tested negative for estrogen receptors (ER-), progesterone receptors (PR-), and HER2/neu. None of the 6 axillary lymph nodes excised were positive for malignancy.
Conclusion: ACC of the breast is a rare entity that should be differentiated from other types of invasive breast carcinomas; Although hormone receptors and HER2 are typically negative in ACC of the breast, it is defined as a carcinoma of low malignant potential by the WHO classification.

PS-01-067
Evaluation of Ki67 expression in breast cancer (pT1-2N0) using tissue microarrays and image analysis
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Objective: Ki67 index in breast cancer seems to be strongly prognostic and according last St. Gallen recommendation can predict response to chemotherapy. However, there is no consensus on counting areas or cut-off values for patient stratification.
Method: We examined a retrospective series of breast cancer pT1-2N0 treated within 2000–2009 years (n = 733) using TMA. After whole slide scanning TMA blocks was constructed using 2 mm punches and TMA master device (3DHistech, Budapest). The percentage of Ki67 positive nuclei was evaluated by image analysis within each core.
Results: Mean of tumour cells in breast carcinoma in 1 mm2 of histology slide was 6828,981 + \\- 207,5860 cells, median—6413,727 cells. Mean of Ki67 positive cells in 1 mm^2 was 1360,73+/−92,91 in absolute numbers of cells. Ki67 index = 19,92 %+/−1,36.
Conclusion: For breast cancer TMAs (with big diameter core) are an efficient and reliable alternative to WS IHC staining for Ki67. This technique allow reduce time, reagent and finally cost of each type of analysis. Using image analysis for evaluation of Ki67 index is essential.

PS-01-069
Benign hepatocellular nodule as regression of a breast cancer liver metastasis: Case report
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Objective: The surgical excision of breast cancer liver metastasis (BCLM) is a relative uncommon procedure. Consequently, the report of the histological features of the regression of BCLM after neoadjuvant chemotherapy (NACh) is almost unknown.
Method: We report the case of a patient with BCLM confirmed by biopsy with histological complete regression after NACh with features of a regenerative hepatic nodule.
Results: A 43 years-old woman was diagnosed with a cT2 N0, G3, breast invasive carcinoma, estrogen receptors positive (100 %) progesterone receptors negative, ERBB2 3+, with a synchronous liver metastasis with 16 mm by ultrasonography, confirmed by biopsy. After NACh, the liver metastasis reduced to 10 mm by ultrasonography, and the patient underwent hepatectomy and breast lumpectomy. Histologically, a breast tumour bed with 6 mm with 5 % of overall cancer cellularity, and a 10 mm hepatocellular nodule with steatohepatitis and regenerative features, were found. Posterior radiologic evaluation of the liver confirmed the surgical excision of the metastatic nodule. The patient is alive and well 6 months after surgery.
Conclusion: We illustrate a regenerative hepatic nodule as a form of total BCLM regression. The histologic re-evaluation of BCLM after NACh may be as important as the re-evaluation of the primary tumour to appraise the degree of regression.

PS-01-070
Breast cancer incidence, demographic, and pathological characteristics in Bosnia and Herzegovina
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Objective: Breast cancer is a leading cause of cancer morbidity and mortality in women in less developed countries. No epidemiological, pathological, and clinical data for breast cancer in Bosnia and Herzegovina have been published so far. In addition, there is no screening program for breast cancer in our country. We present 10 years data from a tertiary level institution covering a representative population of Bosnia and Herzegovina.
Method: Medical records from the Department of Pathology, dating from 2005 to 2015, were searched for breast cancer cases. Demographic, pathological, and molecular characteristics of the cases were recorded. Epidemiological data were approximated based on the population number covered by our institution.
Results: There were 296 new cases per year, per 438 000 population covered (crude incidence rate 68/100 000 persons/per 10 years). The average age of the patients was 58.4 years (range, 26–99 years). The most affected age group was 51–60 years (28 %), followed by age 61–70 (24 %), 41–50 (22 %), while 7 % of the affected women were less than 40 years old. The most frequent histotype was invasive ductal carcinoma NOS (70 %), followed by lobular carcinoma (10 %), mixed type carcinoma (5 %), and all special types (15 %). The majority of the tumours were Nottingham histologic grade 2 (47 %), followed by grade 3 (40 %) and grade 1 (13 %). The most frequent tumour stage was pT2 (53 %), followed by pT1 (27 %), pT4 (11 %), and pT3 (9 %). Her-2/neu overexpression was observed in 15 % of the cases. The most common molecular type was Luminal A (74 %), followed by triple negative cancer (11 %), Luminal B (8 %), and Her2 enriched type (7 %).
Conclusion: Higher pT stage at initial presentation is due to lack of effective screening for breast cancer in Bosnia and Herzegovina. Other histopathologic and molecular characteristics from our cohort are in line with the published data.

PS-01-071
Decreased immunoexpression of vav2 could be a potential marker in breast carcinoma progression
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Objective: The oncoprotein Vav2 has been demonstrated to be expressed in human breast cancer cells, however its association with the clinicopathologic parameters and clinical outcome remains uncertain.
Method: We investigated Vav2 expression by immunohistochemistry in tumour tissue from 250 breast cancer patients who underwent curative resection in Samsung medical center. The median H-score was used to evaluate Vav2 expression, and the score was calculated separately in ductal carcinoma in situ and invasive carcinoma portion. The association of Vav2 expression with clinicopathologic variables, such as molecular phenotype (ER, PR and HER2 status), tumour size, nuclear grade, histologic grade, pN stage, overall survival, and recurrence free survival was analyzed.
Results: The Vav2 was strongly expressed in all normal breast duct and ductal carcinoma in situ. Invasive carcinoma showed significantly decreased expression in comparison with DCIS($p = <0.0001$). In addition, the Vav2 expression was significantly higher in ER(and/orPR)-positive group than ER(and/orPR)-negative group($p = 0.011$). The other variables, including tumour size, nuclear grade, histologic grade and pN stage were not significantly associated with Vav2 expression. No significant correlation was found between Vav2 expression and overall survival and recurrence free survival.

Conclusion: The results showed that Vav2 expression was significantly decreased in invasive carcinoma as compared with non-invasive carcinoma. We also found statistically significant correlation between Vav2 expression and ER/PR positivity. ER-positive carcinomas which are mostly well differentiated and have more indolent disease course, showed significantly higher Vav2 expression. Our findings suggest that Vav2 might play a relevant role in the invasive tumour progression, warranting further investigations.

PS-01-072

Male breast cancer: Clinicopathological and immunohistochemical characteristics

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Objective: Male breast carcinoma (MBC) is an uncommon neoplasm accounting for less than 1 % of all breast cancers. In this study, we reviewed the clinicopathological and immunohistochemical characteristics of this rare entity.
Method: We retrospectively collected 35 cases of MBC between 1997 and 2016.
Results: The mean age at diagnosis was 60 years. All patients presented with a palpable mass. They all underwent surgery and only four of them had neoadjuvant-chemotherapy. Twenty-seven patients had mastectomy and eight had lympectomy. Twenty-eight patients underwent axillary dissection. Macroscopic examination revealed a cystic cavity with endoluminal papillary lesion in two cases and a firm nodule measuring from 1.5 to 9 cm in 31 cases. Histopathology found invasive carcinoma of no special type (NST) in 27 cases while the other cases were: two intacystic papillary carcinomas with invasion, two micro-invasive carcinomas, one invasive lobular carcinoma, one mixed invasive NST and lobular carcinoma with melanotic features, one mucinous carcinoma and one neuroendocrine carcinoma. Angiolymphatic and perineural invasion were found respectively in 18 and 15 cases. Tumours were associated with ductal carcinoma in situ in 11 cases, with gynecomastia in six and with a Paget disease in five. Tumour grade was mostly G2. Axillary status was pN+ in 18 patients. Estrogen and progesterone receptors were respectively positive in 22 and 26 patients. HER-2 was overexpressed in two patients.
Conclusion: MBC's diagnosis is often made at advanced stages. Consequently, patients were submitted to more aggressive treatments, with poorer clinical responses.

PS-01-073

Clinical, histological and immunophenotypical features of high-grade adenosquamos carcinomas of the breast

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Objective: Metaplastic breast carcinoma represents a heterogeneous group of disease, including adenosquamous carcinomas. Clinicopathological data are limited for high-grade adenosquamous carcinoma of breast (HGASC).
Method: Clinicopathological features of 17 cases of HGASC were reviewed. ER, PR, c-erbB2, EGFR and CK5/6 immunostainings were performed and evaluated accordingly.
Results: Mean age was 59 (39–85). Mean tumour size was 5.8 cm (1.5–16 cm). Morphologically, 4 cases showed a nested growth pattern and 5 cases showed low grade adenosquamous like pattern, while 8 cases did not follow a specific pattern. Ductal carcinoma in situ was accompanying in 7/17 (41 %) cases. ER and PR were positive in 4/17 and 2/17 cases, respectively. C-erbB2 was 3+ in 3/17 cases. EGFR was overexpressed (3+) in 37 % of cases, mainly showed cytoplasmic staining in ductal component, in contrast to membranous staining in squamous component. CK5/6 was positive in squamous component of all cases at least focally. 7/11(63 %) cases showed lymph node metastasis, while 4/17(23 %) had distant metastasis. 3/16(18 %) cases were dead after a mean of 12 months.
Conclusion: HGASCs are morphologically and immunophenotypically heterogeneous tumours with relatively poor prognosis. Triple negative phenotype predominates; however, HER2 positive and ER positive cases are also present. EGFR expression is present in a significant number of cases.

PS-01-074

Comparative study of OSNA method and conventional method in axillary staging in breast cancer

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Objective: The aim of our study is to compare sentinel lymph node staging (SLNS) obtained by OSNA method with the one obtained by the conventional method (CM).
Method: 1124 patients with breast cancer and SLN study were collected during the years 2009–2010 and 2012–2013. 590 SLN were studied by CM and 534 by OSNA. We analysed different clinicopathological parameters. Statistical analysis was performed using SPSS using chi-square tests.
Results: SLNS was: pN0: CM 349 (59.2 %) and OSNA 335 (62.7 %); pN0i+: CM 74 (12.5 %) and OSNA 14 (2.6 %); pN1mi: CM 59 (10 %) and OSNA 77 (14.4 %); pN1: CM 108 (18.3 %) and OSNA 108 (20.3 %). Statistically significant differences between the SLNS by OSNA and CM ($p < 0.001$) were found, due to the rates of pN1mi and pN0i+. To determine whether this statistical significance could be attributed to different clinicopathological features, 226 patients were selected from the initial series with SLNS pN1mi and pN0i+.
Conclusion: In our series, the OSNA method shows a significant increase of pN1mi (84.6 vs 44.4 %) and decrease of pN0i+ compared to the conventional study. Those differences are not conditioned by clinicopathological parameters. Most cases (75 %) with pN1mi by OSNA shows less than 1000 copies.

PS-01-076

The importance of immunohistochemical expressions of GATA3 and Fli-1 in triple negative breast carcinomas and their relationship with clinicopathological parameters

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Objective: Triple negative breast cancer (TNBC) is a heterogenous group of tumours that are in need of potential markers for specific therapies. In this study, we aimed to detect the expression levels of GATA3 and Fli-1 (nuclear transcription factor) in TNBC, and the relationship of these levels with clinicopathological parameters.
Method: The study included 53 TNBC examined during 5 years. Fourty eight cases, whose blocks were available, were stained with GATA3 and Fli-1 immunohistochemically. A H-score was detected for each tumour, between 0 and 300.
Results: We detected nuclear positivity in 71,4 and 85,7 % of tumours with GATA3 and Fli-1, respectively. There was a statistically significantly positive relationship between GATA3 and Fli-1 H-score. Cases with higher Fli-1 H-score relapsed sooner. Cases younger than 40 years and cases with lymph node metastasis had statistically significantly higher GATA3 H-score comparing those cases older than 40 years and cases

without lymph node metastasis, respectively. We couldn't determine any relationship between other pathological parameters and GATA3 as well as Fli-1.
Conclusion: Fli-1 may cooperate with GATA3 on the same pathway. GATA3 may be a marker to determine TNBC with potential metastases to axillary lymph nodes. Fli-1 may be a marker to give information about relapse time.

PS-01-077
Progesterone receptor antibody clone 1E2 specificity and binding characterization and comparison to other progesterone receptor antibody clones
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Objective: Determine the epitope and binding characteristics of the VENTANA CONFIRM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody compared to other PR antibody clones.
Method: Epitope mapping for VENTANA anti-PR(1E2), Leica(1A6), and Dako(636) antibodies performed using a JPT microarray and a Roche Nimblegen PEPARRAY 61. Western blots incubated with the three antibody clones were performed on AbCam T47D whole cell lysate and recombinant PR. Immunoprecipitation performed on T47D lysate with Ventana Anti-PR(1E2) and mass spectroscopy on identifiable bands. Immunofluorescence localization and confocal analysis was conducted with VENTANA anti-PR(1E2) and Leica(1A6) or Dako(636) with TAMARA and FITC secondary antibodies on FFPE breast tumour tissue.
Results: Epitopes for all three clones are unique but all are present in PR isoforms A, B, and C. Immunoprecipitation with 1E2 identified no notable proteins beyond PR. Western blot shows all three clones identify isoforms A, B, and C. Intensity of Western staining is strongest with 1E2. 1E2 co-localizes to the same nuclei as 636 and 1A6, but at different regions.
Conclusion: The VENTANA anti-PR(1E2) identifies the PR isoforms A, B, and C and immunoprecipitates no unexpected proteins. Variation in different PR antibody clone staining intensities can be explained by differing epitopes, affinities, and regions of detection within cells.

PS-01-078
Papilloma with ductal carcinoma in situ with osteoclastic giant cells of the breast: Case report
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Objective: Breast carcinoma with osteoclastic giant cells (OGCs) is an uncommon neoplasm, described in less than 2 % of breast cancer. OGCs can be seen in invasive ductal, lobular, papillary, or squamous types of breast carcinoma. In situ component may also be present in these tumours, but OGCs within in situ carcinoma without an invasive component have been reported in a few cases.
Method: We present a 42 years old woman who has admitted with a palpable mass in the left breast. Histopathologic examination revealed papilloma with ductal carcinoma in situ with OGCs.
Results: Microscopically, multiple nodules of intermediate-grade ductal carcinoma in situ within papilloma were observed. There were scattered OGCs within the neoplastic ducts. Invasive carcinoma was not present. Immunohistochemically, in situ ductal carcinoma cells were strongly positive for Estrogen, Progesterone, and Synaptophysin. Myoepithelial cells were preserved by p63. The OGCs were strongly positive for CD68, TRAP and VEGF.
Conclusion: Approximately 200 cases of carcinoma with OGCs have been reported in several organs such as gallbladder, liver and thyroid, other than pancreas and urinary tract. The mechanism of formation of OGCs is still unknown. Studies have suggested a less favorable prognosis for patients with carcinoma with OGCs.

PS-01-079
Molecular classification of breast carcinomas correlates with distant metastases and local recurrence: A big study
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Objective: Various clinical and pathological factors have been studied that could influence the rate of local recurrence and distant metastases in breast carcinomas. These have included age, tumour size, nuclear grade, histological subtypes, margin status and nodal involvement. The purpose of our study was to correlate the new molecular classification (StGallen 2013) of breast carcinomas with distant metastases and local recurrence.
Method: We studied 846 carcinomas (collected during the last 6 years at our pathology lab) with a follow-up period of 2 to 6 years. The molecular expression was evaluated using immunohistochemistry. All carcinomas were classified as Luminal A, Luminal B, Her-2 enriched and Triple Negative.
Results: Presence of distant metastases was strong correlated with Luminal B ($p < 0{,}0015$) Triple Negative ($p < 0{,}0020$) and Her-2 enriched (0,0038) breast carcinomas. Her-2 immunophenotype and lobular histology carcinomas were correlated with local recurrence ($p < 0{,}005$).
Conclusion: Luminal B and ripple Negative breast carcinomas seems to be the most aggressive subtype in the rate of distant metastases whereas Her-2 enriched and lobular histology subtypes correlate with local recurrence.

PS-01-080
Correlation between Her2 results in core needle and excision breast biopsy of breast cancer
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Objective: To correlate immunohistochemical results of Her2 in needle biopsy and excision biopsy of breast cancer in patients biopted and operated in Clinical Center of Montenegro.
Method: We correlate Her2 result in needle biopsy and the one obtained after the operation of breast cancer in 74 patients who were biopted and operated in Clinical Centre of Montenegro in 2015. Her2 results are classified into categories: 0 and 1+ (negative), 2+ (borderline) and 3+ (over-expressed).
Results: Her2 negative carcinomas in needle biopsy were 43 (58.1 %) and in excision biopsy 42 (56.7 %). Borderline result showed 16 carcinomas (21.6 %) in needle and 18 (24.3 %) in excision biopsy. Over-expression was found in 15 (20.2 %) needle bioptied carcinomas and 14 (18.9 %) in surgically removed carcinomas. In 2 cases of needle biopsy the result was 3+ and 2+ in excision biopsy, while in one case the result of needle biopsy was 2+ and 3+ in excision biopsy. Discrepancy of the Her2 status between negative and borderline result in needle and excision biopsy was found in 6 cases (6.75 %), while discrepancy between negative and over-expresion result of the needle and excision biopsy was not found.
Conclusion: HER2 status determined in needle biopsy shows high correlations with Her2 status in excision biopsy.

PS-01-081
Expression of Sema4D in invasive breast ductal carcinoma, NOS in relation to tumour angiogenesis and tumour-associated macrophages
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Objective: In vitro and in vivo studies have shown involvement of Sema4D, a Class IV semaphorin, in tumour progression. This study aimed to investigate the relationship between the expression of Sema4D in human invasive breast ductal carcinoma in relation to tumour angiogenesis and tumour-associated macrophages (TAMs).
Method: Expression of Sema4D in 94 patients diagnosed of invasive ductal carcinoma, NOS was evaluated immunohistochemically on paraffin-embedded sections based on 3-hotspot and whole-section intensity distribution scores (IDS). Microvessel density (MVD) and TAMs were assessed by immunohistochemical staining for CD34 and CD68, respectively.
Results: There was no significant correlation between expression of Sema4D and MVD as a surrogate marker for tumour angiogenesis ($p > 0.05$). In relation to TAMs, higher levels of Sema4D expression by the whole-section IDS were observed in lower grades of tumour stromal macrophages ($p = 0.001$). This inverse relationship between the grade of tumour stromal macrophages and categorical Sema4D expression remained significant either by the average 3-hotspot IDS or the whole-slide IDS (both $p < 0.01$). Sema4D expressions had no significant relationship with the tumour nest macrophage counts ($p > 0.05$).
Conclusion: Sema4D expressed in breast carcinomas might have an inhibitory effect on the tumour stromal macrophages. In contrast to experimental studies, proangiogenic properties of Sema4D could not be validated.

PS-01-083
Primary Small-cell Neuroendocrine Carcinoma (PSCNC) of the breast: A case report
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Objective: PSCNC of the breast is a rare entity, accounting for less than 0,1 % of primary breast cancers. Its diagnosis requires the exclusion of non-mammary primary sites and/or histopathological demonstration of an in situ component.
Method: We present a case of PSCNC of the breast, occurring in a woman aged 71 years. Mammography revealed a tumour in the right breast. The patient underwent a modified radical mastectomy after a core biopsy diagnosis of breast cancer was established. Systemic CT detected no other suspicious lesions.
Results: Gross examination revealed a solid, indurated, whitish and partially reddish, ill-defined tumour, beneath the nipple, with a mean diameter of 4 cm. On microscopic examination the cells appeared small and round, with hyperchromatic, oval nuclei and scant cytoplasm. Immunohistochemically, they were Ker8/18+, Ker7+, CD56+, synaptophysin+, CD117/c-kit+, Ker20-, TTF-1(-), chromogranin-, ER-, PR-, c-erbB-2(-), with a Ki-67 index of approximately 80 %.
Conclusion: Differential diagnosis includes lymphomas, certain sarcomas and metastatic carcinomas. PSCNC is considered an aggressive neoplasm, yet early stage tumours may have a more favorable prognosis. No standard treatment exists. The most effective therapeutic option seems to be surgical removal followed by adjuvant chemotherapy.

PS-01-085
Ki67 and estrogen receptor changes in breast cancer local metastases
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Objective: To investigate association between ki67 level of primary tumour and changes of this marker and estrogen receptors (ER) expression level of local metastases in breast cancer (BC).
Method: ER and ki67 immunohistochemical study (clones 1D5 and MIB-1, Dako, Denmark) of primary tumour and local metastases by 83 BC patients without neoadjuvant therapy was performed using the Dako autostainer. ER expression was evaluated according to Allred score, ki67—as the percentage of stained tumour nuclei. ER and ki67 status switches and expression level shifts while metastasizing were registered. Regression analysis (method of least squares, Gretl soft) was used (dependent variable—primary tumour ki67 level, predictors—primary tumour ER-status, ER and ki67 status switches and expression level shifts in metastases). Model's goodness of fit was evaluated.
Results: ER expression shift and ki67 status switch of metastases were considered insignificant ($p > 0.05$). Significant association with primary tumour ki67 level was detected for primary tumour ER status (regression coefficient −24,8, $p < 0.001$), ER status switch (−13,2, $p = 0.02$) and ki67 level shift (12,7, $p = 0.002$). The adjusted R2 for this model was 0.42.
Conclusion: Higher primary tumour Ki67 level correlates with higher probability of its shift, saving ER status and lower ER expression in primary tumour when breast cancer metastasizes.

PS-01-086
Age-related gene expression patterns and subtype profile in breast cancer
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Objective: Breast cancer in adolescents and young adults (AYAs; 15–49 years at diagnosis) is associated with aggressive tumour features. Here, we explored pathologic and biological characteristics of the AYA group.
Method: Three cohorts were analyzed: two population based cohorts of FFPE tissue: one AYA series ($n = 378$), one series of patients aged 50–69 years ($n = 546$), and a TCGA gene expression data set ($n = 520$), including BRCA1/2 germline mutation data.
Results: The AYAs associated with aggressive histopathologic tumour features, ER negativity, locally advanced disease ($p = 0.02$), the basal-like phenotype, BRCA1 germline mutations, and shorter disease specific survival (all $p \leq 0.004$). Genes differentially expressed between AYAs and patients ≥50 years identified one AYA cluster that associated with BRCA1 germline mutations ($p = 0.02$) and ER/PR negative tumours ($p < 0.0005$). All basal-like cases were included in this subcluster (OR = 21, 95 % CI = 9.1-50.0). Gene expression programs reflecting ER loss, stem cell profiles, and hereditary breast cancer were enriched in this subcluster.
Conclusion: In a population based series, we confirm aggressive tumours in AYA breast cancer. An age-related gene expression signature identified all basal-like AYA cases, and points to programs reflecting ER-related biology, stemness and hereditary breast cancer.

PS-01-087
Assessment of cell density in initial, intermediate CNB and in resection specimen after neoadjuvant chemotherapy
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Objective: cell distribution and cell density are the main characteristic for tumour pathology especially in neoadjuvant settings. We performed image analysis tool to characterize cell density within tumour before, during and after neoadjuvant therapy.
Method: The study included 52 breast carcinomas before, during and after neoadjuvant therapy. We analyzed a total number of tumour cells in breast cancer from a 1 sq mm sample of histology slide.
Results: Mean absolute tumour cells in 1 mm2 of histology slide was in first sample of breast cancer before neoadjuvant therapy was 6332.78/mm2, in intermediate CNB after 2–3 cycles of neoadjuvant therapy cell density come down to 4963,03/ mm2 and in final resection specimen there was different level of cell dencity reduction from 4052/mm2 (no response) to 432/mm2 (complete response) according Miller and Payne grading system.

Conclusion: image analysis is a good and objective tool to determinate cell density in neoadjuvant settings.

PS-01-089
Unusual presentation of metastatic breast cancer
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Objective: The most common locations of breast cancer metastasis are lung, bone, liver and brain. This paper aims to present few unusual sites of metastatic breast cancer.
Method: We performed a retrospective analysis of metastatic breast cancer with particular location diagnosed between 2010 and 2016. To determine the origin and the type (ductal vs. lobular) of the tumours, immunohistochemical stains with mammaglobin, Ck7, ER, PR, and E-cadherin were performed.
Results: We identified four patients with unusual sites of metastatic breast cancer (53, 58, 69 and 75 year-old). First case was an incidental breast cancer discovered due to ureterostenosis produced by metastatic tumour; the second patient presented with kidney tumour (renal cell carcinoma) and after radical nephrectomy was diagnosed with ureteral, lymph node and periadrenal tissue involvement by metastatic breast cancer. The other two patients, already known with primary breast cancer, presented, both, with gastro-intestinal symptoms and ascitic syndrome and secondary involvement of epiploon and stomach in the former, and stomac and colon in the later.
Conclusion: Metastatic breast cancer in stomach, colon, epiploon and ureter is possible, even uncommon, and pathologists must consider it in their practice, as a primary manifestation or as a late dissemination of disease, many years after de diagnosis of primary tumour.

PS-01-090
Digital quantification of Ki67 in breast cancer
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Objective: Ki-67 index is a predictive and prognostic factor in breast cancer (BC). Standarize its determination and establishing a relevant cut-off point is still under debate. The aim of this study is to evaluate the concordance between Ki-67 obtained by visually assessment and automated digital image analysis (DIA).
Method: We evaluated 154 biopsies of patients diagnosed of BC in 2010. Ki-67 immunostained slides were eye ballen assessed (EB) with optic microscopy in hot spot, by general pathologists (GP) and 2 breast pathologists (BP) and DIA by one BP considering 500 cells in hot spot.
Results: Comparing EB between GP and BP, the difference in Ki-67 mean value (MV) was 7 points. Concordance (Kappa), classifying Ki-67 into three groups (0-14/15-29/30-100), was 0.42. The difference in Ki-67 MV among EB of GP and DIA was 19 points and Kappa 0.26. The difference in Ki-67 MV using EB of BP and DIA was 12 points and Kappa 0.36.
Conclusion: There are major differences regarding the mean value and Kappa of Ki-67, both among GP, BP and digital quantification. These results throw into question the use of Ki-67 cut-off points for clinical treatment and the need to standardize its assessment.

PS-01-091
Touch imprint cytology of sentinel lymph nodes in breast cancer: One institution's experience
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Objective: To asses touch imprint cytology (TIC) of sentinel lymph node (SLN) as intra-operative diagnostic tool for breast cancer patients.
Method: We analysed 120 SLN from 99 patients. The excised sentinel lymph nodes were freshly examined and bisected longitudinally or serially sectioned at 2 mm intervals on the long axis. Each cut surface was imprinted on the glass slide. Cytology smears were air dried and stained with May-Grünwald-Giemsa (MGG Quick stain). Results of touch imprint cytology were compared with permanent histology sections. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) and accuracy were calculated.
Results: The comparation between TIC and permanent sections showed 102 (85 %) true negative imprints, and 13 (10,8 %) true positive imprints. There were 5 (4,1 %) false negative imprints (2 macrometastasis and 3 micrometastasis). The overall sensitivity was 72 %, specificity 98 %, PPV 87 %, NPV 95,3 % and accuracy was 95,83 %.
Conclusion: TIC is simple, rapid and inexpensive diagnostic method in intra-operative evaluation of SLN metastases with breast cancer patients. However, it also has a series of limitations, especially in detecting micrometastases.

PS-01-092
Evaluation of Caveolin-1 expression in molecular subtypes of breast cancer
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Objective: Development of breast carcinoma is regulated by many factors. CAV1 is a protein that humans is encoded by CAV1 gene. The scaffolding protein encoded by this gene is the main component of the caveolae plasma membranes found in most cell type. Recent studies have shown the loss of stromal CAV1 expression in breast carcinomas may have a prognostic importance. In our study, we purposed to evaluate the interactions between stromal CAV1 loss and its association with different pathological and clinical parameters status in breast carcinomas.
Method: CAV1 expressions were studied in 297 formalin-fixed, paraffin-embedded breast carcinoma specimens and its association with different pathological and clinical parameters was evaluated.
Results: Loss of stromal CAV1 expression was detected in 196 (72.3 %) of 297 cases. Statistical significant association was found between loss of stroman CAV1 expression and large tumour size and tumour volumes ve lenf node involvment ($p < 0{,}001$).
Conclusion: Identification of specific biomarkers is very important for prediction of clinical outcome in breast tumours. We demonstrated loss of stroma CAV1 expression in breast cancer correlate with tumour size, HER2 amplification, stage and lenf node involvement. These results suggest that CAV1 may play a role in the biology of breast cancers.

PS-01-093
Percutaneous radiofrequency ablation in breast cancer: Assessing cell death
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Objective: To evaluate the effectiveness of Radiofrequency Ablation technique (RFA) in Breast Cancer using different cell viability staining methods.
Method: Patients diagnosed on core biopsies of Infiltrating Breast Carcinoma of No Special Type with tumour size ≤2 cm underwent RFA. A new core biopsy pre-RFA was performed followed by lumpectomy. NADH, COX and SDH staining were made using frozen sections, and in paraffin embedded sections H-E, TUNEL, CK19 and CK18 were performed.

Results: Fifteen patients were included. NADH was positive in 12/12 pre-RFA and negative in 9/12 post-RFA. CK18 was positive in 14/15 pre-RFA and negative (10) or focally positive (4) in 14/15 post-RFA. CK19 was positive in 15/15 pre-RFA and negative (12) or focally positive (3) in 15/15 post-RFA. TUNEL was negative in 13/15 pre-RFA and positive in 14/15 post-RFA. COX was positive in 10/12 pre-RFA and negative in 10/12 post-RFA. SDH was positive in 11/11 pre-RFA and negative in 7/11 post-RFA.
Conclusion: Breast Cancer treated with RFA exhibits a decreased expression of NADH, COX and SDH and increased TUNEL positivity. Cytokeratins 19 and 18 have an excellent correlation with the results obtained by the rest of the markers, all of which are indicators of cell death.

PS-01-094
Changes in ER, PgR and HER2 after neoadjuvant chemotherapy
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Objective: After NCT tumours, which do not achive pCR can became new characteristics and change preview.
Method: 145 patients with primary operable breast cancer who received NACT at Petrov oncology institute. Oestrogen receptor (ER), progesterone receptor (PR) and HER2 status were compared between pretreatment and post-treatment residual samples.
Results: Pathological complete response (path CR) was achieved in 21 cases (14.5 %) of patient. In rest 124 cases there were change in ER/PR/HER2 status occurred in 15, 14 and 19 % of cases, respectively, as a switch from negative to positive status for ER and PR in half (8 and 6 %) of the cases and from negative to positive status for HER2 in 13 % cases.
Conclusion: Changes in hormone receptors and HER2 status in 15–19 % cases occur after NACT. Assess of changes after NCT lead to re-testing all of those markers.

PS-01-095
Breast cancer molecular subtypes defined by estrogen receptor progesterone receptor and human epidermal growth factor receptor type 2 status: Association with clinicopathologic parameters in Ivorian patients
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Objective: To determine the prevalence of molecular breast cancer subtypes and to assess their associations with classical clinicopathologic parameters for better therapeutic decisions in breast cancer patients.
Method: Formalin-fixed and Paraffin-embedded blocks of primary breast carcinoma patients were subjected to immunohistochemical assay for the assessment of estrogen receptor (ER), progesterone receptor (RP), and human epidermal growth factor type 2 (HER2) expression. The one-way analysis of variance and the chi-square test were used to compare tumour subtypes with clinicopathologic prognostic parameters.
Results: The positivity rate of ER, PR, and HER2 was 56, 49, and 15.6 %, respectively. Half of patients (51.6 %) had luminal A followed by triple negative (32.1 %). Other subtypes were luminal B (10.1 %) and non-luminal HER2+ (6.3 %). Tumour subtypes were not significantly associated with mean age ($p = 0.52$), menopausal status ($p = 0.76$), histological type ($p = 0.59$). However, breast cancer subtypes were closely correlated with tumour grade ($p < 0.00001$).
Conclusion: The current study should primarily contribute to the reevaluation of the systematic use of adjuvant hormonal therapy and has prognostic and therapeutic implications for the breast cancer management in Ivory Coast.

PS-01-096
Accuracy of the duration of tissue formalin fixation and the molecular profiles of primary breast cancers in a tertiary hospital of Rwanda
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Objective: Breast cancer (BC) is the second most commonly diagnosed cancer in women in Rwanda. BC molecular profile requires optimal tissue fixation duration; no corresponding study yet published in Rwanda. The aim is finding out effect of fixation duration on BC receptors in Rwanda for good clinical and laboratory practices.
Method: Were included 45 BC cases diagnosed from 2013 to 2015 in a tertiary hospital in Rwanda. Optimal fixation duration was defined to be 24–48 h. Histological typing, grading, oestrogen receptor, progesterone receptor and HER2/neu receptor status was evaluated through blind reviews. Data analysis used Stata 13.0. Two-tailed ($P < 0.05$) was considered significant. Ethical clearance was obtained from Hospital Ethics Committee.
Results: Mean age was 51.9 (35–74) years. Tissue fixation duration was optimal in 24.4 %, [mean 141.8 (24–720) hours]. Histological types were ductal carcinoma (75.6 %), lobular carcinoma (13.3 %) and metaplastic carcinoma (4.5 %). Most cases were grade III (42.2 %). Molecular types were luminal A (45.2 %), luminal B (19.4 %), HER2+ (6.5 %) and triple negative (29.0 %). No significant association seen between age and BC molecular type; molecular type and adequacy of fixation or between molecular type and histological type.
Conclusion: Larger studies are recommended to determine the optimal fixation duration for consistent BC molecular profile.

PS-01-098
Quantification of Cytokeratin 19 mRNA burden and correlation with axillary dissection positivity in breast cancer patients
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Objective: The study of sentinel lymph node by cytokeratin 19 mRNA quantification using One-Step Nucleic Acid Amplification (OSNA) in patients with breast cancer may be useful to decide axillary dissection. This study analyzes tumoural burden as a predictor of metastasis at axillary dissection specimen.
Method: We reviewed 54 cases of breast cancer patients who underwent surgery with sentinel lymph node macrometastasis determined by OSNA and examined the results of axillary dissection from those patients.
Results: Cases presented 1 to 4 sentinel lymph nodes positive for macrometastasis. Axillary dissection was positive for macrometastasis in 27 cases (50 %). Mean CK 19 mRNA tumoural burden was 472,620 copies/μL for cases with negative axillary dissection and 1,520,485 copies/μL for cases with positive axillary dissection ($p = 0,11$).
Conclusion: We found no statistically significant difference between the two study groups in axillary dissection positivity. Previous studies support that high tumoural burden correlates with positive axillary lymph nodes after dissection. This method may be helpful when deciding which patients may undergo axillary dissection.

PS-01-099
Angiosarcoma of the breast: A single-institution experience
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Objective: Breast angiosarcoma (BA) is a rare and aggressive tumour. Our aim was to characterize all cases of BA diagnosed at Portuguese Oncology Institute-Porto (IPO-Porto).

Method: Retrospective review of BA diagnosed at IPO-Porto between 2000 and 2016. Clinical and follow-up data were collected. All slides were re-evaluated and additional immunohistochemistry was performed in some cases. When possible, tumours were graded according to Rosen's method.
Results: Fourteen cases were identified: 3 primary BA (2 high-grade, 1 intermediate-grade), 10 radiation-therapy (RT) associated BA (7 high-grade, 1 low-grade) and 1 case associated with Stewart-Treves syndrome (high-grade). Average post-RT time interval was 86.8 months. All patients were female, average age was 59.2 years-old (range 29–89) and average tumour size was 5.75 cm (1.8–14). Twelve patients were treated surgically and 7 underwent adjuvant treatment. Average follow-up time was 22.3 months (range 0–74). Local recurrence occurred in 2 patients (2 and 4 months after diagnosis) and two developed metastasis (7 months after diagnosis). So far, 5 patients have died of disease (average 19.6 months after diagnosis).
Conclusion: The majority of BA diagnosed at our Institution was RT-associated. There were no clinical or histological differences between primary and secondary tumours. In our series, all local recurrences and metastases occurred in high-grade BA.

PS-01-100
Secretory breast carcinoma: Clinical, pathological and molecular analysis
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Objective: Characterization of secretory breast carcinoma(SBC) cases diagnosed at Portuguese Oncology Institute-Porto(IPO-Porto).
Method: Retrospective review of SBC cases diagnosed and treated at IPO-Porto (2000–2016). Clinicopathological data was retrieved. All slides were re-evaluated. Immunohistochemistry study with hormonal receptors (ER, PR, AR), HER2 and GCDFP-15, and fluorescent in situ hybridization (FISH) for ETV6 gene rearrangements was performed.
Results: Five cases were identified: all female; median age: 57 years (range 41–75); median tumour size: 16 mm (range 8–25); 4 cases were Nottingham grade1 and one was grade2. All presented ETV6 rearrangement. ER expression was low (1-10 %) in 3 cases; 2 cases were triple-negative. AR was negative in 4 cases and one had low expression (1-10 %). All were positive for GCDFP-15. Initial treatment was surgical (4 lumpectomy with radiotherapy and 1 mastectomy); sentinel lymph node was negative in all patients. One patient was submitted to additional chemotherapy and two to hormonotherapy. All remain disease-free(median follow-up 36 months, range 21–108).
Conclusion: SBC is a rare breast carcinoma with specific histological and genetic features, usually with favorable prognosis. Traditionally seen as a triple-negative low grade carcinoma, there are increasing reports of higher histological grades, low expression of hormonal receptors(ER and AR) and positivity for GCDFP-15. Our series also parallels the treatment heterogeneity reported, precluding conclusive statements on its effectiveness.

PS-01-101
Expression of MDM2 and CDK4 in liposarcoma arising in malignant phyllodes tumour—a case report
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Objective: Malignant Phyllodes tumours (MPT) are rare fibroepithelial tumours of the breast with infrequent heterologous sarcomatous differentiation including liposarcoma, fibrosarcoma, osteosarcoma and rhabdomyosarcoma. There is limited published literature on molecular profile of these sarcomatous elements. We report a case of malignant phyllodes with liposarcomatous differentiation. Understanding their molecular profile may have important therapeutic implications for such tumours. The aim of this study was to find the MDM2 and CDK4 gene expression in liposarcomatous elements in MPT.
Method: A 21 year old pregnant lady presented with left breast mass. Biopsy of the mass confirmed the malignant phyllodes tumour. Subsequently, she underwent simple mastectomy which showed malignant phyllodes tumour with liposarcomatous differentiation. MDM2 and CDK4 which are used in identifying primary soft tissue liposarcoma were performed on a formalin-fixed paraffin-embedded sample.
Results: Despite being histologically identical to the primary soft tissue liposarcoma, MDM2 and CDK4 were negative underlying a different molecular pathogenesis.
Conclusion: Our results suggest that the heterologous liposarcomatous differentiation in MPT lack the expression of MDM2 and CDK4, characteristic of primary soft tissue liposarcoma. This possibly favours the concept that heterologous differentiation may have originated from metaplasia of stromal cells that underwent a malignant change negating the potential use of MDM2 inhibitors and CDK4 antagonists.

PS-01-102
Breast cancer in young women: A clinicopathological study of an argentinian population
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Objective: Breast cancers in young women (diagnosis before 40 years) are a biological and genetic distinctive subset of tumours with more aggressive course. In our population the clinicopathologic characteristics hasn't been yet described.
Method: 52 cases where retrieved from our files in a 9 year period. A retrospective and descriptive study was performed with clinicopathological prognostic factors according WHO criteria.
Results: The mean age was 36 years. The great mayority were ductal NOS (67.3 %) with high nuclear grade (87 %), high histological architecture (81 %) and medium mitotic activity (36.5 %). 61.3 % show angiovascular invasion and 76.9 % low TIL response. T2 stadium was the more frequent (42.3 %) with mean size 2.36 cm, 36.2 % has no lymph node metastasis. The predominant phenotype by immunohisotchemistry was Luminal B (39,13 %).
Conclusion: As others studies, these subset of cancers exhibit more aggressive features including a distinct predominant phenotype not yet described in other studies.

PS-01-103
Digistain: A novel biomarker imaging platform for grading breast DCIS using routinely processed paraffin sections
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Objective: "Digistain" is a new and validated imaging technology that enables the quantification of a newly conceived biomarker that is present in routinely processed, and unstained FFPE sections. By using a unique optical signature to analyse the chemical make-up of the biopsy quantitatively, the technique circumvents the subjectivity inherent in grading. Within minutes of loading a slide it yields a highly reproducible and user independent numerical score reflecting the Nuclear: Cytoplasmic ratio. We term this the Digistain Index (DI).
Method: In a double-blinded study, 42 breast DCIS biopsies were reviewed and graded by an experienced breast pathologist. A new section was cut from each block, left unstained and loaded into the Digistain instrument. A region of interest (ROI) defined by the pathologist was analysed to generate a DI for each case.

Results: A positive correlation is seen between DI score and histological grade (as assessed by the pathologist) thus validating this index as a viable indicator of histological grade.
Conclusion: We believe the new Digistain approach provides for the first time, a cost effective, reproducible and quantitative measure of breast DCIS grade. This technique can be further developed to deliver an effective assessment of prognosis and recurrence risk that reaches beyond traditional qualitative measures based on H & E staining.

PS-01-104
Intratumoural heterogeneity can impact on the definition of the HER2 "double equivocal" category in breast cancer
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Objective: To investigate whether prevalence and pattern of intratumoural HER2 genetic heterogeneity in breast cancer may affect the definition of the HER2 equivocal category.
Method: We collected 131 score 2+ carcinomas that underwent fluorescence in situ hybridization (FISH), scored according to the ASCO/CAP 2013 guidelines. HER2 and CEP17 copy numbers, HER2/CEP17 ratio, prevalence/type of heterogeneity were recorded for each case. For cases displaying HER2 genetic heterogeneity FISH results were reported as a whole (mean of HER2 and CEP17 copy numbers of amplified and not amplified cells) as well as discrete populations (mean HER2 and CEP17 copy numbers calculated within the two populations).
Results: Ninety-seven (74 %) cases were FISH-negative, 34 (26 %) were FISH-positive, of which 27 displayed heterogeneity of HER2 amplification (range: 11–43 %). In the latter subgroup, when FISH raw values were calculated in the entire population 4 were still positive based on HER2/CEP17 ratios > =2, whereas 23 were labeled "equivocal" (HER2/CEP17 ratio <2, HER2 copy number 4-6).
Conclusion: Presence of >10 % of HER2 amplified cells (HER2 > =6) in a tumour population may lead to equivocal ISH results. Interpretation of type of heterogeneity (discrete clone versus scattered cells) is crucial to diagnose these cases either as equivocal ("double equivocal") or positive for HER2 amplification in a subpopulation of tumour cells.

PS-01-105
Expression of Human Epididymal Secretory Protein 4 (HE4) is negatively correlated with HER2 status in breast carcinomas
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Objective: Epididymal Secretory Protein 4 (HE4) is originally described as an epididymis specific protein but more recently suggested to be a putative serum tumour marker for some tumours including the breast carcinomas. In this study, we purposed to investigate the interactions between HE4 expression and molecular subtypes of breast carcinomas.
Method: HE4 expressions were studied in 258 formalin-fixed, paraffin-embedded breast carcinoma specimens and its association with different pathological and clinical parameters was evaluated.
Results: Decreasing HE4 expression rate was 34.64 %, while diffuse strong expression rate was 10.8 %. We demonstrated that there were no associations between the HE4 expression in breast cancer with tumour size, stage, survive and lymph node involvement. It was only detected that HE4 expression was negatively correlated with HER2 amplification and/or CErbB2 expression (0.009).
Conclusion: Identification of specific biomarkers such as HER2 is very important for prediction of clinical outcome and therapy responce in tumours. In this study, we demonstrated the significant association between HE4 and cErbB2 expressions. These results suggest that HE4 may be a predictor for behavior of breast cancers.

PS-01-106
Loss of nuclear ARID-1A expressions is associated with status of hormon receptors in breast carcinomas
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Objective: Breast cancer is the most common cancer among women worldwide. Development of breast carcinoma is regulated by many factors. AT-rich interactive domain IA (ARIDIA) is a tumour suppressor gene involved in chromatin remodeling and it encodes the ARIDIA protein. Recent studies have shown the loss of ARIDIA expression in different carcinomas may have a prognostic importance. In our study, we purposed to evaluate the interactions between ARIDIA loss and molecular subtypes of breast carcinomas.
Method: ARIDIA expressions were studied in 292 formalin-fixed, paraffin-embedded breast carcinoma specimens and its association with different pathological and clinical parameters was evaluated.
Results: Loss of ARIDIA expression was detected in 89 cases. Mean nuclear expression percentage of ARID-1A was 70. There was no statistical association between ARID-1A expression and molecular subtype of breast carcinomas. Contrary, there was significant association between ARIDIA expression and presence of estrogen (P = 0.003) or progesterone receptors (p = 0.002).
Conclusion: Identification of specific biomarkers is very important for prediction of clinical outcome in tumours. In addition, some parameters such as HER2 also provide therapeutic benefits. In this study, we demonstrated loss of ARID1A expression positively correlate with status of hormone receptors. These results suggest that ARID1A may play a role in the biology of breast cancers especially of triple negative subtypes.

PS-01-108
Comparison of prognostic factors and survival rate of primitive breast sarcoma and sarcoma phyllodes
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Objective: Compare the prognostic factors, the overall survival (OS) and the recurrence-free survival (RFS) between Sarcoma phyllodes of the breast (SP) and Non-phyllodes primary breast sarcoma (NPS).
Method: A retrospective study conducted at the Institute Salah Azaïz between 2004 and 2013 has allowed to collect 18 SPs and 12 NPSs. We studied the correlation between these histological subtypes and the clinicopathological criteria.
Results: An analytical study of the parameters age, tumour size, mammographic features, presence or absence of metastases and locoregional recurrence showed no correlation with histological type (p > 0,05). In univariate analysis, the median OS was 10 months for SP against 60 months for NPS. The influence of the histological type was not significant (p = 0,08). RFS was 7 months for SP and 23 months for the NPS. The influence of the histological type was not significant (p = 0,081). In multivariate analysis, the retained independent prognostic factors for OS were age (p = 0,06) and tumour necrosis (p = 0,02).
Conclusion: The same therapeutic strategies must be indicated for SP and NPS. Surgical treatment is the most important. The role of radiotherapy and chemotherapy are debated.

PS-01-109

Increasing diagnostic accuracy of fibroadenoma and benign phyllodes tumour in core biopsy using histopathologic scoring system

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Objective: Fibroadenoma is very difficult to differentiate from benign phylllodes tumour especially in core biopsy. This study was aimed to identify histopathological features needed to differentiate those tumours and to verify whether using scoring system on those histological features will improve diagnostic accuracy in core biopsy.
Method: 57 cases with paired core biopsy and excision/mastectomy with diagnosis of fibroadenoma and benign phyllodes tumour were included in this Study. Reassessment of histological features were done blindly, with and without scoring system, and excision/mastectomy served as the gold standard. Histopathologic features which assessed were stromal cellularity, nuclear atypia, tissue fragmentation, fat infiltration, mitotic figure, stromal heterogeneity. The scoring system were very mild (0), mild (1), moderate (2) for stromal cellularity and nuclear atypia; low (1), moderate (2), marked (3) for mitosis; none (1) and present (2) for fat infiltration, stromal heterogeneity and tissue fragmentation. Analytical statistic, diagnostic test and accuracy test were done.
Results: Stromal cellularity, stromal heterogeneity and tissue fragmentation mostly found in benign phyllodes tumour compare to fibroadenoma ($p = 0{,}001$; $p = 0{,}000$; $p = 0{,}021$). The Specificity in scoring system increased by 17,9 % whereas positive predictive value, negative predictive value and accuracy increased in scoring system (11,9 and 5,1 %). Area under curve increased by 8,9 %.
Conclusion: Scoring system improve the diagnosis accuracy of fibroadenoma and phyllodes tumour as shown by the increasing specificity, positive predictive value, accuracy and AUC. This can be used as reference to diagnose and differentiate fibroadenoma and benign phyllodes tumour especially in core biopsy.

PS-01-110

Neoadjuvant chemotherapy in young breast cancer in women of western Algeria: Survival study

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Objective: The aim of this study is to define the impact of neoadjuvant chemotherapy (NCT) on survival patients of less than 39 years of age.
Method: A retrospective analysis was made on survival data of 84 patients with operable breast cancer, admitted from January 2008 to June 2014 in the oncology department of Sidi Bel Abbes (Algeria), for NCT cures followed by surgery and adjuvant treatments. Patients were stratified into three age groups (group 1, ≤39 years; group 2, 40–44 years; group 3, ≥45 years). The overall survival (OS) and the disease free survival (DFS) were calculated using the Kaplan-Meier method. The 5-year survival was analyzed according to age at diagnosis. The log-rank test was used in univariate comparison.
Results: The median follow up was 30.5 months. The 5-year disease free survival rates were 42.9 % in the youngest patients, compared with 80 and 70 % in groups 2 and 3, respectively ($P = 0.014$), with a median 5-year DFS of 48 years (95 % CI 8.316-87.684). Group 1 patients also had significantly a lower 5-year overall survival rates (50 % versus 90 % and 72 %; $P = 0.045$).
Conclusion: The patients in the youngest age group remained at a high risk for recurrence and a worse overall survival.

PS-01-111

E-cadherin, P-cadherin, beta-catenin and p120-catenin expression in Luminal B (HER-2 positive) subtype of invasive lobular breast cancer

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Objective: The aim of the research was to study a relation between E, P-cadherins, beta- and p120-catenins in HER-2/neu, ER, PR-positive subtype of breast cancer.
Method: 50 cases of Luminal B (HER-2 positive) subtype of breast cancer were explored. IHC study was conducted with use of automatic staining systems Ventana (USA) and DAKO (Denmark) and specific antibodies to E-cadherin (Clone EP700Y, Cell Marque, USA), β-catenin (Clone14, Ventana, USA), p120-catenin (Clone98, Ventana, USA), P-cadherin (Clone56C1, Monosan, the Netherlands), c-erb-2/HER-2 (Clone4B5, Ventana, USA), KI-67 Antigen (CloneSP6, Spring Bioscience, USA), ER (CloneSP1, Spring Bioscience, USA), PR (CloneSP2, Spring Bioscience, USA).
Results: Loss of E-cadherin expression was found in 2 (4 %) cases. We observed cytoplasmic β-catenin staining in 16 (32 %) cases, p120-catenin—in 50 (100 %) cases. Coexpression of E- and P-cadherins was found in 48 (96 %) cases. The correlation was determined between β-catenin and p120-catenin ($V = 0.32$, $p < 0.05$), PR ($V = 0.32$, $p < 0.05$), HER-2 ($V = 0.20$, $p < 0.05$); p120-catenin and PR ($V = 0.28$, $p < 0.05$).
Conclusion: The results speak about appearance of aberrant P-cadherin expression connected with E-cadherin expression in Luminal B (HER-2 positive) subtype of breast cancer, destruction of cadherin-catenin complexes and release of β-and p120-catenin molecules which activate signaling pathways leading to increase of motility, migration, invasion and proliferation of breast cancer cells.

PS-01-112

Do NY-BR-1 and CD10 have a prognostic participation in invasive ductal breast carcinoma? An immunohistochemical correlational study

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Objective: To study immunohistochemical expression of NY-BR-1 and CD10 in invasive mammary ductal carcinoma, correlate their expression to different clinicopathological parameters to elucidate their effect on prognosis.
Method: Eighty cases of invasive mammary carcinoma were classified according to their ER, PR and Her-2 expression into luminal, Her-2 Positive and triple negative groups. NPI was calculated and pathological stage was recorded for each individual case and cases were classified into different prognostic groups. NY-BR-1 and both stromal & tumour cell CD10 expressions were evaluated immunohistochemically, their expression compared to DCIS & normal breast tissue, and correlated to different prognostic variables.
Results: NY-BR-1 and both stromal & epithelial cell CD10 expression varied significantly between studied groups. Invasive ductal carcinoma cases showed NY-BR-1 positivity in >70 % of tumour cells in 57.5 % of cases. NY-BR-1 showed a significant correlation to NPI, tumour stage, hormonal and her-2 immunoprofile. CD10 expression in tumour epithelial cells correlated significantly to hormonal and her-2 immunoprofile, while CD10 stromal expression had a significant correlation to LN status and tumour stage.
Conclusion: NY-BR-1 is a differentiation antigen of the breast, which is present in normal and tumourous mammary epithelium. High prevalence of both NY-BR-1 and CD10 in hormone negative tumours and higher stages indicate that they could be a valuable targets for development of novel therapies.

PS-01-113

Expression of MHC class II-associated invariant chain (Ii; CD74) in invasive breast carcinoma: Its relation to Nottingham prognostic index, hormone-receptors' & Her-2 immunoprofile

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Objective: To study the immunohistochemical expression of CD74 in series of invasive breast carcinomas classified according to their ER, PR & Her-2 immunoprofile and explore its correlation to Nottingham prognostic index (NPI) and tumour pathological stage to determine if it has a prognostic value.
Method: One hundred and sixty cases of mammary carcinoma were classified broadly according to their ER, PR and Her-2 expression into luminal, Her-2 Positive and triple negative groups. NPI was calculated and pathological stage was recorded for each individual case and cases were classified into different prognostic groups. CD74 expression was evaluated immunohistochemically and correlated to different prognostic variables.
Results: CD74 immunohistochemical expression in invasive breast carcinoma was significantly higher in triple negative tumours, higher tumour grade, presence of lymph nodal metastasis, higher tumour stage and higher Nottingham prognostic index score.
Conclusion: CD74 immunohistochemical expression in invasive breast carcinoma was significantly higher in triple negative tumours, higher tumour grade, presence of lymph nodal metastasis, higher tumour stage and higher Nottingham prognostic index score.

PS-01-116
Breast sebaceous carcinoma - a rare entity. Clinicopathological description of two cases
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Objective: To describe clinicopathological features of two cases of primary breast sebaceous carcinoma (BSC) managed at our institution and compare them with the only 11 cases reported.
Method: We reviewed the histologic slides, patients' clinical data and pertinent articles indexed in PubMed.
Results: Two women with 65 and 71 years-old presented with a palpable nodule with 70 mm (patient 1) and 37 mm (patient 2). Grossly, both tumours were well-circumscribed, yellow-tan. Histologically, they were lobulated, with solid and nested pattern, composed of high-nuclear-grade clear cells with abundant microvacuolized cytoplasm rich in lipids (RedOil), coexisting with smaller darker cells at the periphery. Immunohistochemical profile (ER, PR, Her2) was discordant between the cases, except for diffuse EMA expression. At diagnosis: patient 1 = pN2; patient 2 = pN0, without evidence of distant metastasis. Patient 1 refused further treatment, and died 9 months after surgery, due to recurrence. Patient 2 is alive with no signs of recurrence after 90 months of follow-up. No microsattelite instability (MSI) was found in the tumour.
Conclusion: Our cases support that BSC has a distinct morphology, variable immunoprofile and may behave aggressively, although it is unknown if it differs from other high grade carcinomas. MSI is not characteristic of BSC, contrasting with cutaneous counterpart.

Monday, 26 September 2016, 09.30–10.30, Hall 11.3
PS-02 Cardiovascular Pathology

PS-02-001
Interaction of persistent chlamydiapneumoniae infectionin endothelial cell swithcell-mediated immune response on the surface of human atherosclerotic plaques
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Objective: Examining inflammatory cells interaction during Chlamydia pneumoniae(CP) persistence in endothelial cells (EC).
Method: Autopsy material collected from 46 patients aged 35–92. It received imprints of fatty streaks, plaques and unaffected surfaces of 46 aortas subjects. Samples were stained on Romanovsky-Gimsa. CP-infected EC and inflammatory cells and microerosions number were detected. Statistical data were processed using Fisher method.
Results: CP was detected in EC aortas in 26 (56.5 %) from 46 patients. In 39 cases, death cause was cardiac, of which 19 patients had persistent EC CP inclusion forms. Inflammatory infiltration was detected in 17 patients and in 13 patients (76.5 %) coincidence with CP positive identification in EC ($p = 0.04$) was registered. 14 patients (82.3 %) from 17 patients with inflammatory infiltration showed coincidence with positive identification of microerosions on aortic intima ($p = 0.009$). Connection between EC CP identification and microerosions on aortic intima was also statistically significant. Thus, 19 (48.7 %) from 39 patients had persistent EC CP,and 15 patients (78.9 %) demonstrated coincidence with positive identification of microerosions ($p = 0.046$).
Conclusion: Statistically significant relationship between persistent Chlamydia pneumoniae in endothelial cells, chronic inflammation and development of microerosions on the surface of human atherosclerotic plaques was discovered.

PS-02-002
Cardiac papillary fibroelastoma: 15 years' experience of a central institution
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Objective: Primary tumours of the heart are very rare (0.02–0.28 %). Papillary fibroelastoma (PFE) is the third most frequent cardiac tumour (7 %), usually found in the valves. We present a study that evaluates the incidence of these tumours in a central Institution and correlates them with embolic manifestations as form of presentation.
Method: A retrospective analysis of cardiac tumours was performed over a period of 15 years (2001–2015) in Centro Hospitalar Lisboa Norte, being selected (with review of different variables in clinical processes) those which histological diagnosis was PFE.
Results: A total of 103 patients with cardiac tumour, 15 (14.56 %) had PFE: 6 female and 9 male, mean age 64.8 ± 15.5 years. Seven of them had cerebral embolic events. The diagnosis of cardiac tumour was made by echocardiography (in 14 cases), transthoracic and/or transoesophageal, and in intraoperative consultation (1 case). The definitive diagnosis was made in histopathological sections. Treatment was surgical removal of the tumour mass, with valve replacement in 5 cases.
Conclusion: The analysis realized in our Institution verified the rarity of this diagnosis. Although PFE is a benign tumour, its high embolic potential can cause life-threatening complications, so early diagnosis is important because surgical removal is curative.

PS-02-003
Aortic stenosis and regurgitation of the elderly follow different processes of collagen ageing
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Objective: To investigate the mechanism of collagen alteration in aortic valves (AV) due to aging we compared stenosis (AS), regurgitation (AR) and normal aortic valves.
Method: To estimate the stiffness of AV, speed-of-sound (SOS) through fibrosa of AV was measured by scanning acoustic microscopy (SAM). To detect protease susceptibility, SOS after collagenase digestion was compared. Collagen distribution of type 1 and 3, degree of glycation and stabilization were analyzed by immunostaing.

Results: The AS group displayed significantly less SOS values compared to the AR group with an exception of calcified areas. The AS group showed significantly decreased SOS values following protease digestion, whereas the AR showed little reduction. The AS group presented type III collagen in the fibrosa and the ventricularis. In the AR group, both type I and III collagens coexisted at the fibrosa and ventricularis. By advanced glycation end-products staining, the AS group showed sparse, weak staining, whereas the AR group presented a strong positive reaction on the fibrosa. By lysyl oxidase staining the AS group showed scattered positive staining on the fibroblasts, while the AR group displayed negative staining.
Conclusion: AS displayed tissue remodeling with destruction and repair, while AR showed static chemical alterations with slow turnover of collagen.

PS-02-004
Can increased intraplaque microvessels predict acute coronary event? A pathologic study of coronary arteries in 894 human autopsy cases
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Objective: Previous studies suggested that increased intraplaque neovessels were associated with intraplaque hemorrhage and plaque vulnerability. Our aim was to investigate the relationship between intraplaque microvessels and culprit plaque morphology in acute myocardial infarction (AMI).
Method: Hearts were obtained from consequent autopsies (n = 894; median 82.0 years; 497 M) from 2005 to 2015. We only included patients who died of AMI without PCI or CABG. After serial step-sectioning (total 48,901 cross sections), 26 culprits were classified as erosion (n = 14), plaque rupture (n = 5), calcified nodule (n = 4), and stenosis without thrombus (n = 3). The most stenotic culprits were assessed using micro-computed morphometry.
Results: Intraplaque hemorrhage was found in 96.2 % of culprits. The numbers of intraplaque microvessels were medians of 53.5 (range, 8–118) in erosion, 71 (34–83) in plaque rupture, 22 (0–24) in calcified nodule, and 22 (8–121) in stenosis w/o thrombus, respectively. Intraplaque microvessels were significantly increased in erosion ($p = 0.01$) and plaque rupture ($p = 0.01$) when compared with calcified nodule; however, there was no significant difference between erosion and plaque rupture ($p = 0.25$). The number of microvessels was not associated with severity of stenosis, intraplaque hemorrhage, or necrotic core size.
Conclusion: Intraplaque hemorrhage was common in any types of coronary culprits; however, not all coronary culprits were associated with increased intraplaque microvessels.

PS-02-006
Histopathological characteristics and clinical correlations in type A acute aortic syndromes patients
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Objective: The aim of this study was to assess the histopathological characteristics and the clinical correlations of type A Acute Aortic Syndromes (AAS).
Method: Our study population was composed by 158 type A AAS surgically treated patients, for whom we described the aortic medial layer degenerative, inflammatory and atherosclerotic lesions. Moreover, we correlated these findings with the patients' baseline clinical data, long-term follow-up for mortality, major aorta-related and non-aorta-related events.
Results: We identified two histopathological patterns: 122 patients with degenerative alterations (77.2 %) and 36 (22.8 %) with mixed degenerative-atherosclerotic lesions. Patients with moderate/severe overall degenerative alterations showed a higher prevalence of translamellar mucoid extracellular matrix accumulation (T-MEMA), laminar collapse and severe elastic fibre fragmentation. Patients with mixed alterations were older and presented a higher prevalence of translamellar collagen increase (TCI). Non-significant differences were found between the two subgroups with respect to 6-year mortality and major aorta related events, although the mixed group showed a trend to a poorer prognosis.
Conclusion: although degenerative medial alterations are the essence of AAS, atherosclerosis is a relevant finding among older patients. TCI (i.e. fibrosis) increase showed a strong correlation with atherosclerotic lesions while MEMA was more prevalent among the degenerative subgroup. Elastic fibre fragmentation was an ubiquitous finding.

PS-02-008
Phospholamban immunostaining is a highly sensitive and specific method for diagnosing PLN p.Arg14del cardiomyopathy
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Objective: The pathogenic p.Arg14del phospholamban (PLN) mutation has been identified in 12-15 % of Dutch patients with arrhythmogenic cardiomyopathy and/or dilated cardiomyopathy. Recently, we showed that PLN p.Arg14del cardiomyopathy may be diagnosed by PLN immunohistochemistry which allowed microscopic detection of PLN-containing aggregates that were concentrated in cardiomyocytes in dense perinuclear aggresomes. The objective of this study was to determine the sensitivity and specificity of PLN immunohistochemistry to diagnose PLN p.Arg14del cardiomyopathy in a cohort of 26 diverse genetic cardiomyopathies with known pathogenic mutations.
Method: Included were apical left ventricular myocardial specimens, harvested during left ventricular assist device (LVAD) implantation, from 26 well-documented genetic cardiomyopathy cases (5 PLN p.Arg14del cases and 21 cardiomyopathy cases with other pathogenic mutations). Immunohistochemistry (IHC) with monoclonal phospolamban antibody 2D12 (1:10000, Abcam, Cambridge, MA, USA) was used to visualize PLN protein aggregation. Blinded histologic assesment of PLN aggregates in LVAD samples was performed by 2 independent observers.
Results: IHC analysis revealed typical dense perinuclear globular PLN-positive aggregates (representing aggresomes) in all 5 PLN p.Arg14del cases. In 20 cases no IHC staining was observed and one case was inconclusive.
Conclusion: In this genetic cardiomyopathy cohort, PLN IHC analysis in LVAD samples was found to have a very high sensitivity (100 %) and specificity (95 %) for demonstration of PLN protein aggregates in PLN p.Arg14del cardiomyopathy.

PS-02-009
Aortopathy: A surgical pathological analyses of 34 cases
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Objective: Aortopathy refers to non-atherosclerotic and non-inflammatory changes that occur in the media, which are implicated in producing several thoracic aortic diseases. These not only occur in the young population, but are also devastating and fatal. We present our experience on aortic excisions for aortopathy over a period of 8 years.
Method: The clinical and pathological features of aortectomies performed for aortopathy between January 2008 and December 2015 were analyzed. The degree and extent of histological characteristics of aortopathy (Extracellular matrix alterations, Elastic fiber alterations, Smooth muscle cell alterations and Collagen alterations) were studied, and were correlated to the underlying risk factors and the clinical manifestation.

Results: Among the 34 cases encountered, Marfan syndrome, bicuspid aortic valve and hypertension were the most common predisposing conditions for the aortopathy. The patients manifested as ascending aortic aneurysms and surprisingly as chronic type A dissections.
Conclusion: With improved imaging techniques along with successful surgical outcomes, a need towards increased screening and a lower threshold for elective surgery is becoming the current protocol.

PS-02-010
Autopsy study of pediatric Takayasu's Disease
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Objective: To study the clinico-pathological features of Pediatric Takayasu's Disease (PTD).
Method: Autopsy records of 25 years (1991–2015) were reviewed and cases of PTD (ages < 18 years) were retrieved. Demographic characteristics and clinical features were noted. The pattern of involvement of the aorta was classified as localized, multifocal or diffuse.
Results: Of the 55 cases of Takayasu's disease diagnosed at autopsy in 25 years, 23 patients were less than 18 years of age (range of 2 to 18 years, mean of 9.3 years) and included 10 males and 13 females. Four cases had been diagnosed in the ante-mortem period. Localized disease was seen in 11 cases; arch localization in 3 and thoraco-abdominal localization in 8. Multifocal disease was seen in 5 cases, while 7 had diffuse disease. The manifestations were varied, but common modes of presentation included chest or abdominal pain, hypertension, fever, breathlessness, vomiting. Seven cases showed active disease. Pulmonary artery and/or coronary artery involvement was seen in 10 cases. Three children had concomitant rheumatic heart disease.
Conclusion: PTD is a rare entity with varied manifestations in different populations. It often remains unsuspected. Autopsy studies can establish the diagnosis in unsuspected cases and improve the understanding of this disease.

PS-02-011
Persistence of left ventricular myocardial sinusoids in an infant
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Objective: The fetal heart initially has a sinusoidal vascular pattern. Epicardial mesenchymal cells undergo vasculogenesis to form the right and left coronary arteries, which eventually connect to the aorta. As the vasculogenesis process is completed, the myocardium is compacted and the primitive sinusoids disappear.
Method: We present the case of a female 10 month old infant with high grade fever and increased respiratory activity for one day. She had a history of past admissions with similar complaints at 7 and 9 months of age. The heart rate was 170/minute and respiratory rate was 68/minute. Bilateral coarse crepitations were auscultated. A clinical impression was acute bronchiolitis. The child expired within 24 h.
Results: At autopsy the heart was globular in shape with biventricular dilatation (left more than right). Microscopically, features of dilated cardiomyopathy were seen. In addition, dilated endothelium-lined sinusoids were seen in the myocardium of the posterior and lateral walls but no connection could be demonstrated with the ventricular cavity or the epicardial coronaries. The lungs showed changes of bronchopneumonia.
Conclusion: Persistent myocardial sinusoid of the left ventricle is very rare, and may result in abnormal wall motion or ischemia due to coronary steal phenomenon.

PS-02-012
Acute metabolic effects of high glucose alter resistance of cardiomyocytes to oxidative stress
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Objective: The objective of the study is to investigate effects of acute, high glucose (HG, 20 mM)-induced changes in mitochondrial membrane potential on cardiomyocyte resistance to oxidative stress.
Method: Metabolic effects of HG were tested in freshly isolated rat cardiomyocytes by measuring: oxygen consumption, NAD(P)H fluorometry, generation of reactive oxygen species (ROS), mitochondrial membrane potential, opening of mitochondrial permeability transition pore (mPTP) and cell survival. Cells were preconditioned with isoflurane (APC).
Results: HG increased oxygen consumption, NAD(P)H production and mitochondrial membrane potential, which indicated rapid metabolism of excess glucose by cardiomyocytes. This was associated with elevated production of ROS, accelerated opening of mPTP and increased H2O2-induced cell death. Uncoupling agent dinitrophenol reversed HG-induced mitochondrial hyperpolarization, reduced ROS production and reversed cytotoxicity to cytoprotection by HG. Hyperosmotic mannitol control moderately elevated ROS production and exerted cytoprotection. HG prevented APC-induced mitochondrial depolarization and abrogated APC-induced cytoprotection.
Conclusion: HG acutely hyperpolarizes mitochondria leading to excessive ROS production that is detrimental to cardiomyocytes and abolishes APC. Reduction of ROS production by preventing mitochondrial hyperpolarization exerts cytoprotection probably via small amount of ROS that trigger preconditioning.

PS-02-013
Methods of estimation myocardial remodelling in cardiopathy
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Objective: Pathology anatomy of cardiovascular diseases dominates in routine work of pathologist. Implementation of new surgery interventional methods of treatment requires to diagnose degree of involvement cardiac remodeling in thanatogenesis. The aim of our study is objectivization and documentation special morphological aspects of cardiac remodeling due to hypoxic, ischemic and diabetic cardiopathy.
Method: Autopsy material of hearts from newborns (n = 35), under-1 children (n = 32) with hypoxic cardiopathy, from patients 65-75-years-old, died from ischemic (n = 37) and diabetic (n = 35) cardiopathy was analyzed. Comparison groups were hearts of newborns (n = 6), under-1 children (n = 4) and 60-76-years-old adults (n = 9), who were died from accidents resulting in injuries. Macroscopic investigation, separately weighing, computer morphometry and 3D-modelling were performed.
Results: Total heart weight and sizes were significantly enlarged in relation to the same parameters in comparison groups, but cardiac remodelling is performed by different heart chambers: in cases of hypoxic cardiopathy in newborns and under-1 children—by right ventricle, in cases of hypoxic cardiopathy in adults—by left ventricle realized in dilatation type, in cases of diabetic cardiopathy in adults—by left ventricle realized in hypertrophic type.
Conclusion: 3D-modelling offers the possibility to get significant dates, to prognose type of cardiopathy and estimate its involvement in thanatogenesis.

PS-02-014
The influence of clinical determinants on cardiac wall geometry: An autopsy morphometric study
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Objective: The authors compared heart wall geometry in two distinct groups, divided by the cause of death (COD) established after autopsy.
Method: The studied material consisted of heart tissue fixed in buffered formalin from 81 patients deceased during hospitalization and autopsied. Group A included patients with cardiovascular (CV) COD and Group B, patients with non-cardiovascular (NCV) COD. The average thickness of main cardiac wall segments (left and right ventricle and inter ventricular septum) were determined with an image analysis software.
Results: Clinical profile included a patient, usually man over 60 years aged in Group A and around 50 years Group B. Overall, the mean thickness of different segments of the cardiac wall was bigger in Group B than in Group A, in men than women in Group B and in women than men in Group A. Irrespective the COD, the anterior segment of the left ventricular wall was the thinnest, the thickness increasing towards the posterior segment of the left ventricular wall and having the highest values in the interventricular septum.
Conclusion: Cardiac wall undergoes a remodeling process influenced by gender, the ageing process and the cause of death. Further studies on larger series are required to validate these observations.

PS-02-015
Pericardial pathology: Biopsy or cytology?
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Objective: The pericardium is frequently involved in cardiac and extracardiac pathology. Yet, the diagnosis is not always straightforward. The authors intended to evaluate the adequacy of pericardial biopsy (PB) and pericardial effusion cytology (PC)—each per se or together—as diagnostic tools.
Method: The hospital files of 78 cases, referring to a time-span of 11 years, were retrospectively reviewed, concerning demographic and clinico-pathologic data; which was afterwards submitted to statistic analysis.
Results: Patients mean age was 54.1 years (range, 4 months–82 years), 75 were Caucasian and 54 males. There were 64 PB and 43 PC; 26 cases had both specimens. PB was diagnostic in 18 cases, PC in 11 and both in 6. Concordance with clinical diagnostic hypothesis occurred in 25 PB and in 18 PC. Pericardial pathology consisted in reactive mechanical alterations, inflammations / infections (acute and chronic) and tumours (primary and metastatic).
Conclusion: Both specimens, per se, reach conclusive anatomopathologic diagnosis, either concordant or not with the clinicoimagiologic suspicion. When the pericardial biopsy and pericardial effusion cytology are used together, the diagnostic accuracy may increase.

PS-02-016
Loss of second harmonic generation signal (SHG) in the wall of dissected aortas
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Objective: The generation of second harmonic signals (SHG) indicates the presence of non-centrosymmetric molecules, e.g.collagen, in histologic preparations, but cannot be seen as a surrogate for collagen stains, since collagen may be present without a SHG-inducing configuration. The aim of this study was to compare the intensity of the SHG signals in histologic slides of aortas of normotensives, hypertensives and patients with dissection.
Method: We compared aortas from 22 normotensives, 38 hypertensive patients and 14 hypertensives with acute dissection. SHG was generated in paraffin sections by multiphoton laser microscopy using a SHG device.
Results: In all patients there was a sharp increase of the SHG signal at the outer layers. In dissected aortas this region formed the external border of the blood channel. Furthermore, in these patients we noticed an important loss of SHG signals in all layers.
Conclusion: Non-centrosymmetric collagen might be an important element for the srenght and resistance of the aorta. During dissection the outer layers prevent complete vessel rupture, probably due to their increased content of non-centrosymmetric collagen. The overall decreased content of SHG-collagen in dissected aortas might be the cause, but also the consequence of the dissection process.

PS-02-017
A novel method to obtain endothelial cells from coronary arteries in situ for diagnostic purposes
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Objective: Despite their prominent role in the development of atherosclerosis, until now there are no established methods to routinely harvest arterial endothelial cells in vivo and in situ. The only ethically feasible opportunity is to investigate endothelial cells adherent to the surface of a balloon catheter after angioplasty using liquid based cytology (LBC) techniques.
Method: A total of 64 patients with acute coronary syndrome who underwent stenting of the coronary arteries were studied. After the intervention, the surfaces of the balloon angioplasty catheters were used as probes for obtaining cells from the coronary arteries. The cells were studied on LBC and further characterized using immunocytochemistry.
Results: About 500, mostly polygonal non-nucleated cells with immunocytochemical features of endothelial cells and scant components of atherosclerotic plaque as for instance cytoplasm of smooth muscle cells and cellular detritus of atherosclerotic lipid core were identified from the surface of each balloon catheter.
Conclusion: During balloon angioplasty, only a small amount of cellular material could be obtained from the surface of the arterial walls. But by identifying the presence of cells of atherosclerotic core on LBC preparations it is possible to confirm the presence of a ruptured plaque and to take prompt clinical action accordingly.

PS-02-018
Atypical presentation of aortic arch aneurysm associated with Fallot's Tetralogy
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Objective: Aortic aneurysms are very uncommon in infants and are regarded as connective tissue disorder. We experienced an unusual fetal case of a giant aortic arch aneurysm.
Method: We described an aortic arch aneurysm associated with Fallot's tetralogy. These malformations were detected in a female fetus at 23 weeks of gestation. The pregnancy was not terminated and the infant was born at 38 weeks. She died at the first day of life because of cardiac failure. A complete autopsy was achieved.
Results: On macroscopic examination, a giant assymmetric fusiform aneurysm involved the aortic arch. It measured 7 cm in length. Upon opening, the aortic aneurysm was surprisingly multilocular with thickned walls. On microscopic examination, the lesion was seen to be an aggregate of benign spindle cells with a myofibroblastic appearance. No inflammatory or specific degenerative changes were seen. In this fetus, the lesion was solitary, and the rest of the arterial system was normal.
Conclusion: The combination of Fallot's tetralogy and aortic arch aneurysm has never been reported in the literature to our knowledge. The mechanisms underlying aortic aneurysm are incompletely understood. But, the aspect of the aneurysm in our case suggests that it arises from hamartoma.

Monday, 26 September 2016, 09.30–10.30, Hall 11.3
PS-03 Endocrine Pathology

PS-03-002
Prognostic criteria for pituitary adenomas
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Objective: To determine prognostic criteria for pituitary adenoma depending on hormone production.
Method: We studied the hormonal state and Ki-67 prolifirative index in 142 patients with pituitary adenomas. MRI was used to estimate the tumour size and to monitor its growth. Tumours exceeding 10 mm in size were defined as macroadenomas, and those smaller than or equal to 10 mm as microadenomas. Immunohistochemical staining was carried out with anti-bodies against Ki-67 and 6 pituitary hormones.
Results: Macroadenomas were mainly mammosomatotropinomas or gonadotropinomas with tumour with invasive growth and recurrence. Proliferative activities of micro- and macroadenomas were not significantly different. The average size of recurrent adenomas was 29 ± 12 mm (the non-recurrent ones were 17,6 ± 10 mm, $p < 0{,}001$), their proliferative activities did not differ. The proliferative activity of invasive adenomas was significantly higher than in non-invasive. Gonadotropinomas were more often recurrent and demonstrated invasive growth without clinical signs of hormonal hypersecretion.
Conclusion: Our study showed that the most part of gonadotropinomas did not have any clinical signs. In all the cases they were macroadenomas and often recurrent. The tumour proliferative activity more than 2,6 % can be used as a prognostic criterion only for gonadotropinomas.

PS-03-003
Somatostatin receptor subtype 2A and 5 expression in medullary thyroid carcinoma
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Objective: The aim of the study was to assess somatostatin receptor subtype 2A and 5 (SSTR 2A and 5) expression and clinical significance in Medullary Thyroid Carcinoma (MTC).
Method: Twenty-seven MTC patients were retrospectively evaluated. Immunohistochemical expression of receptors was studied in the primary and metastatic tumours using monoclonal antibodies against SSTR 2A (clone UMB-1) and SSTR 5 (clone UMB-4). The staining results were correlated with various clinico-pathological and outcome parameters.
Results: The diagnosis of MTC was based on the pathological features and positive immunoreactivity of the tumours for calcitonin and CEA. We identified the SSTR 5 as the most frequent receptor subtype in these tumours. SSTR 5 showed positive immunohistochemical expression in 16 of 27 (59.3 %) MTC samples as compared to 8 of 27 (29.6 %) for SSTR 2A. No case showed only SSTR 2A expression. Analysis of primary tumours and their lymph node metastases revealed a similar pattern of SSTR immunoreactivity. SSTR 2A and SSTR 5 protein expression was not related to clinical parameters or outcome.
Conclusion: The presence of SSTR 2A and 5 receptors in MTCs may be an important indication for the diagnostic procedures and targeted therapy with somatostatin peptide radioligands. A prognostic value of these markers should be further evaluated.

PS-03-004
Morphological study of papillary thyroid carcinoma with biomineralization
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Objective: Papillary thyroid carcinoma (PTCa) is the most common form of malignant tumours of this organ, covering approximately 70 % in the structure of morbidity. One of important prognostic PTCa factors is pathological biomineralization. The purpose is to study morphological value of biomineralization in papillary thyroid cancer.
Method: Histological, histochemical techniques and scanning electron microscopy with microanalysis and X-ray diffraction were used to study the samples of PTCa.
Results: The first group of patients included 27 women and 3 men and the average age was 56.93 ± 2.18 years old. In patients with symptoms of mineralization the largest tumour size was 1,84 ± 0,13 cm, in seven cases metastases were found in peripheral lymph nodes. Patients, who had no signs of PTCa mineralization, made up the second group of 30 people—24 women and 6 men. The largest tumour size averaged 1,44 ± 0,09 cm ($p < 0.07$), in eight cases metastases were found in peripheral lymph nodes. Comparing the number of patients with metastases in both groups (7—Group I, 8—Group II) and describing the size of tumour, subject to presence and absence of metastases in patients (2,09 ± 0,2 cm and 1,31 ± 0,17 cm), there was significant difference found between indicators of clinical cases of studied groups ($p < 0.02$).
Conclusion: Mineralized samples of papillary thyroid cancer reach larger compared to cases without evidence of calcification. Comparing the first and second series of samples PTCa showed no connection between biomineralization and age of patients. Hydroxyapatite is the main mineral, which is formed during pathological biomineralization PTCa.

PS-03-005
Synchronous pheocromocytoma and gastrointestinal stromal tumour in a patient with germline mutation in the TMEM127 gene
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Objective: Germline mutations in the TMEM127 (transmembrane protein 127) gene have been detected in familial pheocromocytoma/paraganglioma and more recently in familial pheochromocytoma and renal cell carcinoma syndrome. Carney-Stratakis syndrome (Carney dyad) is characterized by a pheocromocytoma (PHEO)/gastrointestinal stromal tumour (GIST) dyad, secondary to SDHB, SDHC or SDHD gene mutations. We report a synchronous PHEO and GIST case in an individual with TMEM127 germline mutation.
Method: A 70-year-old woman presented with both a left adrenal nodule and a small gastric tumour (antrum wall), incidentally discovered during follow-up for horseshoe kidney. Both tumours (101 and 35 mm respectively) were excised with pathological, immunohistochemical and molecular studies following.
Results: Pathological examination showed a PHEO immunopositive for chromogranin, synaptophysin and Ki-67(<1 %) but negative for cytokeratins (AE1/AE3). The GIST was positive for CD34, CD117(c-kit), DOG1, smooth muscle actin (focal) and Ki-67 (5 %) but negative for cytokeratins, desmin and S100. Sequencing analysis was used for KIT gene screening in the PHEO and for KIT and PDGFRB in the GIST with negative results. Germline mutational analysis showed a heterozygous missense mutation in exon 4 of TMEM127: NM_017849.3:c.620C>T (p.Ala207Val) (Chr2(GRCh37):g.96919643G>A).
Conclusion: This is the first case of synchronous PHEO and GIST (Carney dyad) associated with germline mutation in the TMEM127 gene.

PS-03-006
Thyroid findings in a patient with Birt-Hogg-Dubé syndrome
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Objective: Birt-Hogg-Dubé syndrome (BHDS) is an autosomal dominant genodermatosis caused by heterozygous mutation in the gene encoding folliculin (FLCN) on chromosome 17p11. BHDS is characterized by fibrofolliculomas, renal tumours, and lung cysts with recurrent pneumothorax, but its association with thyroid nodules is unclear. We report thyroid findings in a BHDS patient.
Method: A 55-year-old man presented with a left thyroid lobe nodule. He had a history of Burkitt lymphoma, bilateral renal cell carcinoma, poorly differentiated nasal carcinoma, facial fibrofolliculomas and lung cysts with recurrent pneumothorax. Total thyroidectomy was performed after aspiration biopsy of the nodule indicated follicular neoplasm (class IV, Bethesda system).
Results: The thyroid showed a multinodular cut surface. Microscopically, an encapsulated follicular carcinoma with no vascular invasion (14 mm diameter), 2 follicular adenomas and C-cell hyperplasia were found in left lobe, with 4 papillary microcarcinomas), nodular hyperplasia with oncocytic change and lymphocytic thyroiditis detected in both lobes. Germline mutational analysis showed a deletion of non-coding exons 1 and 2 of the FLCN gene (NM_144997): c.(?_-504)_c.(-114_-113)del. No somatic NRAS, KRAS nor BRAF mutations were detected in follicular carcinoma.
Conclusion: Multiple, bilateral benign and malignant thyroid tumours in this patient suggest a relationship with BDHS, but more studies are needed to confirm this association.

PS-03-007
Hypercalcemic crisis and oncocytic histology may have risk for malignant potential in parathyroid neoplasms
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Objective: Diagnosis of parathyroid carcinoma relies either on histological documentation of distant metastasis or presence of absolute histological features of malignancy in primary tumour, even though histological features do not accurately predict aggressive behavior. Immunohistochemical (IHC) markers have been used to differentiate benign from malignant parathyroid neoplasms (PN) considering histology as gold standard. This study correlated expression / loss of IHC markers (parafibromin, APC, Galectin-3 and PGP9.5) with clinicopathological features in PN to find out if any feature/s that are thought to predict malignancy can independently predict expression / loss of these IHC markers.
Method: IHC for parafibromin, APC, Galectin-3 and PGP9.5 was performed on 227 PNs and correlated with clinicopathological features.
Results: Parafibromin loss, and Galectin-3 and PGP9.5 overexpression alone or in combination showed significant association (p value <0.05) with one or more features—hypercalcemic crisis, low serum vitamin D, raised serum alkaline phosphatase, diffuse sheet like pattern, predominant oncocytic cells, macronucleoli, thick fibrous bands, capsular, vascular and adjacent tissue invasion.
Conclusion: Hypercalcemic crisis (biochemical) and predominant oncocytic cells (histological) showed significant association with all three IHC markers. These features may be incorporated in the existing criteria to diagnose risk of malignancy in PN.

PS-03-008
Follicular variant of papillary thyroid carcinoma: Clinico pathological study at SKMCH
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Objective: Follicular variant of papillary thyroid carcinoma (FVPTC) is most common subtype of papillary thyroid carcinoma. This study is institutional based review of FVPTC, described its prognostic and therapeutic significance.
Method: 69 Cases of FVPTC were included in study, diagnosed between 1996 and 2015. All cases were reviewed by two experienced pathologists. Clinico pathological parameters were assessed.
Results: Out of 69 cases, 46(67 %) fulfilled criteria for FVPTC. Among FVPTC, 35(76 %) were completely encapsulated and 11(24 %) were unencapsulated. All 35 encapsulated cases had no evidence of disease(NED)on follow up. Among 11 un encapsulated cases, 7(64 %) cases showed capsular and vascular invasion, 4 un encapsulated cases without vascular and capsular invasion showed no evidence of disease. Out of 7(15 %) widely invasive cases with both capsular and vascular invasion, 1 patient died, 5 had persistent disease and 1 with NED on follow up.
Conclusion: Encapsulated FVPTC, had very good prognosis. Widely invasive un encapsulated FVPTC had bad prognosis with lymph node, lung and bone metastasis.

PS-03-009
Molecular alterations in the cribriform-morular variant of papillary thyroid carcinoma
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Objective: The cribriform-morular variant of papillary thyroid carcinoma (CMV-PTC) is an unusual neoplasm usually associated with familial adenomatous polyposis syndrome (FAPS). The molecular pathogenesis of sporadic CMV-PTC is not completely understood. We investigate the typical mutations of sporadic thyroid tumours and mutations related with the WNT pathway in a series of 10 patients with CMV-PTC.
Method: Out of the 10 patients, there were six sporadic cases (5 female, 1 male), three associated with FAPS (2 female, 1 male), and one without information. The mean age of patients was 32.2 years (range 18–45 years). Beta-catenin expression was evaluated by immunohistochemistry. Sequencing analysis was used for screening of BRAF, NRAS, HRAS, KRAS, TERT, APC and CTNN1 gene mutations, and fluorescence in situ hybridization for detection of RET/PTC and PAX8-PPARgamma rearrangements.
Results: Tumour cells showed cytoplasmic and nuclear staining for beta-catenin in all cases. Somatic mutations were detected in APC (4 of 10 cases), AXIN1 (2/10), KRAS (1/8), and RET/PTC (1/2). No mutations were found in CTNN1 (0/9), BRAF (0/10), NRAS (0/10), TERT (0/4), HRAS (0/2), nor PAX8/PPARgamma (0/2).
Conclusion: We describe for the first time the presence of AXIN1 mutations in CMV-PTC, and confirm the role of WNT signaling pathway molecular alterations in both sporadic and familial CMV-PTC.

PS-03-010
Histopathological profile of papillary thyroid carcinoma in North East region of Romania (Moldavia)
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Objective: The aim of this study was to describe recent trends in the incidence rates of papillary thyroid carcinoma (PTC) in Moldavia, an iodine deficient goiter endemic area, and to analyze its histopathological characteristics.
Method: Clinical and pathologic data of PTC diagnosed in the Pathology Department of "Sf. Spiridon" Hospital was analised from January 2015 to Marth 2016. PTC were classified using WHO criteria in PTC microcarcinomas—MPTC (less than 10 mm) and classical PTC (over

10 mm) with many histopathological variants. The diagnosis was made using histochemical and immunohistochemical stains (IHC).
Results: The study included 262 cases of PTC, 201 (76.71 %) diagnosed as MPTC and 61 cases (23.28 %) as classical PTC. More than half of MPTC had intraparenchimatous location (64.17 %), minimal capsular invasion (17.41 %), and rare lymph node metastasis (3.48 %). Multicentricity was identified in 33.33 % of MPTC and 85.07 % cases were classified in T1a stage. Classical PTC revealed multicentric involvement in 54.09 %, capsular invasion in 73.77 % and lymph node metastasis in 29.5 % of cases. Almost all PTC cases (90 %) were diagnosticated in T2–T4 stages.
Conclusion: Our study demonstrates that the increasing trend in the incidence of PTC is mainly due to the MPTC, allocated to efficient diagnostic tools principal to IHC methods.

PS-03-011
Papillary thyroid carcinoma and syncron myofibroblastic sarcoma: Two different tumour or papillary carcinoma showing sarcomatous differentiation?
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Objective: We report a case of syncron papillary thyroid carcinoma and myofibroblastic sarcoma. Although these tumours have different immunohistochemical pattern, we hypotethised that they share common origins.
Method: Paraffin embedded tissue blocks, immunohistochemistry including Braf VE1 antibody. After macrodissection BRAF mutation analysis with COBAS 4800 BRAF V600 mutation test, also with inhouse method using mutation specific probe and melting point analysis followed by Sanger sequencing.
Results: TTF1, PAX8 and CK8 scored positive on the papillary tumour but negative on the myofibroblastic sarcoma. The latter was also negative for S100 and p63, but positive for SMA and calponin. According to the immunohistochemistry these tumours were diagnosed as different syncron tumours. Mutation analysis showed the same BRAF mutation in both tumours.
Conclusion: Presence of BRAF mutation in both tumours proposes that these tumours share same origin. Soft tissue tumours usually have no BRAF mutation, except for a low percentage of GIST, MPNST and histiocytic tumours. In our case sarcomatoid melanoma metastasis can be ruled out. Presence of BRAF mutation in both tumours proposes that these tumours share same origin and suggests that the myofibroblastic tumour is a dedifferentiated papillary tumour.

PS-03-012
Comparative study of mitotic count and Ki-67 proliferation index to grade pancreatic neuroendocrine tumour: Inter-observer agreement and correlation
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Objective: Pancreatic neuroendocrine tumour (P-NET) is a rare tumour with an increasing incidence and variable prognosis. Prognosis and treatment of P-NET depend on tumour grade, defined by mitotic count (MC) and/or Ki-67 proliferation index (KI). We compared different techniques evaluating these factors, to define the most time effective one.
Method: 42 P-NET were retrospectively analysed. MC was assessed in 50HPF (10HPF = 2 mm^2) and reported as an average number of mitosis in 2 mm^2. KI was counted manually on 2000 tumour cells. We evaluated inter-observer agreement for both methods, correlation between the two methods, correlation between both methods and KI assessed on a printed picture. Each method was timed.
Results: MC and KI counted manually were concordant (Rho = 0.76). Inter-observer agreement was very good for MC (kappa = 0.83) and KI counted manually (kappa = 0.90). MC and KI counted manually were concordant with the KI on a printed picture (respectively Rho = 0.72 and Rho = 0.90). MC, KI counted manually and KI on a printed picture required respectively 15, 12 and 45 min.
Conclusion: KI counted manually displayed better inter-observer agreement, better correlation with the KI on a printed picture and was quicker than MC. Grade of P-NET could be assessed by evaluation of KI counted manually alone.

PS-03-013
Clinico-pathological features of papillary thyroid microcarcinoma with extracapsular extension
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Objective: To describe histological features and clinical outcomes of papillary thyroid microcarcinoma with extracapsular extension.
Method: Pathological and molecular study of papillary thyroid microcarcinomas (≤10 mm) with extracapsular extension that underwent surgical resection in our institution between January 2005 and December 2015.
Results: Among 392 papillary carcinomas, we identified 29 Papillary microcarcinomas with extracapsular extension in 8 males and 21 females (mean age = 55 years). Tumour's size varied between 3 and 10 mm (mean = 8). All tumours were stage pT3a, nine bilateral and 15 multifocal. Vascular invasion and lymph node metastases were seen in 2 and 9 cases respectively. Tumour was encapsulated in 4 cases. Follicular structures and oncocytic features were seen in 20 and 9 cases respectively. Lymphocytic thyroiditis was observed in 13 cases. V600E-BRAF mutation was identified in all tested tumours (7/7 cases). One patient had early recurrence in regional lymph nodes. All patients are alive without evidence of thyroid cancer at 5 months–11 years of follow-up.
Conclusion: Papillary thyroid microcarcinomas with extracapsular extension represent 7 % of papillary thyroid carcinomas in our series. This tumour is rarely encapsulated and can be associated with vascular invasion and lymph node metastases. V600E mutation is common. However, patient's prognosis seems to be excellent.

PS-03-014
Colorectal neuroendocrine tumours in Japan: Comprehensive multi-institutional survey data
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Objective: Objective in this study is to assess current status in pathological diagnosis of NET in Japan, which will contribute to establish optimal diagnostic system.
Method: We distributed questionnaire to 397 pathology laboratories and 144 institutions affiliated with the Japanese Society for Cancer of the Colon and Rectum. And current status of pathology diagnosis was assessed comprehensively. Colorectal NETs in these institutions were re-evaluated using WHO 2010 and collected to assess clinicopathological relationships.
Results: Most institutions used formalin for fixation, but non-buffered formalin was used in 32.7 % of them. Fixation time was also variable. Most of NETs in Japan were diagnosed using routine immunohistochemistry and histochemistry. Vascular invasion was also diagnosed using them. On the other hand, mitotic count and Ki-67 index were assessed using less cell numbers and fields than those recommended by WHO.

Time only to assess mitotic count and Ki-67 index took 18.0 to 27.3 min. From the data of collected 760 colorectal NETs, risk of lymph node metastasis in rectal NET was confirmed even in lesions smaller than 10 mm, and vascular invasion was important predictive factor.
Conclusion: Our basic data will contribute to establish optimal pathological diagnosis and therapeutic system in the future.

PS-03-015
Differences in the pathological features of papillary thyroid microcarcinomas of <5 mm versus >5 mm: A retrospective analysis of 254 cases
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Objective: The prognostic significance of the tumour size in patients with papillary thyroid microcarcinomas (PTMC) remains unclear. The purpose of this study was to compare the pathological features of PTMCs of ≤5 versus >5 mm in our institution, over a 26 year period.
Method: We performed a retrospective study on 254 PTMCs (123 cases of ≤5 mm and 131 cases >5 mm) registered in the Department of Pathology, Tîrgu-Mureş Emergency County Hospital between 1990 and 2015. Pathological data were retrieved from database registers and pathological reports.
Results: The multifocality ($p = 0.040$), the extrathyroidal extension ($p = 0.0001$), the positive resection margin ($p = 0.046$) and the presence of associated thyroiditis ($p = 0.002$) were all found to be significantly more prevalent among PTMCs of >5 mm, compared to PTMCs of ≤5 mm. Other parameters, like tumour histological type or lymph node involvement did not differ significantly among the study groups ($p = 0.458$ and $p = 0.949$, respectively).
Conclusion: Our study revealed important differences in the pathological features of PTMCs of >5 mm, compared to PTMCs of ≤5 mm. Such results might suggest that PTMCs of ≤5 mm should be managed in a different way than other PTMCs. Further studies, on larger number of cases, with long follow-up data are however needed to confirm this.

PS-03-016
Detection of BRAFV600E point mutation on archived thyroid FNA smears: Assessment of a feasible, reliable DNA extraction technique, validated by successful application in downsteam molecular analysis
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Objective: Molecular techniques have recently emerged as a potential valuable tool that could improve the diagnostic accuracy of thyroid FNA biopsy. The aim of our study was to investigate the feasibility of BRAFV600E point mutation detection using archived thyroid FNA smears (AT-FNAs).
Method: Eleven AT-FNAs, corresponding to the Bethesda diagnostic categories II ($n = 4$), III ($n = 2$), IV ($n = 3$) and VI ($n = 2$) were included in our study (one smear/case). The DNA extraction protocol was based on a precipitation method (MasterPureTM DNA purification kit, Epicentre), according to the manufacturer instructions and optimized in our laboratory. All cases were subject to RT-PCR amplification and high resolution melting analysis for a housekeeping gene (GAPDH) and for BRAF gene, respectively.
Results: We successfully isolated good quantity and purity DNA from all our cases (mean concentration 62.47 ± 37.55 ng/μl; mean purity: 1.47 ± 0.13). Moreover, the BRAFV600E point mutation could be specifically amplified in all these cases (2 positive, 9 negative), whereas the GAPDH target was amplifiable in all cases, except for two (DNA concentration 15.3 and 13 ng/μl, respectively).
Conclusion: Detection of BRAFV600E point mutation from AT-FNAs is feasible. Our DNA extraction technique offered a good range of DNA quality, concentration and purity, allowing reliable applications for further molecular analysis.

PS-03-017
Biomarkers and microRNA expression on gastroenteropancreatic neuroendocrine tumours
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Objective: To establish the relationship between ATRX, HES1, mTOR, NOTCH1, PDGFR-β, VEGFR2 and MGMT expression with predictive significance on gastroenteropancreatic neuroendocrine tumours (GEP-NETs) and its correlation with microRNA expression (miR-19a, miR-96, miR-145, miR-182, miR-200a).
Method: A retrospective evaluation of the total samples diagnosed as GEP-NETs (period 2003–2016) was conducted, clinical and pathological characteristics were evaluated in all cases. Biomarkers expression was assessed trough immunohistochemistry using tissue microarrays. Simultaneously, microRNAs that were possibly regulating biomarkers expression in small intestine and colon were identified applying a bioinformatic approach. For the 5 microRNAs identified we measured the expression by qRT-PCR.
Results: 143 cases of GEP-NET average age 55(11–83 years-old). Mainly from ileum/jejunum (23,8 %), appendix (19.6 %), colon/cecum/rectum (16,8 %), pancreas (15,4 %) and stomach (14 %) were included. Expression was positive in Hes1 (95.8 %), Notch 1 (91.6 %), ATRX (89.5 %), VEGFR2 (74.8 %), PDGFR-β (62.9 %), mTOR (39.9 %), and MGMT (23.8 %). We also found 4 microRNAs upregulated (miR-96, miR-145, miR-182 and miR-200a) and one downregulated (miR-19a) in tumour compare with normal tissue. The high expression of ATRX was correlated with the loss of miR-19a expression and the downregulation of MTOR and VEGFR2 with the upregulation of miR-96 and miR-200a respectively.
Conclusion: Our results must conduct to new studies focused on strict follow up of specific alternative therapies and biomarkers expression to evaluate a possible improve in survival rates of this patients. Finally, epigenetic factors such as microRNA expression regulated key cell signaling pathways involve in GEP-NETs.

PS-03-018
Osteopontin overexpression in papillary thyroid carcinoma with mineralization
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Objective: Pathological mineralization (ectopic calcification) is an often finding in papillary thyroid carcinoma (PTC). The concept of pathological mineralization in papillary thyroid carcinoma included psammoma's bodies, bone formation, stromal and vascular calcification. Osteopontin (OPN) is a glyco-phosphoprotein that is expressed and secreted by numerous human cancers. Osteopontin is upregulated at sites of pathologic, ectopic calcification—presumably at least in part to inhibit debilitating mineralization in these soft tissues. We investigated the expression of OPN and her correlation with pathological mineralization in PTC.
Method: OPN expression was investigated by immunohistochemistry in tumours and adjacent thyroid tissue of 11 PTCs with mineralization and 10 PTCs without pathological mineralization.
Results: OPN expression was increased in PTC with pathological mineralization when compared to those without ectopic calcification ($p < 0.045$, Mann–Whitney U test).
Conclusion: OPN overexpression may be regarded as a protective tissue response to the development of ectopic calcification.

PS-03-019

Involvement of the thyroid gland with lymphoma

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Objective: Lymphoma within the thyroid gland is rarely encountered, accounting for only 2–5 % of all thyroid cancers. The aim of the present study is to review our experience with this uncommon entity.
Method: In our pathology department, we diagnosed 8 cases of thyroid lymphoma between 1992 and 2016.
Results: There were 7 females and one male; their ages ranged from 17 to 85 years with a mean age of 65.8 years. All patients presented with a growing mass in the thyroid gland that compressed or invaded adjacent organs. Six patients had an apparent primary involvement of the thyroid while two patients had a history of preexisting lymphoma in the cervical lymph nodes. Five patients had a biopsy performed while three underwent a total thyroidectomy. Histologically, four patients had diffuse large B-cell lymphoma (DLBCL) while the others had: MALT lymphoma (1 case), DLBCL with MALT lymphoma (1 case), Burkitt lymphoma (1 case) and Hodgkin's lymphoma (1 case). All the patients diagnosed to have a primary thyroid lymphoma had a Hashimoto's thyroiditis associated except for the Burkitt lymphoma.
Conclusion: The diagnosis of primary thyroid lymphoma should be considered when dealing with rapidly growing goitres. Surgical intervention is often required to establish the diagnosis and relieve critical airway compression.

PS-03-020

Thyroglobulin needle washout testing in the monitor of patients with thyroid carcinoma: Analysis of diagnostic accuracy and discrepant results

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Objective: The aim of this study was the assessment of diagnostic utility of fine-needle aspiration biopsy needle washout fluids (FNAB-Tg) in the cases of thyroid carcinoma recurrence and analysis of false-positive and false-negative results.
Method: Two hundred and 13 FNAB-Tg samples from 199 patients with a history of differentiated thyroid carcinoma with suspicious lymph nodes were included in analysis. The wash-out of needle rinsed with 0.5 ml of normal saline solution, using electrochemiluminescence method-ECLIA were performed.
Results: In 62 patients elevated FNAB-Tg levels correlated with positive cytology result. In 13 patients there were no correlation between elevated FNAB-Tg level and cytology result. Three of these patients had cystic metastasis of papillary carcinoma. Eight patients with metastases had not elevated FNAB-Tg levels. In three of them, FNAB revealed carcinoma cells from other malignancies. Two of patients had metastases of dedifferentiated thyroid carcinoma and three had differentiated thyroid carcinoma.
Conclusion: FNAB-Tg of the lymph nodes increases accuracy in the diagnosis of thyroid carcinoma recurrence, especially in detecting of cystic variants and micrometastases or in coexisting malignances of other origin. False-negative FNAB-Tg results may occur in the cases of dedifferentiated thyroid carcinomas or with high serum anti-Tg antibodies.

PS-03-021

Encapsulated versus non-encapsulated, diffuse follicular variant of papillary thyroid carcinoma: Two distinct morphological and biological entities

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Objective: Follicular variant of papillary thyroid carcinoma (FVPTC) has become one of the most common diagnoses in thyroid pathology. The aim of our study was to examine phenotypic and outcomes differences between encapsulated (E) and non-encapsulated, diffuse (NE) FVPTCs in our institution.
Method: We performed a retrospective study on 335 FVPTCs (210 E-FVPTCs and 145 NE-FVPTCs) registered in the Department of Pathology, Tîrgu-Mureş Emergency County Hospital (1990–2015). Pathological data were retrieved from database registers and pathological reports, whereas follow-up data were obtained from the Department of Nuclear Medicine, "Ion Chiricu" Institute of Oncology, Cluj-Napoca.
Results: Compared to E-FVPTCs, NE-FVPTCs revealed a higher rate of multifocality ($p = 0.022$, 31.7 % versus 21 %) and extrathyroidal extension ($p < 0.0001$, 11 cases, 7.6 % versus 3 cases, 1.4 %, all with capsular invasion, two with vascular invasion as well). A persistent disease status at the last oncological assessment and tumour recurrence were more frequent among patients with NE-FVPTCs (8.2 %, $p = 0.046$ and 0.9 %, $p = 0.255$, respectively). Only 1 patient (a case of NE-FVPTC) developed distant metastasis during follow-up (mean 66 months).
Conclusion: NE-FVPTCs seem to present and behave in a more aggressive fashion, compared to E-FVPTCs. Understanding the differences between these entities will probably help guiding treatment strategies in the future.

PS-03-022

From breast to "endocrine brain": The heterogeneous expression of ErbB family members in pituitary adenomas

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Objective: EGFR/HER1 and HER2 assessment related to hormone profile in pituitary adenomas.
Method: 60 retrospective cases of pituitary adenomas, were routine stained for the histopathologic diagnosis, followed by case selection for immunoprofiling and EGFR and HER 2 assessment.
Results: More than 1/3 of the examined pituitary adenomas (33, 33 %) were positive for HER2, exhibiting a membranar pattern in basophilic cells and a predominantly cytoplasmic, granular pattern in acidophilic cells. HER2 expression characterized PRL secreting adenomas ($p = 0.005$). Correlations between FSH-LH ($p < 0.001$) TSH-FSH ($p = 0{,}024$) and TSH-LH ($p = 0.028$) were significant. In situ hybridization confirmed HER2 gene amplification in 33, 34 % out of all HER2 positive cases. EGFR positivity was significant in GH-prolactin ($p = 0.000$) and prolactin-ACTH ($p = 0.045$) co-expressing pituitary adenomas, but also in the peritumoural macrophages and folliculostelate cells.
Conclusion: Differential HER2 and EGFR expression correlated with the hormone profile may be used in order to define different subclasses of pituitary adenomas. Moreover, it could explain the prognostic and therapeutic heterogeneity that occurs in clinical practice. We support the reclassification of pituitary adenomas based on molecular mapping using well certified markers with prognostic and therapeutic impact.

PS-03-023

GFAP and S100 protein game in pituitary adenomas: Single player or multiplayer configuration?

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Objective: S100 Protein and GFAP in pituitary adenomas is less known, few correlations with other prognostic and/or therapeutic factors being available in this field. We aim to elucidate their involvement in the pathogenesis of pituitary adenomas and to correlate their expression with different growth factors and growth factor receptors.
Method: 61 cases of pituitary adenomas were immunohistochemically assessed with GFAP and protein S100 in tumour cells and folliculostelate

(FS) cells in close relationship with the hormone profile. Correlation with VEGF and EGFR expression, previously studied by our team, was also examined.
Results: GFAP and protein S100 were expressed in tumour cells and FS cells. The morphology, distribution and density of GFAP+ FS cells and S100+ FS cells varied depending on the hormone profile. GFAP and protein S100 expression in tumour cells was significantly correlated with the hormone profile and with VEGF and EGFR expression.
Conclusion: GFAP and protein S100 expression in tumour cells from pituitary adenomas depend on the hormone profile. We support the presence of two molecular subtypes of FS cells, GFAP+/VEGF+/S100 and GFAP-/S100+/EGFR+, simultaneously with the classical GFAP+/S100+ variant. S100+/EGFR+ pituitary adenomas may represent a unique group of aggressive tumours, highly capable of invasion and recurrence.

PS-03-024
Minichromosome maintenance protein 7 as marker of aggressive pituitary adenoma
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Objective: Ki-67 labeling index is recognized as a useful prognostic marker of pituitary adenoma clinical behaviour. However, its relevance as an indicator and predictor is far from being universally accepted. In fact, both validations and criticisms are found in the literature. Minichromosome maintenance family proteins, cell-cycle regulator proteins, have been recently proposed as prognostic marker in several tumours. We investigated the expression of minichromosome maintenance protein 7 (MCM7) in comparison to Ki-67 as prognostic marker of clinical behaviour in pituitary adenoma patients.
Method: Pituitary adenomas from patients undergoing transsphenoidal surgery were studied and the prognostic value of both MCM7 and Ki-67 has been evaluated by immunohistochemistry. The data have been analyzed using Cox's regression and Kaplan-Meier analyses.
Results: Twenty-six of 97 pituitary adenoma patients recurred during the follow-up period. Interestingly, high nuclear expression of MCM7 labeling index, unlike Ki-67 labeling index, was significantly associated with a higher risk of recurrence/progression and a poor clinical outcome.
Conclusion: Data from this study indicate that MCM7 is a prognostic marker of clinical outcome in pituitary adenoma patients. Addition of MCM7 to the panel of prognostic markers in pituitary adenoma seems useful, in order to better define the therapeutic choises in each patient.

PS-03-025
Common origin of carcinoids of the lung and gastrointestinal tract identified by miRNA profiling
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Objective: It is still uncertain whether carcinoids of the lung and gastrointestinal tract have a common origin or whether they are closer in origin to carcinomas of the same organs.
Method: To verify whether formalin-fixed paraffin-embedded (FFPE) samples retain the expression signature of the tissue, miRNA expression was compared between FFPE and frozen samples. Then, we selected surgically resected FFPE samples of pulmonary and gastrointestinal carcinoids, as well as other types of tumours and normal tissues from each organ, and compared miRNAs expression patterns. Data were analysed by hierarchical clustering and consensus clustering.
Results: The miRNA expression of FFPE and frozen samples correlated quite well. In the first hierarchical clustering, most of the carcinoids formed one major cluster with loose subpartitioning into each organ type, while the second major cluster mainly comprised adenocarcinomas and normal tissues. The non-negative matrix factorization supported the results. Additional clustering between carcinoids and small-cell lung carcinomas (SCLCs), carcinoids formed a distinct cluster, while SCLCs grouped together with pulmonary adenocarcinomas and normal lung tissues.
Conclusion: Carcinoids had a characteristic pattern of miRNA expression, suggesting a common origin for pulmonary and gastrointestinal carcinoids. The expression profiles were different in carcinoids and SCLC.

PS-03-026
BRAF V600E immunoexpression in papillary thyroid carcinoma and its association with prognostic factors and histopathologic variant
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Objective: The incidence rate of Papillary thyroid carcinoma (PTC) has increased worldwide and also in Indonesia. Several studies indicated BRAF V600E mutation was associated with poor prognosis. Our study using immunostaining with BRAF V600E antibody will provide additional information regarding the clinicopathological characteristics of PTC and predict the prognosis.
Method: Fifty patient with PTC were reviewed to determine prognostic factors microscopically. BRAF V600E mutation was detected by immunohistochemical staining and assesed with H score.
Results: H score ≥326.5 was determined as positive BRAF V600E mutation and <326.5 as negative BRAF V600E mutation. BRAF V600E mutations were detected in 17 (34 %) cases. The cases with positive BRAF V600E mutation had mean age of 44.71 years, and the size of the tumour between 0.1 and 4 cm. Six cases of them are male and 11 female. There were seven cases with extrathyroidal extension (ETE) p 0,04, 11 cases with lymph node metastasis (LNM) $p < 0,001$, and 8 cases with tall cell variant p 0,047.
Conclusion: There are significant correlation between BRAF V600E mutation with ETE, LNM, and tall cell variant. There are no significant correlation between BRAF V600E mutation, either with age, gender, or size of the tumour. BRAF V600E immunohistochemical examination can be performed to predict the prognosis of PTC patients.

PS-03-027
Histopathological pattern of thyroid carcinoma in Sudanese patients: Review of 111 consecutive cases
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Objective: determine the histopathological patterns of thyroid carcinoma in Sudanese patients.
Method: a descriptive retrospective study of thyroid cancer diagnosed at the National Public Health Laboratory (STACK), Khartoum, Sudan (2008–2013). Histopathological reports and archival slides were retrieved from the Histopathology Department and reviewed.
Results: One hundred and 11 cases of thyroid carcinoma were retrieved. The age range was 13–80 years (74 % were females). The common histological type was papillary (54 cases; 48.6 %), followed by follicular (36 cases; 32.4 %), anaplastic (9 cases; 8.1 %), medullary (9 cases; 8.1 %) and poorly differentiated /insular (1 case; 0.9 %) carcinoma. Two cases (1.8 %) represented encapsulated follicular neoplasms of uncertain malignant potential (equivocal invasion).
Conclusion: This study (the first large series of consecutive thyroid carcinoma in Sudanese) highlights potential differences in the frequency of the different thyroid carcinoma subtypes in the Sudanese population with a tendency towards underrepresentation of papillary and overrepresentation

of follicular carcinoma compared to the Western population. These aspects deserve further epidemiological survey to verify the true incidence of the different subtypes, to exclude inadvertent selection bias, and to explore possible relationship to ethnic/geographic origin and variation in relation to iodine deficiency among different regions of the country.

PS-03-028

Importance of immunohistochemical hormone expression in clinically nonfunctional pituitary adenomas

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Objective: About 30 % of pituitary adenomas are nonfunctional (NFA) clinically. Although they are nonfunctional, NFAs may show hormone expression at varying frequencies by immunohistochemistry. We aimed to investigate the hormonal distribution among NFAs.
Method: One hundred and eighty pituitary adenomas (WHO grade I) diagnosed between 2011 and 2016 were evaluated. There were 73 (41 %) women and 107 (59 %) men. The mean age was 49.9 years. Four patients were younger than 18 years. PIT-1, PRL, GH, TSH, ACTH, FSH, LH immunohistochemistry were applied to all cases, along with Pancytokeratin and ER to some cases.
Results: There was no hormone expression in 36 (20 %) cases. One or more hormones expressed in 144 (80 %) cases, of which 66 (37 %) were FSH and/or LH, 23 (13 %) ACTH, 25 (14 %) PRL, 17 (9 %) GH, 1 (1 %) TSH and 12 (7 %) plurihormonal (10/12 both GH and PRL).
Conclusion: The most frequent hormone expression is gonadotropins in NFAs. Almost 10 % are corticotroph adenomas, which are known to have potential of aggressive behaviour. It is reported that NFAs (corticotroph, somatotroph, thyrotroph) can change from silent to clinically active adenoma. It is recommended to document hormone profile immunohistochemically for patient follow up and prognosis prediction.

PS-03-029

BRAF mutation in poorly differentiated thyroid carcinoma

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Objective: Poorly differentiated thyroid carcinoma (PDTC) is a rare tumour with extremely aggressive behavior. Their comprehensive genetic background is still unclear. BRAF mutation is considered a marker of aggressive disease in these tumours, associated with increased cancer recurrence and even loss of radioiodine avidity. The aim of this work was to investigate the frequency of BRAF mutation in a cohort of PDTC.
Method: Twenty-eight patients with PDTC were included in the study between 2004 and 2016. Twenty one of 28 patients were developed from papillary thyroid carcinoma (PTC). BRAF mutation status was determined using a real-time PCR (Cobas® 4800 BRAFV600) method and standard-automated immunohistochemistry procedure (Ventana Anti-BRAF V600E).
Results: 96.4 % of cases (27/28) did not carry BRAF mutation with real-time PCR method and immunohistochemistry procedure. BRAF mutation was detected in one patient with both methods in a case that developed from PTC. Correlation between BRAF mutations and various clinicopathological parameters in PDTCs did not reveal any association with age at diagnosis, gender, tumour size, histological variants of PTC, extrathyroidal invasion, distant metastasis and radioiodine treatment resistance.
Conclusion: Our data did not suggest that BRAF mutation could be a useful marker in patients with PDTC in the cohorts studied.

PS-03-030

Comparison of immunohistochemistry and real-time PCR in detection of BRAF mutation in papillary thyroid carcinoma

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Objective: BRAF mutation is common in papillary thyroid carcinoma (PTC), especially in classical variant PTC where high rates are found (55 %). BRAF mutation is usually detected by molecular techniques, however immunohistochemistry has emerged as an alternative method. We evaluated the expression of the mutated BRAF protein in thyroid carcinoma patients using immunohistochemistry (IHC) and real-time PCR methods and compared these two methods.
Method: We studied 102 patients with classical variant papillary thyroid carcinoma who were under follow up after radioiodine treatment. Formalin-fixed paraffin-embedded tissues of PTC were analyzed for BRAFV600 mutation using real-time PCR (Cobas® 4800) and standard-automated IHC (Ventana Anti-BRAF V600E) procedures.
Results: BRAF mutations were found in 54.9 % of PTC cases by real-time PCR and in 63.7 % of PTC cases by IHC technique. Complete concordance for the two methods was observed for all cases in 90 % of samples. Furthermore, BRAF mutations were found by only IHC in 10 patients, all of whom had classical papillary microcarcinoma with sclerotic stroma.
Conclusion: Our data show that IHC could be used as a first-line method for BRAF mutation detection in daily practice, because it is rapid and more sensitive in the evaluation of microcarcinoma foci.

PS-03-031

Evaluation of prognostic value of 2010 WHO classification of gastric neuroendocrine tumours

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Objective: We aimed to evaluate the clinical and histopathological features of gastric neuroendocrine tumours (NET) and the prognostic value of 2010 WHO classification.
Method: Fifty-eight patients' surgical resection material from two institution (41 patients from Hacettepe University and 17 from Yuksek Ihtisas Hospital) who were diagnosed as neuroendocrine tumour between January 2000-October 2015 were re-evaluated histopathologically and their clinical follow-up was investigated.
Results: Thirty of 58 patients are Grade1, 10 Grade2, 10 Grade3 NET according to WHO2010 classification and 8 don't have residue tumour in resection material. Lymph node metastasis is observed in 13,3 % (4 cases) of G1NET cases. In these four cases with lymph node metastasis, the diameter of tumour is over 1 cm in three of them and the other smaller than 1 cm is invading to submucosa. Also age and male-to-female ratio are increasing with the increase in tumour stage. Four of 10 (%40) G2NET cases with closer Ki-67 proliferation index (%2–%5) to threshold between G1-G2 have lower stage.
Conclusion: From this perspective, tumour diameter and depth of invasion are the points to consider in endoscopic follow-up process. In 2010 WHO classification the threshold for G1 and G2 distinction has a very narrow range, so it is needed to revise it again and reform the treatment algorithms.

PS-03-032

FoxA1 expression in Medullary Thyroid Carcinoma

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Objective: FoxA1, also known as HNF-3A, regulates a variety of tissues during embryogenesis and early life. FoxA1 is reported to have oncogenic and tumour suppressive roles depending on tumour type. In thyroid, FoxA1 expression has recently been shown in C cells and medullary carcinoma (MTC) but not in follicular cells. FoxA1 has also been proposed as potential oncogene in anaplastic carcinoma (ATC). However, FoxA1 expression has not been extensively investigated in a spectrum of thyroid tumours.
Method: 62 MTCs were stained with anti-FoxA1 antibody, and its expression pattern was compared with those of other conventional markers. FoxA1 was also performed on a variety of thyroid tumours.
Results: All 62 MTCs showed diffuse and strong FoxA1 nuclear expression. Expressions of other markers in MTCs were as follows: calcitonin 97.8 %, CEA 94.4 %, chromogranin 100 %, and TTF1 97 %, generally in variable intensity. FoxA1 was completely negative in follicular neoplasms, papillary thyroid carcinomas and poorly differentiated carcinomas while FoxA1 was variably expressed in 62.5 % of ATCs (30/48). FoxA1 was also expressed in C cell hyperplasia as well as solid cell nests.
Conclusion: FoxA1 could be a useful ancillary marker for the diagnosis of C cell hyperplasia and MTC, including atypical MTC (calcitonin negative MTC).

PS-03-034
Proteomic profiling identifies novel potential prognostic biomarkers in lung carcinoids
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Objective: To identify by means of proteomic profiling novel prognostic biomarkers in lung carcinoids.
Method: Two-dimensional electrophoresis was applied to screen differential proteomic profiles in typical (H727) and atypical (H720) lung carcinoid cell lines, and the most relevant differentially expressed proteins were identified using mass spectrometry (Maldi-TOF). Four of these latter (GSTP-1, HSP27, peroxiredoxin-2 and calreticulin), selected based on their biological properties and potential role in carcinogenesis, were validated using immunohistochemistry in a large cohort of 89 lung carcinoid paraffin embedded samples.
Results: Over 150 proteins were differentially expressed in H727 as compared to H720 cells. Among these, 57 were identified by MaldiTOF and belonged to several cellular pathways. Among the four validated using immunohistochemistry, low GSTP-1, high nuclear HSP27 and low peroxiredoxin-2 expression were significantly associated with shorter survival at univariate analysis (all $p < 0.02$) and two of them with aggressive disease status (low GSTP-1, $p < 0.001$; high nuclear HSP27, $p = 0.003$). Interestingly, low GSTP-1 expression was significantly associated with poor outcome also in the group of atypical carcinoids, only.
Conclusion: GSTP-1, HSP27 and peroxiredoxin-2 are novel candidate prognostic biomarkers identified by extensive proteomic profiling in lung carcinoids.

PS-03-036
Proliferation activity and cell cycle regulation in parathyroid pathology: An evidence of heterogeneity
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Objective: To assess the level/heterogeneity of proliferation activity and cell cycle regulator protein expression in parathyroid pathology.
Method: Retrospectively, cell cycle markers and regulators (Ki-67, p21, p27, cyclinD1) were detected by immunohistochemistry in 102 parathyroid adenomas; 27 cases of primary hyperplasia (PPH); 45 normal glands (NG); 5 carcinomas. The lowest (LF), mean and highest (HF) fraction of 500 positive cells was scored by computer-assisted morphometry. Descriptive statistics and Kruskal-Wallis test were applied.
Results: Significant differences between the groups were disclosed regarding the mean fraction of Ki-67 ($p < 0.001$), p21 ($p < 0.001$) and p27 ($p = 0.005$); HF: Ki-67 ($p < 0.001$), p21 ($p < 0.001$), cyclinD1 ($p = 0.002$); LF: cyclinD1 ($p = 0.006$). Considering heterogeneity, lowest-to-highest proliferation fraction ranged 0.2–3.5 % in adenomas; 0.0–2.8 % in PPH, 0.0–11.8 % in carcinomas, and 0.0–1.0 % in NG. The LF-HF of p21-positive cells ranged 2.4–23.7 % in adenomas, 2.5–29.8 % in PPH, 1.5–15.6 % in carcinoma and 2.3–3.8 % in NG. The heterogeneity of cyclinD1 is reflected by following data: 3.4–22.8 % in adenomas, 12.2–42.5 % in PPH, 21.8–41.8 % in carcinoma, 8.8–10.9 % in NG.
Conclusion: The considerable molecular heterogeneity of cell cycle markers in all parathyroid pathologies suggests that heterogeneity is not limited to malignant tumours but could represent a biological mainstay of disease. It must be accounted for in scientific studies and elaboration of diagnostic cut-offs.

PS-03-037
The landscape of intermediate filaments in parathyroid pathology: The expression pattern and heterogeneity
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Objective: To assess intermediate filaments in parathyroid pathology.
Method: The expression of cytokeratin 19 (CK19) and vimentin was immunohistohemically detected in 179 parathyroids: adenoma, 102; primary parathyroid hyperplasia (PPH), 27; normal glands (NG), 45; carcinomas, 5. Applying computer-assisted morphometry, positive parenchymal cell fraction (F) was assessed by intensity level (IL:0–3 scale). The score was computed as sum of ILxF. Descriptive statistics and Kruskal-Wallis test were performed.
Results: The mean vimentin score ranged from 0.3 [0.2–0.4] in NG to 1.1 [0.0–2.4] in carcinomas; $p > 0.05$. Cytoplasmic expression was frequent in positive adenomas: 84.2 % [72.4–91.7] and carcinomas: 100.0 % [51.1–100.0] but NG: 0 % [0.0–18.2]. Perinuclear expression was dominating in PPH, 85.7 % [64.5–95.9]; and NG: 100.0 % [81.8–100.0]. Heterogeneity was frequent: adenomas, 54.9 %; PPH, 70.4 %; carcinomas, 100.0 %; NG, 33.3 %. CK19 was statistically significantly up-regulated in proliferative lesions ($p = 0.012$), scoring in adenomas: 0.8 [0.7–1.0]; PPH: 0.8 [0.5–1.2], carcinoma: 1.0 [0.0–2.7] and NG: 0.3 [0.2–0.3]. Heterogeneity was observed: in adenomas, 60.8 %; PPH, 88.9 %; carcinomas, 100.0 %; NG, 66.7 %.
Conclusion: Vimentin is expressed in parathyroid tissues in cytoplasmic or perinuclear pattern and shows a trend to up-regulation in carcinoma. Proliferative parathyroid lesions are characterised by statistically significant up-regulation of CK19.

PS-03-038
Digital analysis of Adrenocortical Carcinomas' prognostic factors
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Objective: Adrenocortical carcinoma (ACC) is a rare malignant disease. Mitotic count (MC) and Proliferation Index (PI) are pathologically determined probable prognostic factors. We studied clinicopathological and follow-up data of ACC-patients of the 2nd Department of Medicine of Semmelweis University.
Method: Of the 63 ACC-patients 28 histological samples were available. Staging was performed according to ENSAT criteria. MC (HE-stain) and Manual Proliferation Index (MPI, Ki-67 IHC) were determined on scanned slides (Pannoramic 250Flash Scanner), and also an

automatic Digital Proliferation Index (DPI) was counted using NuclearQuant (3DHistech) Software. Consequently, Kaplan-Meier survival graphs were calculated.
Results: MPI had prognostic relevance on Overall Survival (OS, p = 0,043) and Progression Free Survival (PFS, p = 0,024). DPI had also prognostic relevance on OS (p = 0,035) and on PFS (p = 0,029). MC on whole slides and dichotomizing patients by MC per mm2 had better prognostic relevance on OS (p = 0,011) and on PFS (p = 0,023). Best prognostic factor was MC determined on the most proliferating tumour regions: OS (p = 0,005) and on PFS (p = 0,011).
Conclusion: MPI, DPI and MC proved to be prognostic in ACC-patients. MPI was reliable, still DPI had higher significance on OS. DPI is an objective, time-sparing and reproducible, standardizable method, which might improve our pathological reports. The highest significance was found with MC, counted on the most proliferating regions of the tumour. MC is usually counted on 10–50 HPF. Thought, for the reliable inter-study comparison, MC should be rather determined by mm2, since the commercially available objectives examine very different areas (0,159–0k,385 mm2).

PS-03-039
Prevalence of thyroid cancer types among submitted thyroid surgical specimens: A 5-year retrospective study from two referral laboratories in Nairobi, Kenya
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Objective: There is scant data from Kenya on thyroid cancers. We set out to determine the pattern of thyroid cancer occurrence, types and demographic characteristics from a case series at two leading teaching hospital & private laboratories in Nairobi that receive referral specimens from across the country >5500 and >10,000 specimens a year.
Method: Retrospective descriptive review of all pathology reports seen in the two institutions identifying cases diagnosed as thyroid cancer was carried out. At the Kenyatta National Hospital, manual records were reviewed while at Pathologists Lancet Kenya electronic data was retrieved. The period reviewed was January 2011 to December 2015. Data was statistically analyzed using Excel.
Results: A total of 151 cancers were diagnosed over the 5 year period against 1340 thyroid surgical specimens, representing 11.3 % thyroid malignancy rate. Female were most affected at 83 % with a F:M ratio of 4.8:1. The average age of occurrence was 44 years. The most common histological pattern was the papillary carcinoma at 56 %, follicular carcinoma 28 % and anaplastic carcinoma 9 %.
Conclusion: The rate of thyroid malignancy is quite high in these series. The pattern of thyroid cancer occurrence is however fairly similar to those reported in the literature and previous limited case serious in Kenya.

Monday, 26 September 2016, 09.30–10.30, Hall 11.3
PS-04 Infectious Diseases Pathology

PS-04-001
Unusual locations of hydatid disease: A 10-year experience from a tertiary reference center in Western Turkey
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Objective: Report on a series of patients with hydatid disease and specify the unusual locations of the cysts.
Method: The records of patients diagnosed with hydatid disease in our hospital between 2005 and 2016 were analyzed, retrospectively. The cases were evaluated and specified by gender, age and the localization of the cysts.
Results: A total of 329 patients diagnosed over a 10-year period were included in our study. There were 202 females (61.4 %) and 127 males (38.6 %). The hydatid cysts were located in the liver in 257 (78.1 %) patients and in unusual locations in 72 (21.9 %) patients. The most common unusual site for hydatid cysts was the spleen followed by bones, central nervous system, soft tissue, the kidney and the gall bladder. Amongst these 72 patients with hydatid cysts in unusual locations; 33 patients had comcomitant liver hydatidosis, whereas 39 patients had primary involvement of unusual sites. Two patients with malignancies also had hydatid cysts in different locations.
Conclusion: Hydatid disease affects many organs in the body and therefore it can pose a major diagnostic dilemma and mimic other entities. In endemic areas, a differential diagnosis of hydatid disease should be considered for cystic masses in any location.

PS-04-003
Unusually located hydatid cysts: A report of 10 cases
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Objective: Hydatid cyst (HC) is a parasitic disease caused by Echinococcus granulosus. Although this parasite can settle in any part of the human body, it is frequently seen in liver and lungs. Unusual locations have been rarely reported. In this study, we aimed presenting unusual located HC regarding 10 patients.
Method: Retrospective study of HC diagnosed between March 2012 and April 2016. Clinical data were reviewed for each patient.
Results: We had a total of 10 patients between the ages of 30–64 (average age 46,3), 4 of them were men and the others were women. The cysts outside of liver and lung were frequently seen in intramuscular (3/10), spleen (3/10), bone (2/10), kidney (1/10), retroperitoneal (1/10). The most frequent symptom in our patients was a progressive painless swelling for intramuscular cysts. The average cyst size was 7.8 cm. Histopathological examination confirmed the diagnosis in all of the cases. Recurrence was seen in an intrabony lesion.
Conclusion: Hydatid disease is still a serious public health problem in our country. Its clinical presentations vary depending on the involvement of the organ and the size of the cysts. The diagnosis is often suggested by radiology and confirmed by the pathological examination.

PS-04-004
Diagnostic significance of plasma osteopontin in Hepatitis C induced hepatocellular carcinoma in Pakistani population
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Objective: Osteopontin (OPN) a secretory chemokine essential for Th-1 immune response initiation, mainly contributes to the pathogenesis of Hepatitis C virus (HCV) infection. Its protein expression and plasma level might be a useful marker to predict the HCV and its related HCC disease progression. The main objective of the present is to verify the clinical usefulness of OPN as a novel diagnostic, prognostic and therapeutic biomarker against hepatitis C virus infection and grading of carcinoma in Pakistani Population.
Method: In this case-control clinical study HCV viral load and genotype was evaluated through Real time PCR among 100 Pakistani patients including i) normal individuals, ii) HCV infected patients iii) HCV infected patients with HCC. OPN plasma levels was estimated via ELISA and extent of OPN expression in liver tissues in HCV induced HCC patients was established via immunohistochemistry and classified according to the percentage and intensity of staining.

Results: Osteopontin levels were significantly elevated in patients with HCC and in HCV patients in comparison to control group. The plasma OPN level has been correlated well with the severity of liver fibrosis and inflammation in patients with HCV infection. The sensitivity and specificity of OPN for prediction of fibrosis (HCV, HCC and healthy control group) were 85, 73 and 54 %, respectively, at a cutoff value of 4.9 ng/ml suggesting its good diagnostic accuracy in prediction of hepatic fibrosis and carcinoma.
Conclusion: We established for the first time clinical demographic data of Pakistani population showing that, serum and tissue protein expressions of OPN provide the significant clinic-pathological correlation between the HCV & HCC disease progression and interferon based therapeutic response in Pakistani population, thus can be serve as powerful diagnostic, prognostic and therapeutic biomarker against HCV viral infection and related hepatocellular carcinoma in future.

PS-04-005
Abdominal basidiobolomycosis: A case report
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Objective: Basidiobolomycosis is an unusual fungal infection caused by basidiobolus- ranarum. It affects immune competent persons.
Method: Case1: A 2 years old male presented with a history of loss of weight and abdominal mass. Case2: A 10 years old female presented with fever and abdominal mass.
Results: Investigations revealed blood eosinophilia. Computed tomography showed a colonic mass with multiple lymph nodes enlargement. Laparotomy showed right colonic mass with multiple lymphadenopathy. Right hemicolectomy was done and the specimen was sent for histopathology. The gross examination revealed thickening of the colonic wall with multiple lymph nodes ranging in size between 3 and 0.5 cm in maximum dimension. Microscopy showed a colonic wall with extensive infiltration by eosinophils and fungal hyphae surrounded by eosinophilic material and granulomatous inflammation (Splendore Hoeppli phenomenon). The fungal hyphae were positive to Periodic acid Schiff and Gomori's methenamine silver stains. Features were consistent with basidiobolomycosis, which was confirmed by microbiology. The two cases were treated by voricocanazole.
Conclusion: Abdominal Basidiobolomycosis should be included in the differential diagnosis of patients presenting with fast growing abdominal mass and fever.

PS-04-006
Citologic and molecular study about HPV infection in oropharinge
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Objective: Objective: Considering that AIDS patients are more likely to develop cancer, this study investigated HPV infection in HIV-positive oropharynx patients.
Method: Methods: We evaluated 100 patients with AIDS. The clinical and behave partners habits were assessed. The collect was done with brushes. The cytological analysis used the Bethesda'criteria for double blind study. Immunocytochemistry assessed the p16INK4 protein. The hybrid capture researched the high and low risk HPV DNA using KIT DAN-PAP Digene.
Results: Results: HPV high and low risk were detected in 8.2 and 16.7 % of samples. For high-risk and low-risk HPV, the mean ± SD (high-low) of the relationship RLU / CO (estimate viral load) was 2.9 ± 2.58 (1.09 to 7.87) and 1.61 ± 0.65 (1.07 to 2.68). The heterosexual patients had more HPV(9,5 %) with predominance in heterosexual women(5.5 %). No smokers, patients who didn't consume alcohol and patients with CD4 between 201-500/mm3 had more chance to have HPV. Patients with less than one partner per year were associated (p 0.003). There was no association between oral HPV infection and oral lesion, antiretroviral therapy, marijuana, other drugs, oral and anal intercourse, condom use and STDs. The conventional cytology showed atypical cells of undetermined significance in 2 samples.
Conclusion: Conclusion: Cancer was not observed.

PS-04-008
Do not forget the H&E: Power and limitation of histology in the diagnosis of ID
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Objective: Infectious disease diagnoses are most often suspect from the H&E appearance of an inflammatory pattern. The goal of this session is to highlight the value of an H&E for a variety of infectious and address the real limitations of the H&E for making patient care decisions.
Method: A series of cases will be used to illustrate different types of infection (bacteria, mycobacteria, fungus, viral, and parasite) with pearls and pitfalls about each type of organism and the use of the H&E.
Results: Algorithms for how to approach infections on the H&E and how to word pathology reports with the most helpful clinical impact will be discussed.
Conclusion: The H&E is the first, most important tool in detecting and infection which can, with proper approach, yield a great deal of information for the clinicians to act upon as well as direct ancillary tests for final diagnosis.

PS-04-009
Prevalence of HBV and HCV in Sukkar, Pakistan
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Objective: The aim of our study is to determine the prevalence of HBV & HCV infection in Sukkur Sindh.
Method: Total 205 Blood samples were collected from the male & female participants & were screened for the HBV & HCV by ICT/ELISA followed by PCR . Results were analyzed by using SPSS.
Results: Out of 205 participants, 24 (11.7 %) were positive for Anti-HCV in which 13 (6.3 %) were male and 11 (5.3 %) were females. On the other hand 12 (5.8 %) were positive for HBsAg in which 9 (4.3 %) were males and 3 (1.4 %) were females. Whereas only 1 (0.4 %) was positive for both Anti-HCV & HBsAg. Out of these 24 Anti-HCV positive samples 17 (8.2 %) were also positive for HCV by PCR in which 8 were males (3.9 %) & 9 (4.3 %) were females & on the other hand out of 12 HBsAg positive samples 9 (4.3 %) samples were also positive for HBV by PCR in which 7 (3.4 %) were males & 2 (0.9 %) were females. Only 1 (0.4 %) sample were positive for both HCV & HBV by PCR.
Conclusion: Our results indicates very high prevalence of HCV & HBV in this region. Which needs to be address immediately. Another interesting finding of this study is that the frequency of these infections are more in males as compare to females which might be due to the fact that males are more exposed to the high risk activities.

PS-04-010
Trichinella spiralis impact on mesenchymal stem cells: Immunohistochemical study by image analyzer in murine model
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Objective: This study aims to elucidate whether Trichinella spiralis infection or crude antigens administration can stimulate recruitment of CD105+ve/CD45-ve MSCs in the intestine and skeletal muscle of experimental BALB/c albino mice, in comparison to healthy control mice.

Method: Studied mice were divided into: 20 healthy control, 20 with orally induced T. spiralis infection, 20 orally received adult worm crude antigen and 20 received intramuscular larval crude antigen. According to specific timing schedule, mice were slaughtered and tissue sections were examined for MSCs density using CD105 and CD45 immunohistochemical staining and image J image analyzing software, to compare different study groups.
Results: T. Spiralis infection induced a significant increase in MSCs density in both intestinal and muscle sections, similarly the intramuscular injected larval crude antigen caused MSCs infiltration in muscles in comparison to muscle sections from healthy control mice. However, no significant MSCs cell density difference was noticed in intestinal sections after the orally received adult crude antigen compared to healthy control mice.
Conclusion: So, injected T. spiralis crude antigen can be a successful stimulant to MSCs attraction and recruitment in tissues nearby injection site, which may be beneficial for cell regeneration and tissue repair in case of presence of a disease induced damage.

PS-04-011
Detection of latent TB among health care workers vulnerable to TB exposure in Karachi Pakistan
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Objective: To screen the health care workers at risk to occupational exposure for latent TB using QuantiFERON Assay.
Method: 3 ml of whole blood were collected into three specific QFT tubes. (NIL,TB, Mitogen) from 120 health care workers including phlebotomists, Medical technologist, nurses, doctors and faculty members working closely with TB samples or patients. Samples were tested for detection interferon specifically released against TB according to the manufacturer QuantiFERON TB Gold protocol.
Results: Out of 137 samples 27 samples were found positive, 5 samples showed indeterminate result and 105 were found negative. Out of 27 positive samples 20 were from medical technologists working closely since long time with TB samples or TB patients and 4 were from phlebotomists collecting samples from patients.
Conclusion: Health care providers usually work with TB infected samples with minimal infection control measures. This study shows the need for effective latent TB infection control measures and emphasizes on the importance to improve over all biosafety precautions during dealing with the TB patients or samples. The study also provides recommendations for routine and regular screening and checkup of the health care workers working with TB to ensure their safety rather safety of all as no one is safe until everyone is safe.

PS-04-012
Parasites in tropical countries: Own experience from Cambodia
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Objective: Tropical parasitic diseases are rare findings in daily work of pathologists in industrialized countries. However, parasitic disease is one component in the Tropical Neglected Diseases (TND) by WHO in developing countries. They are afflicting more than1 billion people. The burden economy in these countries of parasitic diseases and their consequences are higher than all well-known diseases, like TB and Malaria. With worldwide exploding tourism, these diseases will show up more and more in Medical institutions in Western Countries and should be known to avoid treatment delay by wrong diagnosis.
Method: The Authors reviewed the diagnosis of 38 cases of parasitic diseases submitted to 3 departments of Pathology in Phnom Penh, Cambodia, from 2003 to 2015. About 38 cases (29 intestinal and biliary system and 9 soft part parasitoses) were re-evaluated and reviewed in respect to age, gender and clinical symptoms and residence of patients.
Results: Total 14 cases of Strongyloid Stercoralis, 6 Schistosomiases, 5 Amibiases, 1 Hookworm, 1 Capillaria Phillipinensis, 2 Clonorchis sinenses were found in intestinal biopsies respectively in resection specimen and in biliary system and, 6 Cysticercoses, 2 Sparganoses and 1 Filariasis were respectively detected in soft tissue specimens.
Conclusion: Parasitoses are rare findings in routine pathology. Stool examinations are diagnostic state of art. However, the diagnosis of these diseases needs experience from clinicians and pathologists. In case of travelers in developing countries, parasitoses should be always taken into account of differential diagnosis.

Monday, 26 September 2016, 09.30–10.30, Hall 11.3
PS-05 Digestive Diseases Pathology — Liver and Pancreas

PS-05-001
Electron microscopic investigation in the diagnostics of echinococcosis
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Objective: Parasitic diseases, according to WHO, in more than 32 % of cases are the causes of deaths. In recent years, in the Republic of Kazakhstan a steady increase in the incidence of echinococcosis were noted (up to 1000 or more cases per year). We studied 215 cases of surgically treated liver echinococcosis. One hundred and seventy-nine patients were operated by traditional methods with an impact on residual cavity by various antiseptics. Thirty-six patients underwent an echinococcectomy with cavern sanitation by a physical method that we developed, with the use of underwater electrical discharge.
Method: We conducted an intraoperative sampling of material for morphological study.
Results: By electron microscopic study of Echinococcus cysts that were exposed to chemical attack it was found that all membrane structures of cells of germinal membrane of the hydatid cyst wall were intact and undergone minor changes. In the materials taken after physical method of sanitation of the residual cavity a complete destruction of all cellular elements of brood capsules of Echinococcus were detected. In the cellular detritus small membrane, vacuolar and granular fragments of nuclei and cytoplasm of necrotic cells were seen. From completely destroyed protoscolexes electron-dense debris of hooks and "ghosts" of vacuolated and ruined body components were remained.
Conclusion: Physical method of sanitation of the residual cavity with underwater discharge at surgical treatment is effective in the prevention of recurrence of echinococcosis. This is confirmed by the materials of electron microscopic investigation.

PS-05-002
Colorectal liver metastasis: Post-operative nodular regenerative hyperplasia and sinusoidal obstructive syndrome in oxaliplatin based chemotherapy
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Objective: Sinusoidal Obstructive Syndrome (SOS) and Nodular Regenerative Hyperplasia (NRH) seem to be hepatotoxic effects related

to Oxaliplatin based chemotherapies (OX) in colorectal liver metastasis (CLM). Our objective was to determine incidence of SOS and NRH in patients undergoing liver resection due to CLM and its relationship with chemotherapy regimen. Secondarily, study the correlation of macroscopical and microscopical liver features, type of resection and outcome as hepatic insufficiency.
Method: A historic prospective maintained database of 166 patients with CLM was analysed and followed from January 2007 to December 2014.
Results: Among 130 patients treated with OX 47(38.2 %) presented SOS (Sinusoidal dilatation 2–3), among them 19(40.4 %) presented peliosis and perisinusoidal fibrosis. All 6(4.6 %) with NRH, 9(6.9 %) presenting Blue-Liver Syndrome (BL) and 8(6.1 %) with hepatic insufficiency were treated with OX. All but one in each category underwent a mayor or complex resection.
Conclusion: Severe SOS and NRH are not frequent yet they are present. The only predictive factors for SOS, NRH, BL and/or hepatic insufficiency seems to be OX and the type of surgery performed. Surgeons should have special attention regarding these findings for recurred CLM.

PS-05-003
The expression and role of nuclear EpICD in hepatocellular carcinoma
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Objective: Regulated intramembranous proteolysis mediated loss of an extracellular domain of epithelial cell adhesion molecule (EpEx) and release of an intracellular domain (EpICD) into the cytoplasm, and the sequential association of EpICD with FHL2 forms a nuclear complex with β-catenin and Lef-1, inducing gene transcriptions involved in activation of oncogenic potential of EpCAM.
Method: We examined the immunohistochemical nuclear expression of EpICD in 100 cases of HCC and investigatd the role of EpICD in HCC cell line using EpICD cDNA and small interfering RNA (siRNA).
Results: Nuclear expression of EpICD significantly correlated with nuclear expression of β-catenin, and Ki-67 labeling index. In addition, nuclear expression of EpICD was associated with higher histologic grade and advanced T category. Forced overexpression of EpICD using EpICD cDNA in the HCC cell significantly increased the cell proliferation, migration and invasion. The overexpression of EpICD also increased the expression levels of the active form of β-catenin and c-myc and cyclin D1. Conversely, silencing of EpCAM by siRNA decreased the cell proliferation, migration, invasion and the expression of active form of β-catenin, c-myc and cyclin D1.
Conclusion: Our present data suggest that nuclear EpICD plays important roles in HCC progression by modulating expression of target genes of EpCAM.

PS-05-004
Comparative morphometric characteristics of microvessels in hepatocellular carcinoma of different nodes sizes
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Objective: Comparative analysis of morphometric characteristics of microvessels in hepatocellular carcinoma (HCC) of different nodes sizes.
Method: Studied the surgical specimens of 64 hepatocellular carcinoma nodes of the liver without cirrhosis: 17 cases—diameter nodes less than 5 cm (SN), 24 cases—5–10 cm (MN), 23 cases—over 10 cm (LN). Performed immunohistochemical detection of vessels using the CD34 and CD105 and their morphometric analysis.
Results: The greatest number of CD34+ microvessels were in SN HCC, exceeding by 10.9 and 34,9 % ($p < 0,05$) the figures of MN and LN. The maximum number of CD105+ microvessels installed in MN: by 8.2 % greater than in SN and by 31.4 %—LN HCC ($p < 0.05$). The highest values of the average area of CD34+ microvessels observed in LN, exceeding by 17.1 and 7.0 % of SN and MN HCC. The maximum values of the average area of CD105+ microvessels detected in SN: by 0.5 % greater than in MN and by 19,9 %—LN HCC ($p < 0,05$). The degree of tumour vascularization reduced with increasing the size of HCC nodes.
Conclusion: Morphometric characteristics of microvessels in HCC nodes reflects the processes of tumour angiogenesis, depends on the method of their detection and nodule size.

PS-05-005
Primary giant cell tumour of the common bile duct: No mutation H3F3A found
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Objective: Primitive giant cell tumour (GCT) of the common bile duct is very rare and share similar pathologic features with GCT of bone. Recently, H3F3A mutations were found as highly specific of GCT of bone. The aim of this study was to report a recent observation of GCT of the common bile duct, and to search for H3F3A mutations in the present case and in the pancreatic GCT we previously reported.
Method: The bile duct tumour was fixed in 10 % neutral buffered formalin and included in totality in paraffin. Paraffin sections of the tumour were immunostained. Targeted next generation sequencing (NGS) on the 12 histone H3 genes was performed.
Results: The patient (77-year-woman) presented a pedunculated polypoid mass in the common bile duct consisted of mononuclear histiocytic and stromal neoplastic cells with numerous giant cell stained by CD68 with no reactivity for keratin markers. NGS analysis showed no mutation in the 12 histone H3 genes, including the H3F3A gene recurrently mutated in GCT of bone.
Conclusion: We reported here a sixth observation of primary GCT of the common bile duct. The present result suggests that although GCT of the bone and GCT of extra-osseous location have large similitude, their pathogenesis looks different.

PS-05-006
Severity histologic score of acute pancreatitis in murine models: Preliminary results
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Objective: In acute pancreatitis (AP) five scoring systems have been identified, each one developed for a specific AP murine model and taking only in consideration individual parameters. The aim of this study was the development and validation of a histological score that stratifies the severity of AP severity in several murine models.
Method: 26 Wistar rats were divided into three AP models (caerulein, duodenal occlusion and pancreatic duct occlusion). Animals were sacrificed at 10 and 24 h, depending on model. Lipase and amylase were measured to confirm AP. Histopathologic evaluation for edema, necrosis, inflammatory infiltrate, hemorrhage and vacuolization of acinar cells was performed and graded, and then stratified in four AP levels: none, mild, moderate and severe. The histologic score was correlated with C-reactive protein and procalcitonin.
Results: Histological changes were observed in 62.5 % of animals. Of these, 87.5 % were classified as mild AP and 12.5 % as moderate. Moderate AP was found in the pancreatic duct occlusion model. There was correlation between histological changes and procalcitonin ($p = 0.004$).

Conclusion: Preliminary results seem to validate the proposed histological score of AP. This score will allow greater uniformity of AP severity evaluation in murine models with application in different models for better understanding the AP pathophysiology.

PS-05-007

Immunohistochemical expression of Cadherin 17 (CDH17) in non malignant liver tissues and in Hepatocellular Carcinoma (HCC)

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Objective: This study aimed to evaluate the immunohistchemical expression of CDH17 in non malignant liver tissues and in hepatocellular carcinoma (HCC) with correlation to various clinical and histopathological parameters.
Method: This retrospective study was carried out on 138 liver tissue specimens including 98 HCC. The non malignant liver tissues includes (7 donors, 7 cases of chronic hepatitis C, 2 cases of focal nodular hyperplasia, 2 cases of hepatocellular adenoma, 22 cases of cirrhosis and 66 cases of cirrhosis adjacent to HCC). Tissue microarray technique was used.
Results: The mean percentage of CDH17 expression was significantly higher in non malignant cases (80.5 ± 33.8) compared to HCC cases (55.5 ± 46.7) ($P = 0.003$). Also CDH17 was significantly higher in Cirrhosis without HCC than in Cirrhosis adjacent to HCC ($p < 0.001$). CDH 17 expression was significantly associated with presence of vascular invasion ($p = 0.016$). Also, cases with vascular invasion showed higher H. score (mean ± SD = 146.5 ± 100.3) compared to cases without vascular invasion (mean ± SD = 77.3 ± 104.5) ($P = 0.06$). Using correlation coffecience test there was a significant association between H score of CDH17 expression and decreased survival time ($P = 0.002$) although this was not approved using univariate analysis.
Conclusion: CDH17 was significantly higher in non malignant liver tissue with down regulation in premalignant cirrhosis which may be attributed to a role similar to classic cadherins . Up regulation of CDH17 in HCC is associated with poor prognostic features such as vascular invasion and shorter survival time.

PS-05-008

Evaluation of centrilobular fibrosis in post-transplant liver: Preliminary results

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Objective: We studied centrilobular fibrosis (CLF) in adult post-transplant liver biopsies and assessed possible correlations with histopathological features, collagen proportionate area (CPA) and hepatic stellate cell (HSC) activation.
Method: Thirty seven routine liver biopsies from 20 consented patients (33–65 years, 8 female) were included. The extent and topography of fibrosis and CPA were assessed using sirius red fast green stain. HSC activation was evaluated by α smooth muscle actin (α-SMA) immunostaining. The results were quantified by digital image analysis.
Results: CLF was present in 15 (41 %) biopsies from 12 (60 %) patients. Central vein endotheliitis (CVE) severity was correlated with central perivenulitis (CPV) severity ($p < 0.001$), total parenchymal CPA and the amount of centrilobular α-SMA ($p < 0.05$). CPV did not correlate with CLF. Centrilobular CPA correlated with total α SMA area ($p < 0.001$). CLF did not correlate with age, gender, acute cellular rejection severity or other histopathological features.
Conclusion: CLF is common in adult post-transplant liver biopsies affecting the majority of patients. CVE was the only significant histological feature associated with parenchymal fibrosis and centrilobular HSC activation indicating that it may play a role in activating HSCs in centrilobular areas contributing to CLF development.

PS-05-009

Histopathology of the liver in yellow fever after two months of infection: A case report with literature review

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Objective: Yellow fever is a mosquito-borne flavivirus infection, prevalent in endemic areas and characterized by hemorrhagic fever and rapid deterioration of function of several organs including the liver. Death usually follows within few days of the onset. Few reports describe the liver lesions after the initial acute phase of the disease. We report the case of a 47 year old male patient, traveling to Angola, who presented to our hospital after two months of infection.
Method: The patient was diagnosed with yellow fever on the basis of fever, hematuria and jaundice with positive serological markers. After two month, he was admitted to our hospital for persistent elevation of liver enzymes and cholestasis. Therefore, a liver biopsy was performed.
Results: Microscopic examination showed moderately active portal and lobular hepatitis with regenerative features, ballooning of the hepatocytes, giant cell transformation, hemosiderin laden macrophages and intracellular lipofuscin pigment. There was no evidence of intranuclear viral inclusions. These features were consistent with nonspecific hepatitis as described in surviving liver of yellow fever.
Conclusion: Histological features of yellow fever are well known in the acute stages. In our case, we describe the state of the surviving liver at two month and we review the literature on the subject.

PS-05-010

Immunohistochemical expression of alpha smooth muscle actin (α-SMA) in hepatocellular carcinoma from Egyptian patients and its relation to various clinicopathological parameters

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Objective: To investigate tissue expression of α-SMA in hepatocellular carcinoma (HCC) from egyptian patients and to correlate its expression with various clinicopathological parameters of HCC.
Method: Hematoxylin and eosin stained slides were re-evaluated in 62 HCC cases to assess tumour type, grade, stage, presence of lymphovascular invasion and the status of parenchymal margin (involved or not). Tissue Microarray construction (TMA) was constructed from paraffin embedded blocks (representative of the tumour) and 4-um sections of these tissue array blocks were cut and placed on positive charged slides and applied for immunostaining with α-SMA antibody. The α-SMA staining in the HSCs within the tumour stroma and perisinusoidal spaces was qualitatively classified into the following 4 groups compared with vascular smooth muscle cells (VSMCs): 0, no staining; +1, staining intensity considerably lower than VSMCs; +2, staining intensity lower than VSMCs; and +3, staining intensity similar to that of VSMCs. Also, α-SMA staining was quantitatively classified into the following 4 groups: 0, ≤1 positive cell/high power field (hpf); +1, <10 positive cells/hpf; +2, 10 20 positive cells/hpf; and +3, >20 positive cells/hpf. Qualitative and quantitative classification was performed by a fellowship trained gastrointestinal pathologist without matching knowledge of the clinical data. For statistical analysis, grades 0 and +1 were categorized as low expression and grades +2 and +3 as high expression.

Results: All cases of HCC were positive for α-SMA expression (100 %) in hepatic stellate cells from tumoural stroma. High quantitative (extensive) and qualitative (strong) expression of α-SMA was observed in 33 and 31 of the studied 62 HCC cases respectively, while low quantitative (sparse) and qualitative (weak) expression of α-SMA was observed in 29 and 31 of the studied 62 HCC cases respectively. Regarding the site of HCC, strong and extensive expression of SMA showed high significant association with HCC originating from Left lobes and also from both right and left lobes ($P < 0.008$ and $P < 0.009$) respectively. Strong expression of α-SMA appear to be associated with trabecular pattern of HCC but the association is statistically near significant ($P = 0.08$). Quantitative and qualitative of α-SMA expression failed to show any significant relationship with different clinicopathological parameters of HCC cases.
Conclusion: Expression of Alpha smooth muscle actin (α-SMA) was detected in all HCC cases, mainly those with trabecular pattern, so it may be used to differentiate HCC from other malignancies in liver whether primary or secondary. α-SMA expression has no relation to various clinicopathological parameters of HCC except for tumour site.

PS-05-011
The effect of imatinib in various thioacetamide-induced mouse liver fibrosis models
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Objective: The deposition of collagenous extracellular matrix is an obligate consequence of chronic hepatic injury. The resulting fibrosis is mostly mediated by PDGF-driven hepatic myofibroblasts. Imatinib efficiently suppresses the activity of PDGFR, thus it is a promising candidate for the treatment of hepatic fibrosis.
Method: Thioacetamide (300 mg/l) was given for 18 weeks to male C57Bl/6 wild type and transgenic mice, overexpressing TGF-β1 in the liver. In an additional "therapeutic" experiment thioacetamide was given to wild type mice for 27 weeks. For test animals imatinib was given daily (25 mg/kg per os; in the "therapeutic" experiment from the 19th week). The extent of fibrosis, ductular reaction, the proliferative activity of hepatocytes and ductular cells was monitored.
Results: Imatinib treatment resulted in a transient inhibition of fibrosis progression in wild type mice, but failed to achieve this result in transgenic mice or the "therapeutic" experiment. In each group the extent of ductular reaction changed parallelly with the extent of fibrosis, while the proliferation of hepatocytes remained constant.
Conclusion: Imatinib did not show lasting antifibrotic effect in wild type mice, and it was completely inefficient besides TGF-β1 overproduction or preceding fibrosis. The strong correlation between ductular reaction and fibrosis underlines their close relationship.

PS-05-012
Intrahepatic lymphoepithelioma-like cholangiocarcinoma associated with Epstein-Barr virus: A case report
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Objective: Intrahepatic lymphoepithelioma-like cholangiocarcinomas (LEL-CC) are rare tumours, and are often associated with Epstein-Barr virus (EBV). Here we present a case of LEL-CC associated with EBV infection in an explanted liver.
Method: A 28-year-old male patient with a history of primary sclerosing cholangitis related cirrhosis was transplanted without any clinical sign or symptoms of tumour. Formalin fixed, paraffin embedded liver samples were analysed in detail. In situ hybridization (ISH) for the EBV-encoded small RNA (EBER) was also carried out.
Results: Multiplex tumourous nodules were detected in the explanted liver. Histologically, the tumour was composed of two components: a well-differentiated adenocarcinoma and a lymphoepithelioma-like carcinoma with sheets of undifferentiated epithelial cells and dense lymphoid stroma. Immunohistochemically, both components were positive for pancytokeratin and cytokeratin19. ISH for the EBER was also positive. Tumour cells did not stain with either Glypican-3 or Arginase-1 antibodies.
Conclusion: As far as we know, this is the first case report of EBV-associated intrahepatic LEL-CC in an explanted liver. Although this tumour is not very common, based on literature data it is characterised by favourable overall survival. During the 2 years follow-up despite immunosuppressive therapy—without additional courses of chemotherapy—the patient did not show any evidence of tumour progression.

PS-05-013
Expression of adrenomedullin in chronic inflammatory liver diseases
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Objective: Adrenomedullin (ADM) is a multifunctional neuropeptide which seems to play an immunomodulatory role in different inflammatory processes. Indeed, in a model of rheumatoid arthritis (known to be an autoimmune disease), the administration of ADM, reduced inflammatory damage and restored immune tolerance, by acting on regulatory T lymphocytes. This study aimed to evaluate the expression and the role of ADM in chronic inflammatory liver diseases (CILD), aspects that have never been investigated so far.
Method: We assessed, by means of immunohistochemistry, the tissue expression of ADM in normal liver (10 cases) and in a series of 49 CILD, including 22 autoimmune and 27 viral, type C, hepatitis.
Results: In normal liver, ADM was strongly and diffusely expressed in sinusoidal lining cells and in the hepatocytes. In CILD, ADM expression was less extensive and weaker in most cases. In particular, reduced ADM expression in sinusoidal cells was significantly associated with the autoimmune etiology ($p = 0.01$). Furthermore, a weaker sinusoidal expression of ADM significantly correlated with a more severe necro-inflammatory damage ($p = 0.04$).
Conclusion: This study indicates that expression of ADM is under regulated in CILD, particularly of autoimmune etiology, suggesting that it may play an immunomodulant role even in this context.

PS-05-014
Nectin-1 expression in cancer-associated fibroblasts is associated with poor prognosis of pancreatic ductal adenocarcinoma
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Objective: Nectins are cell adhesion molecules that regulate the formation of adherens junctions and tight junctions. In this study, the immunohistochemical expression of nectin-1 was assessed in tumour cells and in cancer-associated fibroblasts (CAFs) of the pancreatic ductal adenocarcinoma.
Method: Immunohistochemistry for nectin-1 was conducted using tissue microarray blocks constructed from 258 resected cases of pancreatic ductal adenocarcinoma. The immunohistochemical expression of nectin-1 in CAFs was compared with clinicopathological parameters. The percentage of nectin-1 expression in CAFs was classified as negative/focal at ≤30 % and a diffuse at >30 %.

Results: Immunohistochemical analysis demonstrated diffuse CAF nectin-1 expression in 64 cases (24.8 %). Diffuse nectin-1 expression in CAFs is associated with lymph node metastasis ($p = 0.016$), advanced UICC stage ($p = 0.016$), perineural invasion ($p = 0.042$), and tumour in the pancreas head ($p = 0.023$). Patients exhibiting diffuse nectin-1 expression in CAFs had signi_cantly shorter overall survival times than those with focal/negative expression of nectin-1 in CAFs ($p = 0.003$). Multivariate analysis also demonstrated diffuse nectin-1 expression in CAFs to be an independent prognostic factor.
Conclusion: These findings indicate that diffuse nectin-1 expression in CAFs of pancreatic ductal adenocarcinoma is associated with metastasis and patient survival.

PS-05-015
Not only neuroendocrine tumours but also other pancreatic tumours can be accompanied with serous cystic neoplasms even in patients without von Hippel-Lindau syndrome
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Objective: To evaluate serous cystic neoplasms (SCN) accompanying other pancreatic tumours.
Method: We compared clinicopathologic features of surgically resected 15 SCN accompanying other tumours with 259 conventional SCN.
Results: The prevalence of SCN accompanying other tumours was 5 % (15/274). SCN accompanying other tumours had significantly smaller tumour size (2.2 ± 1.5 cm), than that of conventional solitary SCN (3.6 ± 1.9 cm; $P = 0.01$) and they were more commonly observed in head (8/15, 57 %), while conventional solitary SCN were more frequently noted in the body and tail (201/259, 78 %; $P = 0.001$). However, no difference was found in sex and age of the patients and gross pattern (microcystic, macrocystic, mixed, or solid) of SCN. Accompanying neoplasms included 7 intraductal papillary mucinous neoplasms (IPMN), 1 colloid carcinoma arising from IPMN, 6 neuroendocrine tumours (NET), and 1 solid pseudopapillary neoplasm (SPN). Four NET associated with von Hippel-Lindau (VHL) syndrome had multiple NET, while 2 NET without VHL syndrome were solitary.
Conclusion: SCN accompanying other tumours are 5 % of entire SCN and tend to be smaller and located in head. Commonly accompanying tumours are IPMN and NET and other neoplasms, such as colloid carcinoma and SPN.

PS-05-017
Role of metalloproteinase in invasive growth in pancreatic ductal adenocarcinoma
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Objective: The abundant desmoplastic stroma reaction in pancreatic cancer, is considered to be an important reason for its aggressive tumour biology and resistance to chemotherapy.
Method: FFPE -tissue from the pancreatectomy of 100 patients was IHC stained with αSMA, MMP 2 and 9 and TIMP 1,2 and expression for haematoxylin-eosin and Masson's trichrome to assess stroma density.
Results: Tumour stroma in PDA was grading from "loose" in myxomatosis area, "moderate" to "dense" with collagen core. In "loose"—αSMA 1+; in "moderate"—2+ and "dense"—2-3+, but without express in collagen area. Masson's trichrome was positive in all area, but severity expression was different. In "loose" stroma we found some thin blue collagen fibers, separated myxomatosis; in "moderate" and "dense"—the fibers collagen was detected back to back, but in severity areas of collagen expression was strongly positive glaring blue colors. The expression level in carcinoma cells varied from negative to strong positivity and had a tendency to be associated with a low degree of differentiation. There is a direct correlation between the expression of MMP-2 ($r = 0,34$) and 9 ($r = 0,67$), and the presence of perineural invasion, tumour invasion to the duodenum, perineural invasion and peripancreatic tissue. In AC tumour cells strongly express MMP-2, MMP-9.
Conclusion: During invasive tumour growth plays a direct role not only the fact of increasing the production of MMP, create a favorable environment for tumour growth, but also a marked decrease in expression of their inhibitors, which in turn favors more invasive growth.

PS-05-018
KRAS mutation analysis using i-densy in the early diagnosis of pancreatic ductal adenocarcinoma
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Objective: KRAS codon 12/13 mutations have been identified in over 95 % of pancreatic ductal adenocarcinomas (PDACs). The i-densy analyzer can perform rapid gene analyses, including pretreatment, amplification, and detection, automatically on a single platform. We aimed to evaluate the usefulness of KRAS mutation analysis by i-densy using cytological material for PDAC diagnosis.
Method: Seventeen patients were enrolled in this study. Fourteen were patients with clinically suspected PDAC, while the rest of them were chronic pancreatitis patients. KRAS codon 12/13 mutations in pancreatic brush and/or pancreatic juice samples were analyzed using i-densy and conventional cytological diagnostic method, and the results were compared.
Results: KRAS mutations were detected in 11 and wild-type KRAS in five patients, using i-densy. The quantity of sample obtained from one patient was insufficient. Conventional analysis results were positive for nine, negative for seven, and equivocal in one patient. An almost perfect agreement between i-densy results and the final diagnosis was observed, while the agreement between conventional cytology results and final diagnosis was lower.
Conclusion: The diagnostic accuracy of i-densy KRAS mutation analysis was shown to be higher than that of conventional cytology, indicating the potential for its use in clinical applications.

PS-05-019
High accuracy in scoring by digital immunohistochemistry in research pathology in liver cancer
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Objective: To determine the effectiveness of digitally scoring immunohistochemically (IHC) stained slides compared to manual scoring when evaluating the role of epithelial-mesenchymal transition (EMT) in hepatocellular carcinoma (HCC) in background hereditary hemochromatosis (HH).
Method: Expression of two EMT markers (E-cadherin and cytokeratin 18), were evaluated by IHC in paraffin-embedded liver tissue (16 HH-HCC and 4 nonHH-HCC). Manual scoring was conducted by a senior pathologist using light microscopy; digital scoring was performed with ImageJ software using a color separation and diaminobenzidine (DAB) quantification method on scanned slides. Results for both methods were reported using a 0, +1, +2, +3 system combining % of areas and staining intensity. Cohen's Kappa coefficient was then calculated to determine the agreement between both methods.

Results: EMT is characterised by the repression of epithelial adhesion molecules E-cadherin and CK18. Analysis using both methods was performed for these markers (membranous and cytoplasmic patterns) revealed loss of epithelial markers E-cadherin and/or CK18 in tumours that morphologically exhibited greater pleomorphism and/or a mesenchymal phenotype. E-cadherin and CK18 scoring had agreement in 90.0 % with kappa of 0.828 [very good agreement] (95 % CI, 0.596 to 1) and kappa = 0.785 [good agreement] (95 % CI, 0.504 to 1) respectively. Pooled results showed agreement in 90 % of cases and a kappa = 0.817 (95 % CI, 0.644 to 0.99), indicating very good agreement.
Conclusion: These preliminary results using digital analysis demonstrate strong agreement with manual scoring and could be a valuable tool in research pathology. Additional immunohistochemical makers for mesenchymal profile are being further evaluated.

PS-05-020
Compromised liver regeneration as an early step in hepatocarcinogenesis
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Objective: Hepatocellular carcinoma (HCC) develops most often in association with chronic liver disease like viral hepatitis or alcohol toxic cirrhosis. But also in inflammation-free, non-cirrhotic liver HCC can occur. Here, the underlying pathomechanism is largely unclear.
Method: We used histochemical activity staining of cytochrome c oxidase (CCO), a component of the respiratory chain and partially encoded by mitochondrial DNA (mtDNA), to screen for mtDNA damage and to identify clonal liver cell patches. Mutations of the CCO genes in liver cell patches were analyzed by sequencing.
Results: These patches represent presumably lineages of regeneratively active liver cells—potentially stem or progenitor cells. Significantly larger and more numerous patches in HCC-bearing compared to healthy liver suggest a reduced pool of active regenerating liver cells. MtDNA sequencing of the patches demonstrated besides a higher mutational burden also an homoplasmic state of the mutations. Adjacent patches failed to show common trunc mutations, indicating probably independent ancestors.
Conclusion: In conclusion these data suggest a depletion of regeneratively active liver cells as an possible early stage in the development of HCC in non-cirrhotic livers. We present a 3D-reconstruction of liver patches and a model for mtDNA deprivation in liver progenitor cells.

PS-05-021
Combination immunohistochemistry for SMAD4 and Runt-related transcription factor 3 (RUNX3) may identify a favourable prognostic subgroup of pancreatic ductal adenocarcinomas
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Objective: SMAD4/DPC4 mutations have been associated with aggressive behavior in pancreatic ductal adenocarcinomas (PDAC), and recently, it has been suggested using in vitro studies and animal models that RUNX3 expression combined with SMAD4 status may predict the metastatic potential of PDACs. In this study, we evaluated the prognostic utility of SMAD4/RUNX3 status in human PDACs by immunohistochemistry.
Method: Immunohistochemical stains were performed for SMAD4 and RUNX3 on 183 surgically resected PDACs, and the results were correlated with the clinicopathological features.
Results: Loss of SMAD4 expression was associated with poor overall survival (OS) (p = 0.075) and recurrence-free survivals (RFS) (p = 0.079), although not statistically significant. Nuclear RUNX3 expression was associated with decreased OS (p = 0.028) and RFS (p = 0.052), and more frequent in poorly differentiated PDACs (p = 0.018). On combining RUNX3/SMAD4 status, RUNX3-/SMAD4+ PDACs demonstrated longer OS (p = 0.010) and RFS (p = 0.005) compared to RUNX3+/SMAD4+ and SMAD4- groups; RUNX3-/SMAD4+ was a significant independent predictive factor for both OS [p = 0.040, HR 1.817 (95 % CI 1.028–3.211)] and RFS [p = 0.002, HR 2.870 (95 % CI 1.475–5.584)].
Conclusion: SMAD4-positivity with RUNX3-negativity was a significant independent predictive factor for better OS and RFS in PDAC. Thus, combination immunohistochemistry for SMAD4 and RUNX3 may help identify a favorable prognostic subgroup of PDAC.

PS-05-022
Exosomal markers (CD63 and CD9) expression by Immunohistochemistry (IHC) in Pancreatectomy Specimens (PS)
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Objective: Exosomes are important mediators in intercellular communications that play a role in cancer progression and metastasis. Exosomal membranes are enriched in endosome-specific tetraspanins (CD9 and CD63). We explored the expression of CD63 and CD9 utilizing IHC in PS.
Method: Twenty-nine PS were identified. The pathologic tissue (PT) and adjacent normal tissue (ANT) in each PS was stained for CD63 and CD9 using IHC. Two pathologists independently scored the expression of CD63 and CD9. The intensity of staining was graded from 1 to 3. The percentage of stained cells was estimated in 10 % increments. An average Q score (Intensity X Percentage of staining) was calculated. Unpaired t test was used for statistical analysis.
Results: The mean Q score for CD63 and CD9 expression is higher in PT (209 and 72, respectively) compared to ANT (154 and 24, respectively) (p = 0.0044; p = 0.0017). The Mean Q score for CD63 and CD9 expression is higher in the malignant PT (231 and 85 respectively, n = 17) compared to ANT (129 and 25, respectively) (p < 0.0001 and p < 0.0132).
Conclusion: Exosomal markers (CD63 and CD9) expression assessment using IHC is feasible in PS. The expression of CD63 and CD9 is higher in PT and malignant PT compared to their ANT.

PS-05-023
Comparison between rejection activity index and national institutes of health grading system in liver biopsies for the diagnosis of graft versus host
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Objective: The aim of our study is comparison between rejection activity index (RAI) and national institutes of health (NIH) scoring system in bone marrow transplanted patients' liver biopsies.
Method: 20 liver biopsies of 19 bone marrow transplanted patients were reviewed retrospectively and graded using the rejection activity index(RAI) and National Institutes of Health (NIH) Consensus Development Project on Criteria for Clinical Trials in Chronic GVHD.

Results: There were 14 men and 5 women with ages ranging from 4 to 66 years (mean: 26,2 years). The primary diseases were acute myeloid leukemia,acute lymphoblastic leukemia, nonHodgkin's lymphoma, Hodgkin's lymphoma, thalassemia and multiple myeloma. GVHD affected multiple organs in 7 patients. Overall survival is ranging from 3 to 112 months after transplantation (mean: 31,3 months). Seven patients died due to primary disease, transplant related disease and infections. Grading with NIH criteria, 8 patients had 'Likely GVHD', 5 patients had 'Not GVHD', 7patients had 'Possible GVHD'. There was no differences between RAI and NIH scoring system.
Conclusion: NIH Consensus Development Project on chronic GVHD published for defining minimal diagnostic criteria for active GVHD and criteria for an adequate histologic sample in several organ systems, create a standardized terminology for communicating histology results.

PS-05-025
Liver metastases from neuroendocrine tumours: Comparison between neuroendocrine immunohistochemical markers
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Objective: Liver metastases are the most common form of spread of neuroendocrine tumours (NET), often being identified before the primary tumour. This study describes and compares the neuroendocrine immunohistochemical markers of liver metastases from NET.
Method: Immunohistochemical stainings for chromogranin A (CgA), synaptophysin, CD56 e CD57 were performed in 18 liver metastases from NET (small bowel = 5; stomach/duodenum = 5; undetermined = 4; pancreas = 2 and lung = 2). Intensity of marker expression and percentage of positive staining areas were evaluated and compared.
Results: The CD57 was expressed in highest number of cases (94.4 %), followed by CgA (83.3 %), CD56 (52.9 %) and synaptophysin (50 %). As while CgA showed the highest number of cases with more than 80 % of positive staining areas (80 %), followed by CD57 (64.7 %), synaptophysin (55.5 %) and CD56 (33.3 %). CD57 showed moderate/strong intensity of expression in 100 %, CgA-86.6 %, synaptophysin-77.7 % and CD56-44.4 % of the cases. The concordance rate between CgA and CD57 was significant for positive immunostaining ($p = 0.021$) and for intensity of expression/percentage of positive staining areas ($p = 0.014$). CgA showed higher expression in small bowel, pancreas and undetermined; CD56 in pancreas and CD57 in all sites.
Conclusion: CD57 showed results similar to CgA and higher than synaptophysin and CD56 in the characterization of liver metastases from NET.

PS-05-026
Pancreatic mixed adeno-neuroendocrine carcinomas (MANECs) — report of a series of cases
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Objective: Pancreatic MANECs are rare, highly aggressive epithelial tumours with mixed differentiation: neuroendocrine and adenocarcinomatous. They represent less than 1 % of the pancreatic tumours. Identification of neuroendocrine features allows patients to receive a specific treatment with increase of survival and life quality.
Method: We present five consecutive pancreatic MANEC occurring in three middle aged men and two women diagnosed in the last 2 years in our department. They represent about 1.6 % of all pancreatic malignant tumours diagnosed in this period.
Results: All patients had surgical treatment for pancreatic masses with jaundice and severe weight loss. No neuroendocrine signs and symptoms were identified. All specimens were diagnosed as MANEC on microscopic features and immunohistochemical markers as chromogranin A, synaptophysin neuron specific enolase and CD56. Adenocarcinomatous component was moderately differentiated, while neuroendocrine component was poorly differentiated. Postoperative median survival was 10 months, all patients being in an advanced stage at the moment of diagnosis.
Conclusion: Poorly differentiated carcinomas of pancreas can mimic meuroendocrine features, but a thorough microscopic examination and adequate panel of immunohistochemical assays are critical for diagnosing real MANEC, with significant impact on patients outcome.

PS-05-028
Microvessels density in liver metastases
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Objective: Our study focuses on the investigation of angiogenic process in liver primary and recurrent metastases secondary to colorectal cancer.
Method: 24 cases including eight with recurrent metastases occurred after a previous treatment by thermonecrosis (group 1) and 16 with primary metastases treated exclusively by surgery (group 2) were immunohistochemically investigated using anti-CD31 antibody. Microvessels density (MVD) was quantified in 5 hot-spots, separately in intratumoural and peritumoural areas; a mean value was calculated for each case and group. Student's t-test was used for all statistical comparisons.
Results: In group 1, intratumoural MVD was 30.58 ± 13.16, and peritumoural 58.33 ± 23.41, whereas in group 2 intratumoural MVD was 22.26 ± 9.12, and peritumoural 85.03 ± 34.68, with statistically significant differences intratumoural versus peritumoural for both groups ($p = 0.01$, and $p < 0.0001$, respectively). In addition, the comparison between group 1 and group 2 revealed significant differences in MVD only for peritumoural areas ($p = 0.03$).
Conclusion: Our data points out the differences in angiogenic profile between recurrent and primary metastases. Peritumoural MVD mean values, lower in group 1, could be interpreted as a failure of angiogenic potential in metastatic recurrent disease, subsequently to the biological changes induced in tumour liver environment by thermonecrosis.

PS-05-029
Hepatocellular adenoma subtypes in São Paulo, Brazil: A preliminary study
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Objective: To examine hepatocellular adenoma (HCA) subtypes distribution in a preliminary cohort from two tertiary referral hospitals in São Paulo, Brazil.
Method: A preliminary and random set of resection specimens of patients radiologically diagnosed or suspected as HCAs were classified based on morphological and immunohistochemical analysis defined by the current WHO criteria. Between 1994 and 2015, 65 patients underwent partial liver resection and 3 had liver transplantation, accounting for 103 nodules. Our preliminary cohort included 55 nodules from 28 patients in which immunohistochemical reactions were previously performed.
Results: Seventeen nodules (60 %) were further classified as Inflammatory type HCAs, 9 (16 %) as HNF1-a inactivated, 12 (22 %) as unclassified and 1 (2 %) as Beta-catenin activated. One of the liver explant harbored 16 HNF1-alpha inactivated adenomas. One of the unclassified HCAs had evidence of malignant transformation to hepatocellular carcinoma. All HNF1-a inactivated HCA occurred in women (mean 36y).

Conclusion: Preliminary study of 55 HCAs from Brazil showed higher incidence of unclassified HCAs. Distinct epidemiological and environmental factors may be responsible for this trend. Further morphological and molecular analysis of all cases in our institutions is required to better understand the pathogenesis of HCAs in our country.

Monday, 26 September 2016, 09.30–10.30, Hall 11.3
PS-06 Nephropathology

PS-06-001
Proliferative glomerulonephritis with monoclonal IgG deposits associated with membrano-proliferative features
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Objective: Proliferative glomerulonephritis with monoclonal IgG deposits (PGNMID) is a recently described entity. Patients with PGNMID present nephrotic-range proteinuria or nephrotic syndrome, hematuria and renal insufficiency. Clinical evidence of multiple myeloma or B-cell lymphoproliferative disorders are rare. The disease is featured by glomerular nonorganized monoclonal immunoglobulin G deposits. In the renal biopsy various patterns of microscopic pathology can be observed, including mesangial, membranous, and membranoproliferative glomerulonephritis. Diagnostic criteria of PGNMID include the presence of glomerular monoclonal IgG deposits restricted to a single IgG subclass and a single light-chain isotype, the presence of granular deposits by electron microscopy and the absence of clinical and laboratory evidence of cryoglobulin.
Method: We report two cases of PCNMID with IgG3 monoclonal deposits in two females: 44-year-old and 61-yeard-old. At presentation both patients had nephrotic syndrome. Renal insufficiency was seen in an older woman. None of these patients had detectable levels of serum or urinary monoclonal IgG or overt multiple myeloma.
Results: Renal biopsy in both patients showed accentuated glomerular lobularity, mesangial hypercellularity, matrix expansion, segmental endocapillary proliferation, and segmental glomerular basement membrane duplication. By immunofluorescence, deposits were identified along capillary loop and focally in mesangium. IgG was the only immunoglobulin deposited. Both cases showed light-chain isotype restriction (sole positivity for kappa or lambda chain). In a similar distribution to the IgG deposits, glomerular deposition of IgG3, C3 and C1q was detected. Electron microscopy revealed nonorganized electron-dense subendothelial and mesangial deposits.
Conclusion: Our study pointed to the utility of immunofluorescence examination of light chain in the renal biopsy specimens with membrano-proliferative pattern.

PS-06-002
Differential gene expression pattern in biopsies with renal allograft pyelonephritis and allograft rejection
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Objective: Differentiating acute pyelonephritis (APN) from acute rejection (AR) in renal allograft biopsies can sometimes be difficult because of overlapping clinical and histologic features; lack of positive urine cultures and variable response to antibiotics. We wanted to study differential gene expression between AR and APN using biopsy tissue.
Method: 33 biopsies were analyzed using Nanostring multiplex platform and PCR (6 transplant baseline biopsies, 8 AR, 15 APN [8 culture positive; 7 culture negative] and 4 native pyelonephritis [NP]). Additional 22 biopsies were tested by PCR to validate the results.
Results: CXCL9, CXCL10, CXCL11, IDO1 were the top differentially expressed genes, upregulated in AR. Lactoferrin (LTF) and CXCL1 were higher in APN and NP. No statistically significant difference in transcript levels were seen between culture positive and culture negative APN biopsies. Comparing the overall mRNA signature using Ingenuity pathway analysis however, interferon gamma emerged as the dominant upstream regulator in both AR and allograft APN, but not in NP.
Conclusion: Our study suggests that chemokine pathways in graft APN may differ from NP and in fact resemble AR, due to a component of alloreactivity, resulting in variable response to antibiotics alone. Therefore cautious addition of steroids might help in resistant cases of graft APN.

PS-06-003
Familial occurrence of fibronectin glomerulopathy
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Objective: Introduction: Fibronectin glomerulopathy is a rare genetic disease which can lead to renal failure and is characterized by proteinuria, hematuria and hypertension. Inheritance is autosomal dominant and the occurrence is more frequent in the third or fourth decade of life, but can affect any age group and both gender. The demonstration of fibronectin glomerular deposits in kidney biopsy is essential for diagnosis. In this article, we add to the literature two cases of fibronectin glomerulopathy that occurred in father and son, both with nephrotic syndrome, hypertension and hematuria.
Method: CASE REPORT: A 14-year-old male, with nephrotic syndrome during 8 months associated with hematuria (1 + / 4 +), normal serum creatinine (0.73 mg / dl) and blood pressure of 165 × 100 mmHg. Renal biopsy showed all glomeruli with endocapillary hypercellularity, especially at the expense of mesangial cells, associated with large amount of eosinophilic/fuccinophilic deposits, negative to silver and Sirius-Red stains, in the mesangium and subendothelial in capillary loops, with some foci of basal membrane duplication. Congo Red staining for β-amyloid was negative. Immune research by immunofluorescence was negative. Electron microscopy showed large amount of eletrondense deposits, which in high power field, had fine granular appearance, located especially in mesangial and subendothelial in capillary loops, with rare subepithelial deposits. It was suspected of fibronectin glomerulopathy due to the characteristics and location of deposits. The immunohistochemistry for fibronectin was marked positive and immunostaining coincided with mesangial and capillary loops deposits. Thus, the case was diagnosed as fibronectin glomerulopathy. The patient was treated with angiotensin-converting enzyme inhibitor. Three years later, his renal function remained stable and 24 h proteinuria was varying between 3.0 and 5.0 g. Two years after the diagnosis of his son, the 24-h proteinuria research in the parent was 5.0 g and serum creatinine was 1.2 mg / dl. Scrutiny of 4 years ago already showed 24 h proteinuria of 4.98 g, but he had not a nephrology follow up. Also, there was hematuria and hypertension treated with angiotensin receptor blocker. Renal biopsy showed the same morphological findings of his son. Treatment was instituted with Losartan 100 mg; however proteinuria levels was the same up to date, 3 months after the biopsy.
Results: DISCUSSION: These cases document the familial occurrence of fibronectin glomerulopathy. This entity was first described in 1980, with the name "familial glomerulopathy with giant fibrillary deposits" due to diffuse deposits, subendothelial, but often transmembranous and mesangial. In 1995, it was demonstrated deposits immunoreactivity to fibronectin and the disease was called "familiar glomerulonephritis with fibronectin deposits". In 2008, it was associated with mutations in the gene encoding fibronectin (FN1), located in 2q34, which occurs in 40 % of cases of disease.

Conclusion: The diagnosis can be challenging, especially if there is no clinical suspicion, family history or previous serum tests. Therefore, in the morphological analysis of renal biopsy, all routine recommended diagnostic methods should be made. Fibronectin is an extracellular matrix glycoprotein with multiple functions. The mechanism of fibronectin deposition in glomerulus not well understood. A circulating form, which is synthesized by hepatocytes4 is deposited in glomerulus. There is no specific treatment up to date and prognosis is uncertain.

PS-06-006

Associated glomerular lesion in urologic neoplasm: A study based on the evaluation of the non-neoplastic kidney

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Objective: Single kidney is one of the relative contraindication to renal biopsy. Therefore, we evaluated the incidence of glomerular lesion from non-neoplastic portion of the nephrectomy specimen.
Method: We examined a total of 97 patients with nephrectomy from urologic neoplasm for 6 years. Twenty-one cases were excluded because of end stage renal disease. The light microscopic findings of 76 cases of non-neoplastic kidney were evaluated, with immunofluorescence microscopy and electron microscopic examination. The mean age of patients was 62.1 years and the male to female ratio was 54:22. The diagnoses of neoplasm included 65 cases of renal cell carcinoma, 9 cases of urothelial cell carcinoma, one case of angiomyolipoma, and one case of hemangioma.
Results: The diabetic nephropathy was the most common glomerular lesion in 19 (25 %), followed by 11 cases of IgA nephropathy (14.4 %), 6 C1q nephropathy (7.9 %), 2 membranous nephropathy, 1 C3 nephropathy, 1 IgM nephropathy, 3 diffuse glomerulomegaly, and 3 hypertensive nephrosclerosis. Normal appearing kidney was 32 cases (42.1 %).
Conclusion: The glomerular lesion is not infrequent in non-neoplastic kidney, though most glomerular lesion is early in stage. So, the examination of non-neoplastic kidney in the nephrectomy specimen is needed.

PS-06-007

Keratin 17 marks a specific subset of tubular cells arising during renal injury

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Objective: To comprehensively analyse Keratin 17 (K17) expression in healthy and diseased murine and human kidneys.
Method: Five murine models of renal injury were analysed for K17-expression using immunohistochemistry, immunofluorescence, qRT-PCR and Western blotting. Human non-fibrotic and fibrotic kidney were investigated using immunohistochemistry and immunofluorescence.
Results: In healthy murine kidneys showed no K17 expression. In response to injury K17 was expressed de novo in tubular cells, first in single cells which expanded and later on marked whole tubular cross-sections of collecting duct and distal tubules. Parietal epithelial cells (PECs) also showed de novo expression in a glomerular injury model. K17 did not co-localize with markers of tubular injury or proliferation. In healthy human kidneys, K17 was expressed at the basolateral side of distal tubular cells. This changed to a circumferential type of expression in response to renal injury. PECs, which were negative in healthy kidneys, showed strong K17 positivity in cases with periglomerular fibrosis. In fetal human kidney K17 was expressed in ureteric bud segments in a circumferential manner similar to disease state.
Conclusion: We show that K17 is expressed de novo in response to renal injury in mice and in human glomeruli and marks a specific subpopulation of tubular cells.

PS-06-008

Pattern analysis in renal amyloidosis: Its role in predicting patient outcome

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Objective: Detailed histopathologic analysis of renal amyloidosis may have great impact on predicting patient outcome. We, hereby, propose a histopathologic pattern analysis of renal amyloidosis in correlation with clinical findings and prognosis.
Method: This is a retrospective study including 38 patients diagnosed as AA amyloidosis by renal biopsy. The pattern of glomerular amyloid deposition was specified as hilar, mesangial, nodular and membranous. Glomerular enlargement due to amyloid deposition was evaluated by histomorphometric analysis. Laboratory findings of renal function were retrieved from patient files. Student's t and Spearman's rank correlation tests were used for statistical analysis.
Results: Mesangial, hilar, nodular, and membranous patterns were identified in 100, 30.5, 58.3, and 58.3 % of the cases, respectively. Amyloid in interstitium, tubular basement membrane and peritubular capillaries were noted in 75, 58.3 and 83.8 % of the cases, respectively. Nodular pattern was significantly correlated with severe proteinuria ($p = 0.022$). Glomerular enlargement and global involvement were correlated with higher grades of tubular atrophy, interstitial fibrosis and inflammation ($p < 0.05$). Multivariate analysis revealed global amyloid deposition as the only risk factor for end stage renal disease ($OR = 18.75$, $p = 0.01$).
Conclusion: Pattern analysis of glomerular amyloid deposition may aid to predict outcome and is therefore a valuable tool for better patient care.

PS-06-009

Clinical donor variables and vascular changes noted in pre-implant donor kidney biopsies have no significant influence on graft survival rates

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Objective: Morphological studies of "zero-hour" kidney donor biopsies have produced controversial findings over what type of vascular changes, if any, are associated with graft survival. Here, we evaluate this question.
Method: We examined in 91 pre-implant needle kidney biopsies the frequency and severity of arteriolar hyalinosis (AH), intimal fibroelastosis (IFE), tubular atrophy (TA), interstitial fibrosis (IF) and glomerulosclerosis (GS) semi-quantitatively. The wall thickness/lumen (W/L) ratio of each vessel was determined by morphometry. Statistical analyses were then carried out to learn possible clinicopathological correlations. The patients were followed for 12 years.
Results: Graft survival was significantly correlated with recipient age, early delayed graft function, acute rejection, and levels of recipient creatinine clearance measured at 6, 12, 18, and 48 months post-transplantation ($p > 0.05$). Neither donor factors such as age, gender, cause of donor death, HLA mismatch, cold ischemia time, blood group antigens, terminal creatinine clearance, nor morphological parameters including AH, IFE, IF, TA, GS, W/L ratio of vessels significantly influenced the graft survival rate.
Conclusion: Our results suggest that clinical donor variables and vascular changes noted in pre-implant donor kidney biopsies have no apparent influence on graft survival rates.

PS-06-010

Comparison of the two most frequent morphological patterns, excluding amyloidosis, of kidney involvement in monoclonal gammopathy

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Objective: We aimed to investigate renal involvement patterns (excluding amyloidosis) and clinical features of renal damage of monoclonal gammopathy(MCG).
Method: Fifty-one patients have been evaluated for clinicopathological features retrospectively.
Results: The mean age was 54.2 years (26–79). Morphologic patterns consisted of 21(41.2 %) cast nephropathy (CN), 19(37.3 %) monoclonal immunoglobulin (mIg) deposition disease (MIDD), 2(3.9 %) isolated neoplastic infiltration, 2(3.9 %) proximal tubulopathy, 1(%2) proliferative glomerulonephritis and 6(11.8 %) mixed pattern. mIg was kappa in 74.5 % and lambda in 21.6 %. Comparison of creatinine and proteinuria levels along with sedimentation rate between CN and MIDD showed significant difference only for creatinine (7.8 ± 4.4 vs. 3.17 ± 2.35 mg/dL, respectively; $p < 0.001$). MIDD had higher rates of kappa monotypia than CN (89.5 % vs. 57.9 %, $p = 0.027$). Among 30 biopsies in which both immunohistochemistry and immunofluorescence were performed, mIg deposition was detected only by immunohistochemistry in 11. The percentage of cases showing more than 10 % of clonal plasma cell infiltration in bone marrow biopsies, 21 of which pathology reports could be obtained, was 50 and 100 % for cases with MIDD and CN, respectively ($p = 0.018$).
Conclusion: CN and MIDD are the most frequent morphological patterns other than amyloidosis for the renal involvement by MCG. The use of both IHC and IF will increase the rate of definite diagnosis.

PS-06-011

Clinical relevance of TGF-beta signaling pathway downstream effectors expression in kidney biopsies

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Objective: Importance of TGF-β signaling pathway has been already recognized in cell culture experiments and in animal models of kidney fibrosis. However, there is lack of evidence with regard to significance of TGF-β effectors (SMAD2, SMAD3, SNAIL) in nephrotic syndrome of humans and their relations to clinico-pathological parameters.
Method: Clinical and histopathological characteristics of 50 kidney biopsies were analyzed with respect to expression and distribution of SMAD2, SMAD3 and SNAIL molecules, detected by immunohistochemistry, in order to investigate the relevance of TGF-β effectors detection in kidney biopsies of patients with nephrotic syndrome and isolated proteinuria.
Results: SMAD2 and SNAIL nuclear expression in proximal tubule cells correlated with interstitial fibrosis ($p < 0.001$) and tubular atrophy ($p < 0.001$). Significantly higher urea ($p = 0.026$) and creatinine ($p = 0.006$) levels were found in patients with tubular nuclear expression of SMAD2 and SNAIL. These patients had also significantly reduced eGFR ($p = 0.007$) and higher CKD stages ($p = 0.001$) at the time of biopsy. Proteinuria was significantly higher in patients with SNAIL expression in podocytes ($p < 0.001$). Correlation between SMAD3 expression and clinico-pathological parameters was not detected.
Conclusion: Expression of TGF-β downstream effectors SMAD2 and SNAIL in kidney biopsies represent immunomorphological substrate of chronic kidney parenchymal damage, correlating with higher proteinuria levels and decreased excretory kidney function.

PS-06-012

Predictors of chronic kidney disease progression and relevance of NCAM-expressing renal interstitial cells

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Objective: The role and significance of NCAM-expressing renal interstitial cells in different kidney diseases have not been clarified yet. Thus, clinical relevance of NCAM-expressing cells detection and predictors of chronic kidney disease (CKD) progression should be examined.
Method: The study included 69 patients, followed-up for at least 1 year after kidney biopsy. Clinical data, as well as pathohistological features defined optico-microscopicaly and by immunohistochemistry using NCAM antibody, were explored. Predictors of CKD progression were defined by Kaplan-Meier and Cox's regression analyzes.
Results: NCAM expressing interstitial cells were detected in 59.4 % of renal biopsies. The presence of these cells was more frequently observed in the early stages of interstitial fibrosis than in other stages ($p < 0.001$). Patients with NCAM cells detected in the renal interstitium had a significantly lower proteinuria values at the time of biopsy compared to patients without NCAM interstitial cells ($p = 0.024$). Pathohistological diagnosis ($p = 0.026$) and the degree of interstitial fibrosis ($p = 0.002$), as well as serum creatinine ($p < 0.001$) and urea ($p = 0.007$) values were predictors of CKD stage progression.
Conclusion: The presence of NCAM cells in renal interstitium could be a morphological characteristic of early stage of chronic kidney diseases and has been associated with lower degrees of proteinuria.

Monday, 26 September 2016, 09.30–10.30, Hall 11.3
PS-07 Other Topics 1

PS-07-003

C4d deposits and a new diagnostic modality for amyloidosis

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Objective: Amyloidosis is characterized by the deposition of misfolded protein in various organs. The diagnosis of amyloidosis is based on the detection of amyloid deposits by Congo red stain under polarized microscopy. This study was done to investigate C4d deposition in amyloidosis and to determine whether C4d staining can be used as a new diagnostic tool for amyloidosis.
Method: This retrospective study included 32 patients who underwent biopsy at our medical center. The samples were stained by Congo red and C4d immunohistochemical stain, respectively.
Results: The biopsy samples from 18 patients who had been finally diagnosed with amyloidosis were included as the amyloidosis group, and 14 patients diagnosed with fibrosis were included as the control group. C4d was detected in 94.4 % of amyloidosis patients ($n = 17$). On the other hand, in the control group, C4d deposit was not observed in any patient diagnosed with fibrosis.
Conclusion: C4d immunohistochemical staining can be a highly useful modality for the diagnosis of amyloidosis. Furthermore, C4d can be applied as a tool for the differential diagnosis of amyloidosis and fibrosis.

PS-07-004

Trainee perception of graded responsibility for registrar reporting of histology specimens

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Objective: The Royal College of Pathologists supports a competency based framework for independent reporting of histology and cytology specimens. This is achieved using graded responsibilities, roughly intended to correlate with each year of training. The aim of this project was to assess the awareness and attitudes of current histopathology trainees towards such independent reporting.
Method: Prospectively administered structured questionnaire of histopathology trainees in the London training region.
Results: 54 histopathology trainees responded to the questionnaire. Seventy-five percent were aware of the concept, but only 39 % were aware of the Royal College document. Awareness and use of the document increased with seniority but the majority were not yet reporting independently (78 %). Many trainees reported they would feel ready to start reporting independently following completion of Part 1 of the fellowship exam for the Royal College of Pathologists (48 %), but nearly a quarter would like to start earlier than this (24 %).
Conclusion: Although most trainees are aware of the concept of graded responsibility for reporting independently, only 22 % are reporting independently. Uptake of independent reporting needs the backing of the consultant body within the department, but most trainees are keen to participate.

PS-07-006
Multiple organ involvement in IgG4-related disease, misidentified as medical insurance case of asbestosis, leads to sudden death by endocarditis
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Method: A 73-year-old Caucasian male was autopsied, suffering from diabetes type 2, hypertension, cerebral infarction, colon cancer, unclear pancreatic tail lesion, and chronic lung disease. Clinical and radiologic findings were diagnosed as pulmonary asbestosis starting 12 years ago and being accepted as professionally acquired disease by medical insurance. The patient died unexpectedly in cardiorespiratory failure.
Results: At autopsy, the classic triad of lymphoplasmacytic infiltration, storiform fibrosis, and obliterative phlebitis was detected. IgG4: IgG ratio was high (40 %; 50 plasma cells/HPF). Organ involvement included: pancreas, kidneys, spleen, lungs, heart valves, meninges. Diabetes was caused through fibrotic islet destruction. No signs of pulmonary asbestosis were found. Pleural plaque—like fibrotic areas were present. A thrombulcerative endocarditis of the mitral valve enhanced the preexisting hypertensive cardiac failure.
Conclusion: In patients with unusual clinical manifestations and seemingly unrelated organ damage a high suspicion for IgG4-related disease as linking disorder is warranted. This case is notable as the first report of IgG4-related endocarditis with meningeal involvement and death in septic shock caused by multi-organ targeting of IgG4-related disease mistaken as an insurance case of asbestosis related disease, demonstrating the value of a postmortem analysis.

PS-07-007
BAP1 immunohistochemistry and p16 FISH in the diagnosis of malignant peritoneal mesothelioma
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Objective: Peritoneal malignant mesothelioma (PMM) is an uncommon tumour, only 7–9 % of all mesothelioma in Japan. Differential diagnosis between PMM and primary peritoneal serous carcinoma (PPSC), a high-grade serous carcinoma, may be difficult, and separating reactive mesothelial hyperplasia (RMH) from PMM can be even more challenging.
Method: To help differentiate PMM from PPSC and RMH, we used immunohistochemistry to examine BAP1, and FISH to examine for homozygous deletion of 9p21. We used formalin-fixed, paraffin-embedded blocks from 22 PMMs (M:F = 18:4; subtypes: 16 epithelioid, 6 biphasic), 11 PPSCs, and 10 RMHs.
Results: Seventeen of the mesotheliomas were classified as diffuse, while 5 were localized. Loss of BAP1 was seen in 10/21 (45 %) of PMM, but all PPSC and all RMH were BAP1-positive. For the differentiation of PMM from PPSC and RMH of the peritoneum, the sensitivity and specificity for BAP1 in mesothelioma were 43 and 100 %, respectively. FISH analysis revealed homozygous deletion of the 9p21 locus in 11/13 (85 %) of PMM, but in none of RMH.
Conclusion: BAP1 loss is not a sensitive test, although specificity is very high for differentiating PMM from both PPSC and RMH. Homozygous deletion of 9p21 may be helpful for differentiating PMM from RMH.

PS-07-008
Testing tumour cell death and stress responses induced by modulated electro-hyperthermia in 3D cell cultures
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Objective: Modulated electro-hyperthermia (mEHT, oncothermia) generates electric field which can interfere with malignant tumours at 42 °C resulting in low energy density destruction of neoplastic cells. The tumour selectivity of mEHT is due to increased metabolite content and permittivity of tumours compared to normal tissues. In vitro 3D tumour cell cultures mimicking tissue complexity better than cell monolayers were used to test mEHT induced tumour cell death and stress responses.
Method: C26 mouse colorectal carcinoma cells were grown in Matrigel scaffolding (Engelbreth–Holm–Swarm tumour matrix) in LabTek and treated in four groups using: 1) conventional hyperthermia at 42 °C (HT); 2) mEHT with non-contact electrodes, 3) mEHT with contact electrodes and 4) no treatment (control) at 37 °C.
Results: Both mEHT and HT treatments induced chromatin condensation and apoptotic bodies seen in H&E-stained formalin-fixed, paraffin-embedded culture sections. TUNEL assay confirmed apoptosis related DNA fragmentation. The expression of heat stress induced Hsp60 and Hsp70 proteins showed a decreasing gradient in mEHT>HT>control direction. Also, both mEHT and HT treatments resulted in elevated Bax and cleaved caspase-3 protein levels.
Conclusion: In conclusion, our results showed that Matrigel embedded 3D cultures can be useful to test mEHT induced cell death and stress responses and correlate with traditional hyperthermia (HT) effects.

PS-07-009
A comparative morphology of anterior abdominal wall tissues after using bovine-derived peritoneum implant and acellular dermal matrix in the experiment
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Objective: To assess the structural changes of the abdominal wall upon contact with acellular dermal matrix ("Permacol") and a new biological implant—bovine-derived peritoneum in the early stages after implantation.
Method: Open abdominal wall defect was repaired by bovine-derived peritoneum (group I) and "Permacol" (group II) implants in 48 rats. Observation periods: 7,21,30 days. Macroscopical criteria were an infection existence, adhesion and seroma formation. Microscopical criteria were an inflammatory response, neovascularization, connective tissue maturation. A technique of staining with H&E.

Results: Macroscopically, in group I in all cases no seroma or infection was observed, in group II in 13 % cases wounds were infected. In group I in 9 % cases adhesions at the margins of implants and suture sites was registered, in group II adhesions in almost half cases were observed. Microscopically, in both groups, on the 7 day there were the granulation tissue and thin-walled blood vessels formation, the suture-line reactive inflammation. By the 21 day granulation tissue maturation, moderate lymphocytes infiltration were fixed. At the 30 day connective tissue maturation was registered, inflammatory response was absent.
Conclusion: Bovine-derived peritoneum has been showed adequate biocompatibility with the recipient body, without causing severe post-implantation inflammation. These data is allowed to use it for abdominal wall reconstruction perspectively.

PS-07-010

First results (2010–2015) from a pathology based cancer registry of the largest government run diagnostic and reference center of Karachi

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Objective: To analyze cancer data during 2010–2015 at the Dow University of Health Sciences (DUHS) Karachi—the largest public-sector diagnostic center of the province.
Method: A Pathology based cancer registry was established at DUHS and data were extracted, indexed and analyzed to calculate frequency, percentages, crude and age standardized incidence rates for various malignancies.
Results: During 2010–2015, a total of 13,508 cancers were diagnosed. Of these, 5665 (41.9 %) were in males while 7843 (58.1 %) were in females. Incidence rates for all cancers were 72.2 per 1,00,000 (crude) and 152.8 per 1,00,000 (ASR) for males and 116.2 per 1,00,000 (crude) and 235.0 per 1,00,000 (ASR) for females. In males, cancer of lip and oral cavity was the most frequently diagnosed cancer (30.8 %, ASR 42.0), followed by cancers of skin (8.1 %, ASR 14.0) and colorectum (7 %, ASR 9.8). In females, breast cancer was the most frequently recorded malignancy (49.5 %, ASR 112.5), followed by lip and oral cavity (11.2 %, ASR 30.7) and oesophagus (5.6 %, ASR 14.4).
Conclusion: We report that Karachi has the highest incidence of cancers of breast, lip and oral cavity, oesophagus and larynx in females and cancer of lip and oral cavity and larynx in males compared to any of the Asian populations.

PS-07-011

Analysis of histopathology fees in East Africa with comparison to developed countries: Disparities in relation to sustainability and quality of service delivery

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Objective: Little has been published on histopathology test fees in East Africa. This analysis seeks to compare the fees charged in a bid to unravel relevant discrepancies and disparities.
Method: Charges for histopathology services were sought through personal contacts and internet searches of fee schedules from key representative facilities in 5 East African countries, USA, UK, South Africa and Australia.
Results: We present a detailed tabulation comparing the range of fees charged for routine H&E, special stains and immunohistochemistry. Overall we observe that there is a huge disparity in the charges within and between the countries in East Africa, and also with the other countries. The charges for a small routine biopsy in East Africa generally ranged from $5USD to $50USD. Many instances were noted where the fees charged are lower than the cost of rendering the services. Also there is no standardised procedure coding system, which pose challenges for appropriate billing.
Conclusion: The charges for histopathology services in East Africa are substantially lower than developed countries, while the cost of rendering these services are relatively higher. This may impact the sustainability & quality of service provision. Policy makers and stakeholders ought to consider price rationalization for pathology services.

PS-07-012

Documentation and appropriate completion of medical certification of cause-of-death forms by physicians at a first tier tertiary teaching hospital in a sub-Saharan African country

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Objective: This retrospective study was undertaken to answer the following questions: how frequent are death certificates issued for deaths occurring at a tertiary hospital in Nigeria, and whether death certificates are being completed correctly by physicians.
Method: All deaths occurring at the hospital over a 5-year-period were stratified by ward and sex. Also, death certificates issued by physicians at the hospital were retrieved, and the wording and statements on the death certificate examined to determine whether the underlying cause-of-death in each case was listed in an acceptable manner or not. Errors in death certificate's completion were categorized into 4 categories according to the classification system adopted by Tsung-Hsueh Lu et al.
Results: A total of 5392 deaths were recorded, 53.3 % of whom were males; only 350 (6.5 %) death certificates were issued—299 (85.4 %) in males and 51 (14.6 %) in females—out of which only 125 (35.7 %) were completely corrected. The most common type of error was Minor Error 2 (41.3 %).
Conclusion: Cause-of- death certificates are not routinely completed by physicians; more than half of the completed cause-of-death certificate forms contained no useful information for epidemiological studies.

PS-07-014

Bone grafts regeneration with composite based on alkali-free bioglass FastOs®BG and beta-TCP: Histopathological study

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Objective: New synthetic bonegraft material combining moderately degradable alkali-free bioactive glass, FastOs®BG, with pure bioresorbable β-Tricalciumphosphate (β-TCP), doped with Mn/Zn/Sr was evaluated on animal model for possible application in dentistry treatments.
Method: A 4-mm diameter critical-size defect was performed in calvaria of 13-week wistar rats, divided into four groups—5 animals each: kept empty defect or filled with autogenous bone, FastOs®BG/β-TCP or FastOs®BG/dopedβ-TCP. Euthanasia was performed on 28th/63th day after surgery. Bone regeneration was evaluated by radiography and histopathology after decalcification (H&E and Von Kossa).
Results: The highest bone density percentage on 28th/63th days was 84.6 and 92.9 % respectively—defects filled with autogenous bone—28th day was significantly higher than all the other groups ($P < 0.01$). On 63th day, FastOs®BG/β-TCP group had 65.9 % and FastOs®BG/dopedβ-TCP group 67.7 % regeneration—without

statistical difference. Histopathology showed/ graft bone group: new bone formation; FastOs®BG/β-TCP group: angiogenesis and osteoid matrix on 28th day and mineralized bone on 63th day; FastOs®BG/dopedβ-TCP group: repair with vascularized hyaline matrix around foreign material on the 28th day and new bone formation on the 63th day.
Conclusion: The incorporation of Zn, Mn and Sr in the β-TCP improved bone regeneration after FastOs®BG/β-TCP as bone graft substitutes without inflammation inconvenience.

Tuesday, 27 September 2016, 09.30–10.30, Hall 11.3
PS-08 Cytopathology

PS-08-001
To correlate cervical smears with Borderline Nuclear Changes (BNC) with follow up biopsies in women from 2010–2014 at Royal Hospital: A retrospective study
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Objective: • To find the prevalence of Borderline Nuclear Changes (BNC) in Oman. • To determine the outcome for patients with a diagnosis of BNC in biopsies.
Method: A retrospective Cross sectional study was carried out over a period of 5 years between January 2010 and December 2014 at the Royal Hospital Cytology laboratory. Among 639, a total 130 patients had followed up by further cytology PAP (Papanicolaou) smears and biopsies were included. Patient age range is between 24 and 62 year. Ethical approval was obtained from the ethical committee.
Results: Out of 130 cases of women with cytology report of BNC, 62 women (47.7 %) were followed up by repeat cervical smears only and 68(52.3 %) had followed up with cervical smears and biopsy. The biopsy outcome were normal in 31 cases(45.6 %), low grade (koilocytic atypia+CIN 1 (Cervical Intraepithelial Neoplasia)) in 32 cases (47 %) and high grade lesion (CIN2 & CIN3) were seen in 5 cases (7.4 %).
Conclusion: On referral of women for colposcopy with last smear showing BNC, the outcome was high grade in 7.4 % of cases, irrespective of whether the borderline smear was preceded by another borderline smear or a dyskaryotic smear. BNC is a significant diagnosis that should be taken seriously. Further studies might be needed to provide more information to distinguish true precursor lesions that cause cervical carcinoma from those that have no clinical relevance.

PS-08-002
Subtyping of non-small cell lung carcinoma in fine needle aspiration specimens: A study of 252 patients with surgical correlation
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Objective: Accurately subcategorizing non-small cell lung cancer (NSCLC) into adenocarcinoma and squamous cell carcinoma influences clinical decision making and drives appropriate treatment selection. We investigate the diagnostic accuracy of FNA in differentiating NSCLCs of squamous from nonsquamous subtype: to correlete cytological findings with histological features and immunohistochemistry confirmation in some cases.
Method: From 2010 to 2015, a total of 635 transthoracic needle aspirate or transbronchial needle aspirate were performed: 332 cases were diagnosed as NSCLC, with or without an indication of a specific subtype, while 303 cases were not diagnosed as NSCLC. Out of 332 cases diagnosed as NSCLC, 252 had histologic follow-up. Subsequently histological specimens included 161 surgical resection and 91 biopsies.
Results: The specific subtype of NSCLC was provided in 217 cases (86 %) based on cytomorphology which included: 115 (46 %) adenocarcinomas, 102 (40 %) squamous cell carcinomas. NSCLC-NOS by FNA was diagnosed in 35 cases. At histology 251 cases (99.6 %) were subclassified. 122 (48 %) adenocarcinomas, 104 (41 %) squamous cell carcinomas, 11 (4 %) large cell carcinomas, and 14 (6 %) adenosquamous carcinomas. The diagnostic accuracy between cytological and histological typing was found in 181 of 197 (92 %) cases ($K = O.837$; $p < 0.001$).
Conclusion: Our study proved that most NSCLC can be subclassified as adenocarcinoma or squamous cell carcinoma by FNA through cytomorphology and the application of immunocytochemistry.

PS-08-003
Cytological features of ALK rearranged lung adenocarcinoma
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Objective: ALK rearranged lung adenocarcinoma show characteristic histological features such as signet ring cell carcinoma (SRC) and mucinous cribriform structure. The purpose of this study is to clarify cytological findings characteristic for ALK rearranged lung adenocarcinoma.
Method: We compared cytological findings of 16 ALK rearranged cases with 40 ALK rearrangement-negative cases. We examined cytoplasmic features of SRC, such as containment of pink, yellow, or orange mucins, green, vacuolar, or vesicular cytoplasm, and globular green cytoplasmic inclusion, and appearing patterns of SRC, such as single cell pattern or cluster-formation. The formation of mucinous cribriform structure was also studied.
Results: The univariate analysis showed that significantly frequent findings included pink mucin, green, vacuolar, or vesicular cytoplasm, globular green cytoplasmic inclusions, single cell pattern, cluster formation, and mucinous cribriform structure. The stepwise multivariate analysis identified three significant contributing features including pink mucin ($p = 0.03$), vesicular cytoplasm ($p = 0.06$), and single cell pattern ($p = 0.01$). If the cytological specimens showed two or three of these features, the sensitivity and specificity were 88 % in both for the prediction of ALK gene rearrangement.
Conclusion: The pink mucin, vesicular cytoplasm, and single cell pattern of SRC are useful cytological markers to predict ALK gene rearrangement in pulmonary adenocarcinoma.

PS-08-004
Usefulness of Maspin, CA 19.9 and p53 in the diagnosis of ductal adenocarcinoma of the pancreas in cell blocks obtained by ultrasound-guided fine needle aspiration cytology
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Objective: Ultrasound-guided fine needle aspiration cytology (EUS-FNAC) allows a quick diagnosis of ductal adenocarcinoma of the pancreas (DAP). However, the difference between DAP and

chronic pancreatitis remains a very difficult task in the scarce material obtained.
Method: A total of 26 EUS-FNAC procedures have been performed in pancreatic masses during the last 2 years in our Institution. The specimens included conventional cytological slides and formalin-fixed paraffin-embedded cell blocks. Immunohistochemistry was performed with Maspin, p53 and CA19.9.
Results: Seventeen DAP (65.3 %), 4 suspicious cases (15.3 %) and 5 negative cases (19.2 %) were diagnosed using only classic cytological criteria. All DAP and negative cases were confirmed by biopsy or radiologic follow-up. Subsequent biopsies also revealed that 3 of the suspicious cases were actually DAP and one was a neuroendocrine tumour. Immunohistochemistry performed in cell blocks revealed that Maspin, CA 19.9, and p53 were positive in 19/20 (95 %), 12/20 (60 %) and 4/20 (20 %) DAP, respectively.
Conclusion: EUS-FNAC is a safe and quick method in the diagnosis of DAP. Cytological smears and cell blocks are recommended for a more reliable analysis. The accuracy of EUS-FNAC in pancreatic masses can be improved combining classic cytological criteria and immunohistochemistry performed in the cell blocks.

PS-08-005
Rosai-Dorfman Disease diagnosed on fine needle aspiration biopsy in a child: A case report and review of the literature
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Objective: To describe the diagnosis of Rosai-Dorfman disease (Sinus histiocytosis with massive lymphadenopathy) by fine needle aspiration biopsy (FNA) of a lymph node in a young child, and briefly review the literature.
Method: A 3-year-old male child was referred to our regular FNA clinic with a one week history of progressive left neck swellings. On examination he had left cervical firm mobile non-tender lymph nodes measuring 5 cm by 4 cm, 4 cm by 3 cm and 2 cm by 2 cm. FNA was performed under general anaesthesia due to the child's age.
Results: Diagnostic material was obtained. Cytology smears showed a cellular smear of polymorphous lymphoid population with small mature lymphocytes and numerous multinucleated histiocytes in a haemorrhagic background. The histiocytes showed marked lymphocyte emperipolesis. The adenopathy subsequently resolved and the child, now 6 years old, has not had a recurrence.
Conclusion: Rosai-Dorfman disease was successfully diagnosed on FNA of cervical lymph nodes. FNA is a valuable low cost tool in screening patients to determine whether a biopsy is necessary in the management of lymphadenopathy.

PS-08-006
Cytological characteristics of poorly differentiated Squamous Cell Carcinomas (SCC) of the breast: Comparison between cytological findings of invasive ductal carcinoma and apocrine carcinoma
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Objective: The squamous cell carcinoma (SCC) is a very rare subtype of the breast. The cytological diagnosis of non-keratinizing, poorly differentiated squamous cell carcinoma is sometimes difficult with the discrimination from invasive ductal carcinoma (IDC) or apocrine carcinoma (AC) being especially challenging. We aimed to clarify diagnostic cytological features of mammary poorly differentiated SCC.
Method: We investigated cytological findings of poorly differentiated SCC (n = 10), and compared them with those of IDC (n = 15) and AC (n = 14). The following cytological parameters were evaluated: streaming arrangement, nucleolar enlargement, dense nuclei, cannibalism, and necrotic background.
Results: Cytological specimens of SCC cases showed significantly higher incidence of streaming arrangement ($p = 0.002$), nucleolar enlargement ($p = 0.02$) and necrotic background ($p = 0.002$) than those of IDC. Streaming arrangement ($p < 0.001$), cannibalism ($p = 0.002$) and necrotic background ($p = 0.047$) in SCC were more frequent than in those of AC. Detection of two or more parameters described above in SCC showed higher sensitivity (80 %) and specificity (93 %) for correct diagnosis, in comparison with IDC. When differentiating from AC, the presence of parameters in SCC improved sensitivity (80 %) and specificity (100 %).
Conclusion: Cytological features such as streaming arrangement, necrotic background, nucleolar enlargement and cannibalism are useful predictors for diagnosis of SCC of the breast.

PS-08-007
5 year audit of thyroid fine needle aspirate reporting, with emphasis on category Thy3a
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Objective: The Royal College of Pathologists introduced category Thy3a (atypical features) in 2011. Our aim was to assess the use of Thy3a at our institution since its introduction in Jan 2012.
Method: All thyroid FNAs reported between Jan 2011 and Dec 2015 were identified. Frequency and patient outcomes including repeated FNA and surgical resections were analysed, with an emphasis on Thy3a.
Results: The sensitivity (92.31 %) and specificity (99.90 %) of our thyroid FNA diagnoses over 5 years were consistent and within published guidelines. Over the 4 years period, our diagnostic frequency of Thy3a was 1.2 % (16 of 1261 cases). 7 of these 16 cases had repeat FNAs, ultimately reported as Thy1 (n = 1), Thy 1c (n = 1), Thy 2 (n = 3), Thy 3f (n = 1) and Thy 5 (n = 1). 4 cases were follicular adenomas on resection. 1 case was an occult micropapillary carcinoma and 4 cases had no further specimens sent to histopathology.
Conclusion: In our practice, we have a very low rate of Thy3a category use. This has not impacted negatively on our sensitivity or specificity. We suggest that the Thy3a category be critically analysed to establish the appropriate frequency and real benefit of this diagnostic category.

PS-08-008
Cell agglutination is a cheap and accurate complement for fine needle aspiration in order to obtain cell-block material
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Objective: Fine needle aspiration (FNA) is a widely used technique that besides providing diagnosis also attains to get biologic material for cell-block to perform immunocytochemistry and molecular biology techniques. Guidelines for FNA promptly affirm to stop aspirating as soon as material enters the hub/barrel of the syringe and use the material on the needle. We present an alternative and cheaper method for collecting biologic material on FNA.

Method: In an 8 years period, FNA was performed according to international guidelines, but when material entered the barrel of the syringe, aspiration was not stopped in order to get sample in the barrel. Needle material was placed in glass slides for ordinary staining and barrel content was placed directly in to a vial with formaldehyde, where it agglutinates and posteriorly was embed in paraffin. Stained slides were compared using this technique and liquid based cytology.
Results: We obtained cell-block material from different organs such as soft tissue, salivary glands, pancreas, breast and lymph node, with excellent morphologic and immunocytochemistry results. In out method there was better cellular and architecture preservation.
Conclusion: Cell agglutination of biologic material in formaldehyde is a cheap, quicker and accurate way to obtain cell-block, allowing ancillary studies and improving diagnosis capacity.

PS-08-011
Peritoneal fluid cytology in intraperitoneal chemotherapy: Diagnostic pitfalls and cytomorphological findings
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Objective: Intraperitoneal chemotherapy (IPChT) is an emerging modality in the treatment of advanced gastric adenocarcinoma. Cytologic evaluation of peritoneal fluid specimens post-IPChT is important in determining subsequent management. However, the cytomorphological changes induced in benign constituents of peritoneal fluid following direct intraperitoneal exposure to chemotherapeutic agents have not been well characterized in the literature.
Method: In this study, we review 30 peritoneal fluid samples of patients treated with IPChT, and describe the cytomorphological features of both benign and malignant cells with the aid of relevant immunocytochemical interrogation.
Results: Our findings show a significant degree of morphologic overlap between reactive and malignant cells. 'Exploding' mitotic figures, nuclear membrane irregularities, multi-nucleation and cytoplasmic vacuolation were reactive features commonly present in negative fluid specimens, presenting potential pitfalls to accurate diagnosis. The most discriminating feature that favored malignant cells was increased nuclear to cytoplasmic ratio. In addition, the presence of increased eosinophils and 'pseudoparakeratotic cells' were helpful clues indicating prior IPChT.
Conclusion: Post-IPChT peritoneal fluid specimens pose unique diagnostic challenges. Awareness of the extent and spectrum of atypical features exhibited by benign constituents, coupled with the judicious use of immunocytochemistry are key to accurate cytologic interpretation.

PS-08-012
Efficiency of stylet capillary suction and standard suction technique of Endoscopic Ultrasound-guided Fine Needle Aspiration (EUS-FNA) in solid pancreatic tumours
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Objective: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is the recommended sampling procedure for solid pancreatic cancer. There are no guidelines about the sampling and processing techniques, therefore, they vary substantially across medical centers.
Method: We aimed to compare the diagnostic yield of samples obtained with stylet or suction in 75 prospectively enrolled patients with pancreatic masses. The number of smears, cellularity and bloodiness were assessed, and considering our results, we established a recommendation for sampling.
Results: EUS-FNA resulted in diagnostic samples in 77.33 % of the cases: with suction in 57 and with stylet in 52 cases. The number of smears were significantly higher in the suction group (1.87 vs. 3.5; $p < 0.001$), with no difference in the cellularity (1.75 vs. 1.52; $p = 0.2556$). The bloodiness of smears obtained by suction was increased ($p < 0.001$), which made the diagnostic rate lower (47.36 vs. 33.23 %; $p = 0.003$). The washing fluid of the needle and cell blocks was diagnostic in 38.6 % and in 67.50 %, respectively. Needle type, tumour size and location had no influence on the diagnostic yield.
Conclusion: Both stylet and standard suction are effective in the EUS-FNA sampling of pancreatic masses. Suction is recommended for desmoplastic tumours; the bloodiness of vascularized tumours decreases the diagnostic yield of sampling.

PS-08-013
Prepare cytological samples from washed, peritoneal and bronchoalveolar lavage and cerebrospinal fluid by "Plasmo-Thromboplastin" method
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Objective: Despite the cell block be considered a diagnostic method of wide applicability in routine practice, the indication of each method according to the different types and aspects of cytological samples is not well established. Thus, the aim of this study was to evaluate the applicability of the plasma-thromboplastin (PT) method in pleural, peritoneal, pericardial, cerebrospinal fluids, peritoneal and bronchoalveolar lavage, urine and aspirated cystic lesions.
Method: Conventional smear, cell block and immunocytochemistry were prepared for each cytological sample ($n = 299$).
Results: The PT method was applicable in samples without sediment or small amount of sediment and with sediment of blood, 88.3 % of the samples. Samples with large amount of sediment and anticoagulant (11.7 %) were prepared by agar method. Adequate cellularity and cellular distribution with preservation of the morphology of groups and cells were observed in both methods. The immunocytochemical staining pattern was similar to that usually observed in conventional smears. Agreement was observed in 96.9 %, between the diagnoses of cell block and conventional smears. In some samples, cancer was detected only by cell block.
Conclusion: The plasma-thromboplastin method is applicable in most samples, has high diagnostic agreement with conventional smears and may decrease the false-negatives of cytological analyses.

PS-08-014
The rate of high-risk Human Papilloma Virus (HPV) in liquid-based cervical samples from Turkish women
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Objective: Cervical cancer is the second most common cancer among women, with an estimated 500.000 new cases occuring each year in the world. According to Ministry of Health registry data, cervical cancer is the ninth most common cancer among female cancers in Turkey.
Method: The study population consisted of 1252 women attending a gynecological outpatient clinic between Nowember 2013 to May 2015 in Umraniye Education and Research Hospital. In our clinic, cervical cancer screening were performed by the combination of HPV testing (Cervista HPV HR and Cervista HPV 16/18) and liquid- based cytology testing (ThinPrep Pap Test).
Results: Out of 1252 cases, 330 cases (26.4 %) were with abnormal cytology and 922 cases were (73.6 %) with normal cytology. HR HPV was detected in 18.7 % of NILM samples, in 80 % of abnormal cytology (in 72.5 % of ASC-US samples, in 83.3 % of

LSIL samples, in 87.8 % of ASC-H samples, in 100 % of LSIL-H, and HSIL samples). Of all 435 positive samples, 310 (71.3) were HR HPV non 16/18; 110 (25.3 %) were HPV 16; 17 (3.9 %) were HPV 18.
Conclusion: The aim of this study is to investigate the rate of HPV DNA among Turkish women with normal and abnormal cytology. HPV rate and type distribution in this study were similar to that reported worldwide at least in our study population. However, HPV prevalence was more common compared with previous studies reported from Turkey.

PS-08-015
Synchronous primary breast carcinoma and pancreatic neuroendocrine neoplasm: Role of EUS-FNAC
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Objective: Pancreatic neuroendocrine tumours (pNETs) are infrecuent neoplasms with variable outcome, where progesterone receptor (PR) expression and proliferation index (PI), measured with Ki67, have shown usefulness as prognostic and predictive markers.
Method: A 59-year-old woman with invasive ductal breast carcinoma is presented. A staging CT scan showed a 9 mm round mass in the tail of the pancreas. In order to stablish a correct staging (metastatic vs synchronous disease), an endoscopic ultrasound-guided fine needle aspiration cytology (EUS-FNAC) was requested.
Results: Cytologic study showed discohesive cellularity with minimal atipia, and rounded nuclei with finely stippled ("salt-and-pepper") chromatin. No mitotic figures were detected. Immunohistochemical staining using cytological slides demonstrated reactivity for chromogranin, synaptophisin and progesterone receptors, with a low proliferation index (3–5 %) measured with Ki67, leading the diagnosis of pNET, suggesting low/intermediate grade and starting with the oncologic and surgical management of the breast cancer (T2cN2M0).
Conclusion: EUS-FNAC is considered the technique of choice for the diagnosis of pNETs, being a non-invasive, highly sensitive (80–90 %) and specific (100 %) procedure with minimal complications. Factors, such as experienced endoscopists and cytopathologists, together with immunohistochemical markers, including PR (correlated with low aggressiveness) and Ki67 (necessary for grading the neoplasm), provide crucial information for the patient management.

PS-08-016
An audit of a pathologist performed US-guided FNAC outpatient clinic: 3 years experience from Akershus University Hospital
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Objective: Review of the institutional experience of pathologist-performed US-guided examination and FNAC of superficial lesions in collaboration with the surgery department.
Method: Audit of 467 FNAC performed between August 2013 and April 2016. Patients were referred from within the hospital or primary care. US-guided FNAC were performed by either a cytopathologist or a surgeon. When performed by a surgeon, a cytopathologist provided onsite evaluation of specimen adequacy.
Results: Of the 467 patients, FNAC was performed on 448 patients. These included 239 thyroids (51 %), 139 lymph nodes (29 %), and 30 salivary gland,(6.4 %), 35 soft tissue (7 %) and 31 neck lesjons (6.6 %). Malignancy was diagnosed in 51 cases (10.9 %), including 35 metastatic lymph-nodes, 10 thyroid and 2 breast carcinomas and an acinic cell carcinoma of the parotid gland. No lesions were identified in 19 patients (4 %). Inadequate material was obtained in 12 cases (2.5 %).
Conclusion: US examination is a valuable tool to visualize lesions, secure material from relevant regions of the lesions and to identify cases with no focal lesion/tumour. Collaboration between pathologists and surgeons concerning FNAC has resulted in fewer non-diagnostic/equivocal cases, improved selection of surgical candidates and a reduction in follow-up of patients.

PS-08-019
Accuracy of intraoperative touch imprint cytology of breast lesions using core-needle biopsy specimen: A comparison with frozen section diagnosis
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Objective: Image guided needle-core biopsy (CNB) generally replaces the role of fine needle aspiration cytology due to benefit of diagnostic accuracy recently in breast lesions. However, rapid pathological diagnosis is required for various reasons. This study aims to evaluate the accuracy and usefulness of touch imprint cytology (TIC) using CNB specimen comparing with frozen section diagnosis (FSD).
Method: We made two touch imprint slides in 100 cases before performing FSD with 73 CNB and 27 biopsy specimens requested for FSD in a total of 82 patients. Two pathologists examined TIC separately. Diagnostic categories were benign, atypia, suspicious for malignancy, malignancy, and defer. The results were compared with FSD and permanent section diagnosis.
Results: Of the 100 specimens, 44 were confirmed to be malignant, and 56 benign in permanent section. In the TIC, the sensitivities of the pathologists were 90.9 %, 95.5 % respectively, and specificities 98.1 % and 96.2 %. Positive predictive values were 97.6 %, and 95.3 %, while negative predictive values 92.7 %, and 96.2 %. The coincidence between the pathologists was 95.5 % in the malignant lesions, 89.3 % in the benign lesions, and 92 % in total cases. In false positive cytologic diagnosis, papillary neoplasm was 2 cases. In comparison of diagnostic accuracy with FSD, the sensitivity of FSD was 95.5 %, the specificity 100 %, the positive predictive value 100 %, and the negative predictive value 96.6 %.
Conclusion: Although diagnostic accuracy is slightly superior in FSD, TIC is accurate, simple, & cost effective method for rapid diagnosis especially in malignancy. It can replace the FSD to avoid frozen artifacts, and consumption.

PS-08-020
Spindle cell tumours of the salivary gland
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Objective: Fine Needle Aspiration (FNA) of salivary glands spindle cell lesions is very challenging with a wide range of benign/malignant tumours and reactive lesions.
Method: 4 cases of salivary gland FNA with cytology and cell block: 74-year-old man with tumefaction of left parotid; 91-year-old woman with painfull swelling of left mandibular gland; 63-year-old woman with painless swelling of left submandibular gland; and 59-year-old woman with nodule of left parotid.
Results: 74-year-old revealed fusiform cells, with oval/elongated nuclei with fine dispersed chromatin, moderate pleomorphism

and rare mitotic figures, some with cytoplasmic melanin pigment granules, positive for HMB-45, S100 protein and vimentin—melanoma metastases. Ninety-one year-old woman showed neutrophils, cells with large cytoplasm and eccentric nucleus, positive for CD68—granulomatous inflammatory lesion. Sixty-three-year-old woman presented spindle cells with mild nuclear pleomorphism and round cells arranged in monotone fibrillar matrix—suggestive of fusocellular tumour of uncertain malignant potential (UMP). Fifty-nine-year-old woman presented large and clarified cytoplasm cells, arranged around fibrous structures, positive for CK7, P63 and calponin and negative for desmin and alpha-1-antitrypsin—UMP myoepithelial tumour.
Conclusion: Cytology of spindle cells lesions encompasses a wide variety of lesions, with potential pitfalls. The conjugation of morphology, immunocytochemical and clinical aspects is fundamental for accurate diagnosis.

PS-08-021
Contribution of BRAF p.V600E mutational study by pyrosequencing in detection of papillary carcinoma by thyroid fine needle aspiration
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Objective: OBJECTIVE: As BRAFp.V600E gene mutation is considered specific of papillary carcinoma (PC) in thyroid, the aim of our study is to determine the contribution of its detection by pyrosequencing on material obtained by thyroid fine needle aspiration (FNA) to improve preoperative diagnosis of PC.
Method: METHODS: Inclusion criteria: thyroidectomized patients with histological diagnosis of PC and representative FNA before surgery with Bethesda categories II to V, registered at our institution between October 1989 and March 2014. Design: Retrospective observational study. Methodology: Identification of cases; blind reassessment of cytological diagnoses according to Bethesda classification if needed; BRAFp.V600E mutational study by pyrosequencing on histological material, and on FNA material in cases with detected mutation.
Results: RESULTS: 35 cases fulfil inclusion criteria. BRAFp.V600E mutation was detected in 15 tumours, while 20 tumours had no detectable mutation. 17 FNA corresponding to the 15 mutated cases were identified, being able to detect the mutation in 14 (82.3 %). No mutation was detected in cases with follicular variant of PC.
Conclusion: CONCLUSION: Mutational study of BRAFp.V600E on thyroid FNA would contribute to diagnosis of papillary carcinoma in 14 of 41 non-diagnostic FNA prior to surgery (34 %), which would improve management of these patients.

PS-08-022
Metastatic cancers to thyroid gland and their primary mimickers: A cytomorphologic comparison
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Objective: Metastatic cancers to thyroid might be presented with thyroid lumps and subsequently, be subjected to fine needle aspiration (FNA). Diagnostic dilemma to differentiate secondary from primary thyroid mimickers occurred when clinical information was unavailable. This study is to explore cytomorphology of these cases.
Method: Thyroid FNAs, performed during January 2007 and March 2016 at Chiang Mai University Hospital, Thailand, were retrieved under diagnoses of "metastatic cancer", "metastatic cancer cannot be excluded" or "primary versus metastasis". Cytological slides were reviewed along with their histologic correlates and clinical data.
Results: Out of 2444 thyroid FNAs, 20 with definite or equivocal diagnoses of metastatic tumours were encountered. Eight of which were confirmed to have metastatic nature. These include 1 squamous cell carcinoma from tonsil, 1 osteosarcoma, 3 pulmonary adenocarcinoma, 1 hepatocellular carcinoma, 1 endocervical adenocarcinoma and 1 unknown primary. Two metastatic cases were presented without prior clinical cancer history. Primary thyroid mimickers include anaplastic, medullary and papillary carcinomas. Certain cytological patterns could be readily diagnosed.
Conclusion: Although certain distinct cytological patterns may be of diagnostic, those with pleomorphic and papillary cellular patterns may be problematic. Presence of normal thyroid counterparts, clinical data and ancillary studies are helpful with these diagnostic challenges.

PS-08-023
Oral cytology and high risk HPV distribution in the oral cancer risk-groups
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Objective: There are no screening programs for oral cancers in Georgia.
Method: We investigate abuse of alkohol n = 33, cigarette smoking n = 28, multipartners n = 23, women with cervix pathology n = 53 and control group n = 46. Oral smears were stained using the Papanicolaou technique. For detecting high risk HPV subtypes was used chromogenic in-situ hybridization (Zyto Fast PLUS CISH).
Results: In abuse of alcohol atypical cytology was detected in 57.2 % and HR-HPV −14.2 %. In cigarette smoking group atypical cytological changes −70.8 %,HR-HPV −16.7 %. In Multipartners atypical cytology −66.7 %, HR-HPV −33.3 %. Women with cervix pathology,atypical cytology was 59.2 %, HR-HPV −36.4 %. In control group atypical cytological changes −38.1 %, HR-HPV −4.8 %.
Conclusion: Women with cervix pathology have the same changes as the classical groups of oropharyngeal cancer. Despite the same data of atypical cytology in cigarette smoking and alcohol abuse groups high risk HPV was revealed 2 times less than in multipartners and women with cervix pathology. This may indicate to oropharingeal carcinogenesis independence from HPV. Because of detecting atypical changes and high risk HPV in control group, it is recommended to carry out oral cancer screening program in the whole population and not only in risk-groups.

PS-08-024
Telomere length of mesothelial cells in pleural effusion measured using quantitative fluorescence in situ hybridization (Q-FISH) method
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Objective: Telomeres are repetitive DNA sequences at the ends of chromosomes, which generally shorten by 50 to 200 base pairs with each cell division and telomere shortening increases the risk of malignancy. In this study, we estimated telomere lengths of mesothelial cells in pleural effusion to examine the correlation between the telomere length and mesothelial carcinogenesis.
Method: Cell blocks obtained from 26 cases of non-neoplastic pleural effusion (NN), 8 cases of carcinomatous effusion by lung adenocarcinoma (LA), and 9 cases of malignant mesothelioma (MM) were examined. Telomere lengths were measured by quantitative fluorescence in situ hybridization (Q-FISH) method and were shown by normalized telomere:centromere ratios (NTCRs).
Results: The mean NTCRs of mesothelial cells of NN, tumour cells of LA and MM were 1.53+/−0.29, 1.02+/−0.23, 1.05+/−0.33, respectively.

The NTCRs of LA and MM were significantly lower than NN. CD146, IMP3 and Glut-1, which are known as malignant markers of mesothelial cells, rarely express in NN and tend to be seen in the cases with lower NTCRs.
Conclusion: The results indicate that telomere shortening of mesothelial cells might be associated with the development of malignant mesothelioma.

PS-08-025
Diagnostic accuracy of a limited immnuo-panel of Calretinin and Ber-EP4 for diagnosis of malignant effusions
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Objective: To evaluate the diagnostic accuracy of limited immuno-panel of two antibodies for differentiation of reactive mesothelial cells and malignant epithelial cells in effusions; Calretinin and Ber-EP4 respectively.
Method: The study was conducted at the Histopathology, Oncology and Surgical departments of Allama Iqbal Medical College, Jinnah Hospital Lahore, Pakistan over a period of 1 year (October 2014 to October 2015). A total of 97 suspected malignant pleural and peritoneal effusions were collected. Cytological smears and cell blocks were prepared from centrifuged deposit of aspirates. Giemsa and Papanicolaou stained smears were screened for malignant cells. Immunohistochemical markers (calretinin and Ber-ER4) were applied to the cell block. The cytological diagnosis of malignant cells and reactive mesothelial cells was verified with the cell block histopathological diagnosis and immunohistochemistry results.
Results: Out of total 97 cases, cytological examination diagnosed 55 cases as definitive malignant, 21 cases as confirmed benign, 18 were suspicious for malignant cells and 3 were inconclusive due to low cellularity. Application of antibodies (calretinin and Ber EP4) on cell blocks revealed 77 serous effusions positive for malignant cells and 20 were negative. Cross tabulation was done between results of Immunocytochemistry on cell blocks and histopathological diagnosis which is taken as gold standard. This showed that Sensitivity of Ber-EP4 is 98.6 %, specificity is 100 %, PPV is 100 % and NPV is 96 %. Sensitivity of Calretinin is 100 %, specificity is 70.8 %, PPV is 91.3 % and NPV is 100 %.
Conclusion: Limited immono-panel of calretinin and Ber EP4 has a high positive and negative predictive value and is cost effective in resource limited set up for differentiation of Adenocarcinoma cells and Reactive Mesothelial cells in serous effusions.

PS-08-026
Reliability of Bethesda System - based evaluation of thyroid Fine Needle Aspiration Biopsy specimens in cytohistologic correlation
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Objective: Analysis of clinical usefulness of Fine Needle Aspiration Biopsy (FNAB) in thyroid carcinoma diagnostics.
Method: 16,656 FNAB reports were made from 2010 to 2015 in the Department of Tumour Pathology, Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Gliwice Branch (IO). All FNABs were performed by pathologists with the assistance of radiologists, under ultrasound guidance. The smears were fixed in 95 % alcohol and stained with hematoxylin-eosin. Each case was assessed by two pathologists dealing with thyroid pathology. Cytological reports were correlated with histopathological results of operations performed in IO.
Results: Benign lesions (diagnostic category II of the Bethesda System—DC II) comprised 85 % of diagnoses, DC III—2,37 %, DC IV—2,11 %, DC V—1,7 %, DC VI—0,66 %. Non-diagnostic cases constituted 8 % of FNABs. Histopathological outcomes proved that the highest ratio of cancer in final pathology report was in DC VI (100 %) and DC V (75 %). In DC III and IV the decision on the surgery was made for clinical indications. In these categories, the proportion of malignant lesions was 22 and 19,23 %, respectively.
Conclusion: The diagnosis of cancer or suspicion of malignancy in FNAB should be an absolute indication for surgical treatment.

PS-08-027
Immunocytochemistry for monitoring of early reccurency of bladder carcinoma
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Objective: One of the goal of urine cytology is to detect lesion, especially for recurrence lesion before they can be detect cystoscopically.
Method: 40 patient with high grade urothelial carcinoma were examined during clinical follow-up within 3, 6 and 12 month after TUR with routine PAP test and p53 and HER2 to monitoring early recurrence.
Results: Negative for HGUC was in 19 cases, only in one case from this group HER2 was expressed as strong membrane stain less than 10 % cells, in 4 cases was weak nuclear stain of p53. In 2 cases in AUC group was no reaction with HER2, and weak stain with p53 in one case. AUC-H (2 cases) both with strong reactivity with HER2. In urothelial carcinoma LG in 9 cases we had strong HER2 stain in 5 cases and p53 positive in 4 cases. Recurrence of urothelial carcinoma was diagnosed in 8 cases within 12 month of clinical follow-up and there was strong positive stain both with HER2 and p53.
Conclusion: Urine cytology could be useful approach to detect early recurrence of HGUC and immunocytochemistry can help to discriminate them as recurrence or not.

PS-08-029
Could a sarcomatous component seem like an "atypical glandular cell"?
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Objective: Malignant neoplasms, other than squamous and adenocarcinoma may be seen in Pap smears. They appear on Pap smears either as exfoliated cells or via direct sampling of tumours that involve cervix by direct extension.
Method: A 71-year-old postmenopausal women with abnormal vaginal bleeding was referred to our hospital. On her gynecologic examination she had a protruding mass from her cervical os. She was evaluated by a Pap smear first. Her Pap smear revealed irregular and discohesive cell groups that had ill defined and transparent cytoplasm, peripherally located nuclei, vesicular chromatin and, conspicious nucleoli. There was no spindle cell component seen. The Pap smear was diagnosed as AGC, NOS.
Results: On pathological examination of the endometrial curettage and following hysterectomy specimen, the tumour was diagnosed as mullerian adenosarcoma. Detailed examination of the sarcomatous component revealed the remarkable resemblance of the cells that was seen on Pap smear.
Conclusion: Adenosarcoma is composed of a benign epithelial component admixed with a malignant mesenchymal component. Although it is well known histologically, its cytological features are rarely described. Adenosarcomas are rare lesions but should be considered in the differential diagnosis when the cell clusters unlike typical AGC are noted in a Pap smear.

PS-08-030
Follicular dendritic cell sarcoma: A case report of a frequently unrecognized entity in fine needle aspiration cytology
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Objective: Follicular dendritic cell sarcoma (FDCS) is a neoplastic proliferation of antigen-presenting accessory cells of the immune system. Despite having distinctive cytological features, it remains a commonly misdiagnosed entity. We report a case of FDCS unrecognized by fine needle aspiration cytology (FNAC) that was only diagnosed after excision.
Method: We describe the clinicopathological features of a case of FDCS, with a review of the literature.
Results: A 69-year-old woman presented with a left cervical mass. FNAC was performed and smears showed atypical spindle cells, isolated or in syncytia, admixed with small lymphocytes. No definite diagnosis was rendered and excision was recommended. Microscopically, it consisted of a whorled proliferation of spindle to ovoid cells with indistinct cytoplasm and bland vesicular nuclei, interspersed with small lymphocytes. Neoplastic cells were CD21+. A diagnosis of FDCS was made. Smears were reviewed and CD21 was performed on cytology specimens. The FNAC findings, in conjunction with the immunocytochemistry results, would have been diagnostic if the entity had been suspected.
Conclusion: The main challenge in the diagnosis of FDCS results from failure to consider it in the differential diagnosis. Increased awareness of FDCS may improve the recognition of its distinctive cytological features, rendering a specific pre-operative diagnosis.

PS-08-031
Ultrasound guided fine needle aspiration on evaluation of axillary lymph nodes status on primary breast cancer
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Objective: The aim of this study is to determine the sensivity, specificity, positive (PPV) and negative predictive value (NPV) and general acuity of Ultrasound (US) guided fine needle aspiration (FNA) for pre-surgical evaluation of axillary lymph nodes status on primary breast cancer.
Method: Retrospective study of 328 patients with a pathological diagnosis of primary breast cancer between 2010 and 2014, who had performed US guided FNA for axillary lymph node evaluation and posterior sentinel lymph node biopsy (SLNB) or axillary dissection. The patients were selected consecutively from our department database and the cytological and histological diagnosis were compared.
Results: We obtained 24,5 % false negative and 2,2 % false positive results, resulting on a sensivity of 80,55 %, 95,91 % specificity, PPV of 97,32 %, NPV of 72,27 % and general acuity of 84,89 %.
Conclusion: US guided FNA at our institution showed good correlation with the histological results with a high specificity and PPV and good acuity and can be routinely used on axillary lymph nodes evaluation. The results were discrepant mainly when there was obtained scant material on FNA or when the cytology showed isolated atypical cells of unknown significance. This technique avoids SLNB and shortens the waiting time for axillary dissection and neoadjuvant chemotherapy start.

PS-08-036
Cytologic features of acinar cell carcinoma of the pancreas: A report of four cases
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Objective: Pancreatic acinar cell carcinoma (ACC) is a rare neoplasm with few cytologic descriptions. Cytology may resemble that of islet cell tumours. The purpose of this study is to report our experience with four cases of ACC that were evaluated using FNA.
Method: Four cases of ACC in which FNA was performed preoperatively were selected. Two corresponded to endoscopic US-guided-FNA and two to percutaneous FNA. All tumours had a complete histologic evaluation.
Results: Smears were hypercellular and revealed numerous poorly cohesive clusters as well as single cells. Aggregates were irregular, with cellular crowding, occasional vessels and pseudopapillary structures. Acinar or rosette-like groups were present in three cases. Cytoplasmic fragility and naked nuclei were a frequent finding. When preserved, the cytoplasm was slightly granular. Although marginal nuclear location was seen, plasma cell morphology or binucleation were absent. All cases showed evident nucleoli. Relevant anisonucleosis was present in two cases. Two cases were diagnoses as neuroendocrine tumours, one as adenocarcinoma and in the remaining one the possibility of ACC was suggested.
Conclusion: Cytology of pancreatic ACC shows peculiar morphologic features. Although it may resemble neuroendocrine tumours some findings such as prominent nucleoli, granular cytoplasm, acinar clusters and no evident plasma cell morphology should alert the pathologist.

Tuesday, 27 September 2016, 09.30–10.30, Hall 11.3
PS-09 Electron Microscopy

PS-09-002
Electron microscopy (EM) is a useful method to discover Primary Ciliary Dyskinesia (PCD)
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Objective: Kartagener syndrome is characterized by the combination of chronic sinusitis, bronchiectasis and situs inversus. It is related to the Primary Ciliary Dyskinesia (PCD). Electron microscopy is the gold standard method to determine PCD. The purpose of this study is to show a case report where EM was a useful diagnostic tool.
Method: The current case is a 39-years old woman with known situs inversus and asthma. CT-Scan showed bilateral bronchiectasis and she was referred to the Department of Respiratory Diseases. Where bronchoscopy was made based on the suspicion of Kartagener syndrome. Bronchial brushes were sent to EM. After plastembedding, sectioning and staining, several pictures were taken for analysis.
Results: 46 cilia were counted. The average of outer dynein arm was 1.2, inner dynein arm 0.9 and nexin link 3.9, and orientation was varying. Ultrastructural analysis showed PCD.
Conclusion: The diagnosis of Kartagener syndrome is not difficult to suspect. The difficulty is to keep this diagnosis in mind since the symptoms are non-specific. However, the association with situs inversus should help to raise the diagnostic suspicion. The importance of early diagnostic and symptomatic treatment as well as prevention of infections is emphasized by the progressive degeneration in respiratory function in patients with PCD if untreated.

PS-09-003
Ultrastructural markers of dysangio- and dysnephrogenesis in Congenital Hydronephrosis (CH)
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Objective: reveal similar ultrastructural changes in malformed vessel and hypoplastic parenchyma in CH.
Method: renal biopsies obtained from 34 children from 3 days to 7 years old. We used routine EM processing.
Results: abnormal vessel wall architecture was present in all specimen—irregular thickness of basement membrane (BM); kinking of arterioli

lined with immature o-chaped endothelium; chaotic orientation of immature tall SMC with round large nuclei, thin cytoplasm rim, hydropic changes and poorly formed organells; fragmentated internal and external elastic membrane. Parenchymal hypoplastic lesions included: deficiency of capillary loops in glomeruli and their indistinct lumens; irregular BM thickness with layer rarefaction; immature glomerular endothelial cells with significantly increased nucleus/cytoplasm ratio; different sizes of podocytes and their dislocation, absence of well formed foot processes in same of them, hydropic changes of cytoplasm; large cuboidal epithelium lining undifferentiated tubules, irregular thickness of tubular BM. The percentage of these vessel and parenchymal lesions correlated with clinical symptomatic. So similar changes of arteriolar and glomerular BM and endothelial cells were revealed.
Conclusion: the most severe morphological changes in renal parenchyma were found in children first weeks of life. Ultrastructural changes in malformed vessels correlated with dysnephrogenesis features.

Tuesday, 27 September 2016, 09.30–10.30, Hall 11.3
PS-10 Gynaecological Pathology

PS-10-001
Diagnostic performance of miRNA and HPV E6/E7 mRNA assay on formalin fixed paraffin embedded cervical cancer tissues
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Objective: MiR-9, miR-21, miR-155, and miR-944 are known to promote cell growth, migration and invasion in human cervical cancer cells. The aim of this study was to investigate expression levels of miRNAs (miR-9, miR-21, miR-155, and miR-944) in 53 formalin fixed paraffin embedded (FFPE) cervical cancer samples and 50 FFPE normal samples.
Method: The expression levels of miR-9, miR-21, miR-155, and miR-944 from FFPE samples were analyzed using quantitative reverse transcriptase PCR (RT-qPCR). RNU6B miR was used as an internal control.
Results: MiR-9, miR-21, miR-155, and miR-944 were useful markers for discriminating cancer samples from normal samples with an area under the ROC curve (AUC) of 0.7565 [95 % confidence interval (CI) 0.6624 to 0.8507], 0.8325 (95 % CI 0.7530 to 0.9120), 0.8492 (95 % CI 0.7736 to 0.9249), and 0.8522 (95 % CI 0.7779 to 0.9265), respectively. Moreover, the expression levels of miR-9 (P = 0.0039), miR-155 (P = 0.0039), and miR-944 (P = 0.0154) were significantly higher in tissue samples which are positive to HPV E6/E7 expressions than those which are negative.
Conclusion: In conclusion, miR-9, miR-21, miR-155, and miR-944 seem to be up-regulated in cervical cancer samples and the up-regulation seems to be related to HPV oncogene expression.

PS-10-002
The expression of prolactin and prolactin receptors in ovarian epithelial tumours
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Objective: Accumulating evidence suggests a role for prolactin (PRL)/prolactin receptor (PRL-R) signaling in ovarian cancer. The aim of this study is to investigate the profile and significance of expression of PRL and PRL-R in ovarian epithelial tumours.
Method: We studied the expression of PRL and PRL-R in 503 ovarian epithelial tumours using immunohistochemistry. The tumours included 431 carcinomas, 46 borderline and 26 benign tumours.
Results: All tumours expressed PRL-R in their epithelial cells. Benign tumours showed significantly stronger expression than other categories ($p < 0.001$). PRL-R expression in malignant tumours was significantly higher with higher grade and stage ($p = 0.013$ and $p = 0.037$). PRL was expressed in tumour epithelial cells and/or stroma. Stromal expression was seen in 58 % of cases, which was significantly higher in borderline tumours as compared to other categories ($p < 0.001$). Expression in tumour epithelial cells was seen in 17 % of cases, 85 % of which were malignant. In these tumours there was a significant correlation with shorter patient survival ($p = 0.033$).
Conclusion: The expression of PRL and PRL-R in ovarian epithelial tumours indicates the presence of an autocrine loop, which appears to influence clinical outcome. Our results show the potential of PRL and PRL-R as prognostic biomarkers and therapeutic targets in ovarian carcinoma.

PS-10-003
The usage of atomic power microscopy in nano-histological studies (at the example of preeclampsia)
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Objective: Recent years the method of atomic power microscopy(APM) has become the one of fundamental methods, which allows to make first steps in nano-pathology of the human
Method: APM was conducted with help of microscope «Ntegra-Aura». The specimens of uterus (endometrium, myometrium), blood, placenta, umbilical cord of 30 women were researched.
Results: The alteration of cytoarchitectonics of erythrocytes in women on background of preeclampsia was shown with help of APM. The sizes of cells did not differ authentically from control group (6,8 ± 0,4 μm and 7,0 ± 0,3 μm). The number of cells with degenerative changes and erythrocytes with hemolysis was increased. The depth of discocytes was 0,25 ± 0,04 μm (0,38 ± 0,05 μm). The anatomy of pores was violated. The alteration of microrelief of endothelium was in blood vessels of umbilical cord. The number of normocytes was decreased significantly up to 42,0 ± 2,0 % (85,0 ± 4,0 %). The microcytes with diameter 5,5 ± 0,5 and thickness 1,95 ± 0,4 μm prevailed among blood cells. At the pathological course of pregnancy the smoothing of relief in terminal villi due to narrowing or complete absence of the lumen of the blood vessels was revealed (1,5 ± 0,2 μm и 3,2 ± 0,5 μm).
Conclusion: APM is reliable and effective method for research of biological objects in pathology. This method can be used as the method for express-diagnosis, particularly for research of system "mother-placenta" at complicated pregnancy.

PS-10-004
The usage of scanning microscopy for exploration of pathology of macro- and microelements in system "mother-placenta-fetus" at eclampsia
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Objective: Pre-eclampsia and eclampsia, the most severe complications of pregnancy that can lead to maternal and perinatal morbidity and mortality.
Method: The materials of patients (biopsy specimens, umbilical cord, placenta), pregnancy of whom was complicated by preeclampsia(65) and eclampsia(10), were researched. The precise elemental analysis was conducted with usage of detector for registration of spectra of the characteristic X-ray radiation, which was integrated with raster electron microscope.
Results: The content of oxygen in erythrocytes of vascular bed in endometrium was 35,22 ± 2,01 % at preeclampsia and 30,12

±2,31 % at eclampsia; 45,12±2,35 % in control group. The same tendency for oxygen, magnesium, phosphorus was detected inside and outside of spiral arteries of myometrium. The quantity of oxygen in arteries of umbilical cord was 33,46±1,45 % at pre-eclampsia, 29,81±2,06 % at eclampsia and 43,91±2,25 % at normal pregnancy; in veins—24,60±2,30 %; 21,60±2,06 %; 34,60±2,32 % respectively. The decreasing of magnesium was revealed. At pathology of pregnancy the quantity of oxygen was rapidly decreased in vessels of chorion as well in intervillous space(23,85±2,45 %; 21,96±2,48 %; 45,12±2,31 %) while quantity of potassium, sodium, and calcium was increased. The violation of content of macroelements combined with destructive processes and violation of blood circulation were in explored organs and tissues.

Conclusion: The complex usage of biochemical and morphological methods can be the base for development of methods of prophylactics and treatment of pathology of pregnancy

PS-10-005

Turner syndrome with mosaicism and translocation of the SRY-gene

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Objective: to research genetic mosaicism in karyotype in Turner syndrome (TS).

Method: surgical material from six patients 11–24 years old with TS and mosaicism in serum and gonadal tissue was studied. Immunohistochemistrical detection of Ki-67, Vimentin, Desmin, Inhibin-a, AR, ER. The tissue karyotype (TK) and SRY-gene has been detected by fluorescence in situ hybridization and polymerase chain reaction, the serum karyotype (SK)—cytogenetically. Data processing: Statistica 7.0.

Results: Two patients with gonadoblastoma have had 45X/46XY SK and XO, XY TK, and SRY-gene in gonadal tissue (GT). Two patients with dygenetical gonads and fragments of ovarian tissue: 45X/46XX SK and XO TK, the SRY-gene is in one case—in GT. Two other patients with streak-gonads: 45X/46XY SK and XO/XY, XO/XY/XYY TK, the SRY-gene is in both cases—one in serum and another one is in GT. Immunohistochemistrically: streak-gonads—high expression of Vimentin and low of all rest. DGOT—high expression of ER; DGGB—high expression of Inhibin-a, ki-67.

Conclusion: karyotype in TS correlates ($r = 0,32\text{-}0,4$; $p < 0.05$) with different morphology. In two patients with absence of Y-chromosome the SRY-gene was detected that in according to science sources is the result of SRY-gene translocation to X-chromosome during meiotic recombination. The SRY-gene does not always correlate with gonadoblastoma.

PS-10-006

Occult uterine sarcoma in a series of hysterectomies performed for benign indications

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Objective: This study aims to define the incidence of unexpected occult uterine sarcomas among women who underwent hysterectomy for benign indications at our teaching hospital. Patients who were found to have uterine sarcoma on histopathologic examination were considered to have an occult uterine sarcoma.

Method: A total of 3008 hysterectomies for benign gynecologic indications were performed between 2000 and 2015. The most common indications for hysterectomy were leiomyomas and abnormal uterine bleeding.

Results: Among these 3008 hysterectomies, 11 patients were found to have uterine sarcoma, with an overall rate 1 in 270 (0.37 %). These malignancies included six leiomyosarcomas, four endometrial stromal sarcomas (3 cases were high-grade, and 1 cases were low-grade), and one Müllerian adenosarcoma. High-grade endometrial stromal sarcoma was the dominant subtype. Median age was 51 years (range 45–68). Among women found to have occult sarcoma, hysterectomies was performed as a primary indication for leiomyomas (75 %) and abnormal bleeding (25 %). There was no evidence of malignancy in the preoperative histologic examination of the endometrium of these patients. Of these 12 patients, 9 were treated by open hysterectomy and bilateral salpingo-oophorectomy. 3 of these patients underwent total laparascopic hysterectomy.

Conclusion: As a result, the total incidence of uterine sarcoma among patients operated on for benign indication is low in our population (0.37 % or 1 in 270). The FDA estimates that 0.3 % of all women undergoing hysterectomy for the treatment of myomas are found to have an unexpected uterine sarcoma. No reliable predictors of uterine sarcoma present and attention is warranted in preoperative planning for hysterectomy.

PS-10-007

Ovarian uveal melanoma metastasis showing MLH1/PMS2 protein loss in a patient with Lynch Syndrome

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Objective: An increasing number of extra-colonic neoplasms are being described in Lynch Syndrome patients. Uveal melanoma is not included in Lynch Syndrome tumour spectrum, despite evidence suggesting a role of microsatellite instability in its sporadic tumourigenesis. In this work we aim to describe a patient with Lynch Syndrome that presented an ovarian uveal melanoma metastasis.

Method: The patient was referred for genetic counseling at 45 years-old due to a family history of Lynch Syndrome (MLH1 mutated). She underwent enucleation of her right eye at age 25 due to a uveal melanoma which recurred as an ovarian metastasis 22 years later. Histological, immunohistochemical and molecular study of the tumour was performed.

Results: The uveal melanoma ovarian metastasis differed from the primary tumour by exhibiting frequent pseudo-follicles, increased cytological atypia, edema, hemorrhage and necrosis. It showed loss of MLH1/PMS2 protein immunoexpression and high microsatellite instability. No MLH1 promoter methylation nor BRAF mutation were found.

Conclusion: We conclude that the patient's uveal melanoma tumourigenesis was most likely related to the MLH1 germline mutation. To the best of our knowledge this is the first report of a uveal melanoma showing MLH1/PMS2 protein loss in the context of Lynch Syndrome.

PS-10-008

Prognostic value of lymphatic and blood vascular invasion in endometrial cancer

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Objective: Vascular invasion (VI) is a well-established marker for outcome in endometrial cancer. Our aim is to explore whether type of VI, defined as lymphatic (LVI) or blood vascular invasion (BVI) influences the pattern of metastasis.

Method: From a prospectively collected cohort we selected three groups of endometrial carcinoma patients: 56 with positive lymph nodes at primary surgery (LN+), 44 with negative lymph nodes, and recurrent disease (LN-R+), and 100 with negative lymph nodes, and no recurrence (LN-R-). Immunohistochemical (IHC) staining with D2-40 and CD31 antibodies was used to differentiate between lymphatic and blood vessels.
Results: Based on H&E, VI was observed in 25.5 %. IHC staining showed 29.7 % LVI only, 4.2 % BVI only and 2.6 % both BVI and LVI. LN+ patients had significantly more LVI (63.5 vs. 28.6 %) ($p = 0.001$). LN-R+ patients had significantly more BVI (14.3 %) compared to LN-R- patients (2.0 %) ($p = 0.009$). In multivariate analysis BVI in combination with age, tumour type and grade, was a significant predictor separating patients with and without future recurrence.
Conclusion: The current study suggests that LVI is associated with lymph node metastasis at primary diagnosis, while BVI is associated with recurrence. IHC for separation of LVI and BVI might contribute to individualisation of treatment.

PS-10-009
Tissue microarray use for biomarkers studies in endometrial cancer
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Objective: To optimise use of tissue microarray (TMA) for immunohistochemical (IHC) staining in endometrial cancer (EC), in preoperative endometrial samples and hysterectomy specimens.
Method: Cores of preoperative and hysterectomy specimens of 14 EC and three atypical hyperplasia cases were collected in TMA blocks. Two 0.6 mm, and two 2.0 mm cores were used from each sample. Different antibodies were tested in TMAs and compared with results of whole slides of hysterectomy. Tested antibodies: ER, PR, p53, Ki-67, MLH1, PMS2, MSH2, MSH6, ARID1A, stathmin, IMP3, L1CAM, PTEN, beta-catenin, p16.
Results: Overall, 2.0 mm cores were more assessable for evaluation than 0.6 mm cores (95.7 % versus 77.5 %, $p < 0.001$). Most antibodies had a substantial to good agreement between hysterectomy TMA and whole slide, with exception of those with heterogeneous expression: PR, Ki-67, stathmin, beta-catenin, p16. Preoperative TMAs showed for most antibodies moderate to perfect agreement with hysterectomy TMAs. There were more cases with positive staining on preoperative TMA and negative hysterectomy TMA than conversely.
Conclusion: Agreement between TMA and whole slide, and preoperative and hysterectomy TMAs varied per antibody. Based on the more frequent loss of cores with smaller core size, 2.0 mm cores are the preferred size for IHC studies in EC.

PS-10-010
Ovarian mucinous epithelial neoplasms arising within mature teratomas: About four cases
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Objective: To study mucinous tumour component in ovarian teratoma.
Method: We reported four cases of ovarian mucinous epithelial neoplasms arising within mature teratomas collected in the pathology laboratory of Salah Azaiez Institute from 1995 to 2016.
Results: The patients' ages ranged from 29 to 70 years. Tumour size ranged from 5 to 27 cm. Grossly, three tumours had cystic appearance with pilosebaceous content. Only one tumour was composed of small to large cysts containing mucinous material. Histologically, in association with mature teratomatous components, one was classified as mucinous cystadenoma, two as mucinous borderline tumours and one as invasive mucinous carcinoma. Pseudomyxoma ovarii was noted in one case of mucinous borderline tumour. Peritoneal pseudomyxoma was found in both cases of carcinoma and cystadenoma. No appendiceal lesions were identified.
Conclusion: Various type of mucinous neoplasms can arise in ovarian teratoma, varying from benign to malignant tumours. In literature, the borderline tumour type is predominant. Thus, meticulous dissection of teratoma should be performed to look for any malignant areas, since management and prognosis vary depending upon the microscopic type and stage.

PS-10-011
Endocervical adenocarcinoma: The impact of pattern-based classification system in clinical decision
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Objective: The objective of this study is to investigate other than classical pathologic factors that could identify better patients with Endocervical Adenocarcinoma (ECA) who are at risk of developing lymph node metastases (LNM).
Method: A retrospective review of records of patients with ECA regarding clinical and pathologic features, tumour size, lymphovascular invasion (LVI) and pattern of tumour invasion were defined. The later categorized as: Pattern A: well confined glands, Pattern B: early invasion of stroma, originating from well confined glands, Pattern C: destructive invasion.
Results: A total of 103 women aged 21 to 79 were identified with ECA. All patients were staged between IA2 to IV, whereas LVI was involved in 42 cases. Stage I were all patients with Pattern A, 71,4 % with Pattern B and 41,6 % Pattern C, while had LNM 11,4 % and 22,9 % respectively (B,C).
Conclusion: Patients with Pattern A, stage I would not need lymph node resection, according to the suggested histologic classification for ECA. Moreover, patients with Pattern B rarely have LNM since 71.4 % of them have stage I disease. Therefore, our data suggest that this new pattern-based method of classifying ECA could be clinically significant since it is simple and consistent.

PS-10-012
The importance of pathological parameters involved in recurrence and survival of patients with vulvar cancer: A novel insight
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Objective: Aim of the study is to determine the impact of clinicopathological parameters on recurrence and survival of patients with vulvar cancer.
Method: Patients ($n = 175$) with squamous vulvar cancer where retrospectively analyzed and further evaluated regarding the prognostic significance of different clinicopathologic variables, including: age, diameter and location of the lesion, depth of invasion, grade, lymphovascular space involvement (LVSI), perineural invasion, pattern of invasion and presence of VIN. Time to recurrence was recorded; disease free survival and overall survival were calculated.
Results: Among all tumour related variables multiple analysis showed that the number of positive lymph nodes (LN) was the only independently associated risk factor for recurrence. Additionally, increased depth of invasion, tumour thickness, invasive or spray invasive pattern, perineural invasion and LVSI were associated with greater risk for recurrence. Also, multiple Cox regression analysis showed that age at diagnosis, free

surgical margins and the total number of positive lymph nodes were independently associated with survival.
Conclusion: Lymph node metastasis and status of surgical margins were confirmed to be independent predictors for poor prognosis in patients with vulvar cancer. Furthermore, number of positive lymph nodes, spray invasive pattern and perineural invasion correlated with increased risk for recurrence.

PS-10-013
Undifferentiated endometrial carcinoma: Experience with cases from a single cancer center
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Objective: Undifferentiated endometrial carcinoma (UEC) is a rare and poorly recognized entity.
Method: Retrospective study on cases diagnosed as UEC.
Results: A total of 17 cases were identified, with a median age of 60 years. Post-menopausal bleeding was the most common symptom. TAH and BSO was the most common treatment (n = 12, 80.0 %). Nine (52.9 %) patients received adjuvant treatment. The median overall survival was 9 months. Grossly, the tumours were mostly friable fungating/polypoid masses (n = 7, 46.7 %), involving the lower uterine segment or cervix in 7 (46.7 %) cases. Pure UEC was seen in 7 cases (41.2 %), while de-differentiated carcinoma in 6(35.3 %). UEC was part of the epithelial component of carcinosarcoma in 3 (17.6 %) cases and was mixed with serous carcinoma in a single case. In all cases but one (n = 16, 94.1 %) focal strong positivity for one or more of the cytokeratins was evident. Vimentin was positive in 9 cases (81.8 %). P16 was diffuse and strong in the undifferentiated component in 6 (50.0 %) cases, while P53 was diffusely positive in 5 (38.5 %). Only 2 out of 11 (18.2 %) referral cases were correctly diagnosed as UEC.
Conclusion: UEC is a rare tumour that is frequently mis-diagnosed. Applying the right immunostains helps establishing the correct diagnosis

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PS-10-014
Amplification of SOX2 transcription factor is strongly related to HPV status of vulvar carcinomas
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Objective: SRY box 2 protein (SOX2) is a transcription factor mainly implicated in stem cell differentiation. The aim of our study was to analyze SOX2 expression along with copy number changes in a large set of vulvar carcinomas.
Method: For immunohistochemical detection of SOX2, we used a rabbit monoclonal anti-SOX2 antibody (clone EPR3131, Epitomics Inc.). Copy number changes of SOX2 were analyzed by commercially available probes according standard procedures (Zytovision, ZytoLight SPEC SOX2/CEN3). Analysis of the HPV status was done with RNA in situ hybridization, utilizing specific probes against pan HPV (ViewRNA, Affymetrix Inc.).
Results: SOX2 was immunohistological detectable in 30/55 (54.5 %) specimens. Amplification of SOX2 was observed in 10/48 (20.8 %) specimens with a valid FISH signal. Furthermore, SOX2 overexpression and amplification were both strongly related to positive HPV status. Tumours which were positive with pan HPV probes in RNA in situ hybridization showed significantly more frequent high SOX2 expression levels as well as amplification than tumours not associated to HPV (57 vs. 18 %, $p < 0.01$ and 40 vs. 9.5 %, $p = 0.02$).
Conclusion: SOX2 overexpression and amplification is strongly related to HPV associated vulvar carcinomas. Our results may give new insights in the molecular pathogenesis of HPV related vulvar cancers.

PS-10-015
Interest of an immunohistochemical panel in mucinous ovarian tumours: A study of 29 cases
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Objective: The diagnostic issues raised by primary ovarian mucinous tumours (POMT) are of two types: the exclusion of metastasis and the grading. The aims of our work were to determine whether immunohistochemistry (IHC) may assist in tumour grading and provide a simple tool to differentiate between primary and metastastic mucinous ovarian tumours.
Method: We studied 29 cases: 12 metastasis and 17 POMT, including 7 cystadenomas, 6 borderline tumours and 4 carcinomas, in a prospective study performed between 2014 and 2015. The following markers were tested: CK7, CK20, CDX2, PAX-8, MUC1, MUC2, MUC4 and MUC5AC.
Results: The expression pattern in POMTs vs metastasis was as follows: CK7 100 vs 50 %, CK20 59 vs 92 %, CDX2 18 vs 83 %, PAX8 35 vs 0 %, MUC2 17 vs 42 %. The expression pattern in benign, borderline and malignant POMTs were respectively: for PAX8, 57, 17, 25 %; for MUC4, 42, 33, 25 %; for CK20, 29, 83, 75 % and for MUC5AC, 29, 83, 50 %.
Conclusion: In most cases, the combination of CK7, CK20, CDX2 and PAX8, in association with the clinical history, is able to distinguish primary and metastatic mucinous ovarian tumours. In POMTs, the expression of PAX8 and MUC4 might help to identify low grade tumours, in contrast to CK20 and MUC5AC, more frequently expressed in high grade tumours.

PS-10-016
High-risk HPV detection rate in patients with parakeratotic cells in cervical cytology and its relationship to the CIN2+ lesion
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Objective: In cytology specimens, parakeratotic cells are either isolated or in sheets and resemble small superficial squamous cells. The cytoplasm, however, is more dense than a normal superficial squamous cell, and the nuclei can be more hyperchromatic with variation in size and shape.
Method: A total of 1268 women with normal cytology were included in the study. Out of 1268 cases, 390 cases were reported as normal cytology with parakeratosis, and 878 cases were reported as normal cytology without parakeratosis. Cervista HPV HR test was performed using these samples. Thirty-four women were referred for colposcopy.
Results: HPV infection was detected in 101 of 390 cases with parakeratosis (25.9 %), and in 130 of 878 cases without parakeratosis (14.8 %). Rate of HPV positivity was higher in women with parakeratosis compared to women without parakeratosis ($p < 0.001$). The sensitivity, specificity, positive predictive value, and negative predictive value of presence of parakeratosis in normal cytology were 28.57, 80, 50, 61.54 %, respectively. The presence of parakeratosis has high specificity for detection of CIN2+ in histological follow up.
Conclusion: Presence of parakeratosis in normal cytology is correleated with the cases of HPV infection,which has high specifity for detection of CIN 2+ in histological follow-up.

PS-10-017
The rate of high-risk Human Papilloma Virus (HPV) in cervical cytology and its relationship to the CIN2+ lesion
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Objective: Cervical cancer is the second most common cancer among women in the world and is the ninth most common cancer among female cancers in Turkey. Persistent human papilloma virus (HPV) infection is the main cause for the development of cervical cancer.
Method: A total of 1748 women with normal and abnormal cytology were included in the study. Out of 1748 cases, 485 cases were reported as abnormal cytology, and 1263 cases were as normal cytology. Cervista HPV HR test was performed using these samples. 174 women were referred for colposcopy.
Results: The sensitivity, specificity, positive predictive value, and negative predictive value of HPV testing were 91.89, 14, 44.16, 70 %, respectively. The sensitivity, specificity, positive predictive value, and negative predictive value of cytology were 89.19 %, 25 %, 46.81 %,75.76 %, respectively. The sensitivity, specificity, positive predictive value, and negative predictive value of HPV testing and cytology (co-test) were 98.67 %, 4.76 %, 42.53 %, 83.33 %, respectively.
Conclusion: HPV testing and cytology had high sensitivity but low specificity in Turkey. Sensitivity of co-test was higher than the sensitivity of cytology and HPV test alone.

PS-10-020
Heterogeneity in PD-L1 expression and CD8+ infiltrates in low grade versus high grade serous ovarian carcinomas
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Objective: High grade (HGSOC) and low grade (LGSOC) serous ovarian carcinomas are now known to be tumours with different pathogenesis and outcomes. We investigated tumour infiltrating lymphocytes (TIL), expression of PD-L1 and density of CD8+ lymphocytes in ovarian and peritoneal locations.
Method: Whole tissue sections from 25 HGSOC and 10 LGSOC primitive locations were studied, with paired peritoneal lesions in 8 and 9 cases respectively. Automated immunohistochemistry was performed. Presence of TIL and PD-L1 expression in tumour cells (TC) and immune cells (IC) were semi-quantitatively assessed. Image analysis was performed to quantitatively assess density of CD8+ cells.
Results: LGSOC were characterized by lower density of TIL and CD8+ lymphocytes than HGSOC in ovarian location. Higher densities of CD8+ infiltration were observed in peritoneal locations in both LGSOC and HGSOC, with a high intertumour and intratumour heterogeneity. PD-L1 expression was not observed in LGSOC whereas 8/24 were positive for TC and 9/24 positive for IC in HGSOC. No correlation was found with neoadjuvant chemotherapy and BRCA mutation status.
Conclusion: LGSOC is characterized by lower CD8+ infiltration and absence of PD-L1 expression as compared to HGSOC. Our study highlights tumour heterogeneity for these immune markers between ovarian and peritoneal locations.

PS-10-021
Circulating serum interleukin-18 and interleukin-10 levels in early diagnosis of ovarian carcinoma patients: A case control study
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Objective: The aim of this study was exploring the diagnostic role of IL-18, IL-10 and its role in ovarian carcinoma.
Method: A total number of 420 subjects were enrolled in the study after approval of the institutional ethics committee. Out of 420 subjects, 210 biopsy approved patients were included in the study and grouped into various stages as per TMN classification, age and ethnicity matched 210 healthy subjects were recruited as controls within the age range of 20–60 years. Peripheral blood samples of all patients and age matched controls were obtained at baseline and estimation of IL-18 and IL-10 was done by enzyme linked immunosorbent assay (ELISA). Data were analyzed with appropriate statistical tools like ANOVA and Graph PAD.
Results: The baseline levels of IL-10 and IL-18 in all groups of ovarian carcinoma were found to be significantly ($p < 0.05$) higher than the control group. The levels of IL-18 and IL-10 also found to be elevated significantly in stage T3 ($p < 0.05$) and T4 ($p < 0.05$) as compared to stage T2. The levels of IL-18 is found to be well associated with progression of disease of various groups ($r = 0.80$, $p < 0.05$). In contrast, IL-10 showed significant direct association with progression of carcinoma ($r = 0.85$, $p < 0.05$).
Conclusion: Study concluded that serum IL-18 is a better diagnostic marker with higher specificity and sensitivity. IL-10 may be valuable as a prognostic marker in ovarian carcinoma but still more studies on larger sample size is needed for its validation.

PS-10-022
Uterine sex cord stromal tumours: A study of 8 cases
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Objective: Uterine sex cord stromal tumours are rare, and are divided into endometrial stromal tumours with sex cord like elements (ESTSCLE), and Uterine tumours resembling ovarian sex cord tumours (UTROSCT). The aim of the study is to see histomorphological features of uterine sex cord stromal tumours.
Method: From January 2004 to Mid April 2016, we found 8 cases of uterine stromal tumours in our files (3- ESTSCLE, 4- UTROSCT, and one was labelled as mixed stromal-smooth muscle tumour with true sex cord differentiation).
Results: The mean age was 39.3 years (median 38). All ESTSCLE showed typical low grade ESS areas with sex cord elements in trabecular/retifrom pattern. All were positive for ER,PR, CD10. One case had history of carcinoma breast; the same case also showed paraaortic lymph node metastasis. All URTOSCT showed nests, cords, trabeculae. Calretinin, inhibin, MIC-2 were used as sex cord markers (MIC-2 being positive in ¾ cases). EMA was consistently negative. One case showed aortocaval, pelvic nodal metastasis; another showed necrosis, mitotic count of 20/10 hpf and was deemed malignant.
Conclusion: ESTSCLE and UTROSCT are rare uterine tumours. The former behaves as low grade sarcoma; whereas the later, should also be regarded as low grade malignant tumour. Follow up is required.

PS-10-023
HPV detection by the Gene Xpert (Cepheid®) HPV cytology assay applied on the Formalin Fixed Paraffin Embedded (FFPE) material in the cervical bioptical samples
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Objective: the GeneXpert-HPV-assay® is a validated genotyping test of Human Papilloma Virus for cervical cytologic samples based on the cartridge. The aim was to determine the suitability of an easy method of extraction of HPV nucleic-acid (NA) from FFPE cervical-biopsy for genotyping with GeneXpert-HPV-assay®.
Method: a total of 53 cervical biopsies with clinical history HPV-HR infections were extrapolated from cervical cancer screening database (Negative:20 cases, ASC-US:10 cases, L-SIL:14 cases,

H-SIL:9 cases) and 10 μm sections were assessed. The sections were deparaffinised with Xylene in oven, pretreated with 4 cycles in microwave-oven with Citrate buffer at pH6 (Dako®), than treated with Proteinase-K at 37 °C (Vysis-Protease-Abbott®). Tissue slices were detached from the slides, suspended in fixative solution (PreservCyte-Hologic®). The results are matched with in situ-HPV status (Confirm-HPV-Roche®) and p16/Ki67 immunohistochemistry (IHC-Roche®).
Results: 42/53 FFPE samples (79 %) gave valid GeneXpert-HPV-assay® results and in 38 of 42 FFPE (90 %) the results were completely concordant (Cohen's kappa: 0,808). The p16/ki67 IHC status had an agreement with the GeneXpert-HPV-assay® of 90 %.
Conclusion: GeneXpert-HPV-assay® is a fast, easy and reliable test for HPV identification in FFPE samples, working on lysate obtained from cervical biopsies, and correlates with p16/Ki67 IHC status.

PS-10-024
Papillary thyroid carcinoma arising in ovarian strumal carcinoid
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Objective: Thyroid-type papillary carcinoma and strumal carcinoid are the most common neoplasms arising in struma ovarii. However, the coexistence of papillary thyroid carcinoma and strumal carcinoid is extremely rare.
Method: We experienced a case of papillary thyroid microcarcinoma arising in strumal carcinoid.
Results: A 40-year old female presented with a 6 cm-sized, left ovarian solid mass. The cut surface was yellow to white and fibrotic. Microscopically, the tumour was composed of a follicular variant of papillary thyroid microcarcinoma and a strumal carcinoid. The carcinoid tumour was an admixture of trabecular carcinoid and colloid-containing, thyroid follicle-like structure lined by carcinoid cells. The follicle-forming carcinoid cells showed both thyroid and neuroendocrine differentiation (positive for TTF-1, thyroglobulin, CD56, chromogranin and synaptophysin). Benign thyroid follicles or teratoma were not identified. Our patient showed no evidence of local recurrence or distant metastasis at 10 year follow-up.
Conclusion: Strumal carcinoid is universally benign, with rare exceptions. Thyroid- type carcinoma arising in strumal carcinoid should not be diagnosed as malignant strumal carcinoid to avoid suboptimal treatment and miscommunication. The prognosis of papillary thyroid carcinoma arising in strumal carcinoid is still unclear because of its rarity, but might have a favorable prognosis.

PS-10-025
Variables predicting persistent and/or recurrent squamous intraepithelial lesions of the cervix after large loop excision of transformation zone
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Objective: The intent of this study was to determine variables that may predict the rate of persistence and/or recurrence of squamous intraepithelial lesions (SIL) of the cervix in patients undergoing the large loop excision of transformation zone (LLETZ) procedure.
Method: We performed a retrospective review of histological results of all women treated by LLETZ procedure at General Hospital Celje from January 2013 until December 2015.
Results: Residual and/or persistent disease was observed in 8.9 % (58/653) of women included in our study. Multivariate analysis showed patients' age, positive endocervical and overall excision margins and worse definitive histological diagnosis (high grade cervical intraepithelial neoplasia or invasive carcinoma) to be statistically significant ($p < 0.001$) in predicting higher recurrence/persistence rate, whereas positive ectocervical excision margin was not quite statistically significant ($p = 0.0447$) and cone depth was not statistically significant at all ($p = 0.181$).
Conclusion: Majority of our findings are in accordance with results of other studies reported so far. Different variables can help identify an important subset of women requiring careful follow-up after LLETZ procedure to successfully treat persistent or recurrent disease.

PS-10-026
Adenocarcinoma arising in sacrococcygeal mature teratoma in a 44-year-old female
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Objective: Sacrococygeal teratoma (SCT) is an extragonadal germ cell tumour which is generally diagnosed in infants. It is seen in adults very rarely. Even it has no immature component, can be fatal by carcinomatous transformation.
Method: We report a case of a 44-year-old female patient with adenocarcinoma arising from mature SCT 1 year after the first diagnosis.
Results: Pelvic magnetic resonance imaging (MRI) revealed a perirectal heterogenous, mainly cystic tumour. Histomorphologically, a multiloculated cyst consistent with mature teratoma was present. One year later MRI demonstrated a pelvic cystic lesion with no solid or invasive component radiologically. Surgical resection specimen contained two separate cysts measuring 8 × 3 × 0,6 cm and 4 × 3 × 1cm. On histomorphological examination, adenocarcinoma infiltrating the wall of the larger cyst and invading the bony compartments was identified. Along with the malignant component, some parts of the cyst walls were lined by squamous and columnar epithelium. Nine months after the diagnosis of adenocarcinoma, multiple metastasis to liver, lymph nodes and skin developed and the patient died 2 years after the first diagnosis.
Conclusion: SCT should be considered in the differential diagnosis of presacral tumours in adult age group. Complete resection and close follow-up is crucial for the patient management due to its rare but fatal consequences.

PS-10-027
Endometrial expression of Leukemia Inhibitory Factor (LIF), LIF-Receptor and HOXA-11 but not HOXA-10 is significantly impaired in women with unexplained infertility during implantation window
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Objective: Main objective of the study was to define whether endometrial expression of HOXA-10, HOXA-11 and Leukemia Inhibitory Factor (LIF) with its receptor (LIF-R) is significantly different between fertile and infertile women during implantation window.
Method: >Women having delivered at least one alive newborn were the study's control group (fertile, group 1) while infertile women the patients' group (infertile, group 2). An endometrial biopsy was obtained on 7th-8th postovulatory day. Expression of HOXA-10, HOXA-11, LIF and LIF-R was assessed in both epithelial and stromal cells by immunohistochemistry. Primary outcome was h-score.
Results: Endometrial tissue was obtained by 20 fertile and 55 infertile women (22 with poor ovarian reserve, 13 with tubal infertility, 5 with endometriosis and 15 with unexplained infertility). Mean age was 31.1 + −4.8 years for group 1 and 37.5 + −3.8 for group 2 (P = .001). LIF and LIF-R h-score was significantly decreased in epithelial cells of infertile women compared with fertile controls (P = .05 and P = .006 respectively). No significant difference was observed regarding HOXA-10 and HOXA-

11 epithelial endometrial expression as well as stromal expression of all molecules between two groups. LIF, LIF-R and HOXA-11 epithelial h-score presented their lowest values in women with unexplained infertility.
Conclusion: Endometrial expression of LIF, LIF-R and HOXA-11 but not HOXA-10 is significantly impaired in women with unexplained infertility during implantation window. Our results indicate the significant role of HOXA-11, LIF and LIF-R in the aitiopathogenetic drawback complex of unexplained infertility.

PS-10-028

Immunohistochemistry expression of progesterone and avb3 integrins in the endometrium of fertile and infertile women

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Objective: Main objective was to study whether endometrial expression of Progesterone receptors type A and B and integrins avb3 differ significantly between fertile and infertile as well as within sub-groups of infertility during implantation window.
Method: Women having delivered at least one alive newborn during the last year consisted the control group (group 1) while infertile the patients' group (group 2). Infertile were also categorized to those with ovarian failure (group 2a), tubal factor (group 2b), endometriosis (2c) or unexplained infertility (group 2d). Endometrial biopsy was obtained by Pipelle on 7th-8th postovulatory day. Total progesterone receptors' (TPR), type-B receptors' (PRB) and integrins' avb3 expression was evaluated by immunohistochemistry. Primary outcome was h-score.
Results: Endometrial tissue was obtained by 20 fertile and 55 infertile women. Mean age was 31.1 ± 4.8 years for group 1 and 37.5 ± 3.8 for group 2 (P = .001). TPR and PRB expression was significantly decreased in epithelial cells of infertile women compared with fertile. No significant difference was observed in the epithelial expression of integrins avb3 (P = .52). Furthermore, no significant difference was observed regarding the expression of any biomarker in stromal cells. When adjusting for the cause of infertility, TPR and PRB epithelial expression were significantly decreased in sub-groups 2a and 2d.
Conclusion: Progesterone receptors' but not integrins' expression is significantly decreased in epithelial cells of women with unexplained infertility and poor ovarian reserve. Endometrial biopsy should be performed in all women intending to perform IVF in order to evaluate endometrial receptivity.

PS-10-029

Tubal-peritoneal junction as a trigger zone for high-grade serous carcinoma pathogenesis

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Objective: As many cancers occurs in transition zone between two types of epithelia tubal-peritoneal junction (TPJ) was also supposed to be predisposed for neoplastic changes.
Method: 150 patients (195 FTs) with extraovarian pathology (n = 30) and ovarian tumours (n = 120) were recruited. All fimbrial parts of FTs were investigated extensively. FTs were investigated morphologically and immunohistochemically (p53,Ki-67,PgR,E-cadherin). Student test with Bonferroni correction was used for statistics.
Results: 378 TPJ were verified. 40,6 % TPJ involved endosalpingeal plicae(43,6 % of them localized on the top of plica, 25,6 %—on the side of plica, 30,8 %—between plicae). Histologically TPJ was flat (52,1 %) convex (40,6 %), concave (7,3 %). Lymphatic/ blood vessels dilatation was diagnosed in most TPJ (closed to the basal membrane). Transition metaplasia was revealed in 33 %, Walthard nests—in 25 %, "ovarian" stroma adjunct to TPJ—in 2 % (out of TPJ—in 20 %). Serous tubal intraepithelial carcinoma (STIC) was diagnosed in patients with serous carcinoma (in 30 %). In 53,3 % of patients STIC was revealed adjunct to TPJ, in 33,3 %—in the fimbrial part of FT (out of TPJ), in 13,3 %—out of fimbrial part ($p < 0,05$).
Conclusion: TPJ is supposed to be an analogue of the transition zones in other organs (gastro-esophageal, cervical squamo-columnar). Proximity of STIC to TPJ in most cases proved the hypothesis about TPJ to be a "hot spot" for pelvic high-grade serous ovarian carcinogenesis. The study results carried on the funds received from RFBR (Project 16 16-34-00666/16).

PS-10-030

A histopathologic review of ovarian germ cell tumours at the Lagos University Teaching Hospital, Nigeria

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Objective: Germ cell tumours are the commonest ovarian neoplasms in developing countries yet little has been published regarding their histologic characteristics in our setting. We aimed to evaluate all the ovarian germ cell tumours within a specified period.
Method: All the ovarian germ cell tumours received in the Department of Anatomic and Molecular Pathology, Lagos University Teaching Hospital from January 1991 to December 2013 were retrieved and characterized
Results: 355 patients with germ cell tumours were seen within the study period. This accounted for 52.5 % of all primary ovarian neoplasms. Of these, 314 (88.5 %) were benign and 41 (11.5 %) were malignant. Mature cystic teratoma was the commonest benign germ cell tumour accounting for 99 % of cases. Yolk sac tumour was the commonest malignant germ cell tumour (34.1 %), followed by immature teratoma (29.3 %) and dysgerminoma (17.1 %). The mean size of mature teratomas was 10.9 cm, 15.3 % underwent torsion, 1.8 % ruptured and 0.8 % underwent malignant transformation. Ectodermal, mesodermal and endodermal derivatives were seen in 100, 66.4 and 28.3 % of cases respectively.
Conclusion: Ovarian germ cell tumours are relatively common in our environment. Benign teratomas occur at a younger age, tend to be larger and are more likely to undergo complications than cases from developed countries

PS-10-031

Mesenchymal tumours of the cervix: Clinicopathological characteristics of 28 cases

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Objective: Mesenchymal tumours are rarely encountered in the uterine cervix, where they constitute less than 1 % of all malignancies. We investigate the clinicopathological characteristics of 28 cases of mesenchymal tumours of the cervix.
Method: A retrospective analysis of the clinical data and morphological features of 28 consecutive cases of mesenchymal cervical tumours diagnosed in our Departments between January 1995 and December 2015 was done.
Results: The mean age of the patients were 47 (range, 29–63). Benign tumours are more frequent (17 cases). The most commonly reported benign mesenchymal tumours, listed in order of decreasing frequency, are leiomyoma (9 cases), fibro epithelial tumours (4 cases) lipoma (1 case), neurofibroma (1 case) and adenomyoma (1 case). The most commonly reported mesenchymal malignancies were leiomyosarcoma (8 cases) associated to rhabdomyosarcoma, adenosarcoma and undifferenciated sarcoma reported with almost equal frequency (1 case).
Conclusion: Each of the aforementioned lesions is associated with a relatively distinct clinicopathologic profile. Distinction between these

entities is important because therapeutic care and prognosis differ, and each case must be evaluated within the context of the reported cases of that specific histologic subtype.

PS-10-032

Histone deacetylase (HDAC) 1, 2, 3, 4, 6 and PhosphoHDAC4/5/7 expression in uterine carcinosarcomas

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Objective: Histone deacetylases (HDACs) are critical regulators of gene expression and have been shown to be overexpressed in many human malignancies, including uterine carcinomas and sarcomas. HDAC inhibitors (HDACi) are promising therapeutic agents. We aim to characterize HDAC1,2,3,4,6 and PhosphoHDAC4/5/7(PhosphoHDAC) immunoprofiles in the different morphological components of uterine carcinosarcomas(UCS) and its association with clinicopathological parameters.
Method: HDAC1,2,3,4,6 and PhosphoHDAC immunohistochemistry was performed in tissue microarrays using 55 UCS and 17 UCS metastases from 55 patients(462 cores). Quantitative and qualitative score were evaluated and combined into an immunoreactivity score.
Results: HDAC1,2,3,4 and 6 were expressed in the majority of tumours[HDAC2(80 %) > HDAC4(78 %) > HDAC1(71 %) > HDAC3(55 %) > HDAC6(53 %)], albeit with different immunoreactivity mean scores[HDAC4(7.04) > HDAC2(6.25) > HDAC1(5.15) > HDAC3(4.44) > HDAC6(2.84)]. There was a strong positive significant correlation of expression of HDAC1,2 and 3 between the epithelial and mesenchymal components($rs > 0,5$, $p < 0,001$), although immunoreactivity scores of HDAC1, PhosphoHDAC(cyt) and HDAC6 were significantly higher in the epithelial component ($p < 0,05$). A strong positive correlation between the expression of HDAC3 and HDAC1,2 and 4 and between phosphoHDAC and HDAC1 and 4 ($rs > 0.5$, $p < 0.001$) was found. Increased expression of HDAC4 in the mesenchymal component was independently associated with an improved overall survival on univariate analysis ($p < 0.05$).
Conclusion: The consistent overexpression of HDACs in both components of UCS supports further investigation of HDACi in the clinical setting, namely in clinical trials.

PS-10-033

Disease distribution in low-stage tubo-ovarian high-grade serous carcinoma (HGSC): Implications for assigning primary site and FIGO stage

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Objective: To examine sites and patterns of disease in low-stage tubo-ovarian high grade serous carcinoma (HGSC). FIGO staging encompasses primary site ascertainment (tubal/ovarian/peritoneal). This is difficult in advanced cases where multiple sites are involved. Less than 10 % of extrauterine HGSC present at stage I/II. Early stage cases allow assessment of disease before wide dissemination, with implications for specimen handling, staging and site assignment.
Method: Anonymised pathology reports of 67 Stage I and II HGSCs from 6 teaching hospitals were analysed. Stage, sites/pattern of involvement, site/size of largest focus and laterality of tubal and ovarian involvement were recorded.
Results: Ovarian involvement without any tubal component was only present in 12/67 (18 %). Bilateral ovarian involvement (66 %) was significantly higher than bilateral tubal involvement (13 %) ($p = 0.012$, Fisher's exact test). There is a trend towards fewer stage I compared to stage II tumours in this study in comparison with historic series.
Conclusion: Identification of tubal disease in 82 % cases, and significantly higher bilateral (suggesting metastasis) ovarian as compared to tubal involvement, both support a tubal origin of most HGSC. Detailed tubal sampling according to current protocols will alter stage distribution in low-stage disease, through detection of microscopic tubal involvement in apparent stage I cases.

PS-10-034

Smooth muscle tumours of the uterine cervix: A clinicopathologic study of 10 cases

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Objective: Smooth muscle tumours (SMT) of the uterine cervix (UC) are rare neoplasms. They consist on leiomyomas and leiomyosarcomas. Leiomyosarcoma of the uterine cervix is extremely rare, with only 25 cases reported in the literature. Its diagnosis is only based on pathologic examination. Our aim is to determine the epidemiologic, clinicopathologic and therapeutic features of cervical SMT.
Method: Among 1435 SMT diagnosed in La Rabta from 1995 to 2015, ten cases of SMT of the uterine cervix are reported. A retrospective study was made based on these 10 patients files and histopathological reports.
Results: In our study, nine patients were diagnosed with leiomyoma and only one with leiomyosarcoma. Mean age was 44.5 years for leiomyoma patients. Leiomyosarcoma patient was 60 years old. Abnormal vaginal bleeding was the most common presenting symptom. Grossly, mean tumour size was 5 cm. Seven patients had total abdominal hysterectomy. Three patients underwent vaginal myomectomy.
Conclusion: Leiomyosarcoma of the uterine cervix is a rare tumour associated with a poor prognosis. We emphasize the importance of sampling all the leiomyomas in order to detect malignant histological features.

PS-10-035

Comparision between two molecular assays (GeneXpert®HPV-Cepheid® vs. Hybrid-Capture2®, hc2-Qiagen®) for detection of HPV-HR and LBC, in a selected women aged screening population (age lower 35 and over 35)

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Objective: We compared the performances of two High Risk HPV molecular assays (GeneXpert ® HPV- Cepheid® vs. Hybrid Capture2®, hc2-Qiagen®) in a group of women aged screening and separately for under 35 and over 35 women. Each molecular assay was compared to Pap-test liquid based cytology (Thin Prep®-Cytyc).
Method: A total of 122 samples selected from women aged 24–65, divided into two age groups (37 under 35 and 85 over 35), were tested with GeneXpert®HPV and hc2® methods. Agreement between assays was assessed. Of each sample was carried out also cytology.
Results: High degree of agreement between two assays has been found in the group as a whole (89 %) and separately for women under 35 (81 %) and over 35 (93 %); with Cohen's K of 0.746, 0.621 and 0.780 respectively. Overall agreement with cytology decreased as absolute value for both methods, with a Cohen's K of 0.508 for GeneXpert®HPV and 0.509 for hc2®, presenting a significantly lower value for GeneXpert®HPV in women under 35, with a Cohen's K of 0.360.
Conclusion: Our data suggested that performance of GeneXpert®HPV cartridge assay was comparable to hc2® test in all aged screening population while providing disagreement with cytology in women under 35.

PS-10-036

Paget disease of the vulva: Immunohistochemical analysis of neoangiogenesis and EMT-related markers with clinical-pathological correlation

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Objective: To evaluate the presence of neoangiogenesis and epithelial-mesenchymal transition (EMT) markers expression in Paget disease of the vulva (PDV) and to verify their role in the pathogenesis of the disease and as potential predictors of recurrence.
Method: 18 cases of PDV, including 10 invasive cases, were analysed for microvessels density (MVD) using CD31 immunohistochemical staining and for the expression of E- / N-cadherin, b-catenin and SLUG. Hot spots of neovascularisation containing the highest number of capillaries and small venules were identified at low power, five fields in each section with the highest number of hot spots were selected. The highest vessel density (HVD) and the average vessel density (AVD) of five fields at ×200 and ×400 was recorded.
Results: AVD at 200x and 400x and HVD at 400x were significantly associated with invasive PDV ($p = 0.029$, 0.05, 0.033 respectively), whereas N-cadherin expression showed a trend with invasive disease ($p = 0.063$). No significant relation between MDV and EMT-markers expression and recurrence rate at 6, 12 and 24 months was found.
Conclusion: These results show that neoangiogenesis, measured as MVD, may be involved in the growth and progression of PDV. EMT could also be related to invasion but larger series are needed.

PS-10-037

The cervical smear epithelial cell abnormality data of 354,725 patients from 38 pathology laboratories and 45 hospitals in Turkey

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Objective: There is no other screening program to have the success of PAPtest. Cervical cytology constitutes a large workload so that quality control in cervical cytology is important for the quality assurance (QA) of the pathology laboratories.In this study, we aimed to collect the cervical cytology results from all over Turkey, and discuss the parameters influencing the quality of the PAPtest.
Method: The study proposal was conducted with Turkish gynecopathology working group and 38 centers (totally 45 hospitals) from 24 different cities agreed to contribute. Study was designed to cover the cervical cytology results during 2013. We conducted an online questionnaire and evaluate the results.
Results: The total number of ECA was 18,020 and the global Epithelial Cell Abnormality(ECA) rate was 5,08 % in the total 354,725 smears and among centers, 0,3–16,64 %. The ASC/SIL ratios changed 0,21–13,94 with an average 2,61. When the centers were asked whether they perform QA studies, 25 centers shared the information, only 11 had a such control study.
Conclusion: There is an increase in ECA rate. There are great differences among centers. Quality control studies including ASC/SIL is important. Corrective and preventive action according to quality control parameters is a must. Cervical cytology subspeciality in every center can be imaginary but dedicated pathologists to the cervical cytology should be discussed.

PS-10-038

Low grade endometrioid stromal sarcoma of the uterus: A clinico-pathological study of 8 cases

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Objective: To determine the epidemiological, clinicopathological characteristics and outcome of uterine low grade endometrial stromal sarcoma (LGESS) in Central Tunisia.
Method: It is a retrospective study of 8 cases of LGESS collected from the Cancer Registry of central Tunisia over a 10-year-period (1996–2010).
Results: Age ranged from 26 to 52 years. The most common symptom was menometrorrhagia. Clinical examination revealed an enlarged uterus, vaginal bleeding andleucorrhoea in respectively 4, 2 and 1 cases. At imaging, initial diagnosis was in all the cases a leimyoma. The final diagnosis was established after endometrial biopsies, curettings or on hysterectomy surgical specimens. At immunohistochemistry: CD10, desmin and WT1 were positive in respectively 6, 4 and 5 cases. SMA was positive in 7 cases. According to the FIGO classification, the tumour stage was: IA in 3 cases, IC in 4 cases and IIB in one case. All patients underwent hysterectomy. Adjuvant treatment included chemotherapy for 2 patients and radiation therapy for 4 patients. Hormonal therapy was indicated for one patient. Five patiens had a favorable outcome and 3 died.
Conclusion: LGESS is a malignant uncommon tumour, occuring in young to middle-aged women, with no specific symptomatology. Its diagnosis is histopathological.

PS-10-039

Mammary serine protease inhibitor and CD138 immunohistochemical expression in ovarian serous and clear cell carcinomas

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Objective: To investigate the immunohistochemical expression of mammary serine protease inhibitor (maspin), and CD138 in primary ovarian high grade serous carcinomas (HGSC) as compared to low grade serous carcinomas (LGSC) and clear cell carcinomas and investigate if the studied markers have a correlation to FIGO stage, Ki67 proliferation index and to each other.
Method: Immunohistochemical expression of mammary serine protease inhibitor (maspin), and CD138 in primary ovarian high grade serous carcinomas (HGSC) as compared to low grade serous carcinomas (LGSC) and clear cell carcinomas was performed and correlated to FIGO stage, Ki67 proliferation index and to each other.
Results: Maspin cellular location varied significantly between studied groups with only nuclear expression seen in 46.7 % of LGSC group, mixed nuclear & cytoplasmic in 13.3, 28.6, 20 % of LGSC, HGSC and clear cell carcinoma respectively and was only cytoplasmic in 26.7, 71.4, 80 % of LGSC, HGSC and clear cell carcinoma respectively. Mean maspin and CD138 counts were significantly higher in HGSC and clear cell carcinoma compared to LGSC. Both maspin and CD138 scores varied significantly between studied groups and were positively correlated with adverse prognostic factors in studied carcinomas including FIGO stage, Ki67 proliferation index. Besides, both maspin and CD138 had significant correlation to each other.
Conclusion: These findings suggest that epithelial cytoplasmic expression of maspin and CD138 may have a significant role in tumourigenesis in ovarian high grade serous carcinomas and clear cell carcinomas; these markers may regulate tumour cell proliferation and their significant correlation to each other may suggest that CD138 probably induces maspin expression to protect tumour growth factors from being lysed by proteolytic enzymes.

PS-10-040

The role of estrogen receptor subtypes (alpha, beta and GPR30) in endometrial carcinogenesis

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Objective: Endometrioid adenocarcinomas are estrogen (ER) dependent cancers and preceded by atypical hyperplasia under hyperestrogenic

effect. The purpose of the study was to evaluate the alterations of estrogen receptor subtypes (ERα, ERβ and more recently defined G-protein-coupled estrogen receptor- GPR30) on endometrial hyperplasia—carcinoma sequence and their potential role on the endometrial effects of Tamoxifen (TAM) treatment.
Method: 30 normal endometrium, 45 endometrial hyperplasia, 30 endometrioid carcinoma, 30 endometrial polyps (15 TAM related polyp) were included in the study. Immunohistochemistry was performed by using ERα, ERβ and GPR30 antibodies and immunoreactivity scores were calculated for each case by multiplying the percentage of positive cells by the intensity of staining.
Results: GPR30 expression showed statistically significant increase ($p = 0.00$) on the endometrial hyperplasia—carcinoma sequence whereas no such relation was found for ERα or ERβ. Endometrial polyps related with prolonged TAM treatment (≥3 years) showed significantly lower ERβ expression ($p = 0.02$) and higher GPR30 expression ($p > 0.05$) than TAM unrelated polyps.
Conclusion: GPR30 receptor seems to play a role on endometrial carcinogenesis and TAM induced endometrial abnormalities. And it may be speculated that the ERβ receptor downregulation contributes to the proliferative effects of TAM on endometrium, as its antiproliferative effects by interacting other estrogene receptors have been shown by some studies.

PS-10-041
Malignant tumour associated with ovarian mature teratoma: A single institution experience
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Objective: We aimed to present clinicopathological features and of cases diagnosed with malignant tumour associated with ovarian mature teratoma.
Method: Single-institution retrospective charts were reviewed to identify all cases of ovarian mature teratoma diagnosed from 1998 to 2015.
Results: A total of 218 ovarian mature teratoma cases were identified during the study period. Of the 218 ovarian mature teratoma specimens, eight (3.7 %) exhibited malignant tumours. The average age for cases of malignancy associated with ovarian mature teratoma was 44.6 years. The average size of tumours was 10.36 cm. On final pathology, histological types of tumours were as follows: two cases each of squamous cell carcinoma and papillary thyroid carcinoma; one case each of mucinous adenocarcinoma, metastatic adenocarcinoma, sebaceous carcinoma and oligodendroglioma. Only one patient died of disease. One patient was alive with metastatic disease 2 months after initial diagnosis. Mean and median follow-up times were 64.1 and 49 months, respectively.
Conclusion: An ovarian mass that has characteristics of a teratoma in a postmenopausal patient should alert for malignancy -regardless of tumour size. Intraoperative consultation is a valuable tool for the detection of malignancy and should be requested to determine the modality of surgical approach.

PS-10-042
Heterogeneity of caveolin expression in ovarian carcinoma
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Objective: Our study aimed to analyze caveolin expression in ovarian cancer (OC), in correlation with clinico-morphological parameters and survival.
Method: 64 cases of OC histopathologically diagnosed as serous (44 cases), endometrioid (7 cases), clear cells (2 cases), mucinous (9 cases), and undifferentiated (2 cases) were immunohistochemically processed using anti-caveolin antibody. Semi-quantitative evaluation was based on two criteria: positive cells percentage and staining intensity.
Results: Caveolin expression was positive in 26 cases (40.62 %), of which 18 were serous, 4 cases—endometrioid and 4—mucinous carcinoma. Intensity of reaction was mostly moderate or weak. 38 cases (59.38 %) were negative. We recorded caveolin positivity in 5 of 12 cases graded G1, 12 of 24 cases graded G2 and 9 of 26 cases graded G3. Caveolin was positive in 8 of 18 cases in stage I, 3 of 6 cases in stage II and 15 of 40 cases in stage III. Statistical analysis revealed significant differences only between caveolin expression and disease free survival for stage III ($p = 0.01$).
Conclusion: Our data supports the heterogeneity of caveolin expression in accordance with histologic subtype, tumour grade and stage. Loss of caveolin expression may be assessed as indicator for tumour progression.

PS-10-043
Detection of high risk human papillomavirus in vaginal cytology from patients underwent total hysterectomy for cervical intraepithelial neoplasia grade 2 or worse (CIN2+)
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Objective: Persistent high risk human papillomavirus (HrHPV) infection is the most salient risk factor for the recurrence of cervical intraepithelial neoplasia (CIN), from which vaginal intraepithelial neoplasia (VAIN) and vaginal cancer can develop. This study evaluated the clinical performance of the HrHPV and 16/18 genotyping tests for detection of HPV in vaginal cuff cytology and to describe vaginal pathology after total hysterectomy (TH).
Method: A total of 121 patients who underwent a TH due to CIN2+ in Health Sciences University of Istanbul Umraniye Training and Research Hospital from 2013 to 2016. All the patients were followed up within 1–20 years after hysterectomy and vaginal samples were tested using cytological diagnostics with a PAP test and for Cervista HrHPV testing. HPV 16/18 genotyping test also performed.
Results: Out of 121 HR HPV tests, the results of 80.1 % (97/121) tests were negative and 19.8 % (24/121) tests were positive. Compared with concordant positive results (HPV positive/Pap positive), providers were more likely to perceive that discordant results (HPV positive/Pap negative) would be too complex for patients to understand (10.7 vs. 9 %). HPV16/18 were detected in 4.9/0.8 % of the cases.
Conclusion: HPV infection can cause vaginal cancer after complete hysterectomy in cases complicated by CIN. HPV should be regularly assessed during the postoperative follow-up period. Primary HPV screening followed by cytological triage could be the optimal strategy to identify VAIN in poor screening attenders.

PS-10-044
Intratumoural heterogeneity of endometrial carcinomas
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Objective: Intratumoural heterogeneity (ITH) is important for diagnosis, prognosis and theranostic purposes. There are few studies of ITH in endometrial carcinoma (EC). Aim: to evaluate ITH of morphometric and immunohistochemical parameters in EC.
Method: Cases series of 10 EC: 8 endometrioid (6-G1, 2-G2), 1 serous and 1 mixed serous/clear cell. Digital image analysis of 20 tumour spots per case. Morphometric and immunohistochemical parameters analyzed: relative percentage of tumour cells;

volume-weighted mean nuclear volume; ER, PR, vimentin and beta-catenin immunoexpression. Statistical measures used: coefficient of variation (CV) and quadratic entropy index (QE).
Results: Relative percentage of tumour cells—mean CV: 0.10 (range 0.05, 0.19), mean QE: 18.5. Volume-weighted mean nuclear volume—mean CV: 0.23 (range 0.16, 0.34), mean QE: 27.3. ER H-score—mean CV: 0.56 (range: 0.17, 1.22), mean QE: 46.2; PR H-score—mean CV: 0.60 (range: 0.09, 1.60), mean QE: 39.3; Vimentin H-score—mean CV: 0.71 (range: 0.24, 1.51), mean QE: 32.6; Beta-catenin H-score—mean CV: 0.55 (range 0.19, 1.35), mean QE: 38.9.
Conclusion: EC seem to present variable, mostly low degree of ITH for the morphological and immunohistochemical parameters evaluated, namely in endometrioid subtype. Nevertheless, larger series and more markers are warranted to clarify ITH in endometrial carcinomas.

PS-10-045
Are eosinophils a specific marker of chronic endometritis?
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Objective: Chronic endometritis is associated with abnormal uterine bleeding and infertility. The gold standard is identification of plasma cells, but this can be difficult. CD 138 immunostain is helpful in identifying plasma cells, but adds time and expense. It has been suggested that the more easily identified eosinophils are a surrogate marker for plasma cells. We hypothesized that eosinophils are not a specific marker of chronic endometritis.
Method: The Pathology database at University Hospital, Newark NJ, was searched for cases of chronic endometritis from 1/1/91-8/1/15. Controls were endometrial biopsies that were proliferative or showed disordered proliferation. Slides were evaluated to confirm the prior diagnosis, and to determine the presence of eosinophils.
Results: 50 cases and 50 controls were reviewed. Sixty-two percent of cases had eosinophils present and 38 % did not whereas in controls 38 % had eosinophils and 62 % did not (Fisher's exact test $p = 0.03$).
Conclusion: While eosinophils were more likely seen in chronic endometritis, they were frequently seen in controls as well. The presence of eosinophils is not a specific marker of chronic endometritis.

PS-10-047
Histological characteristics of Human Papillomavirus-associated and -independent squamous cell carcinomas of the vulva: A study of 1636 cases
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Objective: There are two etio-pathogenic pathways for the development of vulvar squamous cell carcinomas (VSCC), one associated with infection by human papillomavirus (HPV); and another independent of HPV. We aimed to determine whether there are any differential characteristics between the two types in a large series of tumours.
Method: We analyzed 1636 VSCCs. The study included HPV/DNA detection, histological review and p16 immunohistochemistry.
Results: 452 tumours (27.6 %) HPV-positive were basaloid (35.9 %), warty (8.4 %) or non-keratinizing (13.3 %); 42.0 % were keratinizing. HPV-negative tumours were keratinizing (78.1 %); basaloid (5.0 %), warty (2.9 %) or non-keratinizing (12.4 %). Vulvar intraepithelial neoplasia (VIN) was in 68.2 % of the HPV-positive tumours; 51.9 % of the HPV-negative tumours. 85.6 % of the VIN lesions in HPV-positive tumours were of the usual type;14.3 % were differentiated. Conversely, 87.2 % of the VIN lesions in the HPV-negative tumours were of the differentiated type; 12.8 % of them were basaloid/warty. Although several characteristics were frequently associated with HPV-negative VSCC, none allowed differentiation. p16 was positive in 82.0 % of the HPV-positive; 8.4 % of the HPV-negative tumours ($p < 0.001$).
Conclusion: Histological criteria do not allow differentiation between HPV-positive and -negative VSCC. p16 is a good surrogate marker of HPV in the absence of HPV DNA detection.

PS-10-048
Is invasive micropapillary serous carcinoma a low-grade serous carcinoma?
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Objective: "Invasive micropapillary serous carcinoma" has been proposed as a synonym for low-grade serous carcinoma (LG-SC). Although it appears that invasive micropapillary areas in some serous carcinomas exhibit high-grade nuclear atypia, the molecular features of such tumours have not been well characterized. The aim of this study was to verify appropriateness of using the term "invasive micropapillary serous carcinoma" as a synonym for LG-SC.
Method: We selected 24 "serous carcinomas with conspicuous invasive micropapillary pattern (SC-IMPs)" and investigated: 1) their morphological features, 2) the immunostaining pattern of p53 protein, and 3) KRAS/BRAF/TP53 gene mutations.
Results: The 24 SC-IMPs were subdivided into low-grade and high-grade tumours based primarily on the nuclear atypia, with the mitotic rate used as a secondary feature: low-grade ($n = 5$), high-grade ($n = 19$). Low-grade SC-IMPs were characterized by low mitotic activity, absence of abnormal mitosis, presence of serous borderline tumour, occasional BRAF mutation, and infrequent TP53 mutation. High-grade SC-IMPs were characterized by high mitotic activity, presence of abnormal mitosis, conventional high-grade serous carcinoma (HG-SC), frequent TP53 mutation and lack of KRAS/BRAF mutation.
Conclusion: Using the term "invasive micropapillary serous carcinoma" as a synonym for LG-SC is misleading, since HG-SC can show conspicuous invasive micropapillary pattern.

PS-10-049
Diagnostic morphological and immunohistochemical features of molar pregnancies and their relations to the progression to persistent gestational trophoblastic disease
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Objective: To differentiate molar (complete hydatidiform mole (CHM) and partial hydatidiform mole (PHM)) and non molar pregnancies on the basis of routine histopathological criteria and expression pattern of p57Kip2 by immunohistochemistry. Also, to determine whether any of these features can predict clinical behavior and progression to persistent gestational trophoblastic disease (PGTD).
Method: Archival materials of 65 cases of products of conceptions (POCs) were revised histopathologically. The tissue sections were also stained immunohistochemically with antibodies against p57Kip2. Follow-up data concerning progression to PGTD were investigated.
Results: Certain histopathological criteria were found significant in differentiation between CHM and PHM. These include villous shape and

outline, villous trophoblastic hyperplasia and atypia at extravillous trophoblasts. P57Kip2 immunohistochemistry was statistically significant in diagnosis of CHM and distinguishing it from PHM and non molar cases. There were no significant differences in any morphological or immunohistochemical features between cases with or without subsequently developed of PGTD.
Conclusion: The diagnosis of molar pregnancies should be stated after constellation of specific histopathological criteria, especially in early gestational age, in order not to miss a diagnosis of CHM. P57Kip2 immunohistochemistry is valuable in diagnosis of equivocal cases. However, there were no significant features to predict subsequent developed to PGTD.

Tuesday, 27 September 2016, 09.30–10.30, Hall 11.3
PS-11 Haematopathology

PS-11-001
Accuracy of Fine Needle Aspiration Biopsy in diagnosing malignant lymphadenopathy in Yogyakarta, Indonesia
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Objective: Lymphadenopaty is an enlargement of lymph node might be caused by infection, cancer, or autoimmune disease. Only few studies reported diagnostic value of FNAB in lymphadenopathy. This study was performed to provide the diagnostic value of FNAB in diagnosing malignant lymphadenopathy in Sardjito Hospital, Yogyakarta, Indonesia, from January 2012 until December 2014.
Method: This study is a retrospective study with cross-sectional design. Analysis is performed using SPSS program and table 2 × 2 to analize the sensitivity, specificity, and accuracy.
Results: From 57 collected cases, 37 (64,9 %) are malignant lymphadenopathy, consisting 21 metastatic tumour cases, 13 non-Hodkin lymphoma cases, and 3 Hodkin lymphoma cases. The overall diagnostic sensitivity, specificity, and accuracy of FNAB in lymphadenopathy are 78,39, 65, and 73,68 %, respectively. In diagnosing metastatic tumour, FNAB has sensitivity of 90,48 %; specificity of 90,63 %; and accuracy of 90,57 %. The sensitivity, specificity, and accuracy of FNAB in diagnosing non-Hodgkin lymphoma are 58,33 %; 95,12 %; and 86,79 % respectively. In diagnosing Hodgkin lymphoma, FNAB has sensitivity of 33,33 %; specificity of 98 %; and accuracy of 94,34 %. The accuracy of FNAB in diagnosing malignancies in generalized lymphadenopathy, head-neck lymphadenopathy, and inguinal lymphadenopathy are 81,82 %;70 %;and 40 % respectively.
Conclusion: FNAB has low-moderate diagnostic value in diagnosing malignant lymphadenopathy. High diagnostic value of FNAB (>90 %) is found in diagnosing metastatic tumour. Meanwhile, FNAB has limitedness in diagnosing Non-Hodgkin lymphoma and Hodgkin lymphoma, with sensitivity for both less than 60 %.

PS-11-002
The utility of fascin and CD83 in the differential diagnosis of mediastinal large B-cell lymphomas
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Objective: Classical Hodgkin Lymphoma (CHL) and primary mediastinal large B-cell lymphoma (PMBL) are the most common large cell lymphomas arising in the mediastinum and these diseases are thought to be closely related histogenetically. Although the distinction between CHL and PMBL is usually straightforward, some cases have overlapping features and qualify as mediastinal gray zone lymphoma (GZL). Fascin and CD83 are markers of histiocytic/dendritic cells that are frequently positive in CHL, but their expression in PMBL and GZL is less well known.
Method: We retrospectively collected cases of PMBL, CHL and GZL from three institutions. Tissue sections prepared from formalin-fixed paraffin-embedded blocks were stained with fascin and CD83 using routine immunohistochemical methods.
Results: Fascin was positive in neoplastic cells of 100 % (22/22) of CHL, 86 % (18/21) of GZL and 32 % (7/22) of PMBL. Similarly, CD83 was expressed in neoplastic cells of 100 % of CHL (11/11), 93 % of GZL (16/18) and 43 % (9/21) of PMBL. The number of cases assessed with the two markers was variable because of the unavailability of unstained tissue sections of paraffin blocks in some cases.
Conclusion: Fascin and CD83 are very sensitive markers for CHL but they are not specific. Negative results would support PMBL or GZL over CHL. A large panel of immunohistochemical markers is still recommended to distinguish the three entities, in which fascin and CD83 are of additive value.

PS-11-003
CD30 and IgG4 are useful diagnostic markers of sclerosing angiomatoid nodular transformation of the spleen
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Objective: Sclerosing angiomatoid nodular transformation (SANT) is a benign but rare lesion of the spleen, and the etiology is still unknown. In this study, we investigate the usefulness of CD30 and IgG4 as potential diagnostic markers.
Method: We collected various vascular tumours of the spleen, including hemangioma, lymphangioma, littoral cell angioma, splenic hamartoma, Kaposi sarcoma, angiosarcoma, and SANT. The expression of CD30 on endothelial and stromal cells and the number of IgG4+ plasma cells are evaluated.
Results: SANT exhibited expression of CD30 (1~3+) on the endothelial and stromal cells, whereas none of the other vascular lesions expressed CD30 on the endothelial or stromal cells. The average number of IgG4+ plasma cells and IgG4 ratio were significantly higher in SANT compared to the other splenic vascular lesions.
Conclusion: Our study showed that the combination of CD30 and IgG4 immunostains can be helpful in distinguishing SANT from other vascular lesions of the spleen. The expression of CD30+ endothelial and stromal cells and high IgG4+ plasma cell count also suggests that SANT might be a form of IgG4-related sclerosing disease.

PS-11-004
Evaluation of P53 protein expression in patients with Myelodysplastic Syndrome (MDS): Prognostic impact
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Objective: MDS is a disorder of hematopoietic stem cell, which risks to progress in acute leukemia. It is essential a good prediction of the risk of the evolution towards acute leukemia (according to IPSS-R). Strong nuclear staining of the p53 protein by immunohistochemistry has been used as a surrogate marker for TP53 gene mutation.
Method: 74 cases of bone marrow biopsies, with MDS have been examined. Sections of 4 μ were subjected to antigen retrieval with EDTA and immunohistochemistry with DO-7 antibody.

Results: the intensity and the percentage of staining were evaluated. The cases with moderate-strong intensity staining were 28: • 14 have hyper-cellularity of single series; • 14 have hyper-cellularity of two or more series; • 90 % of the medullary fibrosis increased.
Conclusion: • p53 expression was present on bone marrow biopsies of patients, which alteration of a single or more series, while patients with alteration of the megakaryocytic series were immune-negative; • TP53 positivity predicted a worse prognosis and an higher risk class; • the increase of the medullary fibrosis indicates a minor survival possibilities. • The immunohistochemical expression of p53 was useful to assess the risk and the evolution of the MDS but was not enough to impact the overall survival.

PS-11-005
Clinicopathological characteristics and rituximab-plus cytotoxic therapies in patients with rheumatoid arthritis and methotrexate-associated large B-lymphoproliferative disorders
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Objective: To analyse the clinicopathological characteristics and prognosis of 40 rheumatoid arthritis (RA) patients with methotrexate (MTX)-associated large B-cell lymphoproliferative disorders (MTX-BLPD).
Method: At first, Epstein-Barr virus (EBV)-positive tumour cells were detected in tumour tissues by in situ hybridisation (ISH). Clinicopathological studies and prognosis were analysed in the 40 RA cases.
Results: By ISH, EBV was detected in tumour cells of 25 in 40 RA patients with MTX-BLPD (63 %). Immunohistologically, BCL2 expression was detected in 35 % of patients with MTX-BLPD, which was lower than 93 % of control DLBCL patients ($P < 0.01$). Eleven patients with EBV-positive MTX-BLPD (44 %) showed remission after MTX withdrawal. In RA patients with clinical stage III/IV BLPD, 15 with rituximab (R)-plus cytotoxic therapies pursued better prognosis than 10 with R-minus cytotoxic therapies ($P < 0.05$). Among the 15 patients, seven with MTX-BLPD showed better overall survival than nine control DLBCL patients ($P < 0.01$).
Conclusion: In RA patients with MTX-BLPD, immunosuppression by MTX, EBV infection and low BCL2 expression in tumour cells may play roles in tumourigenesis and tumour regression. R-plus cytotoxic therapies as well as MTX withdrawal were highly effective in these patients.

PS-11-006
Detection of Epstein-Barr virus in classical Hodgkin's lymphoma by immunohistochemistry: A study of 60 cases at University of Damascus, Syria
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Objective: EBV is implicated in development of classical Hodgkin's lymphoma (CHL) This is the first study investigating the frequency of EBV positivity in CHL in Syria.
Method: 60 constitutive cases of CHL admitted to two major hospitals in Damascus between 2014 and 2015 were detected for EBV by immunohistochemistry for latent membrane protein-1 (LMP-1).
Results: Of 60 cases, 58 % were males. The mean age for patients was 29.65 years (range 3–75). 65, 22, 10 and 3 % were subclassified as NSCHL, MCCHL, LRCHL and LDCHL, respectively. Of all case, 36 % were positive for EBV LMP-1. EBV positivity was not significantly different between males and females, or histological subtypes. However, EBV positivity was significantly higher in the younger age group (60 % ≤15 vs. 26.6 % >15; $p = 0.0289$). Overall positivity (36 %) is significantly lower when compared to recently published data from some developing countries like Jordan (60 %, $p = 0.0413$) and Turkey (72 %, $p = 0.0007$). However, it is not significantly different from other developing countries; Brazil (45 %, $p = 0.2299$) and developed countries; Germany (34.3 % $p = 0.8888$), Italy (20.9 %, $p = 0.1315$).
Conclusion: EBV overall positivity is significantly lower than Syria's neighbors and in bar with frequencies reported in developed counties. In addition, EBV positivity is higher in CHL patients 15 years of age or younger

PS-11-007
Non Hodgkin's lymphomas of the palatine tonsil: Anatomoclinical study about 21 cases
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Objective: Waldeyer's ring (WR) is the primary site for 5 to 10 % of all non Hodgkin lymphomas (NHL) and the tonsil is the most frequently involved site accounting for more than half of WR lymphomas. We report clinico-pathological features of 21 cases of primitive NHL of palatin tonsil.
Method: It's a retrospective study of 21 consecutive cases of adult NHL of the tonsil among 346 NHL of all sites diagnosed between years 2009 and 2014, representing 6 %. Immunohistochemistry studies for CD20, CD3, CD10,BCL6, MuM1, BCL2, CD30, EMA, ALK and Ki67 were evaluated.
Results: The median age was 50 years. The sex ratio was 4♂/1♀. Grossly all cases have unilateral enlarged tonsil with ulceration in three cases. Ninety percent of cases were in early stage (I-II). The diagnosis was diffuse large B-cell lymphoma (DLBCL) in 90 %. The other diagnoses were follicular lymphoma grade 1–2, and anaplasic large T cell lymphoma (ALCL). All patients with DLBCL had complete remission after RCHOP with adjuvant radiotherapy. Five-year overall survival was 90 %.
Conclusion: NHL of tonsil is rare dominating by DLBCL. Complete remission was achieved in 90 % most likely owed to early stage (I-II) and combined chemotherapy and radiotherapy.

PS-11-008
Autoimmune lymphoproliferative syndrome caused by a rare mutation of the FAS gene: A case report
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Objective: Autoimmune lymphoproliferative syndrome (ALPS) is a rare genetic disorder of disrupted lymphocyte homeostasis as a result of defective Fas-mediated apoptosis.
Method: We report a case of ALPS in a 17-year-old male. At the age of 6, the patient had been diagnosed with hepatosplenic lymphoma following splenectomy. The patient was treated by chemotherapy followed by bone marrow transplantation and was in remission thereafter. At the age of 17, the patient presented with progressive lymphadenopathy in several regions, suggestive of relapse.
Results: Histological and immunohistochemical analysis of the lymph node biopsy showed expansion of interfollicular zones and regressive changes of follicles. Flow cytometry of the lymph node and bone marrow aspirate revealed an aberrant subpopulation of double negative T-cells (CD3+, CD4-, CD8-). A suspicion of ALPS was raised. Genetic analysis showed that the patient was heterozygous for the c.179_188dup mutation in exon 2 of the FAS gene, confirming the diagnosis. As far as we are aware, this variant has not previously been reported in the literature. The initial splenectomy slides were reviewed, and the findings were reconsidered to be an expression of ALPS.
Conclusion: We emphasize the need to consider the possibility of ALPS in patients with chronic lymphadenopathy and splenomegaly.

PS-11-009

Expression of cyclin D1 and p53 protein as prognostic factor at different stages and beta-2 microglobulin level of multiple myeloma

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Objective: was to find out is there any correlation between expression of Cyclin D1 and p53 in malignant plasma cells and clinical stage by Salmon - Durie (S-D) and beta-2 microglobulin level (B2MG) in multiple myeloma (MM).
Method: 70 patients' bone marrow biopsies with primary diagnosed MM were examined for Cyclin D1 and p53. Statistical analyses were performed using Graph Pad Prism 5 software.
Results: MM stages according to S-D system were: IA, B (20 %, n = 14): II A, B (43 %, n = 30): IIIA, B (73 %, n = 26). Patients mean age was 63.61+/− 10.81 years. Cyclin D1 positive patients group had statistically significant higher B2MG level (5.174+/−4.599 mg/dl) than those of the Cycin D1 negative group ($p = 0.0462$, unpaired t-test) land more late stages of MM by S-D ($p = 0.0026$, Mann Whitney U test). p53 positive cases were in later stages by S-D system than those with lack of p53 ($p < 0.0001$, Mann Whitney U test) and higher B2MG level 5.585+/−4.675 mg/dl than those of the p53-negative group ($p = 0.008$, unpaired t-test). A positive correlation by Spearman test was found between Cyclin D1 expression, S-D staging system ($r = +0.363$; $p = 0.002$) and β2MG level ($r = +0.2623$; $p = 0.0487$) and also between p53 expression in PC and β2MKB level ($r = +0.449$; $p = 0.0005$).
Conclusion: Cyclin D1 and p53 positive expressions could prove as negative predictive factors in case of MM.

PS-11-010

Peculiarities of lymphomas in the Volga Region of Russian Federation

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Objective: To assess the peculiarities of Hodgkin and non-Hodgkin lymphomas in the Volga region of Russian Federation.
Method: 300 cases of Hodgkin lymphoma (HL) and 623 B-cell non-Hodgkin lymphomas were analyzed in 2012–2015 from database of Kazan Cancer Centre (serves Volga region of Russian Federation). Diagnosis was based on immunohistochemical analysis with 28 antibodies.
Results: Gender distribution for of HL cases was almost equal: 152 (50.7 %) females and 148 (49.3 %) males while second age peak could not be demonstrated. Compared to Western Europe rates of mixed cellularity (90/300, 30.0 %) and nodular lymphocyte predominance (5/300, 1.7 %) variants were higher in Russia. Lymphocyte-rich (10/300, 3.3 %) and nodular sclerosis (159/300, 53.0 % and 31/300, 10.3 % for NS1&2 respectively) variants of HL were less commonly diagnosed. We revealed lower frequency of follicular lymphoma (26/623, 4.2 %), small lymphocyte lymphoma (40/623, 6.4 %) and MALT lymphoma; while incidence of diffuse large B-cell lymphoma (360/623, 57.8 %), splenic marginal zone lymphoma (17/623, 2.7 %) and Burkitt lymphoma (25/623, 4.0 %) was higher in Russian population.
Conclusion: Peculiarities of age, gender and histological structure of lymphomas in Volga region of Russia could be explained by administrative issues (underdiagnoses of indolent lymphomas, medical tourism) as well as different biologic features of tumours.

PS-11-011

Extranodal Diffuse Large B Cell Lymphomas (EN-DLBCLs): Many sites, many entities?

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Objective: We analyzed the clinicopathological, immunohistochemical and cytogenetic features of 106 EN-DLBCLs from stomach (34 cases), intestine (10), cervico-cephalic region (11), central nervous system (13), testes (21), skin (8), and miscellaneous sites (9).
Method: Hans' algorithm and the immunohistochemical double hit score (DHS) for MYC and BCL2 were applied. Fifty-eight cases were analyzed with FISH for BCL6, MYC, BCL2, CCND1, BCL10 and MALT1. Stage, IPI score and overall survival were known for all patients.
Results: According to Hans' algorithm, cerebral, testicular and cervico-cephalic DLBCL were of non-GC subtype, whereas gastrointestinal and miscellaneous DLBCL were of GC subtype. The immunohistochemical DHS differed significantly according to the site of origin, with testicular and cervico-cephalic DLBCL frequently showing score 2. At FISH analysis, BCL6 and BCL2 were most commonly rearranged in non-GC and in GC cases, respectively. Gastrointestinal lymphomas displayed the highest rate of rearrangements, often with MYC involvement. One testicular DLBCL showed BCL2/MYC double hit. High IPI score, advanced stage, cerebral and testicular site of origin were associated with poor prognosis. Non-GC phenotype, BCL2 expression and DHS2 were also poor prognosticators.
Conclusion: DLBCLs arising at different EN sites are highly heterogeneous entities.

PS-11-013

Hemophagocytic Lymphohistiocytosis (HLH) in burn patients at the University of Texas Medical Branch: Retrospective autopsy study (1992–2014)

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Objective: Retrospective study of HLH in burn patients at an academic institution.
Method: 8370 autopsy records were searched between 1992 and 2014. Forty burn patients were autopsied. Histologic sections from the bone marrow, liver and spleen were examined. We also searched and examined non-burn HLH cases during the same period.
Results: A total of 3 patients were diagnosed with HLH in burn patients. One case did not have evidence of infection. The other two cases had multiple bacterial infections including Acinetobacter baumanni, Pseudomonas aeruginosa, Aeromonas hydrophila, Stenotrophomonas maltophila and Klebsiella pneumoniae. All cases had evidence of hemophagocytosis with activated macrophages in the bone marrow, liver and spleen, >70 % total burn surface area (TBSA), and serum ferritin >10,000 ng/ml. Twelve cases of HLH were diagnosed in patients without burns. Associated conditions included multiple bacterial (Gram negative sepsis), fungal (Fusarium, Absidia, Actinomucor, Histoplasma) and Herpes viruses (EBV, CMV and VZV). None of the HLH cases (burn or non-burn groups) were diagnosed pre-mortem.
Conclusion: Secondary HLH results from overactivation of the diffuse mononuclear phagocyte system due to a strong cytokine/chemokine response to a variety of systemic viral infections such as EBV and CMV. More rarely, other viral, bacterial, fungal and mycobacterial agents have been implicated. To the best of our knowledge, HLH has been reported in a single case of a severely burn patient. HLH is difficult to diagnose pre-mortem and requires a high index of suspicion. Its clinical presentation overlaps with septicemia and systemic inflammatory response syndrome. Prospective studies are currently underway in order to clarify the possible association between severe burns and HLH.

PS-11-014

Evaluation of Castleman disease: A series of 50 cases

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Objective: Castleman's disease (CD) is a lymphoproliferative disorder with unknown etiology, which can be associated with either local or systemic nonspecific symptoms. Therefore CD may not be thought priorly in differential diagnosis by both clinician and pathologist. In present study, patients with CD diagnosed in our institute were examined for prediagnosis, histopathology and clinical findings.
Method: Fifty patients with CD diagnosed between 1990 and 2015 were reevaluated retrospectively in terms of clinical and histopathological findings.
Results: The mean age was 42.5 (4-73y). Twenty-seven patients were (54 %) male and 23 (46 %) were women. Three patients had other organ tumours, two patients had POEMS before CD diagnosis. Angioimmünoblastic T-cell lymphoma was developed in one patient after 7 years. Exposure to toxic substances was shown in one patient with eosinophilia. Two patients were positive for HHV-8 antibody. Monotypic lambda expression was observed in one patient. Twelve of the 15 patients who have admitted from different centers to our department were false diagnosed, pathologically.
Conclusion: CD is an ignorable disease both clinically and pathologically because of nonspecific findings. We emphasized the importance of cooperation between clinician and the pathologist for correct diagnose and treatment of the patients. in the present study.

PS-11-015
Burkitt lymphoma in paediatric Sudanese patients: Sporadic type in endemic area
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Objective: To study the pattern of Burkitt lymphoma (BL) and it's association with Epstein-Barr virus(EPV) among paediatric Sudanese patients.
Method: Fifty-two children diagnosed with BL and referred to Radio-Isotope Centre Khartoum (RICK), were included in this study based on availability of pathology specimens and clinical records, following approval by RICK Ethical Committee. Histopathological diagnosis was performed according to 2008 WHO classification of neoplastic diseases of the haematopoietic lymphoid tissue following immunostaining of formalin-fixed, paraffin embedded (FFPE) tissue blocks. The presence of EPV was investigated using EBV-LMP1 antibody on (FFPE).
Results: BL represented 59 % of paediatric NHL seen in the period of this study. The mean age was 5.9 years (range 2–12). Male to female ratio was 1.8:1. The clinical pattern was mainly sporadic (85 %) while endemic type (15 %). None of cases was associated with immunodeficiency. The most common site of involvement was the gastrointestinal tract (70 %). EBV was detected in 33.4 % of cases. No significant correlation was observed between EBV positivity and disease pattern.
Conclusion: Burkitt lymphoma is a common type of NHL among Sudanese children. Although Sudan is an African country with endemic malaria, BL has sporadic pattern with involvement of the gastrointestinal tract.

PS-11-016
T-cell/histiocyte rich large B-cell lymphoma: Morphological and immunohistochemical evaluation of 42 cases
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Objective: T-cell/histiocyte rich large B-cell lymphoma (THRLBCL) is an unusual variant of non-Hodgkin lymphoma.
Method: We retrospectively reviewed 42 cases of THRLBCL to evaluate its heterogenity based on morphologic, immunophenotypic, presentation features, and bone marrow infiltration. The cases retrieved from our pathology department were collected over a 10 year period from 2000 to 2015. The immunohistochemical panel already stained on archival sections incuded CD20, CD30, CD15, EMA, bcl-2, bcl-6, MUM1, and CD10.
Results: The male to female ratio was 3.2 and the mean age at diagnosis was 52 years. At presentation, THRLBCL was nodal in 64.2 % (27 of 42) and involvement of bone marrow was observed in 16.6 % (7 of 42) of the patients. Three cases presented with micronodular splenic THRLBCL. Bone marrow infiltration was detected in 15.6 % (5 of 32) of patients in long term follow-up. On cases evaluated with Hans algorithm using the immunohistochemical panel including CD10, bcl-6 and MUM1, 35.7 % of the 14 cases were identified as germinal center origin.
Conclusion: The present findings of this study suggest that on immunohistochemical examination of THRLBCL a large proportion of cases exhibit a diversity of morphologic and immunophenotypic features and molecular genetic studies on larger series are required to identify the heterogeneous nature of the entity.

PS-11-017
Burkitt lymphoma variant in the monomorphic B cell post-transplant lymphoproliferative disorders: About clinical and histopathological aspects of 4 cases
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Objective: Post-transplant lymphoproliferative disorders (PTLD) are a complication after solid organ transplants (SOT) and haematopoietic stem cell transplants. Burkitt lymphoma is rarely observed as a PTLD.
Method: To describe the clinicopathological details of Burkitt-PTLD cases reviewed since 2005 from the Department of Pathology of Hospital Universitario Puerta de Hierro.
Results: We evaluated 4 patients (3 females and 1 male) transplanted of lung (2 cases), heart and kidney. The median age at diagnosis was 47,25 years (range: 25–73 years) and the median time of immunosuppressive therapy was 90,75 months (range 43–156 months). The clinical presentation was abdominal mass (3) and an axillary mass. All cases had morphological and immunohistochemical features of Burkitt Lymphoma (CD20+, CD10+, BCL6+, BCL2-, Ki67 index more than 95 %). MYC translocation was demonstrated in all cases and all cases showed EBERs expression. Three patients had advanced disease at diagnosis and were treated with high doses of chemotherapy. Two patients maintain a complete response after 8 and 18 months of follow-up, one died to allograft related complications and one died of the lymphoma.
Conclusion: In our series, Burkitt-PTLD represents 4 cases of 50 PTLD. All cases received SOT and were late onset. All cases were EBV associated. After treatment, almost all patients had complete response.

PS-11-019
Phospho-histone-H3 (phH3) immunohistochemistry based mitotic index identifies histological grade in follicular lymphoma
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Objective: Follicular lymphomas (FL) are categorized into three grades (G1-3) according to the number of centroblasts, however, it has low reproducibility affected by the sample quality. Phosphorylated histone H3 (phH3) was widely tested for the objective detection of mitotic figures in different malignancies. The aim of this study was to evaluate the expression of phH3 in follicular lymphomas with different grades and to compare it with other proliferation parameters.
Method: 48 FL cases and 9 control samples were examined. Hematoxylin-eosin based mitosis index (HE-MI), number of mitotic

figures based on anti-phH3 immunohistochemical staining (phH3-MI) and percentage of Ki-67 positive cells (proliferation index, PI) were evaluated and compared with histological grade.
Results: The phH3-MI value correlated significantly with the HE-MI ($p < 0.0001$) and the PI ($p < 0.0001$). All cell proliferation parameters showed significant correlation with the histological grade (HE-MI: $p < 0.0001$; phH3-MI: $p < 0.0001$, PI: $p < 0.0001$). The phH3-MI value was clearly distinctive between G2 and G1 FL groups ($p < 0.0001$) and was highly increased in G3 FL compared to G2 FL group ($p = 0.0020$).
Conclusion: The phH3 IHC staining is a reliable tool for the identification of mitotic figures. Mitosis index evaluated by this method (phH3-MI) can be recommended as an additional parameter for the precise subcategorization of FL cases.

PS-11-020
Extranodal T/NK cell lymphoma: A retrospective study of 8 cases
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Objective: To determine the epidemiological, clinicopathological characteristics and outcome of extranodal T/NK cell lymphomas (EN-NK/TCL).
Method: It is a retrospective study of 9 cases of EN-NK/TCL retrieved from the Central Tunisian cancer registry department over a 15-year-period.
Results: The sex ratio was of 8/1. The mean age was 48 years. The tumour was nasal and paranasal in 5 cases, the common symptom was nasal obstruction. For the 4 other cases, they were located in the palate, the submandibular gland, skin and in the soft tissues. It was a swelluing of the submandibular gland and of the ankle and a skin nodule. According to Ann_Arbor classification, the tumour was localized (stage I or II) in 6 cases and of advanced stage (III or IV) in 3 cases. At immunohistochemistry: CD3, CD56, Granzyme were positive respectively in 6 and 7 cases. Epstein-Barr virus latent membrane protein1 was experessed in 3 cases. In-situ hybridization for Epstein Barr virus (EBV)-encoded RNA was positive 6cases. Adjuvant chemotherapy was indicated in 8 patients. It was associated to radiotherapy for 5 patients. Surgery was indicated for one patient. Complete remission was obtained in 4 cases. 3 patients had died and 2 were follow-up.
Conclusion: EN-NK/TCL is uncommon in Tunisia. Its diagnosis is based on histological and immunophenotype characteristics and in-situ hybridization; the latter displaying the presence of EBV genome.

PS-11-021
Differential diagnosis of small B cell lymphomas with plasma cell differentation
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Objective: Differential diagnosis of small B cell lymphomas with plasma cell differentation such as: small lymphocytic lymphoma (CLL), splenic marginal zon lymphoma (SMZL), nodal marginal zon lymphoma (NMZL), exstranodal marginal zon lymphoma (ENMZL), follicular lymphoma (FL), lymphoplasmacytic lymphoma/Waldenström macroglobulinemia (LPL/WM), could be difficult. Our aim is to search the impact of new markers for differential diagnosis of these antities.
Method: 154 previouslu diagnosed various small B cell lymphomas from 23 spleen, 70 bone marrow, 43 lymph node, 18 other tissues of 116 cases were examined. Immunohistochemistry performed by using LEF1, MNDA, CD27, IRTA1 and Stathmin1 antibodies.
Results: LEF1 expression was present 47,6 % of 21 CLL cases with uniformly strong nuclear pattern. Higher proportion observed (67 %) for typical cases. MNDA and CD27 expressed in all diagnostic groups and was statistically significant in MZL (p:0.02) and CLL (p:0.019) cases. Five FL cases (71,4 %) and 12 CLL/SLL cases (57,1 %) expressed Stathmin1 on paraimmunoblasts. IRTA1 expression in NMZL ($p < 0.001$) and ENMZL ($p < 0.001$) was statistically significant in monocytoid differentiation areas.
Conclusion: None of these markers were found to be specific for any entity. With high expression profile of LEF1 for CLL/SLL, Stathmin1 for FL, IRTA1 for, ENMZL, NMZL especially with monocytoid differentiation, and MNDA for MZL could be used as secondary supporting markers for the cases with diagnostic difficulty.

PS-11-022
A rare case of Erdheim-Chester disease in a small population island
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Objective: Erdheim-Chester disease (ECD) is a rare, multisystem non-Langerhans cell histiocytosis. It was first described in 1930 by Jakob Erdheim and William Chester and ever since only several hundred cases has been documented in the literature. The disease is associated with significant morbidity, due to histiocytic infiltration of critical organ systems. Among the more common sites of involvement are the skeleton, central nervous system, cardiovascular system, lungs, kidney (retroperitoneum) and skin. Histologically, it is characterized by xanthogranulomatous infiltrates, which are positive for CD68 and negative for S100 and CD1a.
Method: This case report describes a 44-year-old cypriot woman with a progressive course over 5 years. She was presented with obstructive uropathy and symmetrical sclerosis of long bones.
Results: ECD was confirmed clinically, radiologically and histologically.
Conclusion: Erdheim-Chester disease is a systemic histiocytosis caused by non-Langerhans cells and typically foamy histiocytes, involving mainly retroperitoneal space and bones. Recent data, has proved that most of these patients harbor point mutations of the BRAF gene at codon 600. Vemurafenib, a BRAF inhibitor, an oral FDA approved targeted agent to the BRAF protein for melanoma, shows dramatic activity in patients with Erdheim-Chester disease whose tumour contains the same mutation. This therapy has proven highly beneficial in this patient. Diagnosis of this rare syndrome requires a high index of suspicion and increased awareness.

PS-11-023
Renal intravascular large B-cell lymphoma
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Objective: Case report about renal intravascular large B-cell lymphoma (RILBCL) which is a rare type of extranodal lymphoma large B-cell. it is characterized by selective growth of lymphoma cells in the light not of large arteries and veins but of the capillaries particularly.
Method: We report the case of a woman of 60 years with a medical background of treated tuberculosis. She was referred to the neurology department for some neurological symptoms. A Magnetic Resonance Imaging was performed and showed a vasculitis image. She was hospitalized for a probable vasculitis of the central nervous system. Concurrently she had anemia with kidney failure at 18 mg/l. Kidney biopsy was therefore executed. Histological analysis revealed, in the light of the glomerular and peritubular capillaries, centroblastic-like large atypical cells. The immunohistochemical study showed that the lymphoid cells expressed CD20, CD79a and did not express CD3. The final diagnosis was intravascular large B-cell lymphoma.
Results: RILBCL is very rare. The age of the concerned population is between 35 and 85 years with a median age of 60 and a male / female ratio

of 1: 1. Clinical symptoms of RILBCL may be those of proteinuria or renal dysfunction. Renal failure may be due to the circulation glomerular obstruction due to the invasion of lymphoma cells. Histopathology allows the diagnosis of RILBCL by highlighting lymphoma cells in the light of the glomerular and peritubular capillaries. RILBCL is an aggressive lymphoma with poor prognosis in general. However an early treatment provides better prognosis.
Conclusion: RILBCL is a very rare large B cells lymphoma type with poor prognosis. However, the knowledge of this entity improves the patients'caring.

Tuesday, 27 September 2016, 09.30–10.30, Hall 11.3
PS-12 Head and Neck Pathology

PS-12-001
Clinico-pathologic characteristics of head and neck sarcomas: A retrospective analysis of 50 cases in a Tunisian institution
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Objective: Head and neck sarcomas are rare tumours with various histological types displaying different clinical behavior. Our objective is to summarize the epidemiology of sarcomas occurring in the head and neck and identify their clinicopathologic characteristics.
Method: We performed a retrospective analysis of 50 patients with primary head and neck sarcomas diagnosed in our department from 1996 to 2013.
Results: Thirty-eight adult cases and 12 pediatric cases were identified. The mean age was 31 years. Forty-two per cent of the patients were males and 58 % were females. Median duration of follow-up for the entire group was 18.5 months. The most common location was the nasal cavity (50 %). In adults, the most common histologic subtypes were fibrosarcoma (23.6 %), chondrosarcoma (13.5 %), Kaposi sarcoma (14.3 %) and osteosarcoma (14.3 %). In the pediatric cohort, the most common histologic subtype was rhabdomyosarcoma (83 %). Fifteen per cent of patients had evidence of prior radiation exposure. The size of tumours was greater than 5 cm in 26.3 % of the cases and 35.5 % of tumours were high-grade. Margins were positive in 31.2 % of the cases. Lymph node metastasis were rare representing 6.5 %. Among all subtypes, 5-year overall survival was 66 % for adults and 73 % for pediatric patients.
Conclusion: Sarcomas are uncommonly found in the head and neck. In our series, lesions tended to be high-grade with a significant portion of surgical specimens having positive margins.

PS-12-002
The role of PI3K/AKT pathway in cell proliferation and apoptosis in oral Squamous Cell Carcinoma
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Objective: The oral squamous cell carcinoma (OSCC) has high incidence worldwide, representing nearly 95 % of all oral malignancies. The PI3K/AKT pathway has already been studied in several cancers, but its role in OSCC in cell proliferation and apoptosis still merits further investigation. It is known that AKT phosphorylates the serine residue 136 of the proapoptotic protein BAD, leading to its inactivation. The XIAP inhibits apoptosis by binding to caspases 3, 7 to 9. The AKT phosphorylates the XIAP at serine residue 86, which leads to inhibition of XIAP degradation. This work aims to study the role of PI3K/AKT pathway in cell proliferation and apoptosis in OSCC.
Method: The cell line SCC25 of OSCC was chosen because it has constitutive activation of the PI3K/AKT pathway. These cells were treated with LY294002, which inhibits the activation of PI3K, and with the AKT IV, which inhibits the activation of AKT. Protein expression and immunolocalization analyzes for AKT, BAD and XIAP were performed by Western blotting and indirect immunofluorescence assays respectively in the presence of the inhibitors LY294002 or AKT IV. MTT assay was performed to analyze cell proliferation.
Results: A decrease in cell survival was evident after the PI3K/AKT pathway blockage (PI3K or AKT), as well there was as a decrease in both AKT and BAD phosphorylation.
Conclusion: Our data suggest that PI3K/AKT pathway may have an important role in cell proliferation and apoptosis in OSCC.

PS-12-003
Early stage minor salivary gland adenoid cystic carcinoma has favorable prognosis
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Objective: To evaluate outcome of minor salivary and mucous gland (MiSG) adenoid cystic carcinoma (ACC) of the head and neck and to compare the results with our published series on major salivary gland (MaSG) ACC. Our study comprised 68 MiSG ACCs operated during 1974–2012 at the Helsinki University Hospital, Helsinki, Finland.
Method: Medical records and histological samples were reviewed. Patients' follow-up was at least 3 years or until death. Our earlier study with 54 MaSG ACCs were used for comparison.
Results: The most common locations were oral cavity and sinonasal cavities. Most patients presented Stage IV (33.8 %) and I (23.5 %) disease. Primary treatment with curative intent was offered for 64 patients and they received mainly surgery with or without oncological treatment. Disease recurred to 57.8 % of patients of which 42.2 % had recurrence within 5 years and 15.6 % later. The recurrence-free-time interval (<5 vs. >5 years) had impact on survival ($p = 0.000$). T classes 2–4 ($p = 0.000$-0.002) and Stages II-IV ($p = 0.000$-0.011) had negative correlation to survival. MiSG ACC had decreased long-term survival compared to MaSG ACC.
Conclusion: Patients with Stage I MiSG ACC had favorable prognosis compared with those with Stage II and advanced tumours.

PS-12-004
Differential expression of Epithelial Cell Adhesion Molecule (EpCAM) in salivary gland neoplasms
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Objective: EpCAM is the epithelial-specific molecule expressed on various types of epithelial cells. Its function involves cellular adhesion, proliferation and signalling. The purposes of this study were to investigate the EpCAM expression in salivary gland neoplasms and examine its relationship with pathologic characteristics.
Method: Forty-two cases of salivary gland neoplasms, including 20 mucoepidermoid carcinomas (MEC), 11 adenoid cystic carcinomas (ACC), 9 pleomorphic adenomas (PA) and 2 polymorphous low-grade adenocarcinomas (PLGA) were enrolled. EpCAM expression was analyzed immunohistochemically using MOC-31 and BerEP4 antibodies.
Results: The majority of MECs and all PLGAs showed EpCAM expression in more than 50 % of neoplastic cells, whereas most PAs and ACCs did not express EpCAM. In MECs, most EpCAM-positive neoplastic cells were clear cells, glandular epithelial cells and intermediate cells, while squamous cells and mucous cells were largely negative. In EpCAM-positive PAs and ACCs, the expression was limited to ductal epithelium. Decreased EpCAM expression in MECs was significantly

associated with microscopically diminished cystic components, the presence of small nest invasion at invasive front, cellular anaplasia, vascular invasion and high pathologic grade.
Conclusion: EpCAM expression may be useful to as an adjunct to determine MECs grading and could help differentiate between ACC and PLGA.

PS-12-007
Histopathological and immunohistochemical studies of long term administration of nutmeg on parotid salivary glands in albino rats
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Objective: More understanding of the effect of long administration of Nutmeg in different doses on the histology and immunohistochemistry of the parotid salivary gland in male albino rats.
Method: A total number of 60 adult male albino rats (average weight = 200 g) were classified into two main groups; Control group of 20 rats and received 1 ml of distilled water orally, and experimental group of 40 rats and was subdivided into 4 subgroups corresponding to 4 durations (2, 4, 6 and 8 weeks). Each subgroup in turn was further divided into 2 subgroups in which each rat was given 1 ml of the prepared nutmeg aqueous extract orally on a daily basis in the following doses (100 and 500 mg/kg body weight) respectively. By the end of the experiment, parotid salivary glands were obtained for histopathological, immunohistochemical, and image analysis.
Results: Histopathological results revealed normal appearance of the control group. While the experimental group showed pathological changes gradually increased as the duration increased and as the dose administered increased. Immunohistochemical and image analysis results confirmed those recorded by histopathology.
Conclusion: Administration of nutmeg had damaging and teratogenic effects on the parotid glands especially when taken at high doses and for long durations.

PS-12-008
Clinico-pathological patterns of salivary glandtumours among Sudanese patients
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Objective: To identify the Clinico -pathological patterns of salivary gland tumours among Sudanese patients.
Method: A cross-sectional study that involved patients submitted salivary gland biopsies to histopathology departments of four centers in Khartoum State, Sudan. Data were collected from patient's records and the slides were collected and reviewed to confirm the diagnosis.
Results: Out of 110 patients aging 2 to 85 years with a mean of 35 ± 15, there were 62 (56.4 %) males. Fifty percent of the tumours originated from the parotid, 35.5 % from the Submandibular and 12.7 % from minor salivary glands. Of them 34 (30.9 %) were malignant and 76 (69.1 %) were benign. Eighty percent of patients with malignant lesions were below the age of 40. Pleomorphic adenoma was the most common benign tumour (86.8 %), followed by oxyphilic adenoma (5.3 %), and myoepithelioma (3.9 %). The malignant tumours were dominated by adenoid cystic carcinoma (26.5 %), mucoepidermoid carcinoma (23.5 %), acinic cell carcinoma (11.8 %), poorly differentiated carcinoma (11.8 %), papillary adenocarcinoma (5.9 %), basal cell carcinoma (5.9 %), squamous cell carcinoma (5.9 %), malignant myoepithelioma (2.9 %), polymorphous low grade carcinoma (2.9 %), and highly malignant large cell lymphoma (2.9 %).
Conclusion: The pattern of distribution of salivary gland tumours in Sudanese patients share many pathological and epidemiological features with other developing countries.

PS-12-009
Diagnostic accuracy of intraoperative frozen section in thyroid nodules
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Objective: Intraoperative frozen section (FS) is a valuable procedure to confirm the cytological diagnosis of thyroid nodules and identify malignancy in patients with equivocal or suspicious cytological diagnosis.
Method: From 2011 to 2015, the medical records of 130 patients who underwent thyroid surgery were analysed. Frozen section biopsies were taken from 70 (54 %) of the 130 patients. The diagnostic correlations of FS with final diagnosis were evaluated.
Results: FS diagnosis was benign in 40 patients, malignant in 18, and indeterminate (consistent with a follicular or Hurthle cell neoplasm) in 12 cases. Intraoperative management was modified in 58 cases. Of the 58 FS that were interpreted as benign or malign, 16 were true positives, 2 were false positives, 39 were true negatives, and 1 was a false negative. Frozen section had an 94 % sensitivity, 95 % specificity, 89 % positive predictive value, 98 % negative predictive value, and 95 % accuracy when indeterminate results were excluded from the calculation.
Conclusion: The results of our study demonstrate that FS in combination with clinical examination have an important role in the determination of the extent of thyroidectomy for patients with a thyroid nodule and FS is recommended for patients with noduler thyroid disease limited to one lobe of the thyroid gland and atypia/follicular lesion of undetermined significance. There were 2 false positive FS results, and only one false negative results. The underdiagnosis was mainly due to the small size of the tumour. The 2 patients had false positive results included one patient with benign papillary hyperplasia as the final diagnosis and one patient with follicular adenoma. As a result, no patients underwent unnecessary total thyroidectomy.

PS-12-010
Snail and Twist expression in salivary adenocarcinoma, not otherwise specified: A pilot study
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Objective: Snail and Twist are two key transcriptional regulators of the epithelial-mesenchymal transition (EMT), whose expression has been studied in a few salivary gland tumours. The aim of this study was to investigate Snail and Twist expression in salivary adenocarcinoma, not otherwise specified (ANOS).
Method: Nine cases of salivary ANOS were evaluated by immunohistochemistry using antibodies against Snail and Twist. The association between Snail or Twist expression and clinicopathological parameters was analyzed statistically using Fisher's exact test.
Results: The mean age of nine salivary ANOS patients was 52.6 years (range, 35–76 years) with a predilection for male (male-to-female ratio, 2:1). Four cases (44.4 %) occurred in the parotid gland and five cases (55.6 %) involved the minor salivary glands. Five cases (55.6 %) showed regional or distant metastasis, and two cases (22.2 %) showed recurrence. Snail was positive in about half of the cases (4/9, 44.4 %), whereas Twist expression was observed in most cases (8/9, 88.9 %). Snail expression was significantly associated with regional and distant metastasis ($P = 0.048$). Twist expression showed no correlation with clinicopathological parameters.
Conclusion: Our results suggest that Snail and Twist are involved in EMT of salivary ANOS. Snail may play an important role in metastasis of salivary ANOS.

PS-12-011

Chronic invasive fungal granulomatous rhino-sinusitis: A case report with review of literature

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Objective: The aim of this report is to draw the attention of colleagues to the clinical presentation and histopathological diagnosis of the Chronic Invasive Granulomatous form of Fungal Rhino-Sinusitis (FGRS) of the paranasal sinuses, as differential diagnosis in lesions of the maxillofacial region.
Method: We present a 30-year-old Nigerian undergraduate who had a 4-year history of right nasal blockage and 2-year history of proptosis of the right eye. Clinical and radiological findings were reported to be consistent with nasopharyngeal tumour. A trans-nasal biopsy was, initially, diagnosed as Chronic Granulomatous Inflammation (likely tuberculosis). He was started on antikochs with no significant improvement at the referral hospital. The tissue blocks were re-evaluated at our centre.
Results: The granulomatous lesion was confirmed. Periodic Acid Schiff and Gomori Methenamine Silver stains showed presence of numerous septate fungal hyphaes, within the giant cells. An assessment of FGRS was made. He was commenced on voriconazole, and there was a dramatic regression of the lesion.
Conclusion: Fungal infection should be considered in all patients with chronic sinusitis and orbital apex syndrome. The need for a high index of suspicion of fungal origin cannot be over-emphasised. Effective collaboration between the Surgeon, Radiologist, Microbiologist and Histopathologist will ensure early diagnosis and treatment.

PS-12-012

Clinico-pathological features of non-keratinizing carcinoma of nasal cavity and paranasal sinus

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Objective: To study the clinicopathological features, immunophenotype, differential diagnosis and prognosis of non-keratinizing carcinoma(non-KC) of nasal cavity and paranasal sinus.
Method: 26 cases of non-KC of nasal cavity and paranasal sinus were collect. The histopathological features and clinical data were analyzed retrospectively. Immunohistochemistry (20cases) were used to evaluate the expression of CK,P16,P53,Ki-67,and Vimentin,etc.; ISH was used to detect HPV and EBER.
Results: The mean age for the 26 patients(16 males, 10 females)was 51.2 year(rang from 22 to 79 years). Three patients have a history of inverted papilloma. Microscopically the tumours tissue showed an invasive growth, and formed mainly papillary pattern and inverted pattern. Twenty cases(20/20) were strongly positive for CK、P63. Seventeen cases(17/20) were strongly positive for CK5/6. Sixteen case were strongly positive for CK8/18. One case(1/20) was strongly positive for P16. Twenty cases(20/20)were negative for CgA,Syn,CD99, NUT,S-100, HMB45 and MelanA. One case showed HPV18mRNA positive. No case positive for EBER. The follow-up time was 5 months to 8 years and 8 months.
Conclusion: Non-KC is a rare neoplasm with distinct morphological characteristics. Its diagnosis is primarily based on the site of lesions and the histological features. The diagnosis and differential diagnosis could be aided by immunohistochemical staining. The tumour may originate from the epithelium of nasal cavity and sinus, and was not closely related with EB virus and HPV infection; the treatment is primarily surgical excision combined with postoperative radiotherapy.

PS-12-013

A case report of Laryngeal Amyloidosis

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Objective: Laryngeal amyloidosis (LA) is a rare lesion (first reported 1873) representing 0,5-1 % of all benign laryngeal diseases. Although usually primary and localized it can also be a part of systemic disease or secondary to an underlying malignancy. The precise etiology and pathogenesis of LA remain unknown. There is no definite established link with smoking,alcohol or vocal abuse.
Method: A 67 years old heavy smoker woman was presented with a 6 months history of hoarseness and recent onset of a choking sensation. Laryngoscopy revealed an 1,8 cm lobulate ventricle and left vocal cord mass suggesting a laryngeal malignancy. An incisional biopsy consisting of 0,5 × 0,5 × 0,3 cm tissue was performed.
Results: Microscopically showed subepithelial globular depositions of amorphous,acellular eosiniphilic material or bundles of eosinophilic tissue with variable inflammatory reaction including lymphocytes and plasma cells. Foreing-body giant cells were also noted. Congo red staining under polarized light revealed yellow-green birefringence consistent with amyloidosis. There was no evidence of monoclonality in the plasma cells and amyloid by immunohistochemistry(CD138 k,λ). No signs of malignancy were seen. Further work up for systemic amyloidosis was negative. An endoscopic excision was done.
Conclusion: LA is a rare,usually localized lesion. Laryngoscopy may falsely suggests a malignancy. Definitive diagnosis is always established histologically. Long term follow-up is indicated for easy detection of recurrence or subsequent systemic disease development.

PS-12-014

Clinico-pathological characteristics and prognosis of primary nasopharyngeal adenocarcinoma: A report of 73 cases

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Objective: To investigate the clinicopathological features and prognosis of primary nasopharyngeal adenocarcinoma (NPAC).
Method: The data from consecutive patients with NPAC from 1999 January to July 2010 in institute were retrospectively analyzed.
Results: Seventy-three patients with NPAC were included in this study, with 25 % (18/73) stage 1, 26 % (19/73) stage 2, 22 % (16/73) stage 3, and 27 % (20/73) stage 4. Histopathologically, 73 % of NPAC were salivary gland type (53/73) and 27 % were common type (20/73). Significant differences were observed in 5 year OS and DFS rates between patients with and without CT /MRI-detected cranial nerve involvement (73.7 vs. 25.6 %, $p = 0.001$; 56.6 vs. 19.3 %, $p = 0.002$). In 19 patients with early stage disease (stage I-II), significant differences were observed between the surgery group and non-surgery group in both 5 year OS and DFS rates ($P = 0.031$, 0.012, respectively). No statistically significant differences were found in 5-year OS and DFS rates between different pathological types of adenocarcinoma.
Conclusion: Primary NPAC is a distinct entity and an uncommon type in nasopharyngeal tumour and it mainly presents with salivary gland type adenocarcinoma. Cranial nerve involvement is the factors affecting the prognosis of the patients. The surgical treatment can improve the prognosis of NPAC patients in early stage.

PS-12-015

Pituitary endocrine tumours presenting as sinonasal or nasopharyngeal masses: A case series illustrating potential diagnostic pitfalls

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Objective: Retrospective survey of invasive pituitary endocrine tumours presenting as sinonasal or nasopharyngeal masses.
Method: We identified 13 non-ectopic pituitary endocrine tumours presenting as masses of the nasal cavity, sinuses, or nasopharynx, which were biopsied from these sites.
Results: The series included 5 men and 8 women, aged 29 to 69 years. Presentations included nasal obstruction (4), headaches (3), visual defects (3), epistaxis (1), rhinorrhea (1), sepsis (1), and fatigue (1). All tumours originated from the sella and extended inferiorly to involve the sphenoid sinus (10), ethmoid air cells (8), nasal cavity (6), and nasopharynx (3). In three cases the initial diagnosis was incorrect; two were classified as olfactory neuroblastoma, one of those was converted to neuroendocrine carcinoma, and one tumour was initially diagnosed as neuroendocrine carcinoma. In two cases, the wrong diagnosis led to incorrect treatment. Follow-up was available for 10 patients and ranged from 2 to 25 years. Four patients were free of disease and 6 were alive with disease.
Conclusion: Pituitary endocrine tumours can invade sinonasal cavities and/or nasopharynx and when they do, they present a possible diagnostic pitfall with potentially serious consequences. Pituitary endocrine tumours should be considered in the differential diagnosis of a neuroendocrine nasopharyngeal or sinonasal tumour.

PS-12-017
Diagnostic accuracy of Bethesda System for FNA cytology of thyroid nodules measured by likelihood ratios
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Objective: The Bethesda System for Reporting Thyroid Cytopathology (or "Bethesda") encompasses six categories, associated with risk of malignancy. We propose practical application of likelihood ratios (LRs) as determinants of Bethesda system accuracy, making test results comparable across differencet clinical settings.
Method: Population: 3307 patients with thyroid nodules (polulation-based). Index test: Cytology result according to "Bethesda". Reference test: final histopathology (surgical excision specimens) or follow-up. Outcome: diagnostic LR (95 % CI) for each test level; Bayesian probability revision and prediction of malignancy rates (post-test probabilities) based on LRs and pre-test probabilities of thyroid cancers in study polulation
Results: A 291 (8.8 %) of all thyroid nodules underwent surgery. In remainder no thyroid malignancies were diagnosed at 6 month follow-up. "Bethesda" categories show the following LRs, (95%CI): "Malignant" 91.4 (12.8–650); 79–98 % cancer probability "Suspicious for malignancy" 9.9 (9.9 (3–33); 29–86 % probability. "Suspicious for follicular neoplasm" 0.51 (0.3–0.97), 26–27 % probability. "Atypia of unknown significance" 0.56 (0.4–0.9); 2–26 % probability. "Benign" 0.06 (0.02–0.2); 1–4 % probability, and "Unsatisfactory" 0.24 (0.06–1.1); 1–13 % cancer probability .
Conclusion: LRs greater than 10 and Less than 0.1 are helpful in ruling in and ruling out of thyroid malignancies; LRs 0.1 to less than 1, and greater tham 1 to 10 are less accurate and of limited diagnostic accuracy. Due to uncertainly of several "Bethesda" categories highlighted by the LRs, the surgeries continue to be performed for patients with a substantial number of benign lesions.

PS-12-018
Palatal mucoepidermoid carcinoma with acral cutaneous metastasis at presentation
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Objective: Introduction: Mucoepidermoid carcinoma (MEC) is a malignant glandular epithelial neoplasm characterized by mucous, intermediate and epidermoid cells, with columnar, clear cell and oncocytoid features in varying proportions. It is the most common primary salivary gland malignancy in both adults and children. More than 50 % of cases affect major salivary glands however, affectation of minor glands in the palate is not uncommon. Palatal tumours may extend into the upper respiratory tract and skull while distant metastases via lymphatic and haematogenous routes though uncommon, is to the lungs, liver, brain and bones. Metastatic disease at diagnosis is observed in less than 5 % of the cases. Cutaneous metastases though rare, have been reported in the past but we believe this is the first case of acral cutaneous metastatic mucoepidermoid carcinoma at the time of diagnosis of the primary palatal lesion.
Method: Patient: The patient is a 39 year old woman who presented with soft palatal swelling and an ulcerated swelling at the distal end of the left index finger. Clinicopathological correlation was key to arriving at diagnosis.
Conclusion: Metastatic mucoepidermoid carcinoma therefore should be one of the differential diagnosis of numerous primary cutaneous carcinomas and adenocarcinomas especially those producing mucin.

PS-12-019
Patterns of carcinoma of head and neck region in a tertiary hospital in Northern Nigeria: A five year review at Ahmadu Bello University Teaching Hospital, Zaria
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Objective: Despite the high morbidity and mortality of head and neck carcinomas, there is limited data on the epidemiological and morphological patterns in our environment. This study is aimed at determination of epidemiological and histopathological patterns of carcinomas of head and neck region in Zaria, Nigeria.
Method: This is a 5 year retrospective study. Data were extracted from the cancer registry and archived histopathology request cards. The slides were reviewed and the data was analysed using Microsoft Excel.
Results: A total of 154 cases were studied, comprising 106 males and 48 females, the M:F ratio was 2.2:1, the mean age was 46.86 years with peak in fifth decade. The commonest sites were nasopharynx, oral cavity and major salivary glands contributing 30.5, 24.1 and 17.5 % respectively. Of the nasopharyngeal carcinomas, 85.1 % were undifferentiated type. Sixty cases were squamous cell carcinoma, with 35.0, 31.7 and 23.3 % from oral cavity, sino-nasal tract and larynx respectively. Oropharyngeal carcinoma was uncommon. Adenoid cystic carcinoma, mainly from the parotid and minor glands was commonest salivary gland-type carcinoma.
Conclusion: Squamous cell carcinoma and nasopharyngeal carcinoma, which have strong links with tobacco and EBV infections respectively, were common. Further studies are recommended to analyse the possible risks factors.

PS-12-020
Primary intraosseous Squamous Cell Carcinoma (SCC) in keratocystic odontogenic tumour: Two case report
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Objective: Primary intraosseous squamous cell carcinoma arises within the jaws is a type of odontogenic carcinoma that is extremely rare. These tumours have no interaction with oral mucosa so they may develop from the odontogenic epithelium residues or from a benign odontogenic cyst or tumour epithelium.
Method: Here we present two cases of intraosseous squamous cell carcinoma arising from keratocystic odontogenic tumour. Keratocystic odontogenic tumour can be locally aggressive and have a high recurrence rate despite the benign characteristics of odontogenic epithelium.

Results: Twenty-nine years old patient had two recurrences of maxillary keratocystic odontogenic tumour which eventually transformed into malignant tumour. Second patient was 56-years old who had keratocystic odontogenic tumour on his maxilla and had malignant transformation at the time of diagnosis.
Conclusion: The presented cases were discussed from all aspects of clinical history, radiological examination and pathological features.

PS-12-021
Uveal melanoma: Morphological and epidemiological analysis
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Objective: Annually doctors diagnose about 30,000 malignant tumours in Kazakhstan, and in about 1700 cases they have head and neck localization, including neoplasms in the eye. We performed a retrospective analysis (2008–2015) of cases of enucleation on the eyes due to uveal melanoma.
Method: The clinic of the Kazakh Research Institute of Eye Diseases in Almaty, Kazakhstan accepted 79 patients (including 49 women) with complaints of blurred or distorted vision and vision loss. In 36 patients the pathology was observed in the left eye, in 43 patients—in the right eye. The patients mentioned gradual vision loss over the period of 2 months to 3 years along with eye pain. Men were prevalent in the age group from 51 to 60 years old, while majority of women developed this condition in the age group from 61 to 70.
Results: predominant localization of the tumour on the optic nerve (34 cases) and pre-equatorial region (28 cases). The most tumours were of mixed cell type (48 cases) and spindle cell type (20 cases).
Conclusion: In all cases tumours were diagnosed at the late stage; the most tumours were of mixed and spindle cell type; the ratio of women to men was 1.6 to 1; the most often localization was in the optic nerve and pre-equatorial region.

PS-12-023
Thyroid-like low grade nasopharyngeal papillary adenocarcinoma: A case report
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Objective: Thyroid-like low grade nasopharyngeal papillary adenocarcinoma (TL-LGNPPA) is an extremely rare neoplasm characterized by morphological analogy to papillary thyroid carcinoma and abnormal expression of thyroid transcription factor-1 (TTF-1).
Method: A 25 years old female patient was admitted to our Ear, Nose and Throat out-patient clinic with the complaint of nasal obstruction for 1 year. Magnetic resonance imaging showed a 23 × 20 × 19 mm sized polypoid mass on the roof of the nasopharynx and multiple enlarged lymph nodes in bilateral neck region. Thyroid gland was normal and an endoscopic punch biopsy was performed.
Results: Histologically, the tumour consisted of papillary growth of cuboidal or columnar epithelium. The papilla were complex and tightly packed with hyalinized fibrovascular cores. Immunohistochemically, the neoplastic cells were positive for TTF-1, negative for thyroglobulin, CK19, CD56, P63, Napsin A. The pathological diagnosis was consistent with TL-LGNPPA.
Conclusion: TL-LGNPPA is a rare low-grade neoplasm with distinct morphological characteristics. The differential diagnoses included papillary thyroid carcinoma, low-grade papillary adenocarcinoma of salivary gland origin, and a papillary variant of intestinal -type adenocarcinoma. TL-LGNPPA have an excellent prognosis with simple and complete resection.

PS-12-024
The role of caspase-4 gene expression in apoptotic pathway of oral carcinogenesis
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Objective: Squamous cell carcinoma of oral cavity is in the ten most common cancer worldwide. Oral epithelial dysplasia may be described as morphological appearances between normal and malignant epithelial tissue. Here, we evaluated the mRNA expression of caspase-4 and immunohistochemical detection of apoptotic and proliferating cells via DDF-45, and Ki67 antibodies, on oral squamous cell carcinoma, dysplasia, and non-neoplastic epithelial hyperplasia cases intending to emphasize the apoptosis in oral cancer and in the disease's so called early stages.
Method: Ten formalin fixed, paraffin embedded tissues were used for each entity. Caspase 4 expression was analyzed by quantitative RT-PCR. ABC method was used for immunohistochemistry.
Results: Reduced caspase-4 expression was seen in 80, 73, and 54 % in cancer, dysplasia, and hyperplasia samples, respectively. Immunohistochemical analysis of cancer samples from dysplasia revealed high DDF45 immunoreactivity, whereas low immunoreactivity from hyperplasia group. Proliferation index also was higher in cancer cases than dysplasia and hyperplasia.
Conclusion: DFF45 seems to play an important role in the onset of apoptotic process by acting through the regulation of DNA fragmentation. These data suggest that the apoptosis through caspase 3 expression and DNA fragmentation is active in oral epithelial neoplasms especially in squamous cell carcinoma.

PS-12-025
Hormonal factors expression in recurrent pleomorphic adenoma
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Objective: Recurrent Pleomorphic Adenoma (RPA) is a challenging disease mostly due to the difficulty of its treatment. Hormonal factors have been used as adjuvant therapies and prognostic markers in various neoplasms. The aim of this study is to investigate the role of estrogen receptor (ER) and progesterone receptor (PR) in Pleomorphic Adenoma (AP), RPA and RPA with malignant transformation (TRPA).
Method: Twenty cases of PA, 20 of RPA and four TRPA cases were immunohistochemistry studied for ER and PR. A grading system based on nuclear reactivity percentage was assigned on a scale from 0 to 3. Less than 10 % cell reactivity was assigned 0; 11–25 % was assigned 1; 26–50 % was assigned 2; and reactivity greater than 50 % was assigned 3.
Results: Tumours were negative for ER and PR in all cases of PA and RPA. Three TRPA cases were negative for these hormonal factors; and one TRPA case was moderately positive for both ER and PR.
Conclusion: This study suggests that ER and PR are not expression in PA and RPA, indicating that these tumours would not benefit from hormonal adjuvant therapies. However, due to the TRPA rarity, further detailed studies are warranted on a large series.

PS-12-026
Merkel cell carcinoma arising in Warthin tumour: An extremely rare entity with limited experience and little available information in the literature
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Objective: Warthin tumour is the second most common salivary gland tumour. Rarely, either the epithelial or lymphoid component of Warthin

tumour can undergo malignant transformation, with an estimated incidence of less than 1 %. Several malignancies have been described in literature, but only few of Merkel cell. We report a case of a 69-year-old man presenting with distention of his left parotid gland. Parotidectomy was performed.
Method: We received the left parotid gland measuring 6.5 × 3.5 × 2.7 cm. The cut surfaces revealed a well-circumscribed, grayish, solid, partly cystic tumour measuring 2.8 × 2.5 × 2cm.
Results: Microscopically we observed a malignant tumour arising in a Warthin tumour, comprising of solid sheets of small to medium size cells with scant eosinophilic cytoplasm, oval nuclei, dusty chromatin and inconspicuous nucleoli. Numerous mitoses and necrosis were seen. Immunohistochemically, a paranuclear "dot-like" positivity pattern for CKAE1/AE3, CK20 and Neurofilaments was observed. The cells stained also positive for CD-56 and Synaptophysin. Ki-67 was estimated 50–55 %. A diagnosis of Merkel cell carcinoma was made.
Conclusion: The possibility of a metastatic Merkel cell carcinoma from an undetected cutaneous or extracutaneous primary site was considered. CT imaging and FNB revealed metastatic disease in lymph nodes of the mediastinum, however no primary tumour was found in our patient.

PS-12-027
The expression of epithelial-mesenchymal transition and cancer stem cell markers in oral dysplasia and cancer
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Objective: The aim of the study is to analyse the expression of epithelial-mesenschymal transition and cancer stem cell markers in oral epithelial dysplasia and oral squamous cell carcinoma in order to asses their influence on oral carcinogenesis.
Method: The study was conducted on 45 formalin fixed, parraffin - embedded tissue samples consisting of oral squamous cell carcinoma (n:15), epithelial dysplasia (n: 15) and epithelial hyperplasia (n: 15) . The expression of Snail 1 and CD 133-prom 1 was detected by using both quantitative RT-PCR and immunohistochemistry, whereas CD 44 and E-cadherin expression was evaluated immunohistochemically.
Results: The overall Snail 1 up-regulation was seen 56 % of the cases (25 out of 45) where as, prom 1 up-regulation was found 7 % (3 out of 45) which were in the samples from 1 carcinoma and 2 hyperplasia. Elavated mRNA level for Snail 1 was significant in carcinoma cases ($p < 0.05$). The decrease in E-cadherin expression and increase in CD 133 expression was found in the spectrum of oral epithelial hyperplasia to squamous cell carcinoma .
Conclusion: Snail 1 may indicate the potential role as an epithelial – mesenchynal transition marker in the sequence from oral hyperplasia to dysplasia- cancer.

PS-12-029
Clinico-pathological significance of immunohistochemical biomarkers in salivary duct carcinomas: A multi-institutional study of 152 cases
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Objective: Salivary duct carcinoma (SDC) is one of the most aggressive salivary tumours. Our aim is to determine the immunoprofiles of the various biomarkers and their clinicopathological significance in SDC.
Method: 152 cases of SDC were immunostained for HER2, HER3, EGFR, p53, AR, ERβ, CK5/6, MUC1, PLAG1 and Ki-67. Also HER2 gene amplification were examined by FISH.
Results: Immunoreactivity for each biomarker in SDCs was as follows: HER2 (3+ and/or FISH+: 46.1 %), HER3 (1-3+: 68.2 %), EGFR (3+: 32.2 %), p53 (LI >20 %: 57.3 %), AR (81.6 %), ERβ (96.6 %), CK5/6 (2-3+: 30.5 %), MUC1 (3+: 77.2 %), PLAG1 (1-3+: 53.7 %) and Ki-67 (LI >40 %: 57.9 %). Interestingly, overexpression of HER2, HER3, EGFR and Ki-67 was significantly associated with SDCs ex pleomorphic adenoma rather than that in de novo SDCs. Both overall survival and progression-free survival of the patients with higher Ki-67 LI were significantly shorter than those of patients with lower Ki-67 LI. Moreover, both AR-negative and CK5/6-positive groups showed significantly shorter progression-free survival. There was no significant correlation between the other biomarkers analyzed and clinicopathologic parameters.
Conclusion: The present study demonstrated that Ki-67, AR and CK5/6 are regarded as a prognostic factor in SDC. Diverse molecular mechanisms might play in the carcinogenesis of SDCs depending on their origin.

PS-12-030
Neuroendocrine differentiation in mucosal malignant melanomas os sinonasal and oral regions
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Objective: To investigate the frequency and significance of neuroendocrine differentiation in mucosal malignant melanomas of sinonasal and oral regions.
Method: Thirteen cases of oral and sinonasal mucosal malignant melanoma were retrieved from our archieves. Ten cases who had available blocks were included to the study. Prior diagnoses were confirmed reevaluating hematoxylin and eosin stained slides and immunohistochemical stains by two pathologists. Synaptophysin, chromogranin and CD56 expressions were investigated by immunohistochemistry from paraffin-embedded tissues in ten cases of mucosal malignant melanomas. Cases were evaluated with respect to both staining percentage and intensity.
Results: Study cases were epithelioid (6/10), epithelioid and spindle cell (3/10) and plasmacytoid (1/10) morphology. Five cases (50 %) were stained moderately and one case (10 %) stained weakly for CD56. Synaptophysin positivity was observed in 3 cases, focally and in mild to moderate intensity. All cases were negative for chromogranin.
Conclusion: Our findings suggested that neuroendocrine differentiation in mucosal malignant melanomas is not uncommon finding. The awareness of this feature and to apply a broad panel of immunohistochemistry are necessary for distinction of mucosal malignant melanomas from histologically similar malignant tumours.

PS-12-031
Sinonasal adenocarcinoma: A 20-year experience at a single institution
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Objective: Adenocarcinoma is a rare tumour of the sinonasal tract. This study aims at evaluating outcomes in a series of patients treated in a single institution in a 20-year period.
Method: Retrospective review was performed of patients with adenocarcinoma of the sinonasal tract from 1996 to 2016. Demographic data, disease presentation, treatment, and survival rates were collected and evaluated.
Results: 40 patients with sinonasal adenocarcinoma were identified. Twenty-five percent of the patients had wood-related occupations, 15 % working on the cork industry. Average age at time of diagnosis was 67 years (48–84 years). Fifty-eight percent of patients presented with T3 or T4 tumours. Surgery plus adjuvant radiation therapy was the most common primary form of treatment (58 %). 36 had the

intestinal type and 4 had non-intestinal type histologies. Persistence of disease or local recurrence was seen in 26 patients (65 %). The overall 5-year survival was 59 %. Survival was decreased significantly in patients with T3 or T4 tumours and with disease's persistence after initial therapy.
Conclusion: Sinonasal adenocarcinomas are locally aggressive tumours that usually present at high stages. Association with occupational exposure, namely with the local cork industry, was present. Despite treatment, persistence of disease or local recurrence occurs in a significant percentage of patients.

PS-12-032
Thyrolipoma and thyrolipomatosis: 3 case reports
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Objective: Described as uncommun thyroïd lesions with only few cases reported in the literature, thyrolipoma and thyrolipomatosis are two rare distinctive conditions. Here, we report 3 new cases in order to illustrate clinical, morphological and histopathological features of these rare entities.
Method: Our present study concerned 3 cases of fat containing thyroid lesions diagnosed as such in the department of pathology of Sfax Hospital.
Results: The mean age of patients was 60 years with 2 females and one man. All patients presented multinodular goiter in physical examination and underwent total thyroïdectomy. The thyroïd specimens showed either yellow-tan nodules (2 cases) or diffuse yellow-brown appearance (2 cases). Histologic examination revealed 3 different patterns: (1) a well circumscribed fat nodule (thyrolipoma) in one case; (2) a diffuse fat infiltration (thyrolipomatosis) in one case; or (3) fat infiltration involving both patterns in one case. Moreover, a papillary carcinoma and a lymphocytic thyroïditis were identified in one case of thyrolipomatosis.
Conclusion: In summury, we reported 3 cases of thyrolipoma and thyrolipomatosis. Only one case have combined histological pattern with concomitant papillary carcinoma, which is an extremely rare feature in the literature.

PS-12-033
Histopathological differences between primary Sjögren's Syndrome and Sjögren's Syndrome accompanied by scleroderma
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Objective: Investigation of morphological differences in relation with serological variables between primary versus secondary Sjogren's syndrome associated with systemic scleroderma (Scl-SS).
Method: A total of 69 primary Sjogren's syndrome (pSS) and Scl-SS patients were grouped according to the the AECG criteria as pSS and Scl-SS. Hematoxylin and eosin sections of the minor salivary gland biopsy were re-evaluated and the lymphocyte focus score (FS), plasma cell focus (PCF) and fibrosis rates were all evaluated.
Results: There were 43 pSS and 26 Scl-SS cases. Both biopsy and auto-antibody were positive in 16 pSS cases while only biopsy was positive in 25 cases and only antibody in 1 case. Both biopsy and antibody were positive in 5 Scl-SS cases while only biopsy was positive in 18 and only antibody in 3 cases. The PCF was identified in 24 pSS cases while 5 Scl-SS cases. The PCF was statistically significantly higher in pSS cases ($p = 0.003$). No difference was seen between SS subtypes in terms of lymphocyte FS, fibrosis and auto-antibody positivity.
Conclusion: We found that PCFes could be found more frequently in pSS than Scl-SS. Additionally our study reveals that the co-existence of Scl-SS decreases the incidence of FS value ≥1 compared to pSS.

PS-12-035
Salivary gland tumours: The importance of molecular pathology
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Objective: There have been significant progress in our understanding of salivary gland tumours (SGT), with description of chromosomal translocations, that are useful for diagnosis, working as confirmatory test. CRTC1-MAML2 in mucoepidermoid carcinoma (MEC) correlates with better prognostic. EWSR1-ATF1 gene fusion is specifically found in hyalinizing clear cell carcinoma (HCCC). Mammary analogue secretory carcinoma (MASC) was recently described and associated with ETV6-NTRK3 translocation. We aim to report three illustrative cases of SGT: Case 1(MASC)- 23-year old female with a mass in the submandibular gland; Case 2(HCCC)- 51-year old female with a palatal mass with local recurrence after 10 years; Case 3(MEC)- 51-year old female with a lesion of the tongue.
Method: Clinicopathological information was collected from clinical files and pathology reports. Formalin-fixed paraffin-embedded specimens were used for molecular analyses using FISH.
Results: Case1: Microcystic architecture and eosinophilic homogenous bubbly secretion. Immunoprofile: S-100 protein+, DOG-1-. Case2: Admixture of clear and eosinophilic cells, embedded in hyalinized stroma. Immunoprofile: Cytokeratin+, p63+, myoepithelial markers-. Case3: Squamous, intermediate, and goblet cells with mucus production.
Conclusion: Molecular pathology offers new insights in terms of pathogenesis, diagnosis and prognosis that would help to improve the management of patients with SGT, adding value at a therapeutic level, particularly through the search of new biomarkers that could act as potential therapeutic targets.

PS-12-036
Chordomas of the head and neck region
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Objective: Chordomas are rare, locally agressive low grade malignancies that develop from notochordal embryonic residues. They show a dual epithelial-mesenchymal differentiation and account for 1–4 % of all bone malignancies. Chordomas preferentially occur in the sacrum (50–60 %). The head and neck localisation is not common. Here we report chordomas of spheno-occipital, and cervical region diagnosed in our department and summarize clinicopathological characteristics of these cases.
Method: Retrospectively, the cases diagnosed as "chordoma" were reviewed from 2002 to 2015. Clinicopathological features of cases with a tumour at spheno-occipital, and cervical region were assessed.
Results: Of 7 cases (4 males, 3 females) with a mean age of 48.4 (13–75 years). Six cases were diagnosed as conventional chordoma and one was chondroid chordoma. Mean follow-up was 34.5 months (10–110 months). Recurrence was detected in 2 cases and distant metastasis was determined in one case.
Conclusion: Chordomas resist chemotherapy and radiotherapy. Radical surgery and high-dose radiation are the most used treatments. Given the location and invasive nature of these tumours, complete resection is difficult.

PS-12-037
Granular cell tumour: Report of seven cases
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Objective: Granular cell tumour is an uncommon neoplasm of soft tissue that can arise in multiple corporal sites, but is mainly met in the skin, oral

cavity or digestive tract. We report seven patients with granular cell tumour in the oral cavity (four), the skin (two) and the breast (one). Three of the patients were men and three women and their age ranged from 15 to 42 years.
Method: In all cases an excisional biopsy of the neoplasm with safety margins was performed. Tumour sizes ranged between 0,5 and 2,3 cm. All the tumours were processed for histopathological and immunohistochemical study.
Results: The tumours were constituted by a poorly circumscribed proliferation of polygonal cells with central relatively small nucleus and a pronounced eosinophilic and granular cytoplasm. Two cases with spindle-cell morphology and prominent nucleoli, were characterized as "atypical". All tumour cells were positive for S-100 and CD68 and negative for Actin. No recurrence is reported, due to safe resection margins.
Conclusion: The origin of the granular cells is controversial. Granular cell tumours are benign and malignant cases are rare. Some granular cell tumours are called "atypical" in the presence of one or two histological criteria, established by AFIP.

PS-12-038
TERT promoter mutations in laryngeal squamous cell carcinomas
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Objective: Mutations in the promoter region of human telomerase reverse transcriptase (TERT) have been identified in over 50 cancer types, including many associated with ultraviolet (UV) exposure and having low rates of self-renewal cells. The high frequency of TERT mutations in cutaneous squamous cell carcinomas (SCC) have been revealed in many studies, but the data about laryngeal SCC is limited.
Method: In this study a total of 78 laryngeal SCC tissues were obtained, genomic DNA's were isolated from formalin-fixed, paraffin-embedded tumour tissue samples and TERT promoter region (the positions of C228T and C250T) mutations were analyzed by PCR-based direct sequencing method.
Results: TERT promoter mutations were detected in only 4 of 78 cases (5.1 %). Somatic C228T and C250T mutations was demonstrated in 3 and 1 cases, respectively. 4 patients were heavy smokers, 3 cases were stage 1 and one case was stage 3 laryngeal SCC. Only one of them had a recurrence. We did not find any statistically significant clinicopathological features in laryngeal SCC with TERT mutations.
Conclusion: In conclusion, our results demonstrated that TERT promoter mutation in laryngeal SCC is uncommon. This finding was consistent with the role of UV in cutaneous SCC pathogenesis and we did not find any association with prognosis.

PS-12-039
Peripheral odontogenic myxofibroma of the maxilla: A case report and literature review
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Objective: To report an unusual case of peripheral odontogenic myxofibroma (POM) of the maxilla.
Method: We reviewed the clinical chart and pathological report of a POM patient treated at Department of Oral and Maxillofacial Surgery, Chulalongkorn University, Thailand.
Results: A 27-year-old African woman presented with a painless maxillary mass developing a few months ago. She denied previous trauma and any medical history. An excisional biopsy under local anaesthesia was performed. The histologic findings demonstrated a lobulated tumour mass composed of haphazardly arranged stellate and spindle-shaped cells in the myxoid stroma interspersed with variable amounts of collagen fibres. Islands of odontogenic epithelium were also presented. The diagnosis of POM was established.
Conclusion: There have been limited numbers of POM reported in the literature. It is hypothesised that this tumour derives from an abnormal development of the pulpal organ or supportive structures of the teeth. Because of its rarity, there is no universally accepted treatment for POM. Its therapies vary from enucleation and curettage with/without peripheral ostectomy, to radical jaw resection with tumour free margin of 1.5–2 cm and removal of neighbouring teeth. The recurrence rate can be up to 25 %. We also reviewed the literature on this tumour.

PS-12-040
A rare neoplasm of trachea: Inflammatory myofibroblastic tumour
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Objective: Inflammatory myofibroblastic tumour (IMT) is a rare and usually benign soft tissue lesion that mainly occurs in the lung and abdominopelvic region of children and young adults. The most common sites of extrapulmonary IMT are the mesentery and omentum. The IMT also known as plasma cell granuloma or inflammatory pseudotumour.
Method: The surgical specimens were formalin-fixed and paraffin embedded. The section were stained with routinary H&E. Immunohistochemistry was performed.
Results: A 52-year-old woman had a history of breast cancer. After the breast surgery computed tomography showed a solitary mass measuring approximately 12 × 10 mm in the proximal tracheal lumen. The resected tumour appears tan-yellow. Microscopic examination revealed a mixture of spindle cells showing fibroblastic and myofibroblastic differentiation. Admixed with the spindle cell proliferation was an inflammatory infiltrate containing lymphocytes, polymorphonuclear leukocytes and plasma cells. Immunohistochemically, the tumour cells stain strongly for vimentin, anaplastic lymphoma kinase (ALK) and focally for muscle specific actin. The tumour had a low Ki-67 proliferative index. We diagnosed this case as IMT. ALK positivity can be helpful in the differential diagnosis of these neoplasms.
Conclusion: Clinical presentation of IMT can mimic malignant neoplasms. Involvement of trachea by this tumour is extremely rare with only a few published case reports.

PS-12-042
A rare case of NUT midline carcinoma of the parotid gland
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Objective: NUT midline carcinoma (NMC) is a recently described entity with a predilection for young individuals and a poor prognosis. It is characterized by chromosomal translocation of the NUT gene. It usually involves midline structures with a minority of cases presenting outside of the midline axis. We describe an exceptional case of a NMC arising in the parotid gland.
Method: A 34-year-old male presented with a rapidly growing left cervical mass. MRI revealed an isolated lesion of the left parotid gland measuring 30 × 21 mm. Parotidectomy with lymphadenectomy was performed.
Results: Gross examination revealed a 35 mm white solid infiltrating parotid tumour with invasion of the surrounding soft tissue, adjacent to the surgical margin. Histology showed a poorly-differentiated carcinoma with nests of undifferentiated cells merging with foci of necrosis and occasional abrupt foci of well-differentiated squamous epithelium with keratinization. In the context of a primary parotid carcinoma with squamous differentiation in a young patient, t(15;19) was determined by FISH. A diagnosis of NMC without

metastases was rendered. Currently (4 months), the patient is undergoing adjuvant chemo-radiotherapy.
Conclusion: This case emphasizes the importance of considering NMC in the differential diagnosis of poorly differentiated carcinomas of the head and neck region in young adults, even outside of the midline structures.

PS-12-043
Dentin dysplasia type 1 in an orthognathic patient: A case report and literature review
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Objective: To present an unusual case of dentin dysplasia type 1 (DTDP-1) undergoing an orthognathic surgery.
Method: Using a retrospective study design, we analysed the clinical chart and radiographs of an orthognathic patient with DTDP-1.
Results: A 34-year-old Caucasian man was referred to our department for combined orthodontics-orthognathic surgery-prosthodontic treatments. On the initial examination, the patient presented with skeletal class III and edentulous area of the left posterior maxilla. Radiographically, most of the teeth, despite clinically asymptomatic, had short roots. The patient has lost several teeth over the past decade. The diagnosis of DTDP-1 was diagnosed based on the radiographic and history findings. Other family members are free from the disease.
Conclusion: DTDP-1 (OMIM: #125400) is a rare autosomal-dominant form of DTDP and seriously affects dental root development. The patients often have severe tooth mobility, spontaneous early tooth loss, abnormal tooth spacing or malocclusion. Genetic studies and counselling are required because of the familial nature of the disease. Various preventive dental measures is necessary to prevent pulpal/periapical infections and early tooth loss. The careless orthodontics-orthognathic surgery may accelerate the early tooth exfoliation. We also review and discuss clinical, genetic, pathological and therapeutic aspects of this disease.

PS-12-044
Next Generation Sequencing analysis of ameloblastomas
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Objective: Ameloblastomas are benign odontogenic tumours of the jaws that exhibit aggressive biological behaviour with local recurrence. There are various types of this tumour and confusion still exists among clinicians as to its correct classification. A comprehensive molecular prolifing of ameloblastomas was performed to identify novel genomic alterations that will led to recognation of molecular subtypes and influance the new therapeutic approaches.
Method: In this study, a total of 60 formalin-fixed, paraffin-embedded ameloblastoma samples were sequenced using the Ion Torrent PGM and the 30 gene AmpliSeq Library Kit from 10 ng of extracted DNA. Histological subtyping for ameloblastomas was done on hematoxylin-eosin sections.
Results: Next generation sequencing analysis showed that BRAF and PTEN were the most frequent altered genes in all subtypes of the ameloblastomas. Solid/multicystic ameloblastomas displayed remarkable gene mutation compared to unicystic type. There was not any gene alteration in respect to histologic subtypes of the tumour.
Conclusion: This is the first comprehensive genomic analysis of ameloblastomas that will shed new light on fundamental aspects in understanding the molecular pathogenesis of odontogenic tumours and may help in the development of new targeted therapies.

PS-12-045
Rhinosporidiosis: Report of four cases from the Eastern Province of Rwanda
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Objective: Rhinosporidiosis is a tropical disease caused by Rhinosporidium seeberi. Originally described by Seeber in Argentina, the disease is primarily observed in India and Sri Lanka. There is only one brief report documenting the disease in humans previously in Rwanda (1993). The Anatomic Pathology Laboratory at the "Centre Hospitalier Universitaire de Kigali (CHUK), a teaching hospital in Rwanda, started operating in October of 2013. We report four cases of rhinosporidiosis confirmed by histopathology.
Method: We conducted a retrospective search for cases of Rhinosporidiosis in the anatomic pathology files of CHUK from 2013 to 2016. Slides were retrieved and the diagnosis was confirmed for all cases. PAS-D and MSS stains were performed in one case.
Results: Four cases of Rhinosporidiosis were identified. Two cases were diagnosed in 2014, one in 2015, and one in 2016. All four patients were males. Their ages were 7, 12, 13 and 15. All presented with a history of nasal obstruction and had a nasal mass on exam. Of interest, three patients are from the same district (Gatsibo, Eastern Province) in Rwanda.
Conclusion: We document four cases of Rhinosporidiosis from the Eastern Province, Rwanda; three within the same district. The clustering of cases suggests a probable reservoir in the area.

PS-12-047
Sinonasal primitive neuroectodermal tumour: An unusual presentation and outcome
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Objective: To report histopathological features of sinonasal primitive neuroectodermal tumour.
Method: A 56-year-old man, with no medical history, presented with epistaxis.
Results: On otolaryngological examination, a polypoid mass of nasal cavity measuring 1 cm. The craniofacial CT scan showed a heterogeneous soft tissue mass originating from the left maxillary sinus, without bone involvement. The detailed metastatic work-up was negative. The endoscopic biopsy resection revealed small round cell tumour expressing diffusely CD99. The neuroendocrine, lymphoid and epithelial markers were negative. A EWS gene rearrangement was demonstrated by FISH molecular analysis. The patient underwent several cycles of neoadjuvent chemotherapy and he was still under follow-up without features of recurrent disease for 15 months.
Conclusion: PNET is rarely encountered in sinonasal region. It is exceptional in middle-aged adults. We tend to show that despite the aggressive character of PNET, an early diagnosis at a localized stage can improve the outcome.

PS-12-048
Twist, snail, integrin beta-1 and e-cadherin expression in odontogenic lesions
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Objective: The potential role of epithelial mesenchymal transition (EMT) molecules in the tumourogenesis of odontogenic lesions has not been investigated in detail. Here we aimed to evaluate Twist, Snail, Integrin β-1 and E-cadherin expression in

ameloblastoma (ABL), keratocystic odontogenic tumour (KOT), orthokeratinized odontogenic keratocyst (OOKK) and dental follicle (DF).
Method: Twist, snail, integrinβ-1 and E-cadherin expression were examined immunohistochemically and expression of these factors have been scored on the basis of staining intensity and ratio of positive cells.
Results: Mean expression scores of all four markers were highest in DF. There weren't any statistically significant difference in expression scores of snail and twist for the groups however E-cadherin and integrinβ-1 expression values of DF were statistically significant. E-cadherin expression was also significantly higher in OOKK in comparison to KOT and ABL. For solid and unicystic ABL we didn't observe any statistical significance in expression scores of markers.
Conclusion: Higher twist and snail expression in DF may point out to role of these factors in odontogenesis rather than odontogenic tumour pathogenesis. Significant loss of E-cadherin and integrin β-1 expression in ABL and KOT may facilitate loss of adhesion between tumour cells and could be associated with tumour invasiveness and progression.

PS-12-049
Factors that may influence polymorphous low-grade adenocarcinoma progression
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Objective: There is mounting evidence highlighting the importance of some biological processes in tumour growth, such as vascular supply, apoptosis, autophagy and senescence. We have investigated such scenarios in Polymorphous low-grade adenocarcinoma (PLGA) in an attempt to identify those that are relevant for this particular lesion.
Method: We analyzed 31 cases of PLGA using immunohistochemistry for anti-CD34 and anti-CD105 to detect blood vessels; anti-D2-40 to detect lymphatic vessels; anti-Bax, anti-Bcl-2 and anti-Survivin to explore cell apoptosis; anti-Beclin and anti-LCB3 to investigate autophagy and anti-p21 and anti-p16 for senescence.
Results: Immunohistochemical results showed that PLGA containing numerous CD34-positive blood vessels, very low number of CD105 positive cells and scarce lymphatic vessels. Bcl2 was strongly and uniformly expressed whereas Bax expression was weaker and heterogeneous often within the same lesion. Survivin, Beclin and LC3B were strongly expressed in PLGA cells. Regarding senescence, the results showed that PLGA cells do not express p21 and only a small proportion of lesions show positivity to p16.
Conclusion: PLGA progression does not depend on newly formed vessels, it is otherwise promoted by autophagy, sustained by both anti-apoptotic and anti-senescence signals and stimulated by Bcl-2 and Survivin.

PS-12-052
Castleman's disease mimicking a parotid tumour
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Objective: Castleman disease (CD) is a rare benign lymphoproliferative disorder of unknown etiology, typically presenting as a solitary mediastinal mass. The head and neck region is the second most common site; however, the salivary glands are rarely affected. Two clinical (localised and generalised) and three histopathological (hyaline vascular, plasma cell, and mixed) types have been described. We present a case of a 59-year-old male patient with parotid CD of the mixed type as a rare entity.
Method: A 59 year old man presented to our otorhinolaryngology clinic complaining of tinnitus. The patient underwent a left superficial parotidectomy with a clinical prediagnosis of mucoepidermoid carcinoma.
Results: H&E stained sections showed mostly preserved lymph node architecture. Some lymphoid follicles had atrophic germinal centers and mantle zones was expanded with the cells somewhat aligned concentrically. Also there were sclerotic blood vessels radially penetrated the germinal centers, the overall appearance of the follicle may resemble a lollipop. The diagnosis rendered was CD, mixed type.
Conclusion: The wide spectrum of clinical manifestations makes the diagnosis a challenge. It is diagnosed by exclusion with the aid of histopathological examination. Therefore, it is important that physicians consider this clinical entity so patients can receive adequate and early treatment.

PS-12-053
Analysis of BRAF V600E (VE1) protein expression and BRAF mutation status in salivary gland cancers
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Objective: The aim of the present study was the analyses of BRAF V600E(VE1) protein expression and BRAF mutation status in codon 600 in salivary gland cancers.
Method: For identification of BRAF V600E(VE1) protein, the immunohistochemical (IHC) staining was performed on the TMA salivary gland tissue sections derived from 95 patients. Furthermore, the automatic PCR-based diagnostic platform was enriched for the evaluation of mutations in codon 600 of BRAF gene.
Results: By IHC cytoplasmic BRAF V600E(VE1) protein expression was found in 2/95 cases: respectively, 1/3 (33 %) case of adenocarcinoma, and 1/5 (20 %) case of carcinoma ex pleomorphic adenoma. The non-specific nuclear BRAF V600E(VE1) protein expression was evaluated in 14 (15 %) cases of all analyzed samples. In this group there were 9/28 (32 %) cases of pleomorphic adenoma, 3/5 (60 %) cases of ductal carcinoma, 1/9 (11 %) cases of mucoepidermal carcinoma, and 1/5 (20 %) case of carcinoma ex pleomorphic adenoma. All analyzed cases were negative for PCR-based analyzes of BRAF V600 mutations.
Conclusion: In heterogeneous group of salivary gland cancers further molecular analyses are necessary for better understanding the role of genetic alterations. We have found an peculiar BRAF V600E protein expression which was not confirmed by molecular tests.

PS-12-054
The inorganic pyrophosphatase (PPA1) expression as the new potential metastatic parameter in laryngeal squamous cell carcinoma (LSCC)
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Objective: Is PPA1 correlated with unfavorable outcome in head and neck cancers.
Method: Combining the 2D electrophoresis and mass spectrometry performed on three groups of LSCC cell lines, derived from primary tumours, recurrent tumours and metastases, were used for identifying the potential biomarker candidates of relapse and metastasis in LSCC. Furthermore, the immunohistochemical (IHC) analysis were performed for evaluation of selected protein expression and localization in primary LSCC N(0), N(+) and SCC metastases in lymph nodes.

Results: Annexin V, calreticulin and the PPA1 were identified exclusively for significant upregulation in the metastases-derived cell lines. Furthermore, using IHC these selected upregulated proteins were compared according their abundance in primary LSCC N(0), LSCC N(+), and in LSCC metastases in lymph nodes. Our results show a positive correlation between the PPA1 protein expression and the presence of lymph node metastasis ($p < 0.001$). For the other two proteins, there was no statistically significant correlation.
Conclusion: The PPA1 protein could become potentially novel biomarker of metastasis in LSCC. Revealed group of proteins are deregulated in recurrences and metastases of LSCC, and might be useful biomarkers identified in molecular background of LSCC.

PS-12-055
Lymphomas of Waldeyer's Ring: Clinicopathologic study of 22 cases
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Objective: The purpose of our study was to present epidemiological and pathological particularities of Lymphomas of Waldeyer's Ring (WR).
Method: We analyzed Lymphomas of W R registered in the Department of Pathology of Mohamed Tahar Maamouri in Tunisia from January 2005 to march 2016.
Results: We registered 22 cases. There were 16 males and 6 females and their ages varied from 51 to 80 years with a median age of 51 years. Nasopharynx is the most common location (13 cases). In 18 cases lymphomas were of B-cell phenotype (8 cases diffuse large B cell lymphoma, 8 small cell lymphoma, 1 plasmablastic lymphoma and 1 Burkitt lymphoma). They were of T-cell phenotype in 3 cases (1 case LT NOS, 1 case NK/T cell lymphoma, nasal type, 1 angioimmunoblastic T-cell lymphoma, 1). Hodgkin lymphoma was diagnosed in 1 case.
Conclusion: The present study shows that the most common location of Lymphomas of WR is the nasopharynx. Median age in our series was 51 years, most lower than that reported in the literature. Our study shows a predominance of diffuse large B-cell lymphoma sub type as shown in in the literature.

PS-12-057
Papillary carcinoma arising in a thyroglossal duct cyst: A case report
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Objective: The thyroglossal duct cyst (TGDC) is the most common congenital abnormality of the thyroid gland development. It is estimated that it occurs in 7 % of the adult population. However, the highest incidence of thyroglossal duct cyst is encountered among children and adolescents. Only 1 % of TGDC develop carcinomas: 90 % of all carcinomas are papillary thyroid, 5 % squamous cell carcinomas, 2–3 % follicular carcinomas; anaplastic carcinomas are rare and medullary carcinomas have never been described. TGDC carcinomas are more frequent in women, with a sex distribution of 1,5:1 up to 2:1.
Method: We present the case of a 25 year old woman with a pre-laryngeal mass, unrelated to the thyroid. Clinically and imagistically, the thyroid gland was unmodified and no enlarged lymph nodes were identified. The mass was excised using the Sistrunk procedure.
Results: Paraffin embedded sections were stained with hematoxylin and eosin and examined microscopically, revealing a TGDC component with a papillary thyroid carcinoma arising from it, confirmed by immunostaining for cytokeratin 19.
Conclusion: Because total thyroidectomy was not performed in this case, the dilemma of differentiating between primary TGDC papillary carcinoma and metastatic thyroid papillary carcinoma remains unsolved, so long-term monitoring of the thyroid gland is needed.

PS-12-059
Polymorphous low-grade adenocarcinoma of the parotid gland: A case report
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Objective: Polymorphous low-grade adenocarcinoma (PLGA), the most common malignant neoplasm of minor salivary glands, occurs very rarely in major salivary glands, most frequently in parotid gland. Less than 40 cases have been reported to date. Its morphological diversity and exceptional occurrence in major salivary glands make diagnosis difficult.
Method: 52-year-old woman presented with retroauricular oval nodule, present for several years, increasing in size recently. Surgically excised specimen was a circumscribed, partly incapsulated nodule measuring 2,5 cm. Microscopically tumour was composed of monomorphic, cuboidal cells with vesicular nuclei and lightly eosinophilic, focally clear cytoplasms, forming lobular, tubular, trabecular and solid patterns with scant eosinophilic, somewhere myxoid stroma. Tumour focally infiltrated adjacent adipose tissue. Strong immunoreactivity for CK7, Vimentin, S-100, and moderate GFAP positivity was observed. Proliferative index Ki67 was low.
Results: Defining characteristics of PLGA are cellular uniformity and great histologic variability. PLGA may occur either de novo or develop in a pre-existent pleomorphic adenoma. Only 8 cases of de novo PLGA originating in major salivary glands were reported. Pleomorphic adenoma presents the main differential diagnostic dilemma. PLGAs uniformly express CK7, S100 and vimentin positivity and GFAP is usually negative, although some authors reported positive staining in up to 15 % of PLGAs. Pleomorphic adenomas reveal strong positivity for GFAP.
Conclusion: GFAP positivity in major salivary gland PLGA may suggest a malignancy arising in pre-existent pleomorphic adenoma.

PS-12-060
Dedifferentiated epithelial-myoepithelial carcinoma of the parapharyngeal area: Case report
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Objective: Epithelial-myoepithelial carcinoma (EMC) is a rare low-grade salivary gland malignancy of presumed intercalated duct origin comprising 1 % of all salivary gland tumours. High grade transformation in EMC is a recently recognised entity with few cases reported in the literature. Abrupt transition of the myoepithelial and/or ductal component of EMC into high grade carcinoma is referred to as "dedifferentiated EMC". The most common site of involvement was the parotid gland, followed by the submandibular gland, the palate and nasal cavity.
Method: An additional case of dedifferentiated EMC in the parapharyngeal area. The patient was a 65-year-old man presented with a rapid growth of a mass in the left submandibular area which he had first noticed 4 years ago. CT imaging demonstrated a 41 × 30 mm, central necrotic lesion extending from nasopharynx to parapharyngeal area Histologically, most parts of the lesion were high-grade carcinoma with sheetlike and nestlike growth of markedly atypical cells and comedonecrosis, whereas the minor part consisted of typical EMC.
Results: We report this case with histological and immunohistochemical analyses and review of the literature.
Conclusion: The aggressive behaviour of dedifferentiated EMC suggests that it is important to recognise this variant of EMC to avoid misdiagnosis and inappropriate treatment.

PS-12-061
Sporadic endolymphatic sac tumour: Case report and review of the literature
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Objective: Endolymphatic sac tumour (ELST) is a rare neoplasm with benign histopathological appearance and clinically destructive behavior which occurs in the skull base and frequently invades the petrous bone, the mastoid, semicircular canal, cerebellopontine angle structures and cranial nerve. The term "aggressive papillary middle ear tumour" has been proposed to describe this invasive type of middle ear tumour. These tumours can be encountered sporadically or in Von Hippel-Lindau (VHL) disease.
Method: Here we report a sporadic case of ELST in 54-year-old woman. There wasn't any symptoms or history of VHL disease in the patient. She presented with a chief complaints of vertigo and hearing loss approximately 15 year duration. CT imaging demonstrated a destructive lesion of the right petrous bone. MR scanning revealed a 6 × 7.5 mm mass which showed peripheral hyperintensity and central hypointensity on T1- and T2-weighted images. Microscopically the tumour was composed of typical papillary structures lined by a single layer of cuboidal to columnar epithelial cells The stroma of the papillary fronds was richly vascularized. The epithelial cells had uniform nuclei and pale eosinophilic to clear cytoplasm. Immunohistochemically the tumour cells showed positive reactivity with pan-CK, CK7, EMA, vimentin, and focal reactivity with glial fibrillary acidic protein (GFAP) and p53.
Results: Because of the rarity of this tumour, it can easily be confused with other tumours such as paraganglioma, middle ear adenoma, adenocarcinoma, papillary carcinoma of thyroid or choroid plexus papilloma.
Conclusion: These tumours constitute a distinct pathological entity and have clinically destructive behavior.

Tuesday, 27 September 2016, 09.30–10.30, Hall 11.3
PS-13 Pulmonary Pathology

PS-13-002
PD-L1 expression in NSCLC and biopsy size
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Objective: Higher PD-L1 expression in tumour cells predicts better response rate in NSCLC patients treated with immune checkpoint inhibitors. Small biopsies are predominant specimen type available for predictive testing. We analyzed PD-L1 expression in various biopsy size specimens of NSCLC tumours.
Method: The study included resection specimens (N = 63), tissue microarrays prepared from resected tumours (n = 50), and small biopsies obtained during diagnostic procedures (N = 64). FFPE sections were prepared for immunohistochemistry using PD-L1 rabbit monoclonal antibody (clone SP142, Roche, USA) on an automated staining platform (Benchmark ultra, Roche, USA). PD-L1 expression was evaluated on tumour cells with membranous staining. PD-L1 positivity was defined by two cutoff values, 1 and 5 %.
Results: There were 48 % positive cases among resection specimens at 1 % cutoff value, and 38 % at 5 % cutoff value. For tissue microarrays, we obtained 12 and 8 % positivity, at 1 and 5 % cutoff values. For small biopsies, the positivity rate was 16 and 14 %, at 1 and 5 % cutoff values. Higher PD-L1 expression was observed in SCC. Taking 1 % cutoff value, SCC positivity rate was 71 % in resection specimens, 11 % in tissue microarrays, and 16 % in small biopsies.
Conclusion: We conclude that size of biopsy has major impact on PD-L1 tumour positivity most probably due to heterogeneous expression.

PS-13-003
Role of the stem cell niche of respiratory acini in lung tissue remodeling in idiopathic interstitial pneumonia and pulmonary sarcoidosis
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Objective: to study morphology and molecular mechanisms of lung tissue remodeling in stem cell niche of respiratory acini (SCN) in different idiopathic intersticial pneumonia (IIP) and sarcoidosis (S).
Method: Biopsies from 252 patients with IIP and SL were. There were patients with interstitial lung fibroses-118 cases (47 %), nonspecific interstitial pneumonia—35 cases (14 %), desquamated interstitial pneumonia—23 cases (9 %), cryptogenic interstitial pneumonia—18 cases (7 %). S was without and with prominent fibrosis—43 cases (17 %) and 15 cases (6 %). Immunohistochemical detection of Apo-Cas, Ki 67, PCNA, MMP 1, 2, 4, 7 and TIMP, SMA, Desmin, Vimentin, CK 5, 6, 7, 19, CD68, EMA, TGF-β, TNF -α, CD34, PDGF, EGF, FGF-b, Oct.-4, CD 117 with statistical analysis was done.
Results: Cells of SCN may express markers of stem cells (Oct.-4, CD 117, CD34), mesenchymal (SMA, Desmin, Vimentin) and epithelial (CK, EMA) differentiation, play central role in the pathological remodeling and mesenchimal-epithelial transdifferentiation in lungs.
Conclusion: Remodeling of lung tissue in SCN is the key process in structural rearrangements in IIP. Persistent and severe damage of SCN leads to the development of fibrosis and adenomatous hyperplasia and lung cancer.

PS-13-004
The role of TRAP1 in the assessment of invasion in lung adenocarcinoma with lepidic pattern
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Objective: The extent of invasive component in lung adenocarcinomas is associated with clinical outcomes. However, determination of invasion is the most difficult issue in practical pathologic diagnosis. The TNF receptor-associated protein 1 (TRAP1), an important member of mitochondrial heat shock protein 90 family, is involved in neoplastic progression because of its ability to suppress cell death and reorganize cellular metabolic pathways.
Method: We performed immunohistochemical detection of TRAP1 in 57 small (≤3 cm) resected lung adenocarcinomas with lepidic pattern [11 adenocarcinoma in situ (AIS), 24 minimally invasive adenocarcinoma (MIA) and 22 invasive lepidic adenocarcinoma (ILA)] to evaluate relationship between expression of TRAP1 and invasion.
Results: No TRAP1 expression was seen in non-neoplastic alveolar parenchyma. MIA (17 of 24, 70.8 %) and ILA (17 of 22, 77.3 %) more frequently showed expression of TRAP1 than in AIS (4 of 11, 36.4 %). Although the frequency of TRAP1 expression between MIA and ILA did not reach statistical significance, ILA frequently showed high (strong staining in ≥50 % of tumour cells) expression of TRAP1.
Conclusion: The expression of TRAP1 may contribute to local tumour invasion and TRAP1 can be a potentially useful marker for assessment of invasion in lung adenocarcinoma with lepidic pattern.

PS-13-005
Four-year audit on molecular testing in metastatic lung cancer on small biopsy/cytology samples in an Irish rapid access lung cancer centre
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Objective: To assess the frequency of EGFR mutations and ALK fusion over a 4 year period and in advanced stage non small cell lung carcinoma.
Method: Molecular data from the laboratory files were recorded to include sex, age, type of sample (cytology/histology, biopsy vs. surgical) on which molecular testing was performed (RT-PCR and FISH), type of mutations, histological subtypes, and failure rates.

Results: 301 cases were collected, and in 87 %, the sample type tested was non surgical (biopsy/cytology) . Women represented 53 % of the cohort, 30 % of the testing was done on cytological samples, of which 65 % were EBUS samples. Thirty-one percent of testing was done on lung CT guided core biopsy samples. Adenocarcinoma represented 88 % of the tumour subtypes. Regarding EGFR, 13 % of patients were found to harbour mutations with 71 % of these being women. Exon 19 deletions and exon 21 L858R mutation were the most common (51 and 23 %). ALK rearrangement was detected in 3 % of cases, 56 % were women. TTF-1 was expressed by tumour cells in 87 % of EGFR mutated adenocarcinomas and 83.3 % of ALK rearranged adenocarcinomas. In this cohort with a predominance of small samples, failure rate for EGFR testing reached 9 and 15.6 % for ALK FISH testing.
Conclusion: This audit from a single institution with a rapid lung cancer assessment clinic and formal MDT appraisal of all patients diagnosed with lung cancer, provides similar rates of EGFR mutations and ALK rearrangement to that published in non -Asian populations, in a cohort where 87 % of molecular tests were done on biopsy/cytology samples, further emphasizing the feasibility of these techniques on small samples

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PS-13-006
Pulmonary placental transmogrification: The last 16 years in a reference center
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Objective: Placental transmogrification of the lung is an unusual histopathologic pattern first described by McChesney in 1979, characterized by formation of placental villus-like structures in the lung parenchyma. This condition has been described in patients with bullous emphysema and fibrochondromatous hamartomas. The aim of this work is evaluate the prevalence of this rare feature in this type of pathology.
Method: A total of 103 pulmonary hamartomas and 410 bullous emphysema diagnosed in the Centro Hospitalar Lisboa Norte (Lisbon) during 16 years (2000–2015) were retrieved. Histologic slides of all these cases were reviewed for the presence of villus-like papillary projections and/or placenta-like structures.
Results: Placental transmogrification was identified in 3 of 513 cases (0.58 %) of pulmonary resections; 1 case with clinical information of hamartoma and 2 of emphysema. Histologically showed multiple villous structures resembling placental chorionic villi.
Conclusion: Placental transmogrification is regarded as an unusual benign lesion curable by surgical resection. The origin and pathogenesis are still unknown; some authors have hypothesized that this condition is likely a congenital malformation; others believe that a proliferating respiratory epithelium exceeding the stromal component may induce placental papillary projections. In our opinion probably results from the development of oedema, fibrosis, and chronic inflammation in the residual alveolar tissues.

PS-13-008
Experience in determine ROS 1 with immunohistochemistry and FISH in primary lung adenocarcinoma in the 12 de Octubre hospital from 2013 to 2016 (Madrid, Spain)
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Objective: Determine the number of patients with primary lung adenocarcinoma and translocation of ROS-1 gene with immunohistochemistry and FISH, to compare results of both techniques in a period from January 2013 to March 2016 in the 12 de octubre hospital.
Method: In a retrospective observational study, we identified 436 patients diagnosed with primary lung adenocarcinoma in the 12 Octubre hospital from January 2013 to March 2016. All patients were performed determination of biomarkers, including ROS-1.
Results: 436 patients with lung adenocarcinoma, 62 % were males and 38 % female, with an average age of 74 years. 1.1 % of the cases had ROS-1 gene translocation, and the average age was 53 years (60 % were men). 80 % of cases were positive also with immunohistochemistry. There was only one case with ROS-1 positivity by immunohistochemistry and had no gene amplification by FISH.
Conclusion: The incidence of translocation of the ROS1 gene in our study population was 1.1 %. Comparing the two techniques, we observed a high correlation between positive cases. Our results are similar with the published literature that estimate the incidence of ROS-1 in 1 % of patients and could be benefited with anti-tyrosine kinase treatment.

PS-13-009
Fluorescent in SITU hybridization analysis of the ALK gene in 2045 non-small cell lung cancer patients from Northwest Spain (Galicia)
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Objective: Description of our experience as a referral center in the public health care system of Galicia, in Northwest Spain, for the identification by fluorescent in situ hybridization (FISH) of the anaplastic lymphoma receptor tyrosine kinase gene (ALK) rearrangements in advanced non-small cell lung cancer (NSCLC) patients; and the correlation between ALK patterns and clinicopathologic features.
Method: 2045 samples of NSCLC patients were collected from 2010 to 2015 and tested by FISH. We examined 1686 paraffin-embedded tissue specimens and 395 cytological samples (306 cell block preparations and 53 cytological smears), and investigated any correlation between the FISH results and the clinicopathological features.
Results: Tissue samples showed a higher rate of successful evaluation than cytological samples (92.9 versus 84.1 %), but this difference was not significant. ALK rearrangements were identified in 82 (4 %) patients; 65 (79.3 %) in tissue specimens, 15 (18.3 %) in cell block samples and 2 (2.4 %) in cytological smears. This translocation was associated with a non-smoker history, younger age, female gender, stage IV, and an adenocarcinoma histological type.
Conclusion: ALK evaluation by FISH is feasible in both tissue and cytological samples. Clinicopathological features of our ALK positive patient series are similar to those previously reported in the literature.

PS-13-011
Microvascular proliferation is associated with aggressive tumour features and reduced survival in lung adenocarcinomas
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Objective: Despite new treatment options in lung cancer, there is still need for new and better prognostic factors to assist in treatment decisions. Angiogenesis has been associated with tumour growth and dissemination, and our research group has found that vascular proliferation index (VPI) is a valuable prognostic marker. Here, we studied the prevalence and prognostic impact of VPI on cancer specific survival (LCSS) in lung adenocarcinomas (AC).
Method: Selected tumour slides from a cohort of 210 patients surgically treated for AC at Haukeland University Hospital, Bergen, Norway, during 1993–2010, were stained for Nestin/Ki-67 (dilutions 1:50/ 1:100). VPI was evaluated as the ratio between proliferating vessels (pMVD) and the microvessel density (MVD). Cut-off value was set at 1.9 % (median).

Results: High VPI was associated with high tumour grade ($p = 0.012$), a solid growth pattern ($p = 0.039$) and high tumour stage ($p = 0.019$). Further, high VPI was significantly associated with reduced LCSS ($p = 0.020$).
Conclusion: Angiogenesis by VPI can be evaluated by Nestin/Ki-67. High VPI is associated with aggressive tumour features such as tumour grade and stage, and also reduced LCSS, in lung AC. VPI could be a marker for prognosis and should be studied in other cohorts.

PS-13-012
Recurrent chronic thromboembolic pulmonary hypertension due to occult pulmonary intimal sarcoma
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Objective: Pulmonary intimal sarcoma (PIS) is a rare tumour and difficult to diagnose because its clinical features often mimic chronic thromboembolic pulmonary hypertension (CTEPH). We report a recurrent CTEPH case of 65-year-old man to clarify the cause of recurrence of CTEPH by histology.
Method: The excised specimens of the first and the second pulmonary endarterectomy (PEA) were compared histopathologically and immunohistochemically.
Results: The excised specimen of the first PEA composed of organized and hyalinized thrombus without cellular component. The patient showed a good outcome for 5 years after PEA. However, because of recurrence of pulmonary hypertension, re-PEA was performed. The obtained specimen of the second PEA showed undifferentiated intimal sarcoma in peripheral pulmonary artery with gelatinous appearance macroscopically. The histology of the gelatinous part showed spindle-shaped sarcoma cells scattered in myxomatous extracellular matrix. The proximal part of the specimen composed of non-specific hyalinized material like thrombus which was the same appearance of the first PEA specimen. The patient had no underlying disease such as coagulation abnormality, deep venous thrombosis, or any other primary malignant disease. He died after the second PEA for 6 months, although adjuvant chemotherapy was done.
Conclusion: After 5 years of initial operation of PEA, CTEPH re-occurred. The cause of this case of CTEPH finally revealed intimal sarcoma of pulmonary artery. PIS is a rare disease. The histological feature of extracellular matrix of PIS was very similar to organized thrombus of CTEPH. The behavior of PIS occasionally mimics CTEPH because PIS is sometimes slow growing accompanying with rich extracellular matrix like thrombus.

PS-13-013
Histological conformity of primary lung carcinoma type in biopsy and operation material
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Objective: To compare the histological diagnosis of lung carcinoma in biopsy and operation material in order to detect the frequency of morphological conformity.
Method: The retrospective study included 59 consecutive patients who underwent both pulmonary biopsy and resection due to primary lung carcinoma. The histological tumour type was assessed in haematoxylin-eosin (HE) stained slides. Immunohistochemistry was performed upon necessity. Lung tumour classification by World Health Organization, 2015 was applied. Descriptive statistics was performed including detection of 95 % confidence interval (CI).
Results: The study group comprised 59 cases of which 44 (74.6 %; CI = 62.2–83.9) showed morphological conformity of diagnosis in biopsy and operation material by HE. These cases comprised squamous carcinomas (55.9 %; CI = 43.3–67.9), adenocarcinomas (11.9 %; CI = 5.9–22.5), small cell carcinomas and carcinoids (each, 3.4 %; CI = 0.9–11.5). Fifteen tumours (25.4 %; CI = 16.1–37.8) were diagnosed as non-small cell carcinomas by HE in the biopsy. Among these, 11 cancers (18.6 %; CI = 10.7–30.4) were attributed to specific histological subtypes after evaluation of surgical material or by immunohistochemistry but 4 cases (6.8 %; CI = 2.7–16.2) remained as large cell carcinomas.
Conclusion: Three fourths of primary lung carcinoma can be reliably diagnosed by HE in biopsy. The remaining cases necessitate investigation of operation material (if available) and immunohistochemistry.

PS-13-014
The histopathological and immunohistochemical charasteristics of malignant pleural mesothelioma and its microenviroment: A study of 116 cases
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Objective: The aim of our work was to search for morphological and immunohistochemical (PD-L1) prognostic factors of 116 MPM.
Method: We performed a retrospective study on 116 MPM diagnosed at our institution from 1993 to 2015. The following histopathological data were collected: the presence of necrosis, nuclear atypia, nucleo-cytoplasmic ratio, the aspect of chromatin, the size of nucleoli and Furhman grade, mitotic count and the presence of an intra-tumoural lymphocytic infiltration. Immunohistochemical expression of PD-L1 was also studied.
Results: As expected, sarcomatoid, biphasic or desmoplastic subtypes were associated with a poorer prognosis ($p = 0.0006$). Regardless histopathologic subtype, the presence of necrosis ($p = 0.0336$), nuclear atypia ($p = 0.0002$), mitotic count ≥ 3 ($p < 0.0001$), presence of atypical mitosis ($p = 0.0003$), nucleoli ≥ 3 μm ($p = 0.0001$) and Furhman grade >1 ($p = 0.0485$) were associated with a poorer prognosis. Within epithelioid subtype all these factors were significantly related to prognosis. Within sarcomatoid, biphasic and desmoplastic MPM only atypical mitosis was significanly related to prognosis. PD-L1 (E1L3N) expression was significantly associated with a poorer prognosis in epithelioid MPM ($p = 0.0441$). PD-L1 expression was higher in sarcomatoid MPM.
Conclusion: Our work highlights several prognostic factors in MPM, that could help for a stratification for the treatment of patients with MPM.

PS-13-015
Prognostic significance of Glycine Decarboxylase and HIF-1 alpha expression in early stage NSCLC
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Objective: Glycine Decarboxylase (GLDC) is a critical enzyme of tumour-initiating cells (TIC), which have a stem cell phenotype and are held responsible for increased tumourigenicity, therapy resistance and recurrent disease. GLDC is furthermore important in metabolism under hypoxic conditions. Because conflicting results were published concerning the prognostic significance of TIC cell surface markers in lung cancer, our aim was to study the immunohistochemical expression and prognostic significance of GLDC and HIF-1α in a large homogeneous cohort of stage I/II NSCLC.
Method: Immunohistochemistry for GLDC and HIF-1α was validated on two NSCLC cell lines (A549, NCI-H460), evaluated in 428 patients on a tissue microarray with 466 NSCLC, and compared with clinicopathological parameters.
Results: High-GLDC was detected in 33/428 cases (7.7 %), HIF-1α was expressed in 71 (16.6 %) cases—more frequently in SqCC ($p < 0.001$).

GLDC and HIF-1α were significantly associated with worse tumour related survival (p = 0.013, p = 0.021). Patients with low-GLDC/negative HIF-1α showed a significantly longer survival (p = 0.013, p = 0.002), likewise younger patients (p = 0.007), patients with non-large cell carcinoma histology (p = 0.006), and lower pT-category/UICC-stage (p = 0.002/p = 0.001). In multivariate analysis, UICC-stage, age and combinatory GLDC/HIF-1α expression were independent prognostic factors.
Conclusion: Low-GLDC expression without expression of hypoxia markers is a favorable prognostic marker in early stage NSCLC.

PS-13-016
Loss of BRCA1 Associated Protein 1 (BAP1) is rare in lung adenocarcinoma
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Objective: BRCA1 associated protein 1 (BAP1) is a tumour suppressor involved in regulation of the cell cycle, cellular differentiation, repair of DNA damage and apoptosis. Loss of BAP1 protein expression in mesothelial proliferations has so far been shown to be 100 % specific for malignant mesothelioma. However, few studies have investigated the rate BAP1 loss in pleural metastasis of other malignancies. Our objective is to determine the rate of BAP1 loss in lung adenocarcinoma.
Method: Immunohistochemistry for BAP1 was performed on sections from a tissue microarray containing 80 confirmed cases of lung adenocarcinoma. The cases were interpreted as showing BAP1 loss if nuclear staining was completely absent in all tumour cells and present in lung stromal and inflammatory cells serving as internal controls. Cases showing BAP1 loss in the internal controls were excluded.
Results: After exclusion of 11 cases, 1 out of 69 cases of lung adenocarcinoma (1.4 % of cases) showed BAP1 loss. The remaining 68 cases showed preserved nuclear expression of BAP1 in both the lung adenocarcinoma and internal controls.
Conclusion: Loss of BAP1 expression is a rare event in lung adenocarcinoma. Therefore, BAP1 is a potentially useful addition to the immunohistochemical markers used to distinguish mesothelioma from pleural metastasis of lung adenocarcinoma.

PS-13-017
Epithelial-mesenchymal transition in patients of pulmonary adenocarcinoma: Correlation with cancer stem cell markers and prognosis
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Objective: Adenocarcinoma is the most common histologic type of non-small cell lung carcinomas. The existence of lung cancer stem cells (CSCs) and epithelial-mesenchymal transition (EMT) in human tissue is controversy. The aim of this study is to investigate the expression and clinical significance of CSCs and EMT markers and evaluate the correlation between the two in lung adenocarcinoma.
Method: A total of 97 cases comprise the tissue microarray from surgical resection for primary lung adenocarcinoma. Immunohistochemistry for ALDH1 and CD44 as CSC markers and E-cadherin, vimentin, fibronectin, SMA as EMT markers was performed.
Results: High ALDH1A1 expression was statistically associated with female gender (p = 0.001), smoker (p = 0.012), and high pT stages (p = 0.046). High CD44 expression was statistically associated with female gender (p = 0.008), non-smoker (p = 0.000), and no pleural invasion (p = 0.039). High expression of ALDH1 was associated with good overall survival (p = 0.021). High expression of CD44 was correlated with both good overall survival (p = 0.024) and disease-free survival (p = 0.000). Vimentin expression was associated with pT stage (p = 0.001) and pleural invasion (p = 0.028). CSC markers expression was not related to EMT.
Conclusion: Our results showed that the expression of CSCs was associated with a good prognosis in lung adenocarcinoma. The prognostic significance of EMT markers was skeptical in this study. There is a need for more research about CSC, EMT, and the relation between these two in human lung adenocarcinoma.

PS-13-019
External quality assessment of PTEN immunohistochemistry: Challenging pathologist's eye with computer-based intensity measurement in the ETOP Lungscape project
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Objective: The tumour suppressor PTEN serves as surrogate biomarker for hyperactive PI3K/Akt signalling, whereby its protein expression is a valuable read-out. However, no consensus regarding the optimal immunohistochemistry (IHC) protocol for fixed tissue exists. In this ETOP (European Thoracic Oncology Platform) Lungscape project we correlated pathologist's H-scores with computer-generated intensity measurements.
Method: 6 PTEN+ and 6 PTEN- tumour cases were centrally stained on whole sections with 3 different antibodies (MmAb 6H2.1 DAKO, RmAb 138G6 Cell Signaling and RmAb SP218 Spring Bioscience) and the scanned webbook H-scored by ETOP pathologists (range 0–300). Cases were also assembled into an EQA tissue microarray, stained locally with SP218. All stainings were finally analyzed using ImageJ for pixel-based intensity on tumour epithelia.
Results: All 3 antibodies successfully differentiated PTEN+ versus PTEN- cases. Computer H-scores were highly associated to pathologists', but with lower averages. Relative variability between centers was higher for PTEN-. On TMAs, computer scores showed lower inter-center variability. For 138G6 and SP218, sensitivity and specificity were high for moderate values of threshold h (0–20).
Conclusion: SP218 yields a clean IHC and well separates PTEN+ from PTEN- cases, favouring standardization across laboratories. Pathologists tend to H-score higher than the computer, likely due to integration of various signal intensities.

PS-13-020
Is better prognostic stratification of lung carcinoid tumours possible?
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Objective: Lung carcinoid tumours are rare neuroendocrine neoplasms. According to WHO classification typical and atypical forms exist, based on mitotic count and/or necrosis. This grading system is still the best prognostic parameter. Our study aimed to identify markers for subgroups having higher risk of metastasis, progression and worse overall survival.
Method: Patients from two institutions who underwent resection between 1971 and 2015 with adequate clinical information and archived material were identified. Tumours were stratified using mitosis count and/or necrosis. Immunohistochemical assessment of cyclin A, B and E (distinctive expression during cell cycle), neurotrimin, zinc finger protein like 1, and sorting nexin (lost on genomic level as demonstrated previously by arrayCHG and LOH), NCAM isoform 140kdA and Ki67, was performed.
Results: 297 patients (M = 148; F = 149; mean age: 49.3) were identified. 202 typical carcinoids (TC) and 95 atypical carcinoids (ATC). NCAM 140 kdA isoform demonstrated negative reaction in practically all TC, while ATC presented with faint reaction. Overall, cyclin E expression was lower in ATC, while cyclin B and A were higher expressed in ATC,

especially in the ones with higher mitotic rate. Preliminary data demonstrated protein expression loss of neurotrimin, zinc finger protein like 1, and sorting nexin in ATC.
Conclusion: NCAM isoform 140Kd is predominantly expressed in high grade neuroendocrine carcinomas and only minimally in ATC, whereas absent in TC. Different forms of cyclins are activated at specific time during mitosis and better reflect cell-cycle activity compared to Ki67. Staining for cyclins might be better suited for prognostic stratification of patients with carcinoids.

PS-13-021
Contributions of cytology examination in the diagnosis of non small cell lung tumours: A retrospective study
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Objective: Despite great advances in imaging technology for a better visualization and detection of lung cancer, early diagnosis of the neoplasm remains challenging. Cytology has a considerable contribution in the diagnosis of lung cancer; however it has an imperfect specificity for the subtyping of carcinomas. We aim in this study to determine the diagnostic reliability of pulmonary cytology in the diagnosis of non small cell carcinoma (NSCC).
Method: We have compared cytological and histological findings in patients who underwent the diagnostic procedure under suspicion of lung cancer (LC) over a period of 4 years.
Results: Of a total of 981 patients, 167 were microscopically diagnosed with a LC which was classified as NSCC in 83, 83 % of cases. The sensitivity and specificity of cytology were 97.94 and 100 %, respectively. The cytology-histology correlation in NSCC group was 65 %. In 5 cases, cytological specimens were highly suspicious of malignancy but assignment to a NSCC or a SCC was not possible. Microscopically, they were classified as a SCC in one case, adenocarcinoma in one case and squamous cell carcinoma in two cases.
Conclusion: Cytology is a reliable diagnostic tool in the diagnosis of lung malignancies, however, its contribution in tumour typing remains limited.

PS-13-022
Quantitative expression analyses of TTF-1 in NSCLC
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Objective: The aim of this study was to enhance diagnostic sensitivity for the detection of primary pulmonary adenocarcinomas. Therefore we analysed TTF-1mRNA by qRT-PCR and needle microdissection in 199 cases.
Method: TTF-1 mRNA and protein were detected by qRT- PCR and immunohistochemistry (Clone: 8G7G3/1) in FFPE tumour tissues. Overall 51 acinar (AC) and 50 solid pulmonary adenocarcinomas (SOL) were analysed. 49 pulmonary squamous cell carcinomas (SCC) and 49 pulmonary metastasis of colorectal adenocarcinomas (mCRC) served as controls. β2M served as housekeeping gene.
Results: TTF-1 mRNA expression was highest in AC and SOL. The Ct values amounted up to 23 × 10^3. mCRC and SCC showed significantly lower values. TTF-1 mRNA was detected in 88,2 % of AC und 76 % of SOL, but only in 6,5 % of SCC's and 8,1 % of mCRC's. TTF-1 protein was positive in 64,7 % of the AC's and in 60 % of the SOL's. 10 % of SOL's and 25,5 % of AC's were TTF-1 protein neg./mRNA pos.
Conclusion: The quantification of TTF-1 mRNA gives additional tumour specific information in 18 % of the TTF-1 neg. pulmonary adenocarcinomas. Thus, TTF-1 transcript quantification from FFPE tumour tissue can be considered as a valuable diagnostic tool, potentially accelerating clinical procedures.

PS-13-023
Pleural malignant mesothelioma: Evaluation of histopathological types and interventional diagnostic methods
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Objective: We reviewed PMM cases in this study to investigate the diagnostic value and timing of interventional methods and their effects on histopathological types.
Method: A total of 164 subjects were included in the study. The subjects were examined in terms of age, gender, histopathological type, diagnosis of PMM as well as number and type of any previous interventions, results of reports and timing of diagnosis.
Results: Histological types were classified as epithelioid 125 (76.2 %), biphasic 27 (16.4 %), sarcomatoid 10 (6 %), well differentiated papillary 1(0.6 %) and desmoplastic 1 (0.6 %). Diagnostic results of minimal invasive and surgical invasive methods (pleural effusion, closed pleural biopsy, fine needle aspiration and invasive surgical intervention) were determined benign, atypical, malignant and diagnostic sensitivity in order 136, 28, 6, 0.06; 17, 29, 28, 0.37; 4, 8, 3, 0.2; 5, 6, 128, 0.92. No significant difference was found between the interventional diagnostic methods and PMM types.
Conclusion: In conclusion, the first diagnostic intervention option should be the minimal invasive method in pathological approach to pleural diseases. When no satisfactory pathological diagnosis could be achieved in PMM suspected patients through clinical and radiological means, we recommend that more invasive methods should be attempted without delay.

PS-13-024
Histopathological study of pulmonary cysts in Birt-Hogg-Dube Syndrome
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Objective: Birt-Hogg-Dube syndrome (BHDS) is an inherited disorder caused by genetic mutations of folliculin (FLCN). Multiple pulmonary cysts and repeated episodes of pneumothorax are the characteristic features of individuals with BHDS. How to make the differential diagnosis between BHDS-associated pulmonary cysts (BHDSPC) and other cystic lung diseases is incompletely understood in pathology practice.
Method: We investigated the radiological and pathological features of BHDSPC in 73 individuals diagnosed by genetic testing. In addition to surgical specimens, one autopsied case was included. The histopathological features of BHDSPC were compared with those of various cystic lung diseases originally confused with BHDSPC, which included primary spontaneous pneumothorax, lymphangioleiomyomatosis, Sjoegren syndrome and chronic hypersensitivity pneumonitis.
Results: BHDSPC were preferentially located in the lower lobes. Grossly, cysts had very thin walls with a smooth and glistening inner surface, which histopathologically was lined by a layer of flat or cuboidal alveolar epithelium with the surrounding parenchyma showing no fibrosis unless accompanied by inflammation. Many of the cysts were closely associated with or partially incorporated into interlobular septa and/or bronchovascular bundles. Some cysts showed a multi-septate pattern.
Conclusion: The BHDSPC was grossly and histopathologically distinct from other cystic lung diseases. The nature of the cyst may be a hamartomatous formation of giant alveolus-like structure.

PS-13-025

Primary mucoepidermoid carcinoma of the lung: A case report

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Objective: Mucoepidermoid lung carcinoma is uncommon salivary gland-type tumour that usually occurs in youth with nonspecific symptoms. The aim is to present a case of mucoepidermoid lung carcinoma of 60-year-old man with dyspnea.
Method: Solitary pulmonary nodule in right upper lobe was seen radiologically. There were no changes seen during bronchoscopy and transbronchial needle biopsy of the lesion was done for cytological and histopathological examination.
Results: Cytologic smear stained by May-Gruenwald-Giemsa consisted of cylindrical, squamous cells and mucus. In histopathological material stained by hematoxylin-eosin, desmoplastic stroma with moderate lymphoplasmacytic inflammation was mixed with irregular cohesive small and moderate size polygonal cells with eosinophilic cytoplasm and pleomorphic vesicular nuclei. There were also goblet cells with Periodic-Acid-Schiff and Alcian Blue positive basophilic cytoplasm and basal nuclei, arranged in cysts filled with mucus, positive for the same stains. Diffuse cytoplasmic panCK, membrane EMA positivity in both cell types, intensive nuclear p63 positivity in polygonal cells and nonspecific cytoplasmic CD117 reaction were obtained using immunohistochemistry. Low-grade mucoepidermoid lung carcinoma was diagnosed and surgical treatment was indicated.
Conclusion: Mucoepidermoid lung cancer is a diagnostic challenge. Carefully diagnosing is important because most of the low-grade carcinomas have great outcome after surgery.

PS-13-026

PD-L1 expression in primary lung carcinoma and lymph node metastasis

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Objective: PD-L1 expression in tumour cells predicts better response rate in lung carcinoma patients treated with immune checkpoint inhibitors. We wanted to determine connection between PD-L1 expression in primary tumour and lymph node metastasis.
Method: We studied 32 resected primary lung carcinomas (15 adenocarcinomas, 13 squamous, 2 small cell and 2 adenosquamous) and their mediastinal lymph node metastases. FFPE sections were prepared using PD-L1 rabbit monoclonal antibody (clone SP142, Roche, USA) on an automated staining platform (Benchmark ultra, Roche, USA). PD-L1 expression was evaluated on tumour cells with membranous staining. PD-L1 positivity was defined by cutoff value of 1 %.
Results: PD-L1 was expressed in 47 % primary carcinomas (20 % adenocarcinomas, 77 % squamous, 100 % adenosquamous and in 0 % small cell). 25 % lymph node metastases expressed PD-L1 (33 % adenocarcinoma, 46 % squamous, 50 % adenosquamous and 0 % small cell). All PD-L1 positive lymph node metastases had PD-L1 positive primary carcinomas. 47 % of PD-L1 positive carcinomas had PD-L1 negative lymph node metastastasis.
Conclusion: We concluded that the finding of PD-L1 positive metastatic lymph node is diagnostic for PD-L1 expression in primary tumour, while the finding of PD-L1 negative lymph node metastasis is not, since the difference of PD-L1 expression in primary tumour and lymph node metastasis is significantly different.

PS-13-028

Lung adenocarcinoma with enteric differentiation: Immunohistochemical and molecular profiles

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Objective: Lung adenocarcinoma with enteric differentiation (LAED) has been recently recognized in the WHO classification. It is defined as an adenocarcinoma in which the enteric component exceeds 50 % and have to show the expression at least of one immunohistochemical marker of enteric differentiation. Although its definition is very important, above all in the differential diagnosis between a primary lung tumour and a metastasis of colorectal adenocarcinoma, this cancer still lacks a distinctive immunohistochemical and molecular signature.
Method: We recruited a large series of LAEDs and we evaluated the immunohistochemical and molecular profiles of these adenocarcinomas.
Results: In our series, CDX-2 and CK7 were the immunohistochemical markers mostly expressed by PAEDs. There was an inverse relationship between the expression of pnuemocytes-markers, such as TTF-1, and intestinal markers. Molecular analysis revealed K-RAS as the most frequently mutated gene, with very few cases harboring abnormalities affecting EGFR, B-RAF and ALK genes. LAEDs are morphologically very heterogeneous.
Conclusion: The immunohistochemical profile based on CDX-2 and CK7 positivity of LAEDs appears very robust to support this diagnosis, and it is applicable also on small biopsies. KRAS appears as the most important mutated genes in such tumours.

PS-13-029

Rate of EGFR, KRAS, HER2 and BRAF mutations and ALK rearrangement of metastatic lung adenocarcinoma according to the site of specimen: A study of 1400 cases

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Objective: To highlight the rate of these mutations in different organs with metastatic lung adenocarcinoma and its practical significance.
Method: We investigated EGFR, HER2, BRAF mutations and ALK rearrangement in 1400 cases of cytology, biopsy and surgically resected specimens. The rate of these genetic mutations or rearrangement was determined for each organ.
Results: We observed mutated EGFR in 14.97 % of pleural metastasis (31 out of 207), in 4.96 % (8 out of 161) of lymph node metastasis, in 11.36 % of bone metastasis (10 out of 88), in 5.40 % (4 out of 74) of brain metastasis and in 24 % of liver metastasis (6 out of 25). ALK rearrangement was found in pleura (3.86 %), brain (2.70 %) and lymph node (0.62 %) metastasis. Lymph node and liver metastasis showed HER2 mutations in 0.62 % and 4 % respectively. BRAF was mutated in pleural (2.41 %) and lymph node (1.24 %) metastasis. KRAS mutations were present in most metastatic sites with different percent.
Conclusion: Pathologists should be aware that mutation or rearrangement rate is highly different according to the site of the specimen. These results could help pathologist to prioritize molecular studies in case of insufficient material.

PS-13-030

Central versus peripheral carcinoid tumours of the lung

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Objective: Pulmonary carcinoid tumours occur in both central (endobronchial) and peripheral locations, and subtle clinicopathological differences have been observed. Recently we reported OTP (orthopedia transcription factor) as a useful marker for the diagnosis of lung carcinoid, and, during the investigation, found differences between OTP-positive and negative tumours.
Method: 107 resected carcinoid tumours were subdivided to three subgroups based on OTP and TTF1 (clone 8G7G3/1) expressions;

type 1 (OTP-/TTF1-), type 2 (OTP+/TTF1-), type 3 (OTP+/TTF1+), and histopathological parameters were compared among those subgroups.
Results: There were 21 cases in type 1, 32 in type 2, and 54 in type 3. Significant differences were seen between type 1 and 3 in gender, presence of sustentacular cells (STCs), location, circumscription, cell morphology, and presence of neuroendocrine hyperplasia (NH). Type 1 was characterised by male predominance, central location, lesser frequency of STC, well-circumscription, polygonal cell type, and no association with NH while type 3 was characterised by female predominance, peripheral location, presence of STC, and strong association with NH. Type 2 showed features in between.
Conclusion: Given the significant differences between type 1 and 3, lung carcinoid tumours may represent a group of tumours with heterogeneous pathogenesis. Further studies are required.

PS-13-031
Caveolin-1 in the differential diagnosis of malignant mesothelioma and lung adenocarcinoma
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Objective: Caveolin-1 (CAV-1), is a structural protein of the endocytic caveolae plasma membrane, has a profound role in modulating tumourigenic processes. Many researches suggest the eligibility of this protein in discriminating between two malignancies; the lung adenocarcinoma (LAC) and malignant mesothelioma (MM). In this study we aimed to demonstrate the value of Cav-1 staining in the distinguishing between MM and LAC.
Method: Paraffin-embedded blocks from surgical material of 68 MM (51epitheloid, 12 bifasic and 5 sarcomatoid type) and 61 LAC were obtained from the archive of Pathology Department at Gaziantep University. The cases were stained with Cav-1 mouse monoclonal antibody then, percentage of positive tumour cells was scored as negative if there is no staining, and positive if more than 1 % tumour cells have been stained.
Results: Cav-1 expression with a membranous and/or cytoplasmic pattern was detected only in 22 of MM (15 epitheloid, 5 bifasic and 2 sarcomatoid type) and only four cases of LAC showed a positive staining with Cav-1. The internal positive control which was detected in all cases was the alveolar or endothelial cells around the tumour and inside it. Statistically, there was no significant difference between two groups.
Conclusion: Cav-1 has no significant role in differential diagnosis between MM and LAC.

PS-13-032
Pulmonary and cutaneous remodeling in mice model of systemic sclerosis
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Objective: We recently demonstrated an experimental model of systemic sclerosis (SSc) by immunizing healthy New Zealand rabbits with human collagen V (COLV). In the present work, we aimed to characterize histopathological features of pulmonary and cutaneous remodeling in SSc patients and in COL V immunized mice.
Method: Immunized mice (n = 10) 7 weeks old received twice injections subcutaneously with an emulsion of COLV (150 μg) and complete Freud's adjuvant (FA) in a 30 days interval, followed by two intramuscular boosters of COLV and incomplete FA. After 75 days from the first immunization, pulmonary and cutaneous remodeling was evaluated by histomorphometry and immunohistochemistry.
Results: Lung from immunized mice presented a significant higher amount of type I collagen ($p < 0.005$), lymphocytes CD4 ($p = 0.002$), TGF-β ($p < 0.0025$) and CTGF ($p < 0.0001$) when compared to control. In addition IM presented significantly cutaneous inflammatory process ($p < 0.0068$) and predominance of fine fibers compared the thick collagen identified by assessment of picrosírius respectively ($p < 0.0001$).
Conclusion: We demonstrate that all typical manifestations of SSc-related pulmonary and cutaneous remodeling are mimicked by COL V immunized mice, thus emerging as an appropriate preclinical model to study the mechanisms and therapeutic approaches of lung and skin involvement in SSc.

PS-13-033
PTEN and pAKT differs in histological subtypes in NSCLC
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Objective: The PI3K/PAKT/mTOR pathway is activated in many cancers, thus reducing apoptosis and allowing proliferation. On the other hand, it can be antagonized by PTEN. In up to 60 % of squamous cell carcinoma of the lung the PIK3/PTEN/AKT pathway is affected. Therefore we investigated the association of the expression between PTEN and pAKT and correlated these data with histological subtypes of NSCLC.
Method: Expression of PTEN and pAKT was analyzed by double stain immunohistochemistry in tissue microarrays from 444 NSCLC tissues and correlated with clinical and pathological parameters.
Results: PTEN expression showed correlation with age and smoking habit. Furthermore, PTEN was significantly higher expressed in adenocarcinoma ($p = 0.001$). Interestingly, pAKT expression was more intense not only in adenocarcinoma, but also in large cell neuroendocrine lung cancer compared to other NSCLC types ($p = 0.001$). Moreover, a co-expression of PTEN and pAKT in the same cell occurred prevalently in adenocarcinoma ($p = 0.001$).
Conclusion: The different expression profiles of PTEN and pAKT according to histological subtypes of NSCLC hint at diverging regulation of the PI3K/AKT/mTOR pathway in different NSCLC subtypes.

PS-13-034
Subcellular localization of PTEN and pAKT correlates with histological grading in NSCLC
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Objective: The activation of the PI3K/AKT/mTOR pathway as well as the loss of PTEN are known tumour inducing factors. Furthermore, the relevance of the subcellular localisation of PTEN and pAKT was lately described. Therefore, we investigated their expression in NSCLC, with special emphasis on protein localisation.
Method: In 444 NSCLC- and corresponding non-neoplastic lung tissue the nuclear and cytoplasmic expression of PTEN and pAKT was tested by double stain immunohistochemistry and correlated with clinical and pathological parameters.
Results: Both PTEN and pAKT were significantly higher expressed in tumour cells in comparison to non-neoplastic lung tissue. Furthermore, cytoplasmic PTEN showed first upregulation toward poorer differentiated tumours and loss in undifferentiated large cell lung cancer samples ($p = 0.003$). Cytoplasmic pAKT expression got more pronounced with dedifferentiation ($p = 0.009$).
Conclusion: Our data suggest that the subcellular localisation of PTEN and pAKT is important in the dysregulation of the PIK3CA/PTEN/AKT pathway in different histological grading.

PS-13-035

Automated ALK and ROS1 FISH: A comparison between Leica Biosystems Kreatech FISH Probes for BOND and manual FISH

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Objective: A panel of lung cancer fluorescence in situ hybridization (FISH) probes has been released for use on Leica Biosystems' Bond platforms. These FISH probes were tested on non-small cell lung cancer (NSCLC) cases side by side with manual methods to compare the quality of staining and the work flow efficiency of the automated FISH assay.
Method: A study of 10 archival formalin-fixed paraffin-embedded NSCLC cases were tested with the Kreatech ALK and ROS1 FISH probes on the Leica BOND III platform and compared to the results achieved using manual methods.
Results: All automated tests resulted in diagnosable slides with 100 % concordance (n = 20) between the two methods. The hands-on time per sample with the automated probes is reduced by over 1 h.
Conclusion: The comparison study showed that the automated FISH assay resulted in an identical clinical outcome to the manual assay. The reduced hands-on time and the possibility for laboratories to combine automated FISH with routine immunohistochemistry workflow, makes FISH on BOND a promising new addition to the test menu of an Anatomical Pathology laboratory.

PS-13-036

Determination of EGFR by liquid biopsy in patients with primary large cell carcinoma of lung from November 2015 until March 2016 at the University Hospital 12 de Octubre (Madrid, Spain)

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Objective: Analysis of EGFR in plasm and lung tissue in patients with large cell carcinoma of lung in a period between November 2015 and March 2016 at the University Hospital 12 de Octubre of Madrid.
Method: Determination of EGFR by real-time PCR using the Kit System Cobas Z 480 Roche, for genetic screening of mutations, deletions or insertions in exons 18, 19, 20 and 21 of the EGFR gene both DNA circulating blood material and tissue pulmonary.
Results: Were performed 62 determinations of EGFR in patients with large cell carcinoma of lung, with an average age of 72 years, of which 17.7 % were positive in plasm, with good agreement with lung tissue determinations, and 3.2 % were not evaluable. Of the positive cases, there was a jarring case that showed positivity in pulmonary tissue and negativity in plasm. However, another case was positive only in plasm.
Conclusion: Lung biopsy is the currently used technique for diagnosis of malignancy, even it is an invasive method, sometimes difficult. Therefore liquid biopsy may have an important role in genetic determinations. Because of these findings of the present study, it may be considered liquid biopsy as a method for early diagnosis and treatment of lung cancer.

PS-13-037

Prognostic significance of nuclear grade in malignant pleural mesothelioma: A single institution experience

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Objective: Malignant pleural mesothelioma(MPM) is an uncommon aggresive malignancy associated with asbestosis exposure. We investigated whether certain histomorphologic parameters correlated with survival of surgically resected MPM.
Method: From January 2000 to December 2015, we retrospectively reviewed tumour slides of surgical specimens of 30 patients with histologically confirmed MPM. Seven histomophologic features including histological pattern, nuclear grade, depth of invasion, lymphocytic host response(LHR), necrosis, stromal desmoplasia and mitotic index were investigated and analyzed in SPSS 18.0.
Results: We classified 90 % of the patients(27 of 30) as epithelial and 10 % of them(3 of 30) were biphasic type. Subtypes were categorized by histological patterns; solid pattern was most common with 36,7 % (11 of 30). Desmoplasia was observed 63,3 % (19 of 30) of cases. LHR was scored as low in 40 %, intermediate in 36,7 % and high in 23,3 % of patients. Invasion depth was above 5 mm in almost all cases with two cases exceptional. We counted less than 5 mitosis/50 HPF in 56,7 % (17 of 30) and five and more mitosis were counted in 43,3 % of cases. Prognostic datas of 11 patients were collected with five of death after surgery.
Conclusion: High nuclear grade might be considered significantly associated with death ratio in MPM. Larger series are required to determine associations between morphological features and survival.

PS-13-039

Histology versus cytology in the diagnosis of small cell lung cancer: Is it a real advantage?

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Objective: Currently, most cytopathologists are able to correctly distinguish small cell lung cancer (SCLC) from non small cell lung cancer on the basis of cytologic samples, and, indeed, 75 % of lung cancers are diagnosed based on cytology. The authors propose to study the concordance of diagnosis between cytology and histology.
Method: Retrospective study of all cases of SCLC diagnosed over a period of 4 years.
Results: Over a period of 4 years 981 fine needle aspiration samples were obtained from patients with suspicious thoracic lesions. In 167 patients, a cytological diagnosis of malignancy was obtained, and 168 received a parallel or subsequent histological diagnosis. A total of 25 patients with histologically proven SCLC were included. Sex ratio was 8 and the mean age at the time of diagnosis was 64 (34–87). Cytology was performed in all cases. Only 22 cases were conclusive of SCLC. Cytological and histological typing was concordant in 97 % cases (kappa = 0.97). Immunohistochemistry was conducted in 5 cases to correct the diagnosis.
Conclusion: Cytology examination is fairly accurate for typing SCLC and can be regarded as an acceptable procedure for diagnostic. In doubtful cases, the use of ancillary techniques, such as immunocytochemistry, may be required to improve the diagnostic yield.

PS-13-040

Mesenchymal stem cells- and conditioned medium reduce fibrosis in pulmonary parenchyma but promote increased artery adventitia remodeling in bleomycin-injured mice

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Objective: The understanding of pulmonary fibrosis (PF)has been focused on model forinjuries and dysfunctionsof epithelialorendothelial cells. However, recent study showed that pulmonary artery adventitia (PA) and myofibroblastmay act as biological processing center and critical regulator of remodeling. Our aim was to investigate the role of mesenchymal stem cells- and conditioned medium treatment in remodeling of PF.
Method: 15 Wister rats were induced with Bleomycin. After 10d,5 were treated with mesenchymal stem cells (MSC), 5 withconditioned medium

(CM) and 5 without treatment (BLM). Animal were sacrificed 21 days after bleomycincompared to controls (CTR; n = 5). Hematoxylin&eosin,picrossirius red staining, "in situ" immunofluorescence for type I and Vcollagen, and morphometric analysis were performed.
Results: Pulmonary fibrosis collagen I modulated was significantly reducedin MSC and CMcompared to BLM rats ($p < 0.05$), whereasa significant increase in fibrosis collagen V modulated was found in PA from MSC rats ($p < 0.05$).
Conclusion: Pulmonary fibrosis collagen I modulate is reverted byMSC and CM treatment However, MSC and CM treatment modulate collagen V fibrosis in PA, thus suggesting a new important link between pulmonary fibrosis and hypertension.

PS-13-041
Phosphatase and tensin homolog (PTEN) is upregulated in the matricellular stroma of non-small cell lung carcinoma
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Objective: Recently, Trimboli et al. demonstrated that phosphatase and tensin homolog (PTEN) inactivation in stromal fibroblasts of mouse mammary glands accelerates malignant transformation of mammary epithelial tumours and leads to massive remodeling of extracellular matrix (ECM). Based on these findings we investigated the protein expression of PTEN in the immediate peritumoural stroma, called matricellular space, and the corresponding tumour epithelia of non-small cell lung carcinoma (NSCLC) together with relevant extracellular matrix proteins.
Method: Expression of PTEN and ECM proteins were immunohistochemically determined on a tumour tissue microarray of 456 patients with NSCLC of all pT stages. Additionally, 48 cases were evaluated on whole slides.
Results: PTEN expression in both cytoplasm and nucleus was higher in the matricellular cancer-associated fibroblasts (CAFs) than in the carcinoma epithelia. Complete loss of stromal PTEN was infrequent. High PTEN in both stroma and tumour was associated with lower pT and smaller tumour size. High vimentin, versican and collagen but not periostin expression was positively correlated with PTEN in both tumour and stroma.
Conclusion: PTEN loss in both cytoplasm and nucleus occurs more frequently in lung SqCC than AdC. Peritumoural CAFs have a higher PTEN protein expression than the adjacent malignant epithelia. PTEN protein synthesis decreases with increasing tumour size.

PS-13-042
Pulmonary epithelioid haemangioendothelioma—a case report
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Objective: Epithelioid haemangioendothelioma (EHE) previously known as intravascular bronchoalveolar tumour. This is a rare disease, with approximately 50 cases described in the literature.
Method: We report the case of a 60 year old women with treated for myomateux uterus. We discover by chance in CT scan a basi-thoracic mass left. Left lower lobectomy and lymph node dissection were made. Histological examination concluded epithelioid haemangioendothelioma, confirmed by immunohistochemical study.
Results: About 60–80 % of patients with EHE are women. Patient ages range from 7 to 81 years. About 50–70 % of patients are symptomatic at presentation. Imaging show multiple bilateral perivascular nodules, that mimic metastatic cancer or granuloma. At macroscopy, EHE presents with multiple circumscribed nodules with a grey-white cut surface and chondroid appearance. At histopathology, EHE round to oval nodules, composed of strands and solid nests of rounded to slightly spindled cells, with intracytoplasmic lumina containing red blood cells. Most EHE expresses the vascular markers CD31, CD34 and focal cytokeratin expression is present in 25–30 % of cases.
Conclusion: This tumour can affect multiple organs. The prognosis is very unpredictable, with life expectancy ranging from 1 to 15 years. There is no single effective treatment, though spontaneous regression and response to chemotherapy and interferon are reported.

PS-13-043
Sclerosing pneumocytoma—about two cases
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Objective: Pulmonary sclerosing pneumocytoma (SP) is a epithelial tumour, formerly nomed sclerosing haemangioma. We report two cases of SP in two women aged 63 and 45 years. Histological examination and immunohistochemistry was accurate diagnosis of the nature of the tumour.
Method: Case 1: 63 year old women, Chest CT shows solitary mass in the right lower lobe. The patient had a lower lobectomy and lymph node dissection. Histological examination concluded SP, confirmed by immunohistochemical study. Case2: 45 year old women treated for breast neoplasm, CT scan done under the staging. Chest CT shows multiple left parenchymal nodules. Histological examination concluded sclerosing pneumocytoma.
Results: The sclerosing pneumocytoma is benign lung tumour derived from primitive respiratory epithelium. This is a rare tumour usually asymptomatic, occurring in 80 % of cases among middle-aged women. Chest X-ray shows a solitary and well circumscribed mass. Histologically, the SP is characterized by solid, papillary, sclerotic, and haemorrhagic regions. The tumour consists a dual population of surface cells resembling type II pneumocytes and round cells, with slightly different histogenetic profiles. Regional lymph node metastases are rare.
Conclusion: Sclerosing hemangiomas of the lung are generally considered benign lesions, and surgical excision is curative without the need for additional treatment.

PS-13-044
Pulmonary Alveolar Microlithiasis. Case report and literature review
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Objective: Pulmonary Alveolar Microlithiasis (PAM) is a rare autosomal recessive lung Disease, which has been associated with mutations in the SLC34A2 gene. Approximately 400 cases have been reported around the world, the majority in Europe and the Middle East. Countries with highest number of reported cases include Turkey, Italy and the USA. Only rare cases have been described in Africa. We report the first case from Rwanda.
Method: We identified one case in the pathology archives of King Faisal Hospital, Kigali, Rwanda. Diagnosis was confirmed by transbronchial biopsy.
Results: We report a 19 year- old female who consulted for general checkup. X-ray and CT scan images found incidentally diffuse sandstorm images in both lungs. Lung biopsy was done and morphological examination showed numerous round intra-alveolar calcifications consistent with Pulmonary Alveolar Microlithiasis. Her sister who was asymptomatic at that time was also tested in relatives check-up, and her radiologic images showed some diffuse sand like opacities in both lungs.

Conclusion: We document Pulmonary Alveolar Microlithiasis to increase awareness of this rare disease in Rwanda. Definitive diagnosis is obtained by histopathology. There is no specific treatment but disodium etidronate may improve the condition.

PS-13-045

Blood sample-based New Generation Sequencing detects circulating free MicroRNA from acute pulmonary thromboembolism (liquid biopsy)

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Objective: Acutepulmonary thromboembolic (APTE) is a blockage of an artery in the lungs by a thrombo that has traveled from elsewhere in the body through the bloodstream. Our aims was to determinate a plasma microRNA profile as a diagnostic and prognostic biomarker of APTE.
Method: 17APTEpatients and 10 patients and 10 healthy volunteerswere sequentially studied in 2016. All relevant clinical data from medical records andangiotomographyresults were analyzed. An optimized protocol for RNA extraction from plasma samples by Qiagenmirneasy serum/plasma kit in combination with the Vac-Man® Vacuum Manifold were used. The Illumina TruSeq Small RNA-Seq Sample Prep Kit was used to generate small RNA library directly from total RNA. Clustering and sequencing was accomplished using the Illumina NextSeq500. Further databases and software used for analysis were the Diana software.
Results: Dyspnea was the most common symptoms experienced by patients. Only one patient had deep venous thrombosis. All patients had unchanged echocardiography. High-quality RNA were extracted. Circulating microRNAs were differentially expressed and associated with prognostic outcome ($p < 0.05$).
Conclusion: The MicroRNA profile might reflect alterations in Virchow's triadof APTE, providing some clue for biomarker screening, however it still needed to be validated to clinical practice.

PS-13-046

Mutation profile and protein expression for predictive testing in lung adenocarcinoma: A study of 200 patients from Brazil

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Objective: New translational research platforms for selecting and validating clinically relevant prognostic biomarker are needed. Our aims was to determinate the mutational status versus protein expression is related to impact on survival of non-small cell lung cancer (NSCLC).
Method: 200 patients with NSCLC were selected in 2014–2016 for immunohistochemistry and 80 for next generation sequencing. All relevant clinical data from medical records, like survival time, were analyzed. A protocol for DNA extraction from frozen samples by QIAmp DNA kit were used. The Illumina TruSeq Amplicon Sample Prep Kit was used to generate DNA library. Clustering and sequencing was accomplished using the Illumina NextSeq500. Further databases and software used for analysis were the VariantStudio. CD44, EGFR, P53, VEGF, KRAS, HER2, PIK3CA, BRAF and ALK antibodies were used for immunohistochemistry and analyzed by AperioSystem.
Results: Different type of mutation were found. The most of them correlated with the respective protein expression. CD44 mutation is present in 33 % of them and related with CD44 expression in a survival time-dependent manner. Mutation status versus protein expression were differentially expressed and associated with prognostic outcome ($p < 0.05$).
Conclusion: Personalized cancer medicine in DNA-based high-throughput genomic technologies might provide excellent results for biomarker screening, however it still needed to be validated to clinical practice.

PS-13-047

Lung cancer of clinically unknown primary: An autopsy-based study

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Objective: Lung is the most frequent primary site identified by autopsy in the clinical (type-1) Cancer of Unknown Primary origin (CUP) cases. To reveal the factors behind this, our goal was to examine the clinicopathological differences between CUP and non-CUP metastatic lung cancers.
Method: 11,046 autopsy cases of 22 years were analyzed. Clinicopathological factors of 39 CUP and 269 non-CUP metastatic lung cancers were compared.
Results: Significant difference ($p < 0.05$) was found regarding the distribution of histological types; adenocarcinoma was more (56 vs. 41 %), squamous type was significantly less (8 vs. 32 %) frequent in CUPs. Bone metastases (43.6 vs. 9.7 % in total and 50 vs. 22.7 % in adenocarcinomas), paraneoplastic syndromes (31 vs. 13 %), peripheral localization (58 vs. 37 % in total and 90 vs. 57 % in adenocarcinomas) furthermore pain as first clinical symptom (26 vs. 13 %) were significantly more common in CUP cases of the lung.
Conclusion: Higher frequency of the peripheral localization among lung CUPs can contribute to keeping the primary site clinically hidden. Occurrence of these cases can be reduced by taking into consideration clinicopathological differences of the CUP and non-CUP metastatic lung cancers. Autopsy is necessary for the correct post-mortem identification and classification of CUP cases.

PS-13-048

EGFR mutational status in a series of non small cell lung carcinomas: Data from daily practice

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Objective: The prognosis of metastatic non-small cell lung cancer (NSCLC) is still poor. Activating epithelial growth factor receptor (EGFR) mutations are important genetic alterations with dramatic therapeutically implications. Up to now, in contrast to Asian populations only limited data on the prevalence of those mutations are available from patients with European ethnicity.
Method: In this study, routine EGFR testing with real- time PCR assay for 198 patients with NSCLC patients from Bosnia and Herzegovina were tested in various types of tumour samples.
Results: Activating EGFR mutations were found in 6,57 % of all tumours, frequently in women (4,55 %) than in a men (2,02 %) Mutations in exon 19 deletion and 21 (L858R) accounted for 76.92 and 15.38 % and 7.69 % exon 20 insertion. EGFR gene mutations was higher in surgically resected specimens (69,23 %) than in biopsy material (23,08 %).
Conclusion: The incidence of EGFR mutations from clinical routine in Bosnia and Herzegovina was lower than those reported in other Caucasian and European populations.

PS-13-049

Clinicopathological and histomorphological features of congenital cystic adenomatoid malformations: Characteristics of mucinous epithelium

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Objective: Congenital cystic adenomatoid malformations(CCAM) are rare lesions. This study aims to represent characteristic of epithelial lining of CCAM and histomorphological findings contained within CCAM.
Method: Thirteen cases of CCAM type 1 and 2 were identified in retrospective search of the surgical database of our institution from 2010 to 2016. H&E stained slides were evaluated to identify detailed histomorphological features of CCAM. Immunohistochemical stains for mucinous epithelium were evaluated in 3 cases.
Results: The patients were 7 female and 6 male, 9 of cases were younger than 1 year. The accompanying lung tissue was diagnosed as normal pulmonary parenchyma (n = 9), bronchopneumonia (n = 1), bronchiectasis (n = 2) and one did not have any tissue other than CCAM. The cysts of all of the cases were lined by pseudostratified respiratory epithelium. Three cases had multifocal mucinous epithelial lining which formed protruding mucinous tuftings. Mucinous epithelium was positive for MUC5 and negative for MUC1 and 2. Squamous metaplasia was seen in 2 cases. Smooth muscle, mostly focal, around the cysts of CCAM was found in all cases. In only one case, bronchial glands was noted. Within the cystic areas of all of the cases, chronic inflamatory cells were present, and lymphoid follicules was detected within the cystic areas of 6 cases. None but one case had bronchial glands within the cystic area of lesion.
Conclusion: Pseudostratified respiratory epithelial lining, pericystic focal smooth muscle and chronic inflamation are common features of CCAM type 1 and 2. MUC profile of mucinous component of epithelial lining of the cysts was positive for MUC5 and negative for MUC1 and 2.

PS-13-050
Pleural NUT carcinoma with unusual chromosomal rearrangement
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Objective: To introduce the morphological and immunohistochemical characteristics of one case of uncommonly located NUT carcinoma with unusual chromosomal rearrangement.
Method: A 22 years old male patient suffered from rapidly progressive pleural effusion. Multiple pleural nodules were identified in CT examination and were surgically biopsied. The specimen was totally submitted for histological examination, including immunohistochemical staining. Detection of special chromosomal rearrangement by FISH was also carried out.
Results: Histologically, the tumour was predominantly composed of sheets or nodules of small undifferentiated cells with hyperchromatic nucleus and scant cytoplasm, among which some nests of large cell with vesicular nucleus and ample cytoplasm were observed. The transition between the two kinds of cells was abrupt. Large areas of coagulative necrosis and desmoplasic stroma were present. No obvious squamous differentiation was observed. The tumour cells were diffusely immunoreactive with antibodies to p63, Vimentin, CD34 and NUT protein and focally to SMA. Split of Chromosome 15 was detected by FISH, but rearrangement with BRD4 was not identified.
Conclusion: NUT protein positive confirmed the diagnosis, although, in this case, the location, morphology and genetic changes were not typical for nut carcinoma.

PS-13-051
Diffuse pulmonary meningotheliomatosis: A rare entity
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Objective: Multiple minute pulmonary meningothelial-like nodules are incidentally found during pathologic examination of lung biopsies. In some patients, these nodules cause diffuse radiologic abnormalities and restrictive lung disease, which has been called as diffuse pulmonary meningotheliomatosis.
Method: Here in, we present a 60-year-old woman with this uncommon lesion. She had complaints of dispnea and cough. Computerized tomographic evaluation revealed bilateral pulmonary nodules/densities. She underwent open surgery.
Results: Histopathologic evaluation showed multiple interstitial nodules distributed in a randomized fashion. Epithelioid and spindle cells were seen in a vaguely nested growth pattern around vessels. Immunohistochemically, these cells were positive with Vimentin, EMA, Progesterone receptor and Beta-catenin, negative for Melan A, S-100, HMB45, Desmin and estrogen receptor.
Conclusion: In the presence of these features, pathologists should be aware of diffuse pulmonary meningotheliomatosis in the clinical setting of multiple pulmonary micronodules.

Tuesday, 27 September 2016, 09.30–10.30, Hall 11.3
PS-14 Thymic and Mediastinal Pathology

PS-14-001
Mediastinal tumours and cysts: Analysis of 142 cases
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Objective: The present study was undertaken to know the pathological spectrum of mediastinal lesions and to determine the presenting features, location, histology, surgical technique.
Method: We reviewed a series of 142 consecutive patients with mediastinal space-occupying lesions (anterior, middle, posterior compartments) referred to us between January 2009 and December 2014. All patients with undiagnosed mediastinal pathology were referred for tissue biopsy to obtain a tissue diagnosis. There were 51 females and 91 males patients. Average age was 56 years. The youngest patient was 17 years old and the oldest, 82 years old.
Results: The highest incidence of malignancy occured in the first (100 %) and third (65 %) decades and the most common malignancy during the first four decades of life was malignant lymphoma (42 %). The most common presenting symptoms were dry cough (40 %), chest pain(42 %), dyspnea (39), weight loss (22 %) and pleural effusion (10 %). Twelve percent of patients were completely asymptomatic. The majority of tumours and cysts were located in the anterior mediastinum (51 %). 65 (46 %) patients had hilar masses or masses in the middle mediastinum. A minority of lesions (4 %) were in the posterior mediastinum. The highest rate of malignancy was observed in anterior mediastinum (55 % malignancy rate). The most frequent diagnosis were mediastinal sarcoidosis (25 %), malignant lymphoma (10 %), tuberculosis (10 %) and tymoma (7 %).
Conclusion: We conclude that surgical biopsy seems to remain the most important investigation for a successful therapeutic approach to mediastinal masses when less invasive techniques have been unsuccessful. Mediastinoscopy/ mediastinotomy, frozen section and a suitable panel of antibodies were practical approaches to mediastinal masses.

PS-14-002
Primary thymic seminoma emerged from fourth mediastinal branchial cleft cyst-first case reported
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Objective: Primary thymic seminoma is a very rare clinicopathological entity and the incidence of mediastinal branchial cleft cysts

it is even lower. In this report we present a particular case of this condition in a 33 year old male patient, where thymic seminoma emerged within fourth branchial cleft cyst, unusually located in the anterior mediastinum.
Method: The patient underwent thoracic computed tomography which showed an anterior mediastinal mass that was removed by thoracotomy. Histopathological and immunohistochemical assesments were performed in order to establish the diagnosis.
Results: Histopathological examination reveals a cystic cavity lined by epithelium (positive for AE1/AE3, P63) with a seminomatous germ cell tumour proliferation developed within its walls. The large tumoural cells arranged in sheets and separated by fibrous septa show strong positivity for CD 117, PLAP and D2-40. Around the cyst there are areas of thymic tissue positive for Tdt.
Conclusion: The final diagnosis, based on paraclinical, histopathological and immunohistochemical features was primary thymic seminoma. To our knowledge, there are no previously reported cases in literature of primary thymic seminoma originated in a fourth mediastinal branchial cleft cyst. Therefore, considering the novelty of this case, the topic of our presentation might intrigue challenging opinions from the audience.

PS-14-003
Thymolipoma associated to a thymic cyst: A case report
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Objective: To report a case of a thymolipoma associated to a thymic cyst, an association that, to our knowledge, was previously reported only once in the literature. To describe briefly the pathologic aspects of these two benign uncommon entities.
Method: A 63-year-old woman consulted with a persistent cough of 1 year duration. Physical examination was unremarkable. Thoracic CT scan showed an anterior mediastinal oval mass of fluid density. Tumourectomy was performed due to the symptomatic nature of the mass.
Results: The specimen was a 6 × 4,5 × 3 cm mass, weighing 60 g, comprising a solid part of fatty appearance and a cystic cavity of 4 × 3 × 3 cm, with a thin smooth wall, filled with clear liquid. Histologically, the solid part was made of two components: nonproliferative thymic tissue and abundant lobules of mature regular adipocytes. As for the cystic cavity, it was made of a fibrous wall comprising residual thymic parenchyma, lined by simple cuboidal epithelium. The diagnosis of a thymolipoma associated with thymic cyst was retained.
Conclusion: Thymolipomas and thymic cysts are rare tumours of the anterior mediastinum, they can be responsible for non-specific clinical manifestations, only pathological examination confirms the diagnosis. The combination of these two entities is an exceptional occurrence.

PS-14-004
Immunohistochemical expression of p16, a surrogate marker for Human Papilloma Virus (HPV), in oesophageal squamous carcinoma and its clinical significance
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Objective: Evaluation of prevalence and clinical significance of Human Papilloma Virus (HPV) infection in oesophageal squamous cell carcinoma (OSCC) which has not yet been studied extensively as in head-neck and ano-genital malignancies.
Method: The immunoexpression of p16 on tissue micro-arrays of tumour from 100 resected OSCC cases was correlated with clinical and histopathological parameters and response to therapy [assessed by tumour regression grade (TRG) using Mandard's scoring system].
Results: In all, 19 cases were positive for p16 immunohistochemistry (IHC) and 81 were negative. The p16 positive tumours were smaller in size at presentation (mean ± SE = 4.32 ± 0.34 cm) than p16 negative tumours (mean ± SE = 6.02 ± 0.33 cm) (p-value: 0.028). The proportion of p16 positive tumours in the middle third oesophagus (12/19; 63.2 %) was higher when compared to p16 negative tumours which were proportionately more in the lower third oesophagus (46/81; 56.8 %) (p-value: 0.048). The p16 positive tumours revealed a better neoadjuvant therapy response in 25 % (3/12) of cases which had scanty residual viable tumour; whereas only 13 % (10/16) of the p16 negative tumours revealed scanty residual viable tumour with predominant fibrosis (p-value: 0.002).
Conclusion: The expression of p16, a surrogate marker for HPV, could be used as a useful predictive biomarker in assessment of OSCC.

PS-14-005
Primary thymic adenocarcinoma with signet ring cells: An unexpected autopsy finding
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Objective: Thymic adenocarcinomas are a heterogeneous group of malignant epithelial neoplasms showing glandular differentiation and/or mucin production. The extreme rarity and similarity with metastases from adenocarcinomas of other organs makes this a challenging diagnosis, especially in small biopsies.
Method: We present an autopsy case of a 61 year old woman with clinical suspected pulmonary thromboembolism.
Results: The complete autopsy study revealed a large tumoural mass in the superior anterior mediastinum, with whitish and yellowish areas and firm consistency. Microscopic examination showed a poorly cohesive signet ring cell carcinoma in relation with vestigial thymic structures. There were metastases in thoracic and upper abdominal lymph nodes. The lung showed innumerable micrometastic foci and massive neoplastic thromboembolism in small, medium and large caliber vessels. No other lesions were identified in any other organs.
Conclusion: Cause of death was massive pulmonary embolism by a poorly cohesive signet ring cell carcinoma. The presence of the main tumoural mass in the anterior superior mediastinum, coupled with the absence of any other tumoural lesion at autopsy supported the diagnosis of primary thymic adenocarcinoma with signet ring cells (classified as mucinous adenocarcinoma by the 2015 WHO bluebook).

PS-14-006
Mediastinal composite hemangioendothelioma: Case report of rare vascular tumour with unusual location
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Objective: Composite hemangioendothelioma is very rare low/intermediate grade vascular tumour with characteristic mixtures of benign, low-grade malignant and malignant components.
Method: We report the case of composite hemangioendothelioma of the mediastinum in 63-year-old women.
Results: She went on standard chest roentgenogram, to exclude pneumonia after common-cold, which showed centraly located nodular mass. CT revealed nodular mass in posterior mediastinum, measured 40 × 35 mm. Total sternotomy was performed and mass completely resected. Histologic examination showed mixed patern of epithelioid and retiform components embedded in a myxohyaline stroma, also there was areas which resemble arteriovenous malformation. Immunohistochemistry stains (CD31, CD34, ERG) confirmed neoplasm of vascular origin.

Conclusion: Vascular mesenchymal tumours are not uncommon in the mediastinum, but they usually located in anterior or middle mediastinum. This case is presented because posterior mediastinum is unusual and rare location for vascular tumour, especially with this histologic patern.

PS-14-007

A schwannoma arising in a mediastinal lymph node: A case report

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Objective: Schwannoma is an extremely rare primary tumour of the lymph node. Very few genuine cases of benign schwannoma arising in a lymph node have been reported in the literature. We describe a case of a schwannoma that arose in a posterior mediastinal lymph node.
Method: Material: A 43-year old woman had experienced dyspnea for 3 months. A CT scan test was performed which showed a mass of heterogeneous density in the posterior mediastinum. The patient underwent a surgery and the tumour was sent at the pathology lab.
Results: On gross examination the mass measured 2.8 cm in greatest diameter and was totally encapsulated. Histological sections from the mass showed a lymph node exhibiting focal effacement of its arthitecture by a well circumscribed and bland looking spindle cell lesion. The spindle cells were organized in fascicles while areas with nuclear palisading were also present. No atypia or presense of mitoses was found. The spindle cells were positive for S-100 protein and Vimentin while they were negative for smooth muscle actin, desmin and CD34. The diagnosis was that of a primary lymph node Scwhannoma.
Conclusion: Because of the rarity of this intranodal tumour, it is important to distinguish it from other primary and metastatic spindle cell tumours that can arise in a lymph node including palisaded myofibroblastoma. Intranodal Scwhannoma seems to have a totally benign behavior.

PS-14-008

Metaplastic thymoma in 22 year-old male patient

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Objective: Thymoma is the most common neoplasm derived from epithelial cells of thymus. Primary thymic epithelial tumours characterized by a biphasic histologic appearance are uncommon.
Method: 22 year-old asymptomatic man, an anterior mediastinal mass was detected on routine chest radiography. Computed tomography scan reveals a homogenously enhancing soft tissue mass in the anterior mediastinum. Gross examination; the tumours were not capsulated but well circumscribed, and measured 60 × 30 mm.
Results: Microscopic exmination; The tumours were composed of anastomosing islands or broad trabeculae of epithelial cells disposed among delicate spindle cells. The normal thymic tissue was observed at the periphery of lesion. The epithelial cells were oval to polygonal with eosinophilic cytoplasm, vesicular nuclei and small prominent nucleoli. Groove and pseudoincluson seen in epithelial cells. The spindle cells showed a short fascicular or storiform growth pattern, and were bipolar processes. The two components were sharply delineated. mitotic figüre and necrosis was not observed. Rare lymphocytes were observed between the epithelial and spindle component. Immunohistochemically, the epithelial cells were diffusely and strongly positive for cytokeratin and EMA focal positive. While the spindle cells were strongly positive for viementin, and CD-117 were negative. Kİ-67 proliferation index was 5 %.
Conclusion: Metaplastic thymoma is an extremely rare variant of primary thymic epithelial neoplasms with only a few cases reported in the literature. Only 32 cases reported in the english literature, that our patient is the youngest among these cases.

PS-14-009

Clinicopathological and histomorphological features of thymic cysts: Is thick fibrous wall associated with multiloculation?

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Objective: Thymic cysts are rare cystic masses in mediastinum. This study aims to represent characteristic morphological features of thymic cysts.
Method: Eleven cases of thymic cysts were identified in retrospective search of the surgical database of our institution from 2010 to 2016. H&E stained slides were evaluated to identify detailed histomorphological features of cysts.
Results: The patients were 7 female and 4 male ranging from 6 to 66 years (median 33 years). The accompanying thymic tissue was diagnosed as normal thymic tissue (n = 3), atrophic thymic tissue (n = 4), hyperplasia (n = 3), and thymoma (n = 1). One case had parathyriod tissue in pericystic area. Six cases (55 %) were unilocular, and 5 cases (45 %) were multilocular. Thick fibrous wall was found in 8 cases of thymic cysts (73 %), and 63 % of these cases with thick fibrous walls were multilocular cysts and all of multilocular cysts represented thick fibrous walls. Four of 11 cases had ciliated one layer or pseudostratified epithelial lining, and 7 had single or multilayered cuboidal or squamous epithelial lining. Foreign body type giant cells, cholesterol clefts and histiocytes were seen in lumen of cyst and pericystic tissue of 3 cases, keratin was noted in lumen of cyst and pericystic tissue of one case . All of cases containing/with foreign body type giant cells, cholesterol clefts and histiocytes were multilocular cysts. Unilocular cysts showed nothing intraluminal or in pericystic tissue.
Conclusion: Thick fibrous wall and presence of foreign body type giant cells and cholesterol clefts in the lumen and pericystic tissue of cyst is more likely to be associated with multiloculation of thymic cysts.

Wednesday, 28 September 2016, 09.30–10.30, Hall 11.3
PS-15 Dermatopathology

PS-15-001

Skin expression of mammalian Target of Rapamycin (mTOR), Forkhead box transcription factor1 (FoxO1) and serum level of Insulin-like Growth Factor-1 (IGF-1) in patients with acne vulgaris and their relations to diet

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Objective: Acne vulgaris (AV) is a multifactorial disorder of the pilosebaceous unit. Several studies have reported that Insulin-like growth factor-1 (IGF-1), FoxO1 and mTOR interaction is proposed to be the key to understand the influence and link between genetic and environmental factors in acne vulgaris. The aim of this study was to evaluate the immunohistochemical detection of mTOR and, FoxO1 in skin and the serum level of IGF-1 in patients with acne vulgaris.
Method: This study was carried out on 60 participants, 40 acne patients and 20 socio-demographically cross-matched healthy volunteers as controls. A detailed diet questionnaire was taken from acne patients and controls. Serum level of IGF-1 was measured using ELISA technique, skin biopsies were taken from lesion on the back of acne patients and normal skin of the back of healthy volunteers, and FoxO1 and m-TOR expression was detected using immunohistochemistry.

Results: A significantly higher serum IGF-1 level was found in acne patients compared to controls. The cytoplasmic expression of FoxO1 was found significantly more in the acne group while in the control subjects this expression was likely to be nuclear. Both cytoplasmic and nuclear expression of mTOR was significantly higher in intensity in acne patients compared to controls. Excess consumption of high glycaemic load diet was significantly associated with higher serum level of IGF-1 and cytoplasmic expression of FoxO1 and mTOR.
Conclusion: These results suggest that FoxO1, m-TOR, serum IGF-1and high glycaemic load diet may have a role in acne pathogenesis.

PS-15-002
p53 gene mutations in non melanoma skin cancers
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Objective: The aim of the present study was to observe the expression of p53 gene in selected cases of cutaneous SCC & BCC in local population of Karachi, Pakistan.
Method: A total of 64 NMSC cases were selected, morphologically reevaluated and mutations in exon 5–8 of p53 gene were observed.
Results: SCC cases showed 34.3 % p53 mutation, most of which i.e. 45.4 % were seen in exon 6. This was followed by 36.3 % mutations in exon 7 and 18.1 % in exon 8 while no mutation was recorded in exon 5. Amongst BCC cases, exon 5 mutation represented 30.7 % of all, followed by 19.2 and 15.3 % exon 6 and exon 8 mutations respectively. Exon 7 mutations were noted in combination with exon 5 in 7.6 % cases and with exon 6 in. 3.8 % cases. Nodular variant showed 11.5 % cases with single exon 8 mutation. Dual exon 8 mutations were observed in combination with exon 6 constituting 15.3 % of BCC cases. Moreover 3.8 % cases of twin morphologies including nodular and pigmented as well as solid and adenoid combinations each also revealed similar combination of exon 6 and 8 mutations.
Conclusion: Exon 8 of p53 gene was expressed in moderately and poorly differentiated grades of SCC. Similarly exon 8 expressed either singly or in combination with exon 6 amongst BCC cases was a unique finding in the present study which may have some prognostic implications.

PS-15-003
Skin stripping method using proteases to evaluate structural stability by a scanning acoustic microscope
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Objective: A scanning acoustic microscope (SAM) can detect tissue stiffness by speed-of-sound (SOS) because harder tissues show greater SOS. Major structural components such as collagens or elastins alter with genetic background, aging and environmental insults. If chemical modifications of these structure proteins are visible, we can evaluate aging, metabolic disorders and damages. To solve this problem, we have developed tissue stripping (TS) method using proteases.
Method: Young and elderly skin images were observed by SAM and LM. Pepsin or collagenase were applied on the section and SOS of each component was compared before and after digestion.
Results: In elderly skins, dermal fine collagen fibers and degeneted elastic fibers were easily digested by proteases. In younger skins, thick collagen fibers in the dermis showed resistance to proteases. Hypertrophic scars also showed strong resistance to digestions compared with usual wound fibrosis. In the skin of Ehlers-Donlos syndrome, slender dense collagen fibers intermingled with elastic fibers in the dermis showed slower SOS than normal skin. By protease digestion, subtle or no decrease in SOS was found.
Conclusion: Structural stability of tissues alters by different conditions and diseases, which can be objectively evaluated by SOS changes by this TS method.

PS-15-004
Reliability and usefulness of BRAF and NRAS mutational analysis in sentinel lymph nodes of melanoma patients
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Objective: There are conflicting results concerning the usefulness of sentinel lymph nodes (SLN) for the determination of the mutational status of melanoma patients. We tried to elaborate methods for the reliable determination of the mutational status of SLN metastases in routine diagnostics and evaluated its level of concordance between metastases and primary tumours and thus its usefulness for prognostication and prediction.
Method: The mutational spectrum of BRAF and NRAS of SLN melanoma metastases was analyzed by two approaches: 1. DNA was extracted from microdissected SLN-metastases and primaries. The BRAF and NRAS mutation status was then determined by ARMS-PCR and/or Sanger sequencing. 2. RNA was extracted from SLN-metastases, reverse transcribed and analysed by ARMS-PCR. The determined mutational status was compared to that of the corresponding primary.
Results: With ARMS-PCR on DNA from microdissected SLN metastases the mutational status of melanomas can be reliably determined and is highly concordant with the primary tumour. Determination of the mutational status based on cDNA is less sensitive and, therefore, the rate of discordance between SLN metastasis and primary is higher.
Conclusion: With adequate methods the mutational status of SLN metastases of melanoma patients can be reliably determined and is of prognostic and predictive value.

PS-15-006
Recurring multifocal cutaneous leiomyosarcomas in a patient with childhood history of bilateral retinoblastoma
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Objective: Cutaneous leiomyosarcoma is an uncommon malignant tumour arising from the smooth muscle cells of the dermis, accounting for less that 3 % of all superficial soft tissue sarcomas. Most cases develop in adult Caucasian males in the sixth decade of life. Although these tumours may develop virtually anywhere, they tend to have a predilection for the extensor surfaces of the extremities, as well as the scalp and torso. Most of the time they are solitary, measuring between 0.5 and 3 cm in diameter and presenting no regional or distant metastases after complete surgical excision. Recent genetic studies reveal that mutations of the Rb gene may lead to the development of retinoblastoma, as well as leiomyosarcoma
Method: We report the case of a 41 year-old patient, with early childhood history of bilateral retinoblastoma, presenting in 2013 with two tumours located in the left axilla and in the right gluteal region.
Results: The tumours were histopathologically diagnosed as cutaneous leiomyosarcomas. The patient returned in June 2015 with three more cutaneous leiomyosarcomas, which were surgically removed, with negative safety margins. The tumours were located on the left thigh, left axilla

and right pectoral, respectively. In January 2016 the patient had a third presentation, with several new cutaneous leiomyosarcomas: on the left thigh, in the middle third of the right forearm and in the deltoid, subumbilical and the posterior cervical regions.
Conclusion: We believe that this unusual presentation of multiple recurrent cutaneous leiomyosarcomas, as well as the childhood history of bilateral retionoblastoma are most likely linked to a mutation in the Rb gene. However, genetic testing should be performed in order to confirm this assumption.

PS-15-007
Expressomics investigation of MHC II positive areas in melanoma
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Objective: Melanoma has an enhanced immune resistance. One of the mechanisms is immune modulation. Major histocompatibility complex (MHC) class II molecules can be expressed by melanoma cells, thereby participating in immune modulation. MHC class II have a controversial role in melanoma, with some studies associating them with unfavorable outcome and others with regression. To clarify their role in melanoma, we microdissected HLA-DR positive and negative areas in the same melanoma and compared their expressomics.
Method: 58 melanoma metastasis were collected from the Department of Pathology of the KU Leuven. Immunohistochemical staining were obtained for HLA-DR. Two cases with heterogeneous HLA-DR expression were selected. HLA-DR positive and negative areas were microdissected and compared after Next Generation Sequencing. Bioinformatic and pathway analysis were performed.
Results: 70 genes were upregulated in HLA-DR+ areas. Most of them were immune-related. Most of these genes favoured an immune suppressive inflammatory environment. Moreover, they indicated the presence of a mixed B and T infiltrate and of molecules involved in T-B cross talk and germinal center formation. Pathway analysis confirmed these findings.
Conclusion: HLA-DR positive melanoma areas present an immune-related molecular phenotype, with an expressomic signature suggestive for an immune suppressive microenvironment and a germinal center-like reaction.

PS-15-008
In situ evaluation of the correlation between the pattern of tumour infiltrating lymphocytes, INF-gamma levels and MHC molecules expression in melanoma metastasis: Remarks to the current morphologic classification
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Objective: The pattern of tumour infiltrating lymphocytes ("TILs") is a known prognostic factor in melanoma, with a brisk infiltrate having the best, and an absent infiltrate the worst prognosis. Though, there is a lack of knowledge on the functional status of these TILs in these categories in patient's tissue. For stratification of patients that may benefit from immunotherapy, knowledge of this TILs-status is mandatory.
Method: 58 melanoma metastases were collected from the Department of Pathology of the KU Leuven. Immunohistochemical analyses were performed for HLA ABC, TAP1, TAP2, CD8, CXCL9. CD8+ TILs were classified in brisk, non-brisk and absent. CD8, CXCL9 and INFγ levels were measured by qPCR.
Results: MHC I expression correlated with INFγ levels (p:0.04). Though, CD8 mRNA quantification did not correlate with INFγ levels nor with MHC I expression. Considering the CD8 patterns, instead, a correlation was found: the "brisk" category was invariably associated with high levels of INFγ and MHC I overexpression, while the "absent" category invariably had low INFγ. The "non-brisk" category turned out to be very heterogeneous regarding INFγ levels.
Conclusion: A thorough functional evaluation of the "non-brisk" category is needed for further stratification of patients in need of immune checkpoint therapy.

PS-15-009
NAD(P)H dehydrogenase, quinone 1 (NQO1) protects melanin-producing cells from cytotoxicity of rhododendrol
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Objective: We have examined how forced expression of the NAD(P)H quinone dehydrogenase, quinone 1 (NQO1), a major quinone-reducing enzyme in cytosol, affects the survival of Rhododendrol (RD) -treated cells.
Method: The growth inhibitory effect of carnosic acid (CA) and RD or its metabolite on the normal human epidermal melanocyte (NHEM, HEMn-LP/hTERT-1) and B16BL6 cells was assessed by cell counting and WST assay and Western blot. Melanin quantification was detected by spectrophotometry after cells were treated with CA and RD.
Results: We found that treatment of the mouse melanoma cell line B16BL6 or normal human melanocytes with carnosic acid, a transcriptional inducer of the NQO1 gene, notably suppressed the cell killing effect of RD. This effect was mostly abolished by ES936, a highly specific NQO1 inhibitor. Moreover, conditional overexpression of the human NQO1 transgene in B16BL6 led to an expression-dependent increase of cell survival after RD treatment.
Conclusion: Our present results clearly demonstrated that forced expression of NQO1 mitigates the cytotoxicity of RD without notably affecting the inhibition of melanin synthesis. An obvious explanation for this is that NQO1 reduces quinone compounds originating from RD to less toxic catechol forms.

PS-15-010
A unique haematopoietic malignancy in a 73 year old Iranian male
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Objective: A 73 year-old male presented with a 6 month history of an enlarging exophytic lesion on the lower back. The lesion was itchy, the patient had no systemic symptoms.
Method: A biopsy was taken.
Results: Histopathlogy showed an infiltrate of large undifferentiated lymphocytes. MIB1 was expressed in over 90 % of malignant cells. Immunohistochemistry and cMYC rearrangement studies demonstrated that the malignant cells were positive for CD45, CD4 and cMYC but negative for other markers. cMyc translocation was present on FISH analysis. PCR revealed a B-cell clone. Bone-marrow biopsy was negative. PET scanning confirmed extensive lymph-node involvement. The diagnosis was a primary cutaneous haematopoietic malignancy with systemic involvement. The patient was commenced on treatment, there was significant reduction in tumour size at 6 weeks.
Conclusion: This case presented a diagnostic challenge for the following reasons: The indolent clinical presentation and the negative bone-marrow biopsy were not in keeping with the high proliferation rate and primitive nature of the tumour. The neoplasm was exceptionally primitive and thus negative by immunohistochemistry for B-cell markers. Molecular analysis was required to determine a B-cell clone. Similar cases have not been reported in the literature.

PS-15-011

Correlation between clinico-pathological features of oral lichen planus and concomitant treatments

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Objective: The aim of this study is to determine the correlation of the histopathological features and clinical variants of lichen planus, as well as with age, gender or concomitant medical treatments.
Method: We have studied 59 adult patients (36 females and 23 males) cases with firm clinical and histopathological diagnosis of OLP. Clinical parameters recorded included age, sex, location of the lesions in the oral cavity, clinical variant of OLP, toxic habits (alcohol and smoking) and concomitant treatments. Histopathologically, the presence of ulceration, degree of interface lesion, distribution, intensity and composition of the inflammatory infiltrate were evaluated.
Results: Patients treated with several drugs had more erosive forms of OLP (15/20 vs. 14/39, Pearson Chi2 test, $p = 0.018$) and showed atrophy of the squamous epithelium more commonly (13/27 vs. 7/32, Pearson Chi2 test, $p = 0{,}034$). Plasma cells were present in 30 patients and they were more abundant in those cases with the inflammatory infiltrate extending deeper in the subepithelial connective tissue (6/12 vs. 2/47, Pearson Chi2 test, $p = 0.00027$).
Conclusion: Patients taking multiple drugs seem to present a form of OLP more severe with atrophy and erosion of the epithelium Plasma cells are most commonly found in cases showing deeper infiltrate inflammatory infiltration.

PS-15-012

Value of the histopathological features in predicting B-RAF status in cutaneous malignant melanoma

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Objective: Establishing the relation between several histopathological features of cutaneous melanomas (CM) and the presence of V600E B-RAF mutation and infer, if possible, its presence from the pathological characteristics of the neoplasm.
Method: We have retrospectively reviewed 90 cases of CM and have assessed the presence of V600E B-RAF mutation on paraffin embedded tissue (Cobas® 4800, Roche). The histopathological features evaluated were lateral circumscription of the lesion, the percentages of melanocytes along the basal layer and nest formation, predominance of epithelioid or spindle cells and degree of pigmentation.
Results: B-RAF mutated melanomas showed better lateral circumscription than those with wild-type B-RAF (52 vs. 33,3 %) and over 50 % of the neoplastic cells formed well-defined nests (33,3 vs. 21.7 %). The percentages of melanocytes along the basal layer were very similar in mutated and non-mutated lesions. Large amounts of cytoplasmic melanin were only present in non-mutated melanomas (12,5 vs. 0 %) and predominance of epithelioid cells was noted in mutated melanomas (73,1 vs. 65,6 %). Nevertheless, differences were never statistically significant.
Conclusion: According to our results the predictive value of histopathological features is not accurate enough to infer the B-RAF status.

PS-15-013

The first Danish family reported with an AQP5 mutation presenting diffuse non-epidermolytic palmoplantar keratoderma, hyperhidrosis and frequent corynebacterium infections

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Objective: An autosomal dominant form of diffuse non-epidermolytic palmoplantar keratoderma, palmoplantar keratoderma of Bothnian type, is caused by mutations in the AQP5 gene encoding the cell-membrane water channel protein aquaporin 5 leading to defective epidermal-water-barrier function in the epidermis of the palms and soles.
Method: Genomic DNA purified from a blood sample from the proband was analyzed using bidirectional Sanger sequencing of the AQP5 gene.
Results: We report the first Danish family diagnosed with diffuse non-epidermolytic palmoplantar keratoderma in which 14 individuals are potentially affected. The proband, a 36-year-old male had since childhood been affected by pronounced hyperhidrosis of the palms and soles along with palmoplantar keratoderma. He reported a very distinctive feature of the disorder, as he developed pronounced maceration of the skin with translucent white papules and a spongy appearance following exposure to water. The patient presented recurrent fungal infections, a wellknown feature of the condition, but also periodic worsening with pitted keratolysis and malodour due to bacterial infections.
Conclusion: The present case illustrates the importance of Woods light examinations of palmoplantar keratoderma due to the risk of complicating Corynebacterium infections.

PS-15-014

Cutaneous nocardiosis

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Objective: Cutaneous nocardiosis is a rare infectious disease. It is often misdiagnosed because of its rarity and nonspecific clinical presentation. It typically affects immunosuppressed individuals with a history of trauma and can be subdivided into 3 clinical entities that include: Lymphocutaneous infection, superficial skin infection and cellulitis.
Method: The patient (with history of Wegener disease under therapy) presented with a circumscribed, whitish-red skin lesion of left leg and clinical diagnosis of erythema nodosum was considered. Biopsy was performed. Macroscopic examination revealed a whitish-red, circumscribed lesion measuring $1{,}15 \times 0{,}8 \times 0{,}7$ cm.
Results: Histological examination revealed chronic inflammation of the papillary dermis and an area of acute inflammation in the reticular dermis, extending into the subcutaneous tissue, with a small central abscess. This was surrounded by smaller, similar lesions. Staining for PAS and GMS was negative. These findings were compatible with Sweet Syndrome. However later clinical examinations revealed a Nocardia infection. Thus a special modification of GMS was carried out, which showed Nocardia aggregates in the dermis.
Conclusion: In such cases, it is important to take into consideration all clinical information in addition to the histological results, in order to reach a correct diagnosis.

PS-15-015

Squamoid eccrine ductal carcinoma: Report of two cases

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Objective: Squamoid eccrine ductal carcinoma (SEDC) is an extremely rare variant of ductal eccrine carcinoma which represents less than 0.01 % of all cutaneous tumours. As our knowledge is limited to very few case reports, biological potential of tumour is still debatable. We report two cases diagnosed as SEDC in our department.
Results: Case 1: An 80 year-old female patient presented with a lesion on her forehead. A punch biopsy was misdiagnosed as SCC. Excisional biopsy showed squamous and ductal areas, frequent mitosis, and extensive perineural invasion. P63, CEA, and EMA stainings were positive.

Case 2: A 43 year-old male patient presented with a lesion on his lower abdomen. An excisional biopsy performed. Squamous and ductal components, keratin cysts, stromal hyaline degeneration, and perineural invasion were noted. Tumour was positive with P63, P40, CEA, and EMA.
Conclusion: SEDC usually occurs on extremities,scalp, and trunk of middle aged or elder patients. Tumour nests, which are composed of ductal (eccrine) and squamous features,are diagnostic. SEDCs have a better prognosis than other eccrine carcinomas. Differential diagnosis includes SCC, microcystic adnexal carcinoma, porocarcinoma, malign mixed tumour, and metastatic tumours. Further information is needed to understand SEDCs.

PS-15-016
The relations of JAK-STAT signaling expressions to MCPyV-infection and outcome in Merkel cell carcinomas
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Objective: Merkel cell carcinoma (MCC) is a rare and aggressive neuroendocrine skin cancer. Merkel cell polyomavirus (MCPyV) is monoclonally integrated into about 80 % of MCCs. JAK-STAT signaling activation is associated with some cancers. Therefore, we first evaluated the relationship of JAK-STAT signaling expressions to MCPyV-infection and prognosis in MCCs.
Method: 50 MCC tumours (30 MCPyV-positive and 20 MCPyV-negative cases) were assessed immunohistochemically for expressions of p-JAK2, p-STAT3, p-MEK1/2 and p-Erk1/2, respectively, using Allred score. Clinicopathological data were analyzed statistically with SPSS software.
Results: p-JAK2 and p-STAT3 were expressed in 48/50 (96 %) and 39/49 (80 %) MCCs, respectively but not different between MCPyV-positive and -negative MCCs. Allred scores of p-MEK1/2 and p-Erk1/2 expression were significantly higher and lower in MCPyV-positive MCCs than MCPyV-negative ones ($p = 0.002$, $p = 0.019$, respectively). These JAK-STAT signals were not associated with OS or DSS of MCCs. However, in MCPyV-positive MCCs, strong intensity (IS; 2 or 3) of p-MEK1/2 was significantly associated with unfavorable OS ($p = 0.031$).
Conclusion: We first demonstrated the significant association of higher p-MEK1/2 and lower p-Erk1/2 expression with MCPyV-positive MCC, and of higher p-MEK1/2 intensity score with poor prognosis only in MCPyV-positive subgroup.

PS-15-017
Extramammary Paget disease in a seborrheic keratosis: A colonized tumour?
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Objective: Seborrheic keratosis (SK) is the most common benign dermal neoplasms in elderly individuals. Extramammary Paget disease (EMPD) is a type of in situ adenocarcinoma, often with some degree of apocrine differentiation and it's occurrence in combination with seborrheic keratosis is extremely rare.
Method: A 71-year-old female presented to our hospital with a well demarcated pigmented lesion on the scalp, measuring 1,1 × 1cm, which was completely excised.
Results: Microscopically the lesion was well defined, composed of bland and pigmented basaloid and squamous cells, with formation of pseudohorn cysts. Admixed with the epidermal keratinocytes there were neoplastic cells, isolated or forming small nests, with large nuclei, prominent nucleoli and abundant pale cytoplasm (focally PAS+, PAS/D+). These cells were immunopositive for CK7, GCDFP-15, CK8, CEA, EMA and HER2 1+ and focally 2+. S100, Mart1, HMB45, CK20, ER, PR were negative. The patient underwent thorough examination to exclude the possibility of an underlying internal malignancy, with negative results. A diagnosis of EMPD within a SK was established.
Conclusion: Cutaneous neoplasms with two or more distinct cell populations frequently pose a diagnostic challenge to both clinicians and pathologists. Although malignant transformation has been reported in SK, Paget's disease in a pigment SK is very rare and may be overlooked.

PS-15-018
Metastatic malignant melanoma in bone marrow report of a rare case
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Objective: Malignant melanoma usually metastasizes to skin (other areas), lungs and area between lungs, liver, brain, bone, GI tract, heart, adrenal glands, kidneys, spleen and others.
Method: We report the case of a 81-year-old white female who presented with a rapidly growing dark brown lesion on her right ear auricle. A nodular malignant melanoma, 2 cm in greatest diameter, Clark level V and Breslow thickness 0,9 cm was diagnosed and immunohistochemically confirmed. The excision had been successfully carried out and the patient was referred to a centre for chemotherapy.
Results: Six months after the initial diagnosis the patient underwent routine examinations and pancytopenia was detected. The bone marrow biopsy showed 25 % infiltration by atypical melanocytes, a finding consistent with metastatic malignant melanoma. Hypoplasia of all the haematopoetic cell lines was also found. CT examinations didn't reveal other metastatic sites. The patient was referred to a tertiary centre for chemotherapy.
Conclusion: Metastases of malignant melanoma to the bone marrow are very rare. They usually occur in 5 % of patients with disseminated disease and in up to 45 % when an autopsy is performed.

PS-15-020
A case series of cutaneous Penicillium marneffei infection emphasising on histopathology
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Objective: To demonstrate histopathology of Penicillium marneffei infection in AIDS and anti-interferon gamma autoantibodies patients.
Method: Retrospective descriptive study of cutaneous penicillosis confirmed by tissue culture and histology at Thammasat University Hospital during 2007–2015.
Results: Only three patients were available for study. Case 1 had AIDS with multiple umbilicated lesions on face and trunk. Case 2 and 3 had anti-interferon gamma autoantibodies, suggestive of adult-onset immunodeficiency. Case 2 presented with multiple erythematous papules and nodules confluent to plaques at the upper chest, neck, and face. Case 3 had multiple abscesses and ulcers with sporotrichoid pattern at left forearm. The histopathologic features include mixed inflammatory cells interstitial infiltration (2/3 cases), non-necrotizing granuloma (2/3 cases), superficial ulcers (2/3 cases), nodular pattern (1/3 cases), dermal abscesses (1/3 cases), suppurative granuloma (1/3 cases), and lobular panniculitis (1/3 cases).
Conclusion: Cutaneous penicillosis in immunocompromized hosts has variable clinical presentations and histopathologic features. The predominant histopathologic features are interstitial infiltration of mixed

inflammatory cells, non-necrotizing granuloma (often poorly-formed), and superficial ulcers. In AIDS case, the intracellular yeasts are abundant, without granulomatous response. In contrast to anti-interferon gamma autoantibodies cases, the yeasts are rare with granulomatous response.

PS-15-021

Primary cutaneous myoepithelial carcinoma: A misleading tumour

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Objective: Tumours arising from myoepithelial cells are rare and mostly benign. Most malignant variant reported cases arise from salivary gland. Only 11 cases of cutaneous myoepithelial carcinoma (CMEC) were reported. We aim to describe a case of CMEC with a brief review of literature.
Method: A 50-year old woman presented with a nodular well circumscribed flesh-colored lesion of 7 mm, located on the nasal wing. Surgical excision was performed.
Results: Histopathological examination revealed a dermal poorly differentiated neoplasm arranged in a solid pattern. Cells were epithelioid with an abundant eosinophilic cytoplasm and centrally located or eccentric nuclei containing prominent nucleoli. Tumour stroma was fibrous. Surgical margins were infiltrated. Six months later, tumour recurred, showing almost all histological features initially observed with more marked nuclear atypia. Mitotic rate was 4/10HPF. At immunohistochemistry, cells expressed vimentin, CK7 and S100 protein. Mib-1 index was 50 %. Negative staining for cytokeratin/androgen receptors/ PHDLA1 and p63 ruled out an adnexal tumour. Vascular markers (CD34/CD31/ERG), muscular markers (desmin/caldesmon/actin/ myogenin), histiocytar markers (CD68/CD163/MMP11), plasmacytic markers (CD138/mum-1) and melanocytic markers (Melan-A/ HMB45) were negative.
Conclusion: CMEC has variable morphologic and immunohistochemical features, expressing at a varying degree both epithelial and muscle specific markers. CMEC may thus be misdiagnosed as no single profile is diagnostic.

PS-15-022

Intralymphatic nevus cells in benign nevi

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Objective: The histogenesis of nevus cell aggregates in lymph nodes is controversial and various hypotheses have been used to explain their origin. One of them is the transport of cells from cutaneous nevi or lesions to lymph nodes, called mechanical transport theory. We investigated in our cases of benign nevi to obtain evidence to substantiate this theory.
Method: 369 benign cutaneous nevi were prospectively evaluated in excisional biopsy samples. Immunohistochemical stainings for CD31 and podoplanin (D2-40) were performed in the cases with intralymphatic nevus cell aggregate (ILNA), suspected for ILNA and/or intralymphatic nevus cell protrusion (ILNP).
Results: A total of 13 intralymphatic nevus cell aggregates (ILNAs) were found in 10 patients. Six ILNA were verified with their histology as well as immunohistochemically with D2-40 and CD31. Protrusions of nevus cells inside the lymphatics (ILNP) were seen in all cases of ILNA and also in 27 nevi where an ILNA was not observed.
Conclusion: We suggested that ILNAs can be dislodged with local minor trauma and be carried inside the lymphatic vessel to the draining lymph node. Our findings supported the mechanical transport theory.

PS-15-023

Porocarcinoma arising in a sebaceous nevus of Jadassohn: Case report

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Objective: Porocarcinoma is a rare malignant tumour but the most frequently encountered malignancy of the sweat glands. It is a rare association with Jadassohn nevus.
Method: We present a case of a 69 years old female with a porocarcinoma arising in a Jadassohn nevus of the scalp.
Results: The tumour had 1,5/1,5/0,5 cm, white and yellow appearance and ulcerated. Microscopic aspects included basaloid, squamoid and pleomorphic features, with high mitotic rate (22 mitosis/ HPF), a clearly infiltrative growth pattern and connection to underlying epidermis. The tumoural proliferation formed ductal structures. Desmoplasia and little necrosis were present. In the periphery of the malignant lesion, signs of a remaining Jadassohn nevus were present: some acanthosis and papillomatosis, foci of basaloid hair papillae-like proliferations and rare apocrine glands. Tumoural proliferation was positive for panCK, p63, p16 and p53, focally positive for EMA and negative for BerEp4. Endoluminal ductal cells were highlighted by CEA, EMA and CK7. Ki67 index was about 20 %.
Conclusion: Histopathological aspects and immunohistochemical profile sustain the diagnosis of porocarcinoma and a remaining Jadassohn nevus. Probably most porocarcinomas reported in scalp location were developed on Jadassohn nevus which could represent a risk factor.

PS-15-024

Primary extramammary Paget's disease: Report of 13 cases

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Objective: Extramammary Paget disease (EMPD) is a rare neoplasm usually presenting in the anogenital area. We report characteristics of the 13 cases.
Method: We measured the depth from the epidermal surface to the deepest located tumour cell in the adnexa. We used the Allred Score for steroid receptor evaluation and CAP recommendations for HER 2 results reporting.
Results: There were 12 females and 1 male. Median age was 66,9 years. The lesions were solitary and occurred in the anogenital area. Two patients had recurrences of the EMPD. Three patients had history of breast cancer and one had mammary Paget's disease. Morphology was similar in all cases: large tumour cells had clear and pale granular cytoplasm and round nuclei. Tumour cells formed solitary units, solid nests and gland-like structures in the epidermis. Hair follicles and eccrine ducts were the most commonly affected adnexal parts, maximal depth of involvement was 2.9 mm. ERs were positive in 4 cases. PRs were positive in one case. ARs were positive in 8 cases. Her2/neu staining was positive in 4 cases and coexpression of Her2/neu and AR were found in 4 cases.
Conclusion: Described morphological and IGH characteristics of EMPD should be taken into account when planning therapy.

PS-15-025

Cytokeratin 17 and Ki-67: Immunohistochemical markers for the differential diagnosis between Keratoacanthoma and Squamous Cell Carcinoma (SCC)

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Objective: The clinical and histopathological distinction between keratoacanthoma (KA) and squamous cell carcinoma (SCC) is often

troublesome. We investigated the utility of CK 17 and Ki-67 in distinguishing between KA and SCC.
Method: Immunohistochemical staining patterns for CK 17 and Ki-67 were evaluated in 24 KA and 27 SCC cases. The pattern of staining was evaluated as central, peripheral and diffuse according to basal/peripheral and suprabasal/central cell staining in tumour lobules.
Results: We found that 22 of 24 (92 %) KAs stained with a peripheral pattern for Ki-67 and a central pattern for CK 17, while only 2 of 27 SCCs (7 %) displayed the same pattern. The majority of SCCs (16/27, 59 %) stained with the diffuse pattern for both markers. The sensitivity and specificity of the central staining pattern of CK 17 for identifying KA was 92 and 70 % respectively. Additionally, the sensitivity and specificity of the diffuse staining pattern of Ki-67 in favor of SCC was 81 and 100 % respectively.
Conclusion: The diffuse staining pattern of Ki-67 is useful for the diagnosis of SCC, while the central staining pattern of CK17 is in favor of KA. Ki-67 and CK 17 may be useful in differentiating between KA and SCC.

PS-15-026
Merkel cell carcinoma metastasis with coexisting B-cell lymphoma in parotid gland: A case report
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Objective: We presented a case of coexisting diffuse large B-cell lymphoma(DBCL) with primary cutaneous Merkel cell carcinoma (MCC) in metastatic lymph nodes(LNs) in parotid gland.
Method: Female patient, 75 years old. In May 2012 she underwent surgical and radiotreatment for skin tumour MCC d 1 cm of right buccal region. In December 2012 -enlargement of neck LNs on the right side (0,4 to 0,9 cm) and 2 tumour in soft tissues of right buccal region (up to 2,2 cm in parotid gland). The scar was normal. FNAC: small cell carcinoma. Lymphadenectomy and glandectomy were performed.
Results: Part of skin 5 × 2 cm with adipose tissue and salivar gland with grey, ill-defined, homogeneous, nodular mass 2,2 cm. Fat tissue with LNs up to 0,9 cm in diameter. In 2 of 9 neck LNs d 0,4 cm and 1 LN from parotid gland adipose tissue—metastasis of small cell tumour. Parotid gland infiltrated by centroblast and immunoblast-like cells. IHC results: metastasis in LNs: Cytokeratin 20(+), Chromogranin A(+), Synaptophisin(+). Cells of parotid gland infiltrate: CD20(+), CD10(+), bcl6(+). CD5, CD23, CD30, bcl2, Cyclin D1—negative.
Conclusion: Metastasis of MCC in 2 of 9 neck LNs and 1 intraglandular lymph node and Extranodal DBCL of parotid gland.

PS-15-027
Cutaneous adnexal carcinoma: Clinicopathological study of 40 consecutive cases
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Objective: To estimate the frequency of cutaneous adnexal carcinoma (CAC), describe their clinical appearance and histology as well as the particularities of each lesion.
Method: We conducted a multicenter descriptive study over a period of 08 years with a 03 year retrospective step (January 2008 to December 2010) and a prospective step of 05 years (January 2011 to December 2015).
Results: Our global series of 350 adnexal skin tumours includes 40 CAC (11.4 %). A male predominance is noted with a sex ratio of 1.66. The average age is 66.10 ± 18.23 years. The most common site is the head and neck (62.5 %). In most cases it was nodular or nonspecific budding lesions with an average size of 3.6 cm. Sebaceous carcinoma is the most common type (6 cases, 15 %) followed by adenoid cystic carcinoma (5 cases), trichoblastic carcinoma (5 cases), porocarcinoma (4 cases), microcystic adnexal carcinoma (4 cases), Paget disease (4 cases), and trichilemmal carcinoma (04 cases).
Conclusion: This study has allowed us to better understand these rare tumours. The diagnosis is histological because their clinical presentation is often non specific. They are represented mainly by the sebaceous carcinomas, adenoid cystic carcinoma and trichoblastic carcinoma.

PS-15-028
Cutaneous mixed tumours: Clinicopathological study of 41 consecutive cases
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Objective: To estimate the frequency of cutaneous mixed tumours (CMT) and describe their clinical and histological characteristics.
Method: We conducted a multicenter descriptive study which focused on all the mixed tumours over a period of 08 years with a 03 year retrospective step (January 2008 to December 2010) and a prospective step of 05 years (January 2011 to December 2015).
Results: Our series of skin adnexal tumours includes 350 cases with 41 CMT (11.7 %). A male predominance is noted (sex ratio 3.5). The average age is 48 years. The most common site is the head and neck (90.2 %) mainly on the nose (31.7 %) and the upper lip (24.4 %). The clinical appearance is often a nonspecific nodule (73.2 %) with an average size of 1.15 cm. The diagnosis of adnexal tumour was clinically referred only for two cases. All lesions were apocrine. Chondroid differentiation has been objectified in only 58.5 % of the cases.
Conclusion: According to our study, CMT affect male adults, with a predilection for the face. The most common clinical presentation is that of a nonspecific nodular lesion hence the importance of histology diagnosis.

PS-15-029
Hidradénomas: Clinicopathological study of a series of 27 cases
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Objective: Describe the clinical and histological characteristics of hidradenomas.
Method: A multicenter descriptive study was conducted focusing on all hidradenomas over a period of 08 years with a 03 year retrospective step (January 2008 to December 2010) and a prospective step of 05 years (January 2011 to December 2015).
Results: Our global series of 350 adnexal skin tumours includes 27 hidradenomas (7.7 %). We find a female predominance (sex ratio 0.58). The average age is 46.65 ± 14.84 years. The most common site is the head and neck (37 %), mainly on the scalp (22.2 %). The clinical features are those of an unspecific nodular lesion (59.3 %) or a cystic lesion (40.7 %), with an average size of 1.7 cm. The diagnosis of adnexal tumour was clinically mentioned only in one case. It was dermal tumours connected with the epidermis in 11.1 % of the cases, composed of different types of cells having a clear cell component in 55.6 % of cases and of glandular structures in 77.8 % of cases, with sclerotic stroma in 92.6 % of the cases. Local recurrence was observed in 14.8 % of the cases.

Conclusion: According to our study hidradenomas affect female adults, more often on the scalp. The clinical features are those of a non specific nodular or a cystic lesion hence the importance of histological examination. These lesions recur frequently, so it is important to have a complete surgical resection.

PS-15-030

Comparative study of mycological and histological findings on onychomycosis

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Objective: The objective of our study is to specify the contribution of histology compared to mycological examination in the diagnosis of onychomycosis.
Method: A prospective study over a period of 2 months that interested all patients consulting for onychopathy clinically suggestive of onychomycosis and never been treated by antifungal. Each patient had had two types of exams on nail biopsy: mycological and histological.
Results: A total of 40 patients with onychopathy clinically suggestive of mycomycosis were included. The majority of patients were men (63 %) and the mean age at the time of diagnosis was 45. Onychopathy was on the foot in 80 % of our patients, 15 % on hands and only 5 % were in both hands and foots. The Hallux was the primary site of onychomycosis representing 34.73 % of all cases. Mycological examinations showed positivity on KOH on 88 and 57 % on Sabouraud. Histological examination were positive on hematoxilin-eosin in 27 % of cases and 65 % on PAS. Gorcott-Gomori staining was positive in 90 % of all cases.
Conclusion: When highly suggestive clinically onychomycosis and negative or inconclusive mycological examination, we recommend to practice histology with PAS staining initially and if doubt we will pass to Grocott-Gomori staining that remains for us pathologists the Gold Standard.

PS-15-031

Specific cutaneous involvement in multiple myeloma: 2 cases report

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Objective: Skin involvement in multiple myeloma (MM) is uncommon observed in 5 to 10 % of MM. We aim through these cases to describe the clinical presentation, epidemiological and histopathological features of this entity and insist on its poor prognosis.
Method: We describe two cases of MM with skin involvement diagnosed in pathology departments of Sfax and Gabes Hospitals.
Results: We report the cases of two men aged respectively of 56 and 31 years; both presented with multiple violaceous nodules of the trunk. The youngest patient was known carrying a MM in incomplete remission since 1 year, whereas a MM was diagnosed in the first case. Histopathologically, both skin lesions revealed a dense dermal infiltrate of plasmablasts strongly immunopositive for CD138. No karyotype abnormalities were evidenced in the initial karyotype of the second patient while complex abnormalities including 17p deletion were found in the first case. The latter received poly-chemotherapy reaching a partial remission with no recurrences detected within 6 month follow-up while the youngest patient died 1 month after extramedullary-relapse.
Conclusion: Cutaneous involvement in MM is a rare manifestation indicating a deteriorating clinical course. The emergence of cytogenetic profiling may be helpful in identifying genetic subgroups associated with poor prognosis.

PS-15-032

PD-L1 expression in invasive and in situ Squamous Cell Carcinoma (SCC) of the skin and actinic keratosis

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Objective: PD-1/PD-L1 pathway assists tumour evasion from the immune system. We examined the expression of PD-L1 in invasive squamous cell carcinoma (INSCC) of the skin and adjacent in situ squamous cell carcinoma (ISSCC), actinic keratosis (AK) and normal skin (NS) to evaluate for possible PD-L1 implication in tumour progression.
Method: Paraffin tissue sections from INSCC ($n = 114$) were stained for PD-L1. The expression on epithelial cells and tumour infiltrating lymphocytes/dendritic cells was evaluated using Allred score. Statistical analysis was performed using Wilcoxon signed ranks test.
Results: ISSCC, AK and NS were observed adjacent to INSCC, in 43, 112 and 112 cases, respectively. PD-L1 epithelial cell expression was higher in INSCC compared to ISSCC, AK and NS ($p = 0.025$, $p < 0.005$ and $p < 0.005$, respectively) and in ISSCC and AK compared to NS ($p = 0.039$ and $p = 0.034$). PD-L1 lymphocytic/dendritic cell expression was higher in INSCC compared to ISSCC, AK and NS ($p < 0.005$ for all the comparisons), in ISSCC and AK compared to NS ($p < 0.005$ for all the comparisons) and in ISSCC compared to AK ($p = 0.039$).
Conclusion: There is a gradual increase in PD-L1 expression during the progression from non-neoplastic skin to INSCC, through AK and ISSCC, implicating its participation in the neoplastic evolution.

PS-15-033

Merkel cell carcinoma occuring in a dark skinned woman: A rare epidemiologic presentation of an uncommon tumour

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Objective: Report a rare epidemiological presentation of Merkel cell carcinoma(MCC) of the skin, occurring in the right elbow of a dark skinned woman.
Method: 58 years old non "Caucasian" woman who presented a Merkel cell carcinoma of the posterior face of the right elbow. She had a dark skin. She presented first with a stage II disease and had a biopsy excision and was lost of follow up for 4 months. She presented with recurrent disease on the inferior third of the right arm with three metastatic ipsilateral axillary lymphadenopathyconfirmed after biopsy. The treatment decision was to perform an amputation of the right arm and ipsilateral axillary lymph node dissection with adjuvant radiotherapy. She stayed controlled for 6 months after the end of radiotherapy and then presented with lung metastasis and died from respiratory failure.
Results: In our case and in the literature, the MCC resulted in a poor outcome with a high rate of local and distant recurrence despite of radical management.
Conclusion: This case confirmed the literature demonstrating the poor prognosis of patients with Merkel cell carcinoma, however, there is a lack of literature regarding the comparison between the prognosis of this tumour on white and dark skinned populations.

PS-15-035

Clinicopathological evaluation of cutaneous leishmaniasis in the mediterranean region of Turkey

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Objective: Cutaneous leishmaniasis caused by various species of Leishmania (mostly Leishmania tropica) is characterized by long-term

nodulo-ulcerative lesions healing spontaneously with scarring. It is prevalent throughout South-Eastern Anatolia and East Mediterranean region of Turkey.
Method: We evaluated biopsy sections, smear preparations, demographic, epidemiological, and clinical features in 25 patients diagnosed with cutaneous leishmaniasis in 2000–2016 years.
Results: Diagnosis age range from 1 to 74 (median 31,8) years. Thirteen cases were male; 12 were female. The disease was identified more frequently in younger males and females. Eighty-eight percent of cases were diagnosed under the 50 years old. The lesions were localized on face, upper extremities, lower extremities and neck region in 9(%.36), 9(%36), 6(%24) and 1(%4) patients, respectively. Eleven, nine and five of cases were nodulo-ulcerative, papular and nodular respectively.
Conclusion: Increased travel migration of the population from rural areas to the peripheral suburbs with inadequate infrastructure and unhealthy housing are thought to be the main factors for spreading the disease. Immigrations to endemic regions of Turkey from neighbouring countries, where cutaneous leishmaniasis incidence is higher, may lead to increase case numbers, thus more powerful protective measures should be taken in those endemic areas.

PS-15-036
Tumour burden in sentinel lymph node and its correlation to histopathologic characteristics of primary melanoma and status in complete lymph node dissection
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Objective: Sentinel lymph node biopsy(SLNB) is a standard procedure for patients with localized cutaneous melanoma. In this study, sentinel tumour burden was evaluated. Correlation with clinicopathologic characteristics of primary melanoma and non-sentinel lymph node involvement were analyzed.
Method: We included 26 patients in period 2014–2015 who had metastases in SLN(22 males, 4 females, median age52.07, 11–77). Metastases were classified in three group(subcapsular 46.15 %, multifocal 23.08 % and diffuse 30.77 %). SLN tumour burden was evaluated by Rotterdam criteria and correlated with histopathological characteristics of primary melanoma (Breslow index 5.24 ± 4.09), and with further lymphonodal metastases (CLND). Kendall's tau-b was done ($p < 0.05$).
Results: Sentinel lymph node metastases were found as submicrometastasis (<0.1 mm) in 3/26 patients (11.54 %), with tumour burden 0.1–1 mm in 11/26 patients (42.31 %), and >1 mm in 12/26 patients (46.15 %). There was positive correlation between sentinel tumour burden and Breslow thickness ($p = 0.012$). Additional non-SLN involvement was found in 13/26 (50 %) patient with submicrometastasis (<0.1 mm) in 1/3 patients (33.3 %), with tumour burden 0.1–1 mm in 4/11 patients(36.4 %), and >1 mm in 8/12 patients (66.6 %). Correlation between sentinel tumour burden and CLND was without significans ($p = 0.248$).
Conclusion: SLN positivity is more frequent in primary melanoma with greater Breslow thickness. SLN tumour burden are in positive correlation with CLND for submicromatstasis, and in negative correlation for greater tumour burden.

PS-15-037
Borst-Jadassohn phenomenon in clonal seborrheic keratosis: A controversed entity
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Objective: Clonal seborrheic keratosis (CSK) is a rare subtype of seborrheic keratosis with characteristic intraepithelial nests called Borst-Jadassohn phenomenon (BJP). We herein describe pathological findings in two cases of clonal seborrheic keratosis and discuss cutaneous tumours displaying BJP.
Method: Two women aged 70 and 90 year-old presented with a pigmented lesion, 1 cm in diameter each one, located respectively in the left shoulder and the face, developed 5 years ago in the first case and 10 years in the second one. Surgical excision was performed in both cases. An immunohstochemical study with Ki-67, p63, p40 and CK5/6 were made.
Results: Pathological examination showed exophytic proliferation of epidermal basaloid cells evoking seborrheic keratosis. In the first case, well-demarcated clusters of small cells with regular dark nuclei were found within the basaloid proliferation. In the second case, the clusters were made of large clear atypical and mitotic cells.
Conclusion: We illustrate two distinct morphological and immunohistochemical features of BJP in CSK, having benign and malignant appearance respectively. BJP may be observed in different tumours like CSK, hidroacanthoma simplex and porocarcinoma. The mechanism of this nest formation in a subset of intraepidermal neomplasm and the true nature of BJP remains unclear.

PS-15-038
Immunoprofiles of mismatch-repair proteins of sebaceous tumours and their histopathological features
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Objective: The aim of the study is to evaluate the immunohistochemical mismatch repair proteins(MMR) profiles of sebaceous tumours and their histopathological features.
Method: In this study 35 cases diagnosed sebaceous neoplasm were reevaluated. IHC was performed for MSH2, MSH6 and MLH1.
Results: Fifteen sebaceous carcinomas, seven sebaceomas, one atypical sebaceoma and 12 sebaceous adenomas were identified. The mean diameter of tumours were 4.3, 5.71, and 10.4 mm for sebaceous adenoma, sebaceoma, and sebaceous carcinoma, respectively. All sebaceous adenoma and sebaceomas were well demarcated lesions. Sebaceous carcinomas had multinodular and/or infiltrative growth pattern, moderate to marked cytologic atypia and numerous mitosis (mean 36.49/mm2). Mean mitotic count was 3.83/mm2 and 8.14/mm2 for sebaceous adenomas and sebaceomas, respectively. One case with 25/mm2 mitosis were evaluated as atypical sebaceoma. Keratoacanthoma-like architecture or cyctic areas that described in sebaceous tumours with Muir-Torre syndrome(MTS) were seen at 8 and 5 cases respectively. Of these cases seven tumours have loss of either one expression of MMR. While loss of MSH-2 and MSH-6 were seen at two adenomas, two sebaceomas, two carcinomas, one atypical sebaceoma, loss of MLH-1 were at three sebaceous adenomas, one carcinoma. One sebaceoma demonstrated only loss of MSH-6. Concomittant visseral malignancy (colorectal carcinoma) was present at one patient.
Conclusion: Morphological findings were not strongly related with immunohistochemical findings. We couldn't searched the germline mutation. But depending on visseral malignancy the immunohistochemistry results were not associated with possible MTS. Our findings should be reevaluated with studies including germline mutation.

PS-15-039
Melanocytic BAP1-associated intradermal tumours: Report of 3 cases
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Objective: BAP1 gene inactivation mutations were recently reported in association with a novel familial cancer susceptibility syndrome, as well

as with an increased metastatic potential of uveal melanoma and several other sporadic tumours, including melanocytic BAP1-associated intradermal tumour (MBAIT). MBAITs have characteristic morphological features, do not express BAP1 and are usually mutated for BRAF. This paper aims to evaluate the clinical, histological and immunohistochemical features of MBAIT.
Method: We searched the archives of our departments from the last 5 years and found three cases of MBAIT. Their clinical records and histological slides were then reviewed.
Results: All patients were male, ranging from 16 to 44 years old. The lesions were single and located on the face, arm and back. Personal and family records were unremarkable. Histology showed symmetrical, polypoid, predominantly intradermal tumours, composed by epithelioid melanocytes with "spitzoid" features. Maturation was somehow incomplete and mitotic activity was present. Immunohistochemistry showed loss of BAP1 expression in all cases. Clinical follow-up ranged from 21 to 25 months and all patients remain free of disease.
Conclusion: There are only a few published cases of MBAIT, especially when sporadic. Considering their poorly understood biological behaviour, MBAIT should be regarded as atypical lesions needing complete excision and close follow-up.

PS-15-040
Glomeruloid hemangioma in POEMS Syndrome: Report of a case
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Objective: Glomeruloid hemangioma is a rare cutaneous vascular benign tumour, which is strongly associated with POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy and Skin changes) and usually related the Castelman's disease. We present a case POEMS syndrome with multiple cutaneous glomeruloid hemangioma on the trunk.
Method: A 46-year-old woman presented to internal medicine with edema on hands and feet, paresthesia and fatigue. Laboratory tests and imaging studies demonstrated optic neuritis, widespread mixed sensorimotor demyelinating peripheral neuropathy, hepatosplenomegaly, autoimmune thyroiditis, adrenal insufficiency, increased VEGF and IgG monoclonal gammopathy. She was diagnosed as POEMS syndrome. According to these findings, the patient was consulted to dermatology for her skin lesions. Dermatological examination showed hyperpigmentation and hypertrichosis on the face, plethore, multiple erythematous papules on the chest, abdomen and back, non-pitting edema of both hands and feet. Two papules on the chest and the back were removed by shave excision.
Results: Histopathological examination of the two biopsies, coiled capillary vessels contained within enlarged vasculary spaces resembles renal glomeruli. These findings consistent with glomeruloid hemangioma.
Conclusion: POEMS syndrome involves a large number of dermatological manifestation of which glomeruloid hemangioma is considered to be the most spesific markers of the syndrome. Cutaneous lesions are present about one-third of the cases may consist of the strawberry nevus, lobulary capillary hemangioma and glomeruloid hemangioma types. These are located on the trunk and on the proximal segments of the limbs. Light microscopic, clinical features and differantial diagnosis of this tumour are presented here.

PS-15-041
Malignant proliferating trichilemmal tumour (MPTT) an unfrequent entity, that deserve a successful and accurate diagnosis
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Objective: Malignant proliferating trichilemmal tumour (MPTT) is a rare entity, derived from the outer capillary root sheath, originated in the wall of a pre-existing pilar cyst. They are benign, however malignancy is described, 40 cases are described in the literature.
Method: Male 41 with 2 cm scalp skin mobile lesion and slow growth (6 months).
Results: Histologically, squamous cellularity was seen, disposed on layers and lobes, with moderate pleomorphism, hyperchromasia, high mitotic activity and atypical mitosis. Lobes showed abrupt keratinization pattern with invasive growth into surrounding tissue without affectation of the surgical margin.
Conclusion: MPTT, described in 1983 by Saida et al., are rare, normally arising de novo however development over preexisting benign lesions are reported. No specific immunohistochemical marker is known, however the loss of CD34 expression may predict proliferating malignant transformation. This last is evidenced by invasive component with classical trichilemmal keratinization, with or without vascular/perineural invasion. Incidence is unknown, because most are erroneously classified as squamous cell carcinoma, and this represents their main differential diagnosis. This distinction is important because the MPTT have more chance of metastasis and recurrence. We present this case because it is a rare entity, that deserve a successful and accurate diagnosis, due their aggressive behavior.

PS-15-042
Angiolymphoid Hyperplasia with Eosinophilia (ALHE): A heterogeneous entity with frequent plasma cell IgG4
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Objective: Angiolymphoid hyperplasia with eosinophilia (ALHE) is a locally proliferative lesion composed of channels of small blood vessels surrounded by lymphocytes, eosinophils and plasma cells, with etiopathogenesis uncertain.
Method: Clinical-pathological features of seven cases with ALHE were studied. Formalin-fixed, paraffin-embedded skin biopsies were stained for CD31, CD3, CD20, IgG and IgG4 to determine a possible relationship with IgG4 plasma cells.
Results: Five women and two men (age range, 30–66 years) were seen with localized head and neck lesions. Histologically, there were epithelioid vascular proliferation, with mixed inflammatory infiltrate of T-cells CD3+, associated with CD20+ lymphoid aggregates and a variable number of eosinophils (mean 106.8/HPF, range 20–285). Immunohistochemically, most IgG-expressing plasma cells were positive for IgG4 (IgG4/IgG ratio = 51–83 %).
Conclusion: ALHE is heterogeneous condition and share features with cutaneous IgG4-related disease. Further characterization of the disease process is needed to confirm this observation.

Wednesday, 28 September 2016, 09.30–10.30, Hall 11.3
PS-16 Digestive Diseases Pathology — GI

PS-16-001
A parallel between HER2 protein expression in primary gastric carcinoma and corresponding synchronous lymph node metastases
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Objective: Although anti-HER2 treatment is indicated for metastatic gastric carcinomas, patients are selected by HER2 testing in the primary tumour. Our aim was to characterize the concordance rate of HER2 protein expression between primary tumours and correlated metastatic lymph nodes.

Method: Histological slides and pathological reports from 137 primary gastrectomies and corresponding lymphadenectomies performed at a Brazilian university hospital were reviewed. Whole-tissue sections from each primary tumour and from paired lymph node metastases in 85 cases were submitted to immunohistochemistry. HER2 status was confronted with clinicopathological parameters to assess statistically significant associations.
Results: HER2 overexpression was found in 17/137 primary tumours (12.4 %) and 12/85 metastatic lymph nodes (14.1 %). There were associations between intestinal-type tumours and tumour differentiation and HER2 expression in primary tumour ($P = 0.026$ and $P = 0.005$) and metastatic samples ($P = 0.008$ and $P < 0.001$). The concordance rate was of 88.2 % (κ-value: 0.515). There were 10 discordant cases, from which five cases (5.9 %) were HER2 positive in the primary cancer and negative in nodal metastases, while five cases (5.9 %) were negative in the resection specimen and positive in metastatic deposits.
Conclusion: Since eligible patients for anti-HER2 treatment may remain undetected if immunohistochemistry is performed only in primary tumour samples, HER2 testing in lymph node metastases is encouraged.

PS-16-002
Pancreatic-type mixed acinar-endocrine carcinoma arising from the stomach: Clinicopathological, immunohistochemical and ultrastructural analyses

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Objective: Although acinar cell carcinoma (ACC) is usually a neoplasm arising from the pancreas or salivary glands, this tumour has been known to arise rarely from the stomach. We examined ACC with neuroendocrine differentiation of the stomach; this tumour is recently termed as "pancreatic-type acinar-endocrine carcinoma (MAEC) of the stomach".
Method: We selected MAEC from pathology file of Shizuoka Cancer Center, Shizuoka, Japan, during 2002–2015, and examined them clinicopathologically and immunohistochemically. One case was examined ultrastructurally and with double-immnofluorescent staining.
Results: Three cases (0.06 %) of MAEC were extracted; case 1 was 81 year-old Japanese male, who is alive without disease, 3 years after operation; case 2 was 56 year-old Japanese female, who died of disease, 3 months after operation with peritoneal dissemination; case 3 was 62 year-old Japanese male, who died of disease with multiple liver and lymph node metastases, 8 months after operation. Histologically, all cases showed sheet-like or solid nest-like growth of amphophilic ovoid atypical cells, which accompanied with acinar pattern. Immunostaining showed the positivity for both the neuroendocrine markers such as CD56, chromogranin-A, and synaptophysin and the acinar cell markers such as lipase and alpha-amylase. Only case 2 was positive for BCL10. Ultrastructurally, the cancer cells included 200 nm electron-dense neurosecretory granules and 500 nm electron-lucent zymogen granules. Some cancer cells were double positive for chromogranin-A and alpha-amylase.
Conclusion: MAEC of the stomach is extremely rare. This tumour is positive for both neuroendocrine markers and acinar cell markers. Gastric MAEC is limited to the immunopositivity for BCL10, whereas lipase is a useful marker for acinar differentiation.

PS-16-004
Association between the number of dissected lymph nodes and clinicopathological variables in colon carcinoma

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Objective: The number of dissected lymph nodes (NDLN) is varied according to clinicopathological variables in colon carcinoma. We assessed which factors were associated with NDLN.
Method: Between January 2013 and February 2016, 429 cases of resected colon adenocarcinoma, at least pathological T1 (pT1), were obtained. The cases which had treated by preoperative radiation and chemotherapy were excluded. The groups were divided according to NDLN, as less than 12 (lower NDLN group) and 12 or more (higher NDLN group). Relationship between two groups and clinicopathological variables were evaluated.
Results: Forty-five out of 429 cases (10.5 %) were classified into lower NDLN group. Lymph node dissection was performed twice in 42 out of NDLN group cases. Lower NDLN group was associated lower pT stages (T1 and T2, $p < 0.001$), negative pN stage ($p < 0.001$), polypoid growth pattern ($p < 0.001$), well-differentiated tumour ($p = 0.001$), left-sided tumour ($p = 0.004$), smaller tumour size ($p < 0.001$), shorter resected colon length ($p = 0.033$), and resection after polypectomy ($p < 0.001$). Logistic regression analysis demonstrated smaller tumour size ($p < 0.001$), lower pT stages ($p = 0.046$), and left-sided tumour ($p = 0.004$) were associated with lower NDLN group.
Conclusion: For the smaller, T1 and T2, and/or left-sided colon carcinomas, the cutoff value of NDLN should be lower than that of large, advanced colon carcinomas.

PS-16-005
Tumour regression in rectal cancer: What is the most robust tumour regression grade system?

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Objective: Standard care for locally advanced, rectal cancers (LARC) consists of chemoradiation therapy (CRT) followed by surgery. The response rate to CRT has important prognostic impact. Different tumour regression grade (TRG) systems were developed, however no standardization is incorporated in clinical practice. This study aimed to compare distinct TRG systems to assess both inter-observer and intra-observer variability.
Method: Twenty LARCs were prospectively included at the University Hospitals, Leuven. Tumour regression was scored on 4 separate time intervals by four pathologists according to Mandard, Dworak, CAP, Ryan, Becker, Schneider and Rödel. Inter-observer and intra-observer agreement were assessed via kappa-statistics.
Results: Intra-observer agreement was best for Becker ($k = 0.944$) and Schneider ($k = 0.932$). Both systems are based on estimating the percentage of residual tumour, resulting in low inter-observer reliability ($k = 0.576$ and $k = 0.567$). Ryan ($k = 0.742$), Dworak ($k = 0.709$), CAP (0.636) and Mandard ($k = 0{,}633$) scored similar for inter-observer agreement, but intra-observer agreement was best for CAP ($k = 0.888$), followed by Dworak ($k = 0.880$), Ryan ($k = 0.855$) and Mandard ($k = 0.845$).
Conclusion: Assessment of the TRG is important for prognostication. Estimation of residual tumour results in low levels of inter-observer agreement. CAP and Dworak turned out to be the most robust systems.

PS-16-006
Circulating tumour cells, recist and pathological response in patients with resectable colorectal liver metastases

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Objective: To correlate Response Evaluation Criteria in Solid Tumours (RECIST), Pathological Response and Circulating Tumour Cells (CTCs) in patients with resectable colorectal liver metastases (RCLM) and neoadyuvant treatment.
Method: 27 patients with RCLM were chosen for a prospective study. CTCs were quantified in 7.5 ml of peripheral blood pre and post-surgery by the CellSearch® System. Zero CTCs/7.5 ml was chosen as the cut-off.

Clinical response was evaluated according to RECIST. Pathological Regression Grade (PRG) was classified depending on percentage of viable tumour cells in each resected specimen.
Results: CTCs were detected pre-surgery in 12 of 27 patients and post-surgery in 10 of 23; median 1.5 CTCs (range 1–25) and 5.5 CTCs (range 1–24) respectively. Patients with no pre-surgery CTCs achieve better clinical response (RECIST median 2) compared with those with positive pre-surgery CTCs (median 3). Patients with no post-surgery CTCs attain better clinical response (median 2) and PRG (median 2) compared to positive post-surgery CTCs patients (median 3 and 2.5 respectively).
Conclusion: This study suggests that detection of CTCs in patients with RCLM is a surrogate prognosis tool to evaluate the response to chemotherapy.

PS-16-007
Prognostic significance of histopathological variables in colorectal signet ring cell carcinoma
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Objective: To analyze the prognostic significance of histopathological variables (histological grade, vascular invasion, microsatellite instability (MSI), mucin content, pTNM stage) on disease free survival (DFS) and on cancer specific survival (CSS) to colorectal signet ring cell carcinoma (SRCC).
Method: Thirty-two surgical colorectal SRCCs were retrieved from our files among colorectal carcinomas surgically resected between 2003 and 2014. Histological sections of each case were reviewed to assess the above mentioned parameters. In addition, for each case immunohistochemical procedures against proteins of mismatch repair system, CD34 and podoplanin were carried out in order to investigate MSI status, and the presence of venous or lymphatic invasion.
Results: pTNM stage, venous and lymphatic invasion on haematoxylin and eosin (H&E) stain and on immunohistochemistry were significantly associated with shorter DFS and CSS to SRCC. In addition, high histological grade (<50 % of glands) was significantly associated with shorter CSS and also to shorter DFS, although statistical significance was not reached. Venous invasion on CD34 immunohistochemistry and histological grade were significant independent variables at multivariate analyses for CSS and DFS.
Conclusion: If our findings are confirmed in further studies, VI on CD34 immunostaining and histological grade might be included in the histopathological report of colorectal SRCC as significant prognostic factors.

PS-16-008
MicroRNA 429 down-regulates MARCKS expression in ulcerative colitis
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Objective: miRNAs are non-coding RNAs that play important roles in the pathogenesis of human diseases by regulating target gene expression in specific cells or tissues. We have focused on detecting miRNAs related to ulcerative colitis of mouse, identifying their target molecules, and analyzing the correlation between the miRNAs and their target genes in colon cell lines.
Method: UC-associated miRNAs were identified by miRNA microarray analysis of colitis colon tissues and normal colon tissues of mouse. The results were validated by quantitative RT-qPCR. MIR429 target genes were identified by the mRNAs down-regulated in MIR429-overexpressing cells (determined by mRNA microarray analysis). Luciferase reporter plasmids were constructed to confirm the effect of MIR429 on target gene expression. Th protein expression of the target genes was measured by western blot.
Results: 37 miRNAs were identified as UC-associated miRNAs. We investigated one, MIR429, which was specifically down-regulated in UC, and identified 53 genes as targets of MIR429. The association between MIR429 and MRCKS was verified in this study. MARCKS transcript expression was directly down-regulated by MAR429; protein expression was also down-regulated.
Conclusion: Our results suggest that MIR429 could play an important role in the pathogenesis of ulcerative colitis.

PS-16-009
Esophageal squamous papillomas: A retrospective histopathological study of 95 cases from two centers
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Objective: Squamous papillomas (SPs) of the esophagus represent benign polypoid lesions of stratified squamous epithelium. They are usually an incidental finding during upper digestive endoscopy, are frequently underdiagnosed and have low recurrence rates.
Method: We performed a two-institutional retrospective study on 95 cases of SPs diagnosed over a period of 4 years (2011–2015). Our purpose was to evaluate clinical, endoscopic and pathological aspects of esophageal SPs.
Results: From 2011 to 2015 we recorded 48,644 upper gastrointestinal endoscopy procedures in one institution and 8969 in the other one with an estimated incidence for SPs of 0,16 %. Clinically, SPs occurred more frequently in women than in men (1,5:1). The majority of the patients (58,94 %) were 26 to 50 years old, followed by the 51–80 years group. Median size was under 5 mm (90,52 %), but larger lesions have also been observed (11,57 %). Most SPs were solitary (85,26 %) but multiple papillomas have also been detected (11,57 %). Their location was preferential to the distal third of the esophagus (60 %). In 20 % of the patients other coexisting esophageal and gastro-duodenal lesions were present.
Conclusion: SPs of the esophagus remain a rare and, usually, an incidental finding. According to this study, the incidence has increased considerably due to the extensive use of endoscopy outlining great improvement in patient care management.

PS-16-011
An amazing cause of chronic intestinal pseudo obstruction
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Objective: We report the observation of a 37-year woman referred for severe constipation with occlusions becoming worse after pregnancies.
Method: A subtotal colectomy followed 2 years later with proctectomy was examined with immunohistochemistry. During surgery, no peritoneal or genital lesion was noticed.
Results: Histological examination of samples of colon, rectum and distal ileum found a diffuse pathologic muscularis propria affecting both muscular layers at the three intestinal levels: additional disorganized muscle coats filled submucosae and spreaded into subserosae, forming parietal nodular bundles composed with mature bland smooth-muscle cells, stained with actin and desmin, without mitosis, atypia or other cellular component notably endometriosis. CD117, DOG1, S100 stained exclusively normal Cajal cells and normal enteric plexus discarding stromal or Schwann-

cell proliferations. Estrogen and progesterone receptors were expressed in nuclei of muscular bundles.
Conclusion: We retained the diagnosis of a diffuse ileo-colonic leiomyomatosis responsible for chronic intestinal pseudo-obstruction. To our knowledge, this is the first report of digestive leiomyomatosis with such a diffuse small bowel, colonic and rectal presentation without peritoneal location. The peculiarity of our observation is the worsening of symptoms after pregnancies, attributed to hormonal stimulation of the intestinal muscle expressing strongly estrogen and progesterone receptors.

PS-16-012
ERCC1 expression in mucinous and non-mucinous colorectal carcinoma and relation to mismatch repair proteins expression, clinicopathological features and prognosis
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Objective: We aimed at this work to investigate the expression of ERCC1 (as a member of nucleotide excision DNA repair pathway) in colorectal mucinous adenocarcinoma (MA) and non-mucinous adenocarcinoma (NMA), its relation to mismatch repair proteins expression, clinicohistopathological parameters and survival.
Method: Tumour tissue specimens from 75 patients with colorectal MA and 75 NMA were included in the study. All clinicopathological data of these 150 cases were revised with re-examination of all their slides. Three high density manual tissue microarrays were constructed and immunohistochemistry for ERCC1, MLH1, MSH2, MSH6 and PMS2 was done.
Results: ERCC1 showed complete loss of expression in 17 cases (11.5 %) and aberrant cytoplasmic expression in 27 cases (18.2 %). NMA showed significantly more cytoplasmic expression than MA. In NMA, but not MA, loss of ERCC1 expression was significantly associated with MMR deficient status. ERCC1 expression was only associated with presence of lymphovascular emboli, and was not significantly related to survival in both NMA and MA groups.
Conclusion: Loss of ERCC1 expression is strongly associated with MMR deficient status in non-mucinous, but not mucinous, CRC. However, this doesn't affect survival of the patients. Further studies are needed to explore the role of aberrant cytoplasmic ERCC1 in colorectal carcinogenesis.

PS-16-013
A clinico-pathological study of the appendiceal tumours: A 10-years' experience of a Romanian tertiary center
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Objective: The aim of this study is a retrospective analysis of the spectrum of appendiceal tumours registered at the Victor Babes National Institute of Pathology from 2006 to 2016.
Method: We analyzed 53 cases, including the clinical data, imaging, tumour morphology, mural extension and IHC profile: CKs, CDX2, chromogranin, synaptophysin, Ki67, CEA, MUCs.
Results: From 53 cases, 26 cases where NETs, four cases of goblet cell carcinoid, two cases of MANEC, one case of tubular carcinoid, two cases of cystadenoma, one case of sessile serrated polyp, 12 cases of LAMNs, three cases of mucinous adenocarcinoma and two cases of adenocarcinoma NOS. The mean age was 42 years old, with female predominance (F:M of 2.3:1). All NETs measured less than 10 mm in diameter. Neuroendocrine markers were positive in 92 % of cases and CDX2 in three cases from five (60 %). Infiltration of mesoappendix was noted in 25 % of cases. LAMNs were diagnosed in 12 cases, with female predominance (92 %). Infiltration of the subserosa and beyond was noted in 58 % of cases. Other epithelial neoplasms are rarely diagnosed.
Conclusion: Neuroendocrine neoplasms are more frequent among young patients, under 30 years old, whereas the other epithelial neoplasms tend to affect people after the third decade ($p = 0.0008$). We found 7 cases with advanced tumour stage (pT4 and pM1), associated with poor prognosis.

PS-16-014
Evaluation of duodenal biopsies from patients of malabsorption with suspected celiac disease: Histopathological assessment by modified MARSH grading system
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Objective: To apply a uniform system of reporting morphological changes in duodenal biopsies done for malabsorption with suspected Celiac disease to provide a diagnostic tool for celiac disease through a quantitative histopathological assessment by modified MARSH grading system for a better patient management.
Method: This study is a retrospective, cross-sectional study conducted in Sultan Qaboos University Hospital. It included 73 cases presented in 2012 with malabsorption and clinical suspicion of Celiac disease. The biopsies were reviewed by three pathologists, two consultants and one resident and it started on September 2013. The studey was ethically approved Sultan Qaboos University Hospital ethical comittee.
Results: Thirty nine out of 73 (53.4 %) patient were identified to have raised intraepithelial lymphocytes, ten patient were 18 years or below and 29 patients were above 18 years. In our study, we considered the upper limit of normal intra epithelial lymphocytes (IELs) as 25 IELs/100 enterocytes. We applied the criteria for modified MARSH grading system to our patients and we found that most of our cases were classified as normal (33 patients), followed by followed by grade 1 (30 patients) and grade 3 (9 patients) ($P < 0.0001$). 11 patients with modified MARSH grade 1 (36.67 %) were positive for one or more of antibodies, which are antitransglutaminase antibody, antigliadin antibody and anti-endomysial antibody.
Conclusion: In conclusion, the grading system will help and guide for further evaluations for the suspected cases and to start the management early. The finding of a raised IEL count with normal villous architecture is clinically significant and must be highlighted in routine duodenal biopsy reports.

PS-16-015
Inflammatory Fibroid Polyps (IFPs) of the GI tract: Clinical, endoscopical, histological and immunohistochemical features of a series of 19 consecutive cases
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Objective: To investigate the clinical, morphological and immunohistochemical characteristics of a series of 19 cases of IFPs, confirmed or diagnosed in the Victor Babes Institute of Pathology, Bucharest, from 2005 to 2016.
Method: This is a retrospective study, based on the clinical files, endoscopical reports, histopathological and immunohistochemical diagnoses.
Results: A total of 19 cases were collected (11 males, 8 females), ranging from 30 to 76 years, localised in the stomach (ten cases), small bowel (seven cases) and cecum (two cases). The tumours were asymptomatic or with signs of obstruction or abdominal pain. Their size was from 8 to 45 mm. Histologically, IFPs presented with a variable cellularity and vascularity, with perivascular onion skinning in 7 cases, giant cells in 3

cases and with 15 to 1430 eosinophils/10 HPF. Immunohistochemically, panels of antibodies showed variable expression. The PDGFRA was positive in 7 cases from 10. CD 117 and DOG1 were negative in all tested cases. CD 34 was positive in 10 from 18 cases.
Conclusion: Inflammatory fibroid polyps are rare, benign lesions of the gastrointestinal tract, originating in the mesenchimal tissue of the submucosa, most frequently located in the stomach and small intestine, with a span of clinical, morphological and immunohistochemical patterns.

PS-16-016
EGFR, HER2 protein overexpression and gene copy-number variation in distal extrahepatic bile duct carcinoma
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Objective: EGFR and HER2 receptors are one of the most promising therapeutic targets in solid cancer. However few studies have been conducted on EGFR and HER2 receptors in EBD carcinomas.
Method: Immunostains using antibodies against EGFR and HER2 were performed on TMA blocks, consisting of 84 cases of EBD carcinoma. Twenty cases including all high to moderate EGFR, HER2 expression cases and randomly selected weakly positive and negative cases were evaluated EGFR and HER2 copy number variation by FISH and SISH, respectively.
Results: EGFR expression of distal EBD carcinomas was 26.2 %, 6.0 % and 6.0 % in the weakly positive, moderately positive, and strongly positive groups, respectively. HER2 expression was 5.9 %, 3.6 %, 1.2 % in the weakly positive, moderately positive, and strongly positive groups, respectively. All cases of strongly positive EGFR expression showed amplification (n = 1) or high polysomy (n = 4) of the EGFR gene and 3 cases (60 %) of moderately positive EGFR expression also showed high polysomy. One case of strongly positive and 2 cases of moderately positive HER2 expression showed amplification of the HER2 gene. EGFR expression was associated with shorter cancer-specific overall survival (p = .005).
Conclusion: Although further study is warranted, our finding suggests anticancer therapeutics against EGFR and HER2 receptors may be an effective therapeutic options for some subsets of distal EBD carcinoma patients.

PS-16-017
Digestive neuroendocrine tumours: About 32 cases
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Objective: to correlate prognosis of digestive neuroendocrine tumours classified according to WHO 2010 classification
Method: A retrospective review.
Results: The mean age was 50 years. The sex ratio was 0,68. The primary sites were colorectal, appendiceal, ileal, gastric, pancreatic and oesophageal. The WHO 2010 grading: NET grade 1 25 %, grade 2 15,6 %, neuroendocrine carcinoma 40,6 % and mixed adenoneuroendocrine carcinoma 18,8 %. TNM stage: I 13,7 %, II 25 %, III 15,6 % and IV 41 %. Curative surgery was performed in 53 % with a 5-year survival rate of 90 %. This rate was lower than 30 % for the other cases. Mean follow-up was 27 months. Five patients were missing. Seven died: 4 of them were stage IV and 5 with a Ki67 index superior to 20 %. For all patients, the 5-year survival rate was 62 %. The presence of metastasis and TNM staging were major prognostic factors. Indeed, the 5-year survival rate dropped from 80 to 35 % with the presence of metastatic disease.
Conclusion: The Ki67 value, the presence of metastatic disease and the type of treatment were determinant prognostic factors for these tumours.

PS-16-019
CD24 expression in the progression from adenoma to invasive adenocarcinoma of the colon
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Objective: CD24 is known to be a putative marker of stem cell and tumour metastasis. The study aims to verify the clinicopathologic values of CD24 expression in adenoma and colorectal adenocarcinoma (CRC).
Method: A total of 7 whole tissue sections of malignant polyp containing the progression from adenoma to CRC, 48 adenomas and 161 CRCs arranged as tissue microarray were examined by immunohistochemistry for CD24. Associations of CD24 expression with clinicopathologic parameters were also analyzed.
Results: In the normal mucosal epithelia, CD24 was not detected. Cytoplasmic CD24 expression increased from adenoma to well to moderate differentiated CRC and was decreased in poorly differentiated CRC ($p < 0.001$). In the CRCs, cytoplasmic expression of CD24 was inversely correlated with high-grade differentiation (Grade 1 to 3), tumour size and pathologic TNM stage (I-III versus 4) ($p = 0.005$, $p = 0.03$, $p = 0.006$). The statistical associations between CD24 expression and overall and disease-free survival rates were not seen.
Conclusion: Cytoplasmic CD24 plays important roles in carcinogenesis, and the differential pattern of CD24 expression between well to moderate differentiation (G1 and 2) and poorly differentiation (G3) in CRC implies overexpression of cytoplasmic CD24 is an early process, through adenoma to invasive carcinoma.

PS-16-020
Mucin-rich variant of traditional serrated adenoma
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Objective: Traditional serrated adenoma (TSA) is a serrated polyp that has a predilection for the left colon. The aim of the study is to describe a mucin-rich variant of TSAs (MrTSA).
Method: One hundred and forty-one TSA were retrieved in the departments of Pathology (UHN and Oxford). Age, sex, site, presence of conventional dysplasia, association with other polyp types, frequency of ectopic crypt foci (ECF) and content of goblet cells were recorded and compared to classic TSA (cTSA). Arbitrarily, TSAs that consisted of more than 50 % goblet cells were classified as mucin-rich TSAs (MrTSAs). The number of ECFs was quantified as low (1–10) and high (>10). All the TSA included in this study showed the typical serrated pattern.
Results: Of the 141 TSAs, 22 fulfilled the criteria for mrTSA. There was a slightly higher male predominance of mrTSA but no age difference compared to cTSAs. While both occurred most commonly in the left colon, mrTSAs were relatively more frequent in the right (28.6 %) than in the left colon (12.6 %) ($p = 0.012$). Ten of 22 mrTSAs were associated with other polyp types: 8 sessile serrated adenomas (SSA) and hyperplastic polyps (HP) (3 TSA/HP, 2 TSA/SSA and 3TSA/SSA/HP) and 2 with tubular adenomas. mrTSAs showed a lower frequency of ECF than cTSAs ($p = 0.001$). Only 1 of 22 mrTSA showed conventional adenomatous dysplasia.
Conclusion: Our observations highlight a mucin or goblet cell rich variant of TSA characterised by more goblet cells and fewer ECFs than cTSA. Other defining histologic features such as the typical serration pattern were present in all cases.

PS-16-021
Progression of colorectal cancer K-ras positive patients is associated with differential expression of IL-17, IL-22 and IL-23
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Objective: Explore the role of mutant K-ras signaling in inflammation-driven tumourigenesis and the involvement of interleukins in colorectal tumourigenesis progression.
Method: Inhibition of Ras signaling using Manumycin A and Sequence Analysis of K-ras exon 1 in colorectal cancer patients. Immunohistochemical analysis of IL-17, IL-22, IL-23 using ELISA SPOT and correlation with GM-CSF and IFN-γ expression levels in cancer tissues.
Results: Specific interleukins are differentially expressed in K-ras positive patients and the use of K-ras inhibitor Manumycin A decreases both interleukin levels and apoptosis in Caco-2 cells by inhibiting cell viability. In addition, inflammation-driven GM-CSF and IFN-γ levels are modulated through interleukin expression in tumour patients, with interleukin expression in the intestinal lumen and cancerous tissue mediated by aberrant K-ras signaling.
Conclusion: Collectively, the findings a) indicate that interleukin expression is influenced by ras signaling and specific interleukins play an oncogenic promoter role in colorectal cancer, highlighting the molecular link between inflammation and tumourigenesis, and b) accentuate the interwoven molecular correlations as leads to new therapeutic approaches targeting neoplasia.

PS-16-022
Ileal adenocarcinoma in Crohn disease: An unicentric experience emphasizing the importance of screening for dysplasia
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Objective: Association between small bowel adenocarcinoma (SBA) and Crohn's disease (CD) is well-known but rare, following a dysplasia-cancer sequence. We reviewed the clinicopathological characteristics of a series of SBA surgically resected in patients with CD.
Method: A distal ileal SBA was diagnosed in 9 of 441 patients who underwent small bowel resection for ileal CD between 2006 and 2016. They were retrospectively analyzed and followed during a mean time of 20 months [2–71]. Genetic mutations of BRAF, KRAS were tested. MSI phenotype was investigated.
Results: The median age of diagnosis was 46 years; median CD duration was 15 years. Seven patients (78 %) had obstructive symptoms refractory to treatment. Pre-operative biopsies made in 6 patients were informative in 5 (83 %), revealing cancer, dysplasia and indefinite for dysplasia lesions in 2, 2 and 1 patients respectively. SBA developed in active ileitis with adjacent dysplasia in all patients. Two-third of SBA exhibited high grade differentiation, with predominant mucinous and/or signet ring cells component in 44 % of cases. One SBA showed a MSI profile with isolated loss of PMS2 expression. One of the 8 SBA tested exhibited KRAS mutation. None showed BRAF mutation. Five patients (55 %) had advanced stage IV SBA; four of them died within 2 years following surgery.
Conclusion: In our center, an ileal SBA was diagnosed in 2 % of patients resected for refractory CD. Adjacent ileal dysplasia was present in all surgical specimens and could be diagnosed on screening biopsies. This strengthens the importance of neoplasia detection by systematic endoscopy in all refractory CD.

PS-16-023
Molecular biomarkers in a representative sample of Colombian patients with colorectal cancer studied at Fundación Santa Fe de Bogotá
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Objective: The aim of this study was to characterize the molecular and histopathological features of colorectal cancer (CRC) in a sample of Colombian patients.
Method: A representative and aleatory sample of 45 cases was selected from the total cases diagnosed as CRC (2008–2014): 15;<49 years-old (Group 1), 15; 50-64(Group 2) and 15; ≥65 (Group 3). Cases were held on KRAS exon 2 mutational status and those who were wild type were subjected to KRAS exon 3,4, NRAS exon 2,3,4 and BRAF-V600E study by direct sequencing. Microsatellite instability was evaluated with Promega MSI analysis system v.1.2 and Miss Match Repair proteins by Immunohistochemistry. The study was aimed using paraffin embedded tissues.
Results: 45 patients with CRC average age 58.3 years-old, 97 %(44) adenocarcinomas. KRAS exon2 mutations were detected in: Group 1; 11/15 (73.3 %), Group 2; 7/15(46.6 %) and Group 3; 5/15(33.3 %). Among the KRAS exon 2 wild-type patients; 0 % harbored additional RAS mutations (KRAS Exon 2,3,4, NRAS Exon 2,3,4) and 3(13.6 %) presented V600E-BRAF mutation (2 in Group 2, 1 in Group 3). Bethesda panel exposed 2 cases with Microsateliatal Inestability in each group which was correlated with IHQ expression. Statistical analysis revealed that patients with <49 years-old presented more frequency of KRAS exon2 mutations than older ones (p: 0.03; OR: 4,12 IC95% 1,06-16)
Conclusion: The clinicopathologic features and tumour cell gene expression patterns are different according age group, younger patients are phenotypically and molecularly different from elder patients.

PS-16-024
Distinct expression profile of key molecules of crawling type early gastric carcinoma
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Objective: Gastric "crawling-type" adenocarcinoma (CRA) is a tumour histologically characterized by irregularly fused glands with low-grade cellular atypia. To date, the expression characteristics of key molecules in the CRA are still uncovered. Then, using immunohistochemistry and in situ hybridization, we tried to elucidate molecular characteristics of CRA subtype on large series of CRA (n = 94).
Method: We constructed tissue microarrays of 94 CRAs and 72 conventional type differentiated adenocarcinomas (CDAs) of early gastric cancers to evaluate and compare clinicopathological and expression profiles of important molecules in gastric cancer (EBV, MMR protein, HER2, c-MET, EGFR, PTEN, and p53).
Results: CRA was significantly associated with the younger patient age, larger in size, and more frequent involvement of resection margin than CDA ($p < 0.001$, $p = 0.048$ and $p = 0.048$, respectively). None of the CRAs showed MMR protein deficiency (0.0 vs. 5.6 %, $p = 0.036$), HER2 overexpression (0.0 vs. 12.5 %, $p = 0.001$), and loss of PTEN (0.0 vs. 9.7 %, $p = 0.003$). Moreover, other expression alterations, such as c-MET overexpression (4.4 vs. 19.4 %, $p = 0.004$), and mutant-pattern of p53 (either complete loss or diffuse positive, 12.4 vs. 62.5 %, $p < 0.001$) were significantly less common in CRAs than CDAs.
Conclusion: CRA demonstrated a unique clinicopathological characteristics. Furthermore, this subtype showed a distinct expression profile of key molecules. Those results support that CRA is a distinct subgroup of gastric adenocarcinoma.

PS-16-025
Expression of beta-catenin in premalignant lesions of the colon and rectum
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Objective: Beta-catenin acts as intercellular signal transducer in Wnt-signaling pathway. Its abnormal nuclear expression is a marker of "classical" carcinogenesis.
Method: We immunohistochemically assessed distribution patterns of nuclear beta-catenin expression in 24 hyperplastic polyps (HPs), 29 sessile serrated adenomas (SSAs), 14 traditional serrated adenomas (TSAs), 30 tubular adenomas (TAs) and 28 tubulovillous adenomas (TVAs).
Results: HPs and SSAs showed no nuclear beta-catenin expression. Strong or moderate nuclear reaction with beta-catenin was detected in 15,4 % TSAs, 51,7 % TAs, 72,0 % TVAs. Among lesions with nuclear accumulation of beta-catenin sporadic singular positive cells were found in 66,7 % TAs, 44,4 % TVAs; small focuses of positive cells were detected in 20,0 % TAs, 50,0 % TVAs, 7,7 % TSAs; diffuse reaction was revealed in 13,3 % TAs, 5,6 % TVAs, 7,7 % TSAs. Reaction was more prominent superficially in 80,0 % TAs, 55,6 % TVAs, 7,7 % TSAs.
Conclusion: Among serrated lesions only small portion of TSAs showed nuclear accumulation of beta-catenin while conventional adenomas showed pretty high rate of nuclear expression of beta-catenin. This suggests Wnt-signaling pathway plays a small part in malignization of serrated lesions in contrast to conventional adenomas. The reported study was funded by RFBR according to the research project No.16-34-00179 mol_a.

PS-16-028
Surviving expression occurs in precancerous colorectal lesions
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Objective: The risk stratification of patients with colorectal polyps still requires identification of novel molecular markers of carcinogenesis like survivin. Survivin is a member of the apoptosis inhibitors family, involved in regulation of cell division, angiogenesis and inhibition of apoptosis. Our objective was to study the survivin expression in different types of colorectal polyps and adenomas (A/P).
Method: We studied 91 colorectal A/Ps (hyperplastic polyps, sessile serrated adenomas, traditional serrated adenomas and conventional adenomas with low and high grade dysplasia) from the archived biological material of the Pathology Department of the Clinical County Hospital of Tîrgu-Mureş, Romania. We performed survivin (Merck Millipore, Germany, AB3610, 1/1500) immunohistochemistry, using the Dako EnVision system.
Results: Survivin expression was detected in most A/Ps in the cytoplasm and nucleus ($p < 0.05$). There were no statistically significant correlations between clinico-pathological parameters and expression of this protein. Moderate and increased survivin expression was observed most frequently in conventional adenomas and traditional serrated adenomas.
Conclusion: Survivin expression in most A/Ps is suggestive of its involvement in the early steps of colorectal carcinogenesis. Acknowledgements. The study is supported by the Internal Research Grants of the University of Medicine and Pharmacy, Tîrgu-Mureş, Romania (contract no. 20/23.12.2014).

PS-16-029
Correlation between postsurgery pathology studies with presurgery imaging studies in pancreas adenocarcinoma: A retrospective study with 75 patients
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Objective: In the 21st century pancreas adenocarcinoma will be the 4° cancer death cause in the Western world since its rate of incidence equals its mortality rate, assuming a high fatality rate. The intent of this study is to compare the preoperative radiology studies with the postsurgical pathology studies.
Method: A retrospective study was performed with 75 patients with pancreatic adenocarcinoma surgery in Miguel Servet Hospital, Zaragoza (Spain) by the surgery pathology department in collaboration with the radiology department. Several variables were chosen to analyze the correlation between the two studies. A statistical study was performed, including first, a descriptive study and inferential in second term.
Results: The results show that the study population is a good representation of general population, since the results can be extrapolated to articles published to date. It shows that multidetector CT is the best technique today for the preoperative staging of the pieces of DPC, but shows serious deficiencies with the correlation of these pieces in surgery patholoy studies.
Conclusion: 1. The AP remains the "gold standard" in the staging of pancreatic adenocarcinoma. 2. There is a good correlation between both studies in retroperitoneal margin, peripancreatic fat infiltration and duodenum infiltration. 3. There is no statistical correlation between both studies in tumour size and infiltrated regional lymph nodes.

PS-16-030
Prognostic significance of clinico-pathological variables in rectal cancer resected after neoadjuvant chemoradiotherapy
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Objective: To investigate clinico-pathological factors affecting cancer-specific survival (CSS) and disease-free survival (DFS) of patients with rectal cancer after preoperative chemoradiotherapy (CRT) and surgical resection.
Method: The prognostic relevance of clinico-pathological variables on CSS and DFS was analyzed in 238 patients with rectal adenocarcinoma surgically resected after neoadjuvant CRT. Tumour regression grade by using Dworak score, clinical TNM (cTNM) and yTNM staging were evaluated in all the cases.
Results: Dworak grade was 0 in 38, 1 in 84, 2 in 62, 3 in 18 and 4 in 36 cases. Acellular mucin pools in 8 non-mucinous cases were considered as total regression (Dworak 4). Craniocaudal extension <3cms, yT, cN0, yN0, cM0, yM0, total/subtotal regression (Dworak 3/4) were significantly associated with longer CSS and DFS ($P < 0,05$). Mucin pools had not prognostic significance in cases with complete pathological response. Craniocaudal extension and yN were significant independent variables. Regression grade was an independent prognostic factor for DFS.
Conclusion: Pathological tumour regression by Dworak score has prognostic significance in rectal cancer treated by CRT. Presence of acellular mucin pools in surgical specimens is not related with mucinous histotype, while it is associated with clinical behaviour similar to that of cases with total regression and absence of mucin pools.

PS-16-031
Calretinin use for serosal invasion detection in case of colorectal cancer
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Objective: Serosal involvement by colorectal cancer can remain underdiagnosed due to evaluation difficulties, subjective approach and lack of appropriate criteria [Stewart et al., 2011]. Thus, we investigated the validity of immunohistochemical visualization of the mesothelial marker calretinin to detect serosal invasion by advanced colorectal cancer.
Method: Non-perforated colorectal cancers, previously routinely classified as pT3-4 were retrieved from the archives. Immunohistochemistry

(IHC) for leukocyte common antigen (LCA), CD68 and calretinin was applied, followed by case reclassification into five groups: 1.cancer definitely invades serosal surface (SS); 2.invasion into SS reliably excluded; 3.mesothelial desquamation (LCA+, calretinin-); 4.macrophages on SS (LCA+, CD68+); 5.inconclusive.
Results: Study included 61 advanced colorectal cancer cases (pT3-4). After IHC, the tumours were reclassified as follows: 1st group comprised 11.5 % [95 % confidence interval: 5.7–21.8] cases; 2nd: 14.7 % [7.9–25.7]; 3rd: 50.8 % [38.6–62.9] and 4th: 16.4 % [9.2–27.6] of cases. In 2 (5.3 % [1.5–17.3]) cases that were initially diagnosed as pT3 calretinin IHC disclosed clear-cut serosal invasion. In 16 cases (22.5 % [14.4–33.5]) calretinin IHC was useful to identify SS mesothelium.
Conclusion: Calretinin detection does not ease diagnostics of serosal involvement by colorectal cancer. Mesothelial desquamation is the most frequent reaction.

PS-16-032
HER2 status in gastro-oesophageal adenocarcinomas: The 'equivocal' results, their incidence and significance
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Objective: This study reports Her2 status for 224 oesophago-gastric adencoarcinomas using immunohistochemistry (IHC) with follow-up FISH done in 215 cases. We looked at overall results, site specific patterns, IHC/ FISH concordance and cases with HER2 signals > =4, <6 / nucleus ('equivocal' group as defined for breast in ASCO/CAP 2013 update).
Method: IHC was performed on all 224 cases with FISH on 215 cases. HER2 signals/nucleus was noted for all cases. HER2 positivity was defined in accordance with published guidelines (ASCO/CAP 2013).
Results: Overall HER2 positive rate was 23.7 % (n = 53) with a higher rate in oesophageal/oesophago-gastric junction tumours (O/OGJ) (n = 40; 31.0 %) compared with gastric tumours (n = 13; 13.7 %). Twenty-eight tumours (12.5 %) showed HER2 signals in the range > =4,<6 without meeting positive criteria otherwise. This 'equivocal' group was more common in O/OGJ tumours (n = 21; 16.3 %) compared with gastric tumours (n = 7; 7.4 %).
Conclusion: HER2 overall patterns of expression are in line with published data. This study gives detailed information into IHC/FISH concordance across all categories. It identifies a numerically significant 'FISH equivocal' group (12.5 % of all tumours). The possible significance of this 'equivocal' sub-group is discussed in the context of current HER2 reporting guidelines and current literature.

PS-16-033
Actual status of distribution and prognostic impact of extramural discontinuous cancer spread in primary gastric cancer
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Objective: Metastatic nodules in perigastric adipose tissue without evidence of residual lymph node (LN) structure (ND) have been identified in gastric cancer (GC). However, the morphological features and clinical significance of ND have not been clarified in gastric cancer. This study was to clarify the actual status of distribution and prognostic impact of ND in GC.
Method: A retrospective study was performed for 1148 consecutive GC patients underwent curative gastrectomy with regional lymphadenectomy at a single tertiary care center between 1996 and 2009, focusing on the impact of ND detected by routine H&E staining on disease-free survival (DFS) and cancer-specific survival (CSS).
Results: ND was detected in 16.0 % of patients in our cohort. The ND status was significantly correlated with tumour size, infiltration depth, and TNM stage ($P < 0.05$). Patients with ND showed significant shorter DFS and CSS than those without ND ($P < 0.0001$for both). Univariate analysis showed the variables affecting CSS included CA19-9, tumour size, lauren classification, tumour differentiation, gastric wall invasion, LNM, distant metastasis, TNM stage, and ND ($P < 0.05$ for all). Multivariate Cox proportional analysis identified ND as an independent predictor for CSS ($P = 0.022$).
Conclusion: The presence of ND is a risk factor for cancer progress and an independent predictor of poor survival in GC after curative resection.

PS-16-034
Clinicopathological and prognostic characteristics of esophageal sarcomatoid carcinoma: An analysis of 50 patients in a single Chinese center
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Objective: The aim of this study was to explore the clinicopathological characteristics and prognostic factors of esophageal sarcomatoid carcinoma.
Method: Clinicopathological data of 50 patients with esophageal sarcomatoid carcinoma in Sun Yat-sen University Cancer Center from January 2001 to December 2014 were retrospectively analyzed, focusing on the impact on disease-free survival (DFS) and cancer-specific survival (CSS).
Results: Among the patients, the median age was 61.0 years, with a male-to-female ratio of 2.85:1. The 5-year DFS and CSS rates were 53.6 and 68.9 %, respectively. In the univariate analysis, perineural invasion(PNI), pathological stage, serum alkaline phosphatase(AKP), serum C-reactive protein(CPR), white blood cell count, blood neutrophil count, neutrophil to lymphocyte ratio(NLR) and blood mononuclear cell count were significantly correlated with patients' outcome. The multivariate analysis suggested that PNI, AKP, CPR and NLR were independent prognostic factors for CSS; while PNI, CPR and NLR were found to be associated with DFS independent of other clinicopathological parameters. Moreover, the combined prognostic model with PNI, CPR and NLR can significantly stratify the risk (low, intermediate and high) for CSS and DFS.
Conclusion: The proposed new prognostic model might aid to the risk stratification and a personalized therapy for patients with esophageal sarcomatoid carcinoma.

PS-16-035
CD8-Positive Cytotoxic T-Lymphocytes in Colorectal Carcinomas (CRCs): Association with high-level Microsatellite Instability (MSI-H) or germ-line MUTYH mutation
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Objective: High number of tumour infiltrating lymphocytes (TIL) and peritumoural lymphocytes (PTLs) is characteristic for MSI-H CRCs, however their status has not been analyzed yet in another hypermutable CRC entity, i.e. in cancers arising in MUTYH mutation carriers.
Method: CD8+ TILs and PTLs were evaluated in 8 MSI-H CRCs, 2 CRCs from biallelic MUTYH mutation carriers and 1 MUTYH heterozygous patient (as a control). Tissue sections were immunohistochemically stained with CD8-specific antibodies and assessed by the digital image analysis system. TILs and PTLs were counted in 5 high-power fields each.

Results: In two MUTYH-related CRC, the TIL scores were 28 and 76, and the PTL scores were 106 and 129, respectively; this values were 11 and 25 in the CRC obtained from the MUTYH-heterozygous patient. In MSI-H CRCs the mean numbers were 112 (47–179) for TILs and 107 (33–304) for PTLs.
Conclusion: MUTYH-associated CRCs seem to be characterized by elevated infiltration by CD8+ lymphocytes, however the degree of this infiltration in lower than in MSI-H tumours. This work has been supported by the Russian Scientific Fund (grant number 14-15-00528).

PS-16-036
Gastric atrophy in breast and ovarian cancer patients carrying BRCA1 germline mutation
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Objective: High-risk stages (III, IV) of gastric mucosal atrophy are considered to be precursors of stomach carcinoma. Given that BRCA1 mutations are associated with increased gastric cancer risk, we evaluated presence and degree of gastric atrophy in BRCA1 heterozygotes.
Method: 35 BRCA1 mutation carriers were prospectively enrolled in the study (breast cancer: 27; ovarian cancer: 8; mean age: 48 years (range: 22–71 years)). The majority of the patients had relatively low tumour bulk and were analyzed before the chemotherapy. Five biopsy samples were obtained from each of the patients. Slides were stained with hematoxylin/eosin and alcian blue. The evaluation was performed according to OLGA (operative link for gastritis assessment) system by 2 independent morphologists.
Results: 11/35 patients (31.3 %) did not have any evidence of gastric atrophy. 12/35 (34.3 %) cases were classified as OLGA stage I, 10 (28.6 %) as OLGA stage II, 1 (2.9 %) as OLGA stage III, and 1 (2.9 %) as OLGA stage IV. None of the analyzed patients demonstrated evidence for gastric cancer.
Conclusion: These preliminary results warrant further research on the status of gastric mucosa in BRCA1/2 mutation carriers, with the emphasis on yet healthy subjects and comparison with mutation-negative controls. This work was supported by the Russian Scientific Fund (grant number 14-25-00111).

PS-16-037
Cell cycle regulation and its influence on the progression to oesophageal adenocarcinoma using DNA ploidy and immunohistochemistry for Ki-67, p53, and E2F
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Objective: Anomalies in cell cycle regulation can lead to abnormal proliferation resulting in tumourigenesis. The aim of the study is to correlate cell cycle regulation on oesophageal adenocarcinoma progression using chromosomal analysis and protein expression of cell cycle markers.
Method: Samples from 77 patients (squamous n = 12, Barrett's n = 16, low grade n = 13, high grade dysplasia n = 23 and adenocarcinoma n = 13) were immunostained for p53, Ki67 and E2F. DNA ploidy was carried out using image cytometric analysis. Multivariate analysis using Kruskall-Wallis test was used to compare between the histological grades.
Results: Multivariate analysis across the 5 groups showed the strongest association with progression to be with E2F ($p = 0.0007$) followed by Ki67 ($p = 0.0075$) and p53 ($p = 0.0325$) being the weakest. Ploidy data showed increase in aneuploidy in HGD and OAC with average DNA index scores of 1.45 and 1.32 respectively.
Conclusion: E2F is most upregulated marker with strong contribution from HGD and OAC compared to SQ. Ki67 showed upregulation in the earlier NDBE all the way to HGD and OAC. However p53 only showed upregulation in OAC. Ploidy analysis showed aneuploidy increase in HGD and OAC. Taken together, this suggests that cell cycle regulation plays crucial role in the progression to OAC.

PS-16-038
Role of inflammation and T-cell response on Barrett's oesophagus progression to oesophageal adenocarcinoma
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Objective: Barrett's oesophagus (BO) occurs as a consequence of inflammatory response triggered through prolonged reflux and may precede the development of adenocarcinoma (OAC). T-cell activation has been shown to play a role in the progression to OAC. The aim of this study is to assess the potential role of T-cells/immune checkpoints as biomarkers in the BO progression.
Method: 77 patients' samples, including normal squamous (n = 12), non-dysplastic Barrett's (n = 16), low grade (n = 13), high grade dysplasia (n = 23) and adenocarcinoma (n = 13) were stained with antibodies against Survivin, PD1, FOXP3 and CTLA-4. Protein expression was scored with Allred system. Mann–Whitney and Kruskall-Wallis tests were used for statistical analysis.
Results: CTLA4 expression was upregulated in the dysplasia-adenocarcinoma sequence but not at the stage of metaplasia ($p = 0.003$). Survivin was progressively upregulated across the different stages ($p < 0.0001$). There was no significant difference in PD1 or FoxP3 expression between any of the histological groups.
Conclusion: The results show that T-cells / immune checkpoint contribute to the progression of BO to OAC, in addition to survivin. This study adds further evidence to the use of immune checkpoint blockade in upper gastrointestinal cancer, but further studies are needed to assess the relationship of tumour-associated lymphocytes and the metaplasia-dysplasia-adenocarcinoma sequence in BO.

PS-16-039
Expression profiles and clinical impact of MUC1, MUC2, MUC5AC and MUC6 in colorectal cancer
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Objective: Mucin glycoprotein expression can be altered during the carcinogenic process. The impact on the prognosis of patients with colorectal cancer (CRC) is controversial.
Method: We analyzed tumours from 381 patients for MUC1, MUC2, MUC5AC and MUC6 expression by immunohistochemical staining, using tissue microarrays. Progression-free and cancer-specific survivals were determined using the Kaplan-Meier method.
Results: Expression of intestinal mucin MUC2 was lost in 85 (23 %) CRCs, and affected patients showed shorter progression-free survival (PFS, $p = 0.043$). Gastric mucins MUC5AC and MUC6 showed high (>50 %) aberrant expression in 28 (8 %) and 9 (2 %) cases, respectively. High expression of MUC5AC was associated with longer PFS ($p = 0.055$). High expression of MUC6 was associated with 100 % PFS ($p = 0.024$) and longer cancer-specific survival (CSS, $p = 0.043$). MUC1 was expressed in 238 (64 %) tumours and had no impact on outcome. When analysis was restricted to stages II and III, loss of MUC2 was associated with adverse outcome, while overexpression of both, MUC5AC and MUC6 significantly predicted favorable PFS and CSS.
Conclusion: Loss of MUC2 expression proved to be a predictor of adverse outcome, while the gain of aberrant MUC5AC and particularly

MUC6 expression is associated with favorable outcome in CRC, especially in intermediate stages II and III.

PS-16-040

Influential factors and prognostic impact of lymph node count in colorectal cancer

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Objective: Lymph node involvement is a major determinant of prognosis for colorectal cancer (CRC) patients. We analyzed pathological factors related to lymph node retrieval and evaluated the prognostic impact.
Method: The number of retrieved lymph nodes was assessed in 381 CRC patients (excluding patients with neoadjuvant treatment) and was related to different clinicopathological variables. Progression-free (PFS) and cancer-specific survivals (CSS) were determined using the Kaplan-Meier method.
Results: Median number of retrieved lymph nodes was 21 (mean 21, range 1–56) in right-sided, 13.5 (16, 2–57) in left-sided and 17 (19, 3–68) in rectal tumours. It was higher in patients with positive lymph nodes. The number of retrieved lymph nodes was associated with T-classification ($p < 0.001$), UICC stage ($p < 0.001$), tumour size ($p = 0.03$), localization ($p < 0.001$) and length of the operation specimen ($p < 0.001$). In T3/T4 patients ($n = 283$), both PFS ($p = 0.044$) and CSS ($p = 0.029$) were significantly longer, when >12 lymph nodes had been retrieved. Also, in T3/T4 N0 patients ($n = 130$) retrieval of >12 lymph nodes was associated with improved PFS ($p = 0.037$) and CSS ($p = 0.029$).
Conclusion: The number of lymph nodes retrieved was associated with adverse outcome in intermediate stages of CRC. High T-classification, tumour size, localization and length of the operation specimen were associated with increased number of lymph nodes.

PS-16-041

The prognostic significance of Cerb-B2 expression in gastric carcinomas

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Objective: Cerb-B2 overexpression of some solid tumours, particularly breast cancer, has been related with prognosis and response to treatment. But there are a limited number of studies on this subject in gastric cancer. In this study, we tried to determine the relationship between prognosis and Cerb-B2 expression in patients with gastric adenocarcinomas.
Method: 46 patients diagnosed with gastric adenocarcinoma in our department, between 2011 and 2015, were retrospectively investigated with respect to clinical and pathological aspects. All patients were Cerb-B2 positive and some of the patients were re-evaluated with the FISH method.
Results: Clinical follow up 37 of the 46 patients evaluated with Cerb-B2 could be retrieved. Mean follow-up of these patients was 9.6 months and 4 patients had died over this period. 31 of 37 patients had received chemotherapy and metastases were detected in 33 of them. 21 of 46 patients were evaluated with the FISH method. 10 of 11 patients with Cerb-B2 score of +3 were also FISH positive but one of them was negative. Metastasis was identified in 33 patients including; 21 patients with a cerb-B2 score of +3, 9 patients with a Cerb-B2 score of +2 and 1 patients with aCerb-B2 score of +1.
Conclusion: In this study presence of Cerb-B2 expression was seen to led to increased metastasis and aggressive behavior therefore Cerb-B2 positivity and degree can be used as a prognostic factor in gastric adenocarcinomas.

PS-16-042

Role of inflammation induced by the serine-protease Granzyme A in development of colorectal carcinoma in vivo

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Objective: Inflammation supports the different phases of cancer development, being one of the main factors of risk and prognosis in colorectal cancer (CRC). Granzyme A (gzmA) induces an pro-inflammatory response in macrophages and epithelial cells, regulating the production of cytokines in vivo and in vitro. We have now analyzed the contribution of gzmA to the development of CRC of inflammatory origin using different drugs. In parallel the presence of gzmA in colic tissue from patients with CRC has been analysed.
Method: Ulcerative colitis (UC) and CRC was induced in C57Bl/6 wild type (wt), granzyme A KO (gzmA-/-) and granzyme B KO (gzmB-/-) mice using 2,5 % DSS in drinking water alone (UC) or in combination with a single dose of Azoxymethane. Disease evolution was monitored during 2 months. Mice were evaluated after 60 days. The production of inflammatory mediators was quantified in cultures of colic tissue ex vivo. Results were evaluated using two-way ANOVA with Bonferroni's post-test and considered statistically significant if $P < 0,05$.
Results: GzmA-/- mice showed a clinical score lower than wt controls. The survival of the animals in the GzmA-/- group during the phase of acute colitis was higher than 80 % in contrast to that observed in the wt mice (lower than 40 %). Necropsies revealed that macroscopic and microscopic damage were significantly lower in GzmA-/- mice. The analysis of the development of tumours in the distal region of the colon of animals treated with DSS/azoxymethane evidence a lower incidence, number and size in the GzmA-/- group.
Conclusion: This data suggest that inflammation induced by gzmA contributes to CRC development in vivo.

PS-16-044

Anastomosing / crawling-type adenocarcinoma of the stomach

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Objective: Gastric anastomosing/crawling-type adenocarcinoma (ACTAC) is a neoplasm histologically comprising irregularly-fused (holding-hands) glands with low-grade cellular atypia that tends to spread laterally in the mucosa. ACTAC has been recognized as a distinct entity preceding poorly differentiated adenocarcinoma, and frequently showing mixed intestinal and diffuse type.
Method: From 563 T1 consecutive gastric cancer cases resected by endoscopy (326 cases) or surgery (237 cases), lesions including histologic features of ACTAC were selected.
Results: Twenty-five lesions (25 of 563, 4.4 %), including 16 intramucosal and 2 submucosal invasive cancers, were identified. Ten lesions were resected endoscopically. In remaining 15 lesions resected surgically, two (25 %) showed lymph node metastasis. One of those was an intramucosal cancer and the other was a submucosal invasive cancer. Lymphovascular permeation was found in 2 lesions and one of those showed lymph node metastasis.
Conclusion: ACTAC is a distinct subgroup of gastric adenocarcinoma in the early phase. To apply endoscopic treatment to this subgroup, stratification of the risk for lymph node metastasis is needed by histologic assessment.

PS-16-045

Effects of acute exposure to orally administrated acrylamide on histological structure of stomach tissue in Wistar rats

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Objective: Acrylamide is a toxic chemical substance which is in 2002 discovered in foods rich in starch, which are prepared at high temperatures.
Method: The research was carried out 6 groups of 5 experimental animals (Wistar rats). Two control groups orally implicated distilled water. Two experimental groups orally administrated acrylamide in a daily dose of 25 mg/kg, and two dose of 50 mg/kg. Three groups were sacrificed after 24 h and three after 72 h; On histological gastric tissue material is applied qualitative and semi-quantitative histological analysis, stereological measurements of individual compartments of the stomach wall, linear measuring the number of mast cells in the mucosa and submucosa.
Results: Histological changes in the stomach tissue of Wistar rats are seen as a direct slight damage of the surface epithelium, accompanying mild inflammatory reaction and degranulation of mast cells. Directly toxic effect on epithelium leads to the result of the reconstruction of the epithelium, which is confirmed by the presence of immature form of mucoproductive cells. Examined inflammatory and degenerative parameters show a positive correlation with respect to dose and/or a time of exposition to acrylamide.
Conclusion: Knowing the mechanism of action of acrylamide allows to apply adequate prevention and make an appropriate choice of therapeutic methods.

PS-16-046

Telomere measurement of intestinal and cardiac-type mucosae in Barrett's oesophagus using quantitative-fluorescence in SITU hybridization

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Objective: In many countries, Barrett's oesophagus (BE) is defined as columnar-lined oesophagus (CLO) with intestinal metaplasia (IM), IM being considered to have a marked predisposition to cancer development. However, our previous studies have demonstrated a close relationship between Barrett's carcinoma (BC) and cardiac-type (CT) mucosa (Hum Pathol 2011, AJSP 2015). On the other hand, we have revealed excessive telomere shortening with chromosomal instability in precancerous lesions. In the present study, we studied telomere lengths in IM, CT, and BC, where excessive telomere shortening induces chromosomal instability.
Method: In 41 EMR samples containing BC, IM, and CT, we measured telomere lengths using our original quantitative-fluorescence in situ hybridization method (Hum Pathol 2007).
Results: There was no significant difference in telomere length between IM and CT.
Conclusion: Our findings suggest that chromosomal instability due to telomere shortening is not peculiar to IM, and do not support the contention that IM has a special predisposition to cancer development. Therefore, we consider that in accordance with the Japan and United Kingdom definition, BE should be regarded as CLE with/without IM.

PS-16-047

Traditional serrated adenoma or serrated tubulovillous adenoma: Which is which?

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Objective: Epithelial serration, ectopic crypt foci (ECF), and cytoplasmic eosinophilia are typical features of traditional serrated adenomas (TSA); though they may be observed in conventional tubulovillous adenomas (TVA). When there is accompanying adenomatous dysplasia, the differential diagnosis becomes more difficult. The term"serrated TVA" (STVA) has recently been introduced to define TVA with serration. We, hereby, present a series of TSAs with filliform architecture and adenomatous dysplasia resembling TVAs.
Method: Eleven filliform TSAs showing epithelial serration, ECF and cytoplasmic eosinophilia in more than 50 % of the polyp were analysed, using an immunohistochemical panel including CK7, CK20, MUC2, MUC 5AC, MUC6, CDX2, Beta-catenin, p16, p53, and Ki67.
Results: Nine polyps were located in the rectosigmoid while 2 were in the proximal colon. Three cases had intramucosal carcinoma, one had high and the remaining showed low grade dysplasia (7/11). Dysplastic areas showed diffuse positivity with Ki67 and p53, and Beta-catenin. Gastric foveolar differentiation was observed focally in all with MUC5AC expression whereas, 5 polyps showed focal CK7 positivity and 3 demonstrated MUC6 positivity. All polyps were diffusely positive with MUC2, CK20 and CDX2.
Conclusion: Misinterpretation of adenomatous dysplasia in TSAs as a TVA or a mixed polyp may lead to undertreatment of the patient.

PS-16-048

Gastric involvement in Inflammatory Bowel Disease (IBD): Clinical-pathological correlations and utility of step sections analysis

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Objective: Gastric involvement is well known to occur in inflammatory bowel disease (IBD). However, a systematic clinical-pathological correlation has not been evaluated.
Method: We analysed gastric biopsies from 182 cases of patients with IBD (106 with Crohn's disease (CD) and 76 with ulcerative colitis (UC)). Afterwards, we performed additional serial sections.
Results: Symptoms related to upper gastrointestinal tract were present in 45 (42,4 %) CD cases and 40 (52,6 %) UC cases. Endoscopic alterations such as erosions and ulcerations were seen in 42 (39,6 %) CD cases and 35 (46,1 %) UC cases. In original sections, upon histology, we found focally enhanced gastritis in 40 CD cases and 17 UC cases. Granulomas were observed in 7 CD cases and in one UC case, crypt related. On serial sections, focally enhanced gastritis was found in 12 new CD cases and in 5 new UC cases. Additional granulomas were found in 7 CD cases and one crypt related granuloma was observed in one patient with UC.
Conclusion: The introduction of serial sections allowed us to detect the presence of an increased number of gastric lesions, thus indicating that single-level histological evaluation could underestimate their occurrence. Moreover, our study confirmed the gastric involvement by both forms of IBD.

PS-16-049

Diagnostic value of gamma delta intraepithelial lymphocytes in gluten sensitivity: Any better than H&E or CD3?

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Objective: The proportion of intraepithelial lymphocytes (IEL) expressing gamma delta T cell receptor (TCR) expands in gluten-sensitive enteropathy (GSE). We aimed to evaluate the number of gamma delta IELs in comparison to H&E and CD3 counts, within the spectrum of gluten sensitivity.
Method: The study group comprised of a spectrum of normal duodenal biopsies (n = 40), non-GSE IELosis (n = 40), Type 1 (n= 40) and Type 3 (n = 40) serologically diagnosed GSE cases. The number of IELs/100

enterocytes on H&E, CD3 and gamma delta immunostained sections were assessed for each group and compared using Chi square test.
Results: IELs increased significantly through the spectrum (9.00; 19.50; 1.25 in normal, 23.00; 36.50; 3.75 in non-GSE, 38.00; 59.50; 5.00 in Type 1,and 52.50;70.00; 8.00 in Type 3 GSE) on H&E, CD3, and gamma delta immunostains respectively ($p < 0,001$). IEL counts ≥28.50 on H&E, ≥44.50 on CD3, and ≥3.87 on gamma delta immunostains had a sensitivity of 91.30, 83.80 and 85.00 %, and a specificity of 97.50, 91.30, and 68.80 %, respectively, for GSE.
Conclusion: Anti TCR gamma delta antibody proves to be a useful marker and can be used as a supportive tool for the diagnosis of GSE, particularly when dealing with histological equvoical cases.

PS-16-050
Morphological changes of interstitial cells of Cajal, associated with myenteric plexus in animal model of ulcerative colitis
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Objective: The interstitial cells of Cajal associated with myenteric plexus (ICC-MY) play an important role in motor function of gastrointestinal tract (GI). They are affected in GI motor disorders including ulcerative colitis and Crohn's disease. However, morphology of ICC network isn't sufficiently characterized in colitis. Aims: to assess the morphological changes of the ICC-MY in the distal colon using a murine model of acute ulcerative colitis.
Method: Acute colitis was induced in adult male C57Bl/6 mice by 3 % aqueous solution of dextran sodium sulfate (DSS, 40 kDa). Histological sections of distal colon were stained with hematoxylin and eosin. ICC-MY were marked in the whole mount of colon muscular layer with the anti c-Kit monoclonal antibody (ACK4). Digital images were obtained with fluorescence microscopy and analyzed with the ImageJ software.
Results: DSS caused acute inflammation of the distal colon with extensive mucosal ulceration. Vacuolar alterations of smooth muscle cells were found. In control group colonic ICC-MY formed a tight network. In mice with ulcerative colitis there was a decrease in number of cells and in length of their processes. The network density decreased by 20–30 % in colitis. Also specific granularity appeared in some of ICC-MY.
Conclusion: There are morphological changes of colonic ICC-MY, which includes a decrease in their number and a damage of their process.

PS-16-051
The immune score in patients with colorectal cancer: A possible approach for classification and prediction outcome
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Objective: Cancer development is influenced by the host's immune system. Data collected from large cohorts demonstrates that the immune-classification has a prognostic value that may be superior to the TNM-classification. Evaluation with Immunoscore (I) methodology could be a useful prognostic marker in patients with colorectal cancers.
Method: Intratumoural immune reaction was investigated in 20 colorectal tumours from a total of 166 diagnosed in 2011 at Emergency County Hospital Timisoara. Cytotoxic (CD3) and memory (CD45RO) T cells were quantified by immunohistochemical analyses of tissue sections in the center (CT) and the invasive margin (IM) of the colorectal tumours.
Results: The results were correlated with patient survival. Densities of CD45RO(+) and CD3(+) cells in tumour regions (CT/IM) classified the patients into four prognostic groups. The four groups were associated with dramatic differences overall survival (all $P < 0.0001$). The Immunoscore provides a score ranging from (low densities of both cell types found in both regions), to 4 (high densities are found in both regions).
Conclusion: The Immunoscore could be a useful prognostic marker in patients with colorectal cancer. The combined analysis of CD3(+) and CD45RO(+) cells in specific tumour regions could provide a useful criteria for the prediction of survival.

PS-16-052
Changes in the expression of beta-tubulin isotypes are associated with different prognosis and chemosensitivity of colorectal cancer
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Objective: To reveal influence of the expression of betaI- and betaIII-isotypes of tubulin on CRC outcome.
Method: The study was performed on surgical material of 125 CRC. Double immunofluorescence with anti-cytokeratin and anti-betaI- or anti-betaIII-tubulin antibody was performed. Expression was analyzed by image analyses software and was calculated as ratio of integrated density to epithelial region's area and normalized according to positive and negative controls.
Results: The expression of betaI-tubulin was significantly elevated in CRC ($p = 0,000$). Lower values of betaI-tubulin expression in CRC were associated with lower disease-free ($p = 0,008$) and cancer-specific survival ($p = 0,015$). BetaIII-tubulin was almost absent in normal mucosa, but was present in CRC cells ($p = 0,000$). Elevated value of betaI-tubulin in CRC was associated with lower disease-free ($p = 0,002$) and cancer-specific survival ($p = 0,022$). Increased expression of betaIII-isotype in tumour budding was associated with lower disease-free survival in patients on 5-FU chemotherapy ($p = 0,010$).
Conclusion: These results demonstrate for the first time that betaI-tubulin expression is increased in CRC, but lower levels of this isotype are associated with worse survival. Expression of betaIII-tubulin is also increased in CRC, but higher level of it is associated with worse survival. Upregulation of betaIII-tubulin in tumour budding could be important for determination of 5-FU resistant patients.

PS-16-053
Inflammatory Bowel Diseases (IBD) are associated with changes in beta1-tubulin expression epithelial cells
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Objective: To reveal changes in the level of betaI-isotype of tubulin in IBD.
Method: The study was performed on biopsy fragments of colonic mucosa from 61 patients: 12 with Crohn's disease (CD), 27 with ulcerative colitis (UC) and 22 controls. Double immunofluorescence with anti-cytokeratin antibody and anti-betaI-tubulin was performed. Expression was analyzed by image analyses software and was calculated as ratio of integrated density to epithelial region's area and normalized according to positive and negative controls.
Results: The expression of betaI-tubulin was detected in epithelial cells in both inflamed and normal colonic mucosa. In joined IBD group the level of betaI-tubulin was significantly reduced ($p = 0.000$). But in the group of CD the expression was increased comparing with both control ($p = 0.029$) and UC groups ($p = 0.000$). The linear regression revealed significant relation of betaI-tubulin with the presence of dysplasia ($p = 0.000$). No relation was found with disease activity signs, mucus depletion and crypt depletion.
Conclusion: These results demonstrate for the first time that betaI-tubulin expression is altered in IBD and this phenomenon has the opposite directions in CD and UC. Further investigations are needed to understand clinical significance of these findings.

PS-16-054

Florid T-cell lymphocytosis in appendix could be misinterpreted as T-NHL

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Objective: Intravascular lymphocytosis (IVL) in appendectomy specimens is a fairly common phenomenon and should not be confused with chronic lymphocytic leukaemia. Here, an exuberant intravascular T-cell lymphocytosis at the tip of the appendix, extending into the serosa and subserosal tissues is presented.
Method: 28-year-old female referred to hospital with acute abdominal pain. Laparoscopic appendicectomy was performed. The gross examination showed an appendix measuring 49 mm in length and 6 mm in diameter with inflamed tip.
Results: The microscopic examination revealed intravascular accumulation of monomorphic small lymphocytes in the serosal vessels, at the tip of the appendix, which extended into the subserosal tissues. There was no evidence of acute appendicitis. Immunohistochemistry showed that these small lymphoid cells were positive for CD3, CD5 and bcl-2. Staining for CD20, CD10, bcl-6, CD23, TdT, CD34, CD56, MUM-1, Cyclin-D1, CD30, CD3 and EBV (EBER) was negative. Ki-67 staining showed a very low proliferation index. Gene rearrangement for T cell clones demonstrated no evidence of monoclonal T cell population.
Conclusion: Surgical manipulation and the patient's innate immunity are contributary factors to the development of the IVL phenomenon. Pathologists should be aware of this histological artefact in order to prevent overdiagnosis of lymphoid neoplasia.

PS-16-056

Expression of Cdx2 in primary gastric carcinomas

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Objective: Cdx2 is a homeobox domain-containing transcription factor that is important in the development and differentiation of the intestinal cells and served as a potential biomarker of tumour progression in early intestinal-type gastric cancer. The aim of this study was to evaluate the frequency of Cdx2 in gastric carcinomas and to investigate its expression in these tumours.
Method: It was a retrospective study of 32 cases with primary gastric carcinoma that were analyzed over a period of 1year and a half. The follow-up period varied between two and 48 months. The expression of Cdx2 in gastric carcinomas was detected using immunohistochemical method.
Results: Cdx2 expression was detected in 34 % (11 cases/32) of gastric cancer cases. Expression of Cdx2 was significantly higher in intestinal-type carcinomas than in diffuse-type carcinomas (82 versus 10 %; $p < 0,01$). Moreover, positive expression of Cdx2 was mainly found in moderately to well differentiated gastric carcinomas ($p < 0,05$). Howerver, the presence of Cdx2 was not associated with tumour size, TNM stage, vascular and perineural invasion.
Conclusion: Cdx2 plays an important role in the differentiation of normal and neoplastic gastric tissues. Further clinical studies are needed to confirm the role of Cdx2 in clinical practice.

PS-16-057

Expression of TMEM16A (DOG1) by medullary colorectal carcinomas

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Objective: Because calretinin is expressed in medullary colorectal carcinomas (MCRC), we assessed the expression of calcium-dependent chloride channel TMEM16A (DOG1) in these tumours.
Method: Seventeen MCRC were included. DNA mismatch repair status, KRAS and BRAF mutational status, MGMT and p16 expression were assessed. The following immunophenotypic traits were studied: cytokeratin 7, cytokeratin 18, cytokeratin 20, MUC2, MUC4, MUC5AC, MUC6, EPCAM, chromogranin A, synaptophysin, CD56, CD15, calretinin and TMEM16A. Cajal Interstital cells in normal colonic walls served as positive controls for TMEM16A. Seventy six additional non MCRC were immunostained for TMEM16A.
Results: All MCRC but one had MSI-H status. Eight of them displayed BRAF mutation and 9 a loss of p16 expression. The most frequent immunoprofile of MCRC combined the expression of cytokeratin 18 (100 %), EPCAM (100 %), TMEM16A (76 %), CD15 (76 %) and calretinin (70 %). TMEM16A expression was also observed in 13 of the 76 (17 %) non MCRCs. In normal colonic mucosa, TMEM16A was detected in epithelial cells at the bottom of the crypts including goblet cells.
Conclusion: TMEM16A (DOG1) expression by medullary carcinomas suggests that these histologically "undifferentiated" tumours harbour a differentiation state mimicking that of cells from the colonic crypt bottom, involved in water absorption and mucus secretion.

PS-16-058

Screening neuroendocrine component in advanced gastric cancers

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Objective: To conduct the screening of neuroendocrine component (NC) in advanced gastric cancers.
Method: 25 gastric tumours (IIIA-IV stage) after gastrectomy were investigated. The conventional methods, IHC studies with antibodies to chromogranin A, synaptophysin, NSE, Ki-67 were used.
Results: The ratio of M:F—2.1: 1. The average—65 years (43–77). 16 % of tumours (4 patients) had a NC more than 90 %, ulcerative type, were located on the border fundus and antrum, Ki-67 more than 55 %. 1 neoplasm were located in the fundus, protruding type, 4.5 cm diameter, regarded as MANEC (NC—35 % with Ki-67—20 %, exocrine—G3 adenocarcinoma with Ki-67—70 %). 8 infiltrative-ulcerative neoplasms (32 %) of different localization were presented mostly undifferentiated cancers and papillary adenocarcinomas, with spread serosa and multiple metastases in regional lymph nodes (NC—up to 10 %). 7 tumours (28 %) were submitted mainly tubular adenocarcinomas Grade 2 and 3 without the NC. 20 % of tumours had a structure mostly signet ring cell carcinoma, many cells contain both mucus and neuroendocrine granules (amphicrine carcinoma).
Conclusion: 52 % of advanced gastric cancers have neuroendocrine components in different proportions, 16 % of which was the major (more than 90 % of the tumour). Signet ring cell gastric cancers are often amphicrine.

PS-16-059

Cancer stem cell markers CD44, ALDH-1 and Lgr-5: Their relationship with clinicopathologic parameters and survival

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Objective: CD44 and ALDH-1 are well known markers for cancer stem cells (CSC). Lgr5 is a recently found CSC marker in the gastrointestinal tract. The goal of this study is to determine the distribution of CSCs, investigate their relationship with clinicopathologic parameters and survival in gastric adenocarcinomas (GAdC).

Method: CD44, ALDH-1 and Lgr5 immunostains were performed in 153 GAdC cases. Clinicopathologic parameters investigated were age, gender, tumour location, histological type, grade, stage, lymphovascular- perineural invasion and stromal response. Clinical follow up was available in 144 cases.
Results: CD44 staining was associated with intestinal morphology, lymphovascular invasion and desmoplastic response. ALDH-1 staining was seen in proximally located and low grade GAdCs. Lgr5 staining was correlated with low grade and low stage. No relationship was found with CD44 ve ALDH-1 whereas increased survival was associated with Lgr5 staining ($p < 0.05$).
Conclusion: The relationship between CD44 and poor prognostic factors may indicate that CD44+ cells are the actual cancer stem cells and they may play a role in planning the treatment. ALDH-1 staining was closely related with proximal GAdC, reflecting that these stem cells could be particular to this location. Lgr5 staining seen in low grade and early stage tumours may reflect their role in earlier steps of carcinogenesis.

PS-16-060
The relationship between KRAS, NRAS, BRAF, PIK3CA, and TP53 mutations and tumour morphology and behavior in colorectal adenocarcinomas
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Objective: Tumour budding in CRCs is a notable histologic feature associated with an adverse outcome and aggressive histopathologic findings, such as lymphovascular tumour emboli (LVE), perineural invasion (PNI), and an infiltrative growth pattern. We aimed to investigate the associations between molecular alterations and clinicopathologic parameters including tumour budding.
Method: We examined KRAS, NRAS, BRAF, PIK3CA, and TP53 mutations in 90 CRCs using a multi-gene panel with the Sequenom MassARRAY technology platform and analyzed the results.
Results: The incidences of KRAS, PIK3CA, NRAS, BRAF and TP53 mutations were 42.2 %, 12.2 %, 1.1, 2.2, and 23.3 %, respectively. A high tumour budding grade was correlated with KRAS mutations ($p < 0.001$). In addition, KRAS codon 12 and PIK3CA exon 9 mutations were associated with a high tumour budding grade ($p = 0.016$ and 0.006, respectively). LVE and PNI were correlated with KRAS mutations in exon 3 and 4 ($p = 0.044$ and 0.049, respectively). The median disease free survival of patients with PIK3CA mutant tumours in exon 9 was shorter than those of patients without PIK3CA mutation (28.3 vs 47.7 months, $p = 0.030$).
Conclusion: Our results show the associations between certain KRAS or PIK3CA mutations and aggressive clinicopathologic findings such as high tumour budding grade, LVE, and PNI.

PS-16-061
SATB2 is a promising biomarker for identifying colorectal origin in liver metastatic adenocarcinoma
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Objective: SATB2 has been shown to be a sensitive marker of normal colorectal epithelium and colorectal adenocarcinoma (CRC). The aim of the present study was to compare the possible differences in SATB2 expression between primary CRCs and their corresponding liver metastases, and to elucidate the use of SATB2 as a promising biomarker for identifying CRCs in a metastatic setting.
Method: In this study, we utilized immunohistochemistry to stain SATB2 in tissues arrays containing 337 primary and 78 liver metastatic adenocarcinomas from different digestive anatomic sites.
Results: Nonneoplastic colorectal epithelia were SATB2-positive. Among primary digestive system adenocarcinoma, SATB2-positive staining was observed in 99/101 CRCs, 2/97 gastric cancers, 3/82 cholangiocellular carcinomas, 1/30 pancreatic cancer and 0/28 duodenum cancers, respectively. The sensitivity and specificity of SATB2 for CRC detection was 97.0 and 97.5 % in the primary adenocarcinoma. Among liver metastases, positive staining of SATB2 was observed in 53/58 metastatic CRCs, 2/12 metastatic gastric cancers and 0/7 metastatic pancreatic cancers, respectively. For diagnosis of liver metastatic adenocarcinoma, the sensitivity and specificity of SATB2 for colorectal origin detection was 91.4 and 94.7 %.
Conclusion: Our findings suggest that SATB2 staining, as examined by immunohistochemistry, can serve as a promising diagnostic biomarker for liver metastasis of colorectal origin.

PS-16-062
What is the value of radical resection after local excision of early colorectal cancer?
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Objective: To evaluate outcomes of the subsequent resection after local excision of early colorectal cancer (CRC).
Method: From all patients who underwent a local excision for CRC between January 2013 and July 2015, the pathology report and the follow-up were extracted from the national pathology database (PALGA).
Results: In total, 2016 patients with a local excision were identified. Risk factors could not be determined in a substantial proportion. Close resection margins (<1.0 mm) were present in 655 patients (out of 1373, 47.7 %), sm3 invasion was present in 84 patients (out of 197, 42.6 %), 303 patients had Haggit level 3/4 (out of 838, 36.2 %), 228 had lymphatic invasion (out of 1725, 13.2 %). In total 483 patients underwent an additional resection (24.0 %). After radical resection residual carcinoma was present in 152 patients (31.5 %). Positive lymph nodes were found in 82 patients (17.0 %); in 18.5 % of patients with LI and in 16.4 % of patients without LI in the local excision. The percentages of positive lymph nodes per Haggit level (1–4) were 5.9, 13.8, 16.1, and 37.5 %, respectively. For the Kikuchi level (sm1 - sm3) percentages were 0, 33.3, and 18.8 %, respectively.
Conclusion: Existing high risk features do not adequately predict the presence of lymph node metastases.

PS-16-064
Neoangiogenesis and histochemical expression of mucins in colorectal adenocarcinoma
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Objective: The aim of this study was to investigate histochemical expression of mucins comparing to neoangiogenesis in colorectal adenocarcinoma.
Method: From paraffin blocks of 75 patients operated from colorectal carcinoma, the cuts were made and routine HE, histochemical AB-PAS and HID-AB methods, and immunohistochemical ABC method with anti-CD105 antibodies were implemented. After semiquantitative analysis of expression of neutral (fucomucins), slightly acidic(sialomucins) and strongly acidic(sulphomucins), microvascular density (MVD) per mm2 was calculated stereometrically. Software package SPSS (version 13.0) was used.
Results: Moderate and hyper-secretion of sialomucins were the most frequent in colorectal carcinoma (in 88 % of cases), while there was a trace of secretion of fucomucins and sulphomucins(48 %, 53.3 %). In adjacent non-tumour tissue, most frequent finding was moderate and

hyper-secretion of sulphomucins (100 %), while there was a trace of secretion of fucomucins(97.3%of cases) and sialomucins (68%of cases). Expression of sialomucins is with significant and highly positive correlation coefficient (0.44) connected with neoangiogenesis index (mvdIDX). Moderate and statistically significant, but negative correlation coefficient (−0.33) connects sulphomucins with mvdIDX in colorectal adenocarcinoma.
Conclusion: Qualitative and quantitative disorders of epithelial mucin secretion occur in colorectal adenocarcinoma. Mucins-histochemical alterations are in significant correlation with index of neoangiogenesis.

PS-16-065
Diet-related genes polymorphisms are associated with colorectal cancer risk
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Objective: Association between colorectal cancer (CRC), diet and diet-genes stay uncertain. Some authors proposed diet and gene interactions may explain some of the inconsistencies related to diet and CRC association. This study aimed to correlate diet-genes polymorphisms (within lipid, folate, and oxidative stress metabolisms) with CRC risk.
Method: A total of 119 CRC biopsies and 100 blood samples from healthy subjects (control-group) were incorporated in this study. Lipid metabolism(LM): APOA1 APOB, APOC3, APOE, CETP, and NPY; folate metabolism(FM): MTHFR, MTR, and MTRR; oxidative-stress metabolism(OSM): MnSOD, SOD3, GSTP1, GSTT1, and GSTM1 polymorphisms were genotyped using PCR-SSP kits.
Results: LM mutant-genotypes: APOA1(−75)AA ($p = 0.001$); APOC3(3175)GG ($p = 0.0002$); CETP(279)AA ($p = 0.003$), and NPY(7)CC ($p < 0.0001$), were found associated with CRC risk. FM mutant-genotypes MTHFR(677)TT ($\rho = 0.04$), MTHFR(1298)AC ($\rho < 0.0001$), and MTR(2756)GG ($\rho = 0.0002$), were prevalent among CRC subjects. OSM mutant-genotypes MNSOD(175)CC ($p < 0.0001$), SOD3(213)GG ($p < 0.0001$), GSTP1(105)GG ($p < 0.0001$), and GSTT1-null ($p < 0.0001$; OR:7.71; 95%CI:3.83-15.56) were correlated with CRC risk.
Conclusion: A positive association between CRC prevalence and several diet-related genes mutant-genotypes were observed. It seems that deregulation of genes involved in OSM, FM and LM processes seems to have an important role in p53 inactivation. Our results provide preliminary evidence that mutations in diet-related genes may be risk factors for CRC.

PS-16-066
IL-1 common polymorphisms are associated with colorectal cancer risk
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Objective: Interleukin-1 (IL-1) pluripotent cytokine is responsible for the mediation of immunological functions. Inflammation with altered expressions patterns triggers colonic inflammation and cancer susceptibility and development was studied to correlate with colorectal cancer (CRC). We intended to investigate IL-1A, IL-1B and IL-1RA common polymorphisms in CRC development risk.
Method: A total of 50 CRC biopsies and 100 blood samples from healthy subjects control group, were genotyped for IL-1A -889T>C; IL-1B -511C>T, IL-1RA 11100T>C polymorphisms using commercially available kits.
Results: IL-1A and IL-1B, low producer genotypes, IL-1A -889CC (OR = 0.2; 95 % CI:0.1-0.4); IL-1B -511CC (OR = 0.5; 95 % CI:0.3–0.9) were associated with CRC absence ($p < 0.005$), while IL-1B low producer allele, IL-1B -511C (OR = 1.78; 95 % CI:1.0–3.1) was more frequent in control group ($p < 0.05$). We also verified that IL-1RA 11100TT (OR = 0.4; 95 % CI:0.2–0.7) and IL-1RA 11100T (OR = 0.4; 95 % CI:0.4–0.7) were associated with CRC absence ($p < 0.005$).
Conclusion: IL-1 genes revealed a strong linkage with CRC and IL-1A, IL-1B, IL-1RA polymorphisms were associated with IL-1A and IL-1B downregulation (related with pro-inflammatory responses among colonic and rectal carcinomas) and can decrease tumour induction and prevent CCR development. Although not directly linked to the disease, these genes can be important biomarkers for this multifactorial disease.

PS-16-067
Colorectal signet ring cell carcinoma: A clinicopathological study of 10 cases
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Objective: The aim of this study was to analyse the clinico-pathological features of patients with colorectal signet ring cell carcinoma (SRC).
Method: Retrospective study of 340 cases of colorectal cancer including 10 cases of (SRC) diagnosed at our department of pathology over 6 years from 2010 to 2015. Data concerning gender,age, tumour location, macroscopic appearance,lymph node metastasis,pathologic stage and MSI status were analyzed.
Results: The total number of colorectal SRC was 10 cases, which represents 2,9 %, including 7 males (70 %) and 3 females (30 %),aged between 34 to 67 years with median of 48,2 %. The diagnosis was made on surgical resection in 7 cases and only on biopsy in 3 cases. Two patients had Crohn's disease history. The RSC are slightly more common in the left colon 4 cases (40 %) followed by equal frequency in both the right colon and rectum each 3 cases (30 %). Macroscopically, 8 cases (80 %) have an infiltrative gross appearance. Seven patients (70 %) had stage VI with peritoneal carcinomatosis and distant metastases at the time of diagnosis.
Conclusion: The purpose of our study is to demonstrate the aggressiveness of colorectal SRC, which occur more in younger patients, and often at an advanced stage at diagnosis, than usual adenocarcinomas.

PS-16-068
Lanthanum deposition in the stomach and transfer via lymph flow
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Objective: Lanthanum carbonate (LC) is an orally administered phosphate binder for end-stage renal disease patients. Its absorption has been thought to be minimal. Recently, a few cases showing lanthanum deposition in the gastric biopsy specimen were reported in Japan. We evaluated lanthanum deposition and its spreading in the gastrectomy specimen.
Method: 81-year old woman and 67-year old man who undergo hemodialysis and take LC as a phosphate binder were received subtotal gastrectomy for gastric cancer. We checked the specimen microscopically and confirmed LC deposit by scanning and transmission electron microscopy-energy-dispersive X-ray spectroscopy for the former.
Results: Lanthanum deposition were observed in the metaplastic atrophic area extensively and also in the regional lymph nodes. Its deposition was found at neoplastic area, too. They have shown no adverse effect so far.
Conclusion: These findings suggest that lanthanum is absorbed in the stomach and transported via lymph flow. And deposition would be associated with intestinal metaplasia, which might be a reason why lanthanum deposition was reported by only Japanese, who mostly carry intestinal metaplasia in gastric epithelium.

PS-16-069

Immunoexpression and signficance of B-Catenin and Sox2 in adenomatous polyps and adenocarcinomas of colon

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Objective: To investigate the immunohistochemical expression of β-catenin and Sox-2 in adenomatous polyps and adenocarcinoma of colon, also evaluation effect and significance of these markers in adenoma-carcinoma sequence.
Method: There were 56 tubular adenoma with low grade displasia(TALGD), 53 tubular adenoma with high grade displasia(TAHGD), 44 tubulovillous adenoma(TVA), 29 villous adenoma(VA) and 60 adenocarcinoma. Nuclear staining of Sox-2 and β-catenin and also cytoplasmic staining of β-catenin were evaluated. Semiquantitative scoring was performed. Results were compared between groups. The relationship between the findings and clinicopathological parameters were evaluated.
Results: Nuclear β-catenin expression was higher in adenocarcinoma than polyps. The expression in the polyp groups was higher in VA, TVA, TVA than TAHGD, TAHGD and TALGD, respectively. Cytoplasmic β-catenin expression was significantly higher in adenocarcinoma than VA, TVA, TAHGD and TALGD groups; in VA higher than TVA, TAHGD and TALGD; in TVA higher than TAHGD; in TAHGD higher than TALGD. There were significant differences between nuclear β-catenin and tumour differantiation and lymphovascular invasion. Nuclear Sox-2expression was higher in adenocarcinoma and TVA than VA.
Conclusion: B-catenin results were consistent with the literature. High Sox-2 expressions were correlated with malignant potential. Further molecular studies are needed for the effect of Sox-2 in adenoma-carcinoma sequence.

PS-16-071

Changing trends in H. Pylori gastritis: From antral predominant to corpus predominant?

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Objective: Early H. pylori gastritis is antral predominant while advanced gastritis is typically an extensive pan-gastritis involving both corpus and antrum. Prolonged use of PPI affects both the distribution and severity of gastritis which may become corpus predominant. The aim of the present study was to evaluate the variations in the pattern of H. Pylori gastritis within a time span of 10 years.
Method: Pathology reports of cases with a diagnosis of H. Pylori gastritis between 2005 and 2015 years were retrieved from the database evaluated for the histopathologic parameters included in Syndey classification both for corpus and antrum. The results were analyzed using chi-square, Wilcoxon and McNemar and homogeneity tests.
Results: There were 9715 cases with a diagnosis of H. Pylori gastritis, 86.0 % of which showed pangastritis whereas 6 % was corpus predominant and 8 % was antrum predominant gastritis. The incidences of pangastritis, antral and corpus predominant gastritis ranged between 81.5–89.0; 5.0–12.4; 4.1–8.3 %, respectively, over 10 years. There was a significant increase in the incidence of corpus predominant gastritis whereas the incidence of antral gastritis decreased significantly ($p < 0.001$).
Conclusion: Unsuccessful eradication therapies and long-term use of PPIs seem to change the presentation pattern of H. Pylori gastritis, from antral to corpus predominant.

PS-16-072

CD133 expression is related with survivin expression in surgically resected stage II and III colorectal cancers

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Objective: Cancer stem cell has been investigated as a new target for colorectal cancers. We have reported that CD133, cancer stem cell marker, positive cell showed a higher level of survivin expression than siRNA-induced CD133- cell and high survivin expression in CD133+ was related to chemoresistance to 5-FU in vitro study. In this study, we try to know the result of our in vitro study can be applied to the clinical samples.
Method: We investigated CD133 and survivin immunohistochemical (IHC) expression in stage II and III colorectal cancers from 187 patients treated by surgical resection with/without 5-FU based chemotherapy. Terminal deoxynucleotidyl transferase mediated dUTP Nick End Labeling (TUNEL) assay for apoptosis was performed.
Results: Mantel-Haenszel test established a linear association between nuclear survivin and CD133 expression ($p = 0.0178$) although neither had prognostic significance according to the level of IHC expression. There was no correlation between survivin and invasion depth ($p = 0.2674$), lymph node metastasis ($p = 0.7128$) or histologic differentiation ($p = 0.5314$). Apoptotic index (AI) was related with CD133 and survivin expression (Mean ± SD; 4.2308 ± 3.8123 in CD133- vs 5.1654 ± 4.9607 in CD133+ ($p = 0.0336$), 4.1026 ± 3.6906 in survivin- vs 5.1164 ± 4.8941 in survivin + ($p = 0.0443$).
Conclusion: CD133 expression is significantly related with survivin expression and apoptosis in colorectal cancer patients.

PS-16-074

The utility of imprint cytology of gastrointestinal endoscopic biopsies at Kenyatta National Hospital

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Objective: The main objective was to establish the utility of imprint cytology in the diagnosis of GIT pathology at Kenyatta National Hospital.
Method: This study was a cross sectional descriptive study and was carried out on 124 patients in Endoscopy Unit, Kenyatta National Hospital, within a period of 3 months. Imprint smears were made from endoscopic biopsies prior to formalin fixation. Slides were stained with Papanicolaou and Giemsa stains. Cytological features were described. Diagnostic performance of Imprint cytology was calculated and expressed in percentage.
Results: A total number of 124 participants were included in this study and Imprint cytology revealed that 37 (29.83 %) were positive for malignancy whereas 34 (27.41 %) were positive for H.pylori. The overall accuracy of imprint cytology for malignancy and H.pylori was excellent (94 and 90 % respectively).
Conclusion: Imprint cytology has a high accuracy, sensitivity and specificity in diagnosis of malignancy and Helicobacter pylori.

PS-16-075

Crohn's disease first presenting as signet-ring cell carcinoma: A case report

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Objective: The higher risk of small bowel carcinoma (SBC) in Crohn's disease (CD) patients is well-documented, but remains an uncommon event, usually diagnosed after a long-standing history of the latter. We

report a very unusual case of a signet-ring cell carcinoma (SCC) presenting as a first manifestation of CD.
Method: A 59 year-old female, with a prolonged history of colitis of unclear etiology, was admitted with 3 month-long intestinal obstructive symptoms, abdominal pain and weight loss. Computed tomography scans showed severe ileal wall thickening with segmental strictures, suggestive of CD. Diagnostic biopsies revealed SCC and therefore the patient underwent distal enterectomy and sigmoidectomy.
Results: Grossly, there were serosal adhesions, ileal mucosa ulceration with cobblestone pattern and wall thickening, with segmental stenosis along the specimen. Histologically, ileal SCC was confirmed, involving contiguous intestinal loops and sigmoid wall; transmural inflammation, myoenteric hyperplasia and fibrosis in non-infiltrated areas were also evident. The case was signed off as a SCC associated with CD.
Conclusion: Despite being an uncommon complication of CD, small bowel carcinoma should be kept in mind when dealing with enterectomy specimens. The pre-operative diagnostic challenge raises awareness about the absence of surveillance methods for malignancy in the small intestine, namely in inflammatory bowel disease patients.

PS-16-076
A case of gastric carcinoma with intramural lymph node metastasis. How to stage?
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Objective: Intramural lymph node (ILN) spread of digestive carcinomas is an extremely rare event (in the literature there is a single report of an oesophageal carcinoma with metastasis to a gastric ILN). Herein we report a case of gastric carcinoma with ILN metastasis in the submucosa of the stomach and discuss the implications for staging.
Method: A 55-year-old man was referred to our Hospital after the detection, on gastric endoscopy, of an ulcerated lesion (1 cm in diameter) diagnosed as adenocarcinoma. The patient was submitted to radical subtotal gastrectomy.
Results: The histological examination revealed a mixed gastric carcinoma, with tubular and poorly-cohesive cell components and focal invasion of the muscularis propria (pT2). Two submucosal ILNs were identified, localized away from the tumour, both with metastases of the tubular component. No other metastases were found in the remaining lymph nodes identified in the specimen. The tumour was staged as pT2N1, and the patient was started on chemotherapy (XELOX regimen).
Conclusion: To the best of our knowledge, this is the first description of ILN metastasis from a gastric carcinoma, in keeping with the rarity of this situation. For staging purposes, ILNs should be considered as regional lymph nodes and staged as pN1 (x/total lymph node count).

PS-16-077
Endoscopic ultrasonography with fine needle aspiration (EUS-FNA) as essential tool in diagnosing advanced pancreatic neoplasms (PN)
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Objective: PN are frequent tumours usually with silent aggressive behavior. Since patients are diagnosed in advanced stages, when surgery is not an option, EUS-FNA is the only reliable method to obtain tumoural tissue for microscopic diagnostic.
Method: We present the results of the first 47 EUS-FNA performed on pancreatic tumours in Colentina University Hospital. Biologic material was immediately immersed in 90 % alcohol for 2 h; then all fragments were processed for paraffin embedding. There were performed hematoxylin-eosin, specials stains, and immunohistochemical assays.
Results: We examined 41 pancreatic and 6 bile duct lesions. Patients underwent a mean number of 3 ± 0.7 passages each. 32 (68.08 %) of cases were conclusive with 82.5 % accuracy for body or neck, 50 % for the head and uncinate process, and 17 % for bile duct lesions. The diagnostic accuracy did not correlate with the number of passes.
Conclusion: EUS-FNA is a very important diagnosis tool for inoperable pancreatic tumours, allowing an adequate treatment (chemotherapy and specific pain therapy), increasing survival rate and life quality. As more EUS-FNA are performed in one center, sensitivity rises, allowing less passes and better diagnosis.

PS-16-079
Type of pathologic response in liver metastases of colorectal carcinomas related to specific chemotherapeutic agents
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Objective: Correlate the type of chemotherapeutic agents with the grade and type of pathologic tumour response (PTR) in the liver of patients with metastatic colorectal carcinoma (CRC).
Method: Chemotherapeutic agents were divided into chemotherapy alone (QT) or in combination with biological targeted agents (QT+ monoclonal antibodies against the epithelial growth factor [anti-EGFR] or QT+ vascular endothelial growth factor [VEGF]). PTR was assessed using a four grade score based on residual tumour cells. The type of tumoural regression was measured by fibrosis, histiocytes, mucous and necrosis.
Results: Median of PTR was 70 %, greater with QT+ VEGF (median 95 %) followed by QT+antiEGFR (median 75 %) and QT (median 59.50 %). Fibrosis causes a median of regression of 52.5 %, mucous 18.14 %, necrosis 17.38 %, and histiocytes 11.07 %. QT causes more fibrosis when PTR is greater than 90 % compared with the others and QT+ VEGF more necrosis.
Conclusion: Fibrosis is the most frequent form of regression and its increase is associated with greater degree of PTR. Histiocytes don't play a relevant role in this mechanism. The chemotherapeutic agent that causes more regression is QT alone but the association of QT+monoclonal antibodies raises greater liver PTR than only QT.

PS-16-080
Diagnostic yield of biliary brushing cytology: A single centre study
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Objective: a) To determine the percentage of biliary brushing cytology cases with positive, negative, false positive and false negative results. b) To determine the positive and negative predictive value of this test in our centre. c) To see the correlation between cytological, radiological & clinical findings.
Method: This is a retrospective data analysis of all biliary brushing cytology cases reported over 3 years from Jan 2012 to Jan 2014.
Results: A total of 34 biliary brushing cytology cases were reported between 2012 and 2014. Among them 22 were men and 12 were women. Average age was 69 years (Range 24–92 years). Out of 34, 15 cases (44 %) showed presence of malignant cells and all these were true positives with underlying pancreatic and biliary malignancy. Among the remaining 19 cases, 10 cases were true negatives and 9 cases were false negatives. In our cohort, the specificity of biliary brushing cytology was 100 % and sensitivity was 63 %. The positive predictive value 100 % and negative predictive value 53 %.
Conclusion: Biliary brushing cytology in conjunction with radiological investigation and serology is a useful technique in patients with suspected pancreato-biliary malignancy. Our results are comparable to studies done in other centres. To be re-audited.

PS-16-081

EGFR gene amplification is relatively common and associates with outcome in intestinal adenocarcinoma of the stomach, gastro-oesophageal junction and distal oesophagus

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Objective: In contrast to anti-HER2 antibodies, anti-EGFR antibodies have not provided survival benefit in clinical trials for metastatic gastric cancer. Despite the molecular and clinical variation among gastric adenocarcinomas, these studies have not included patient selection based on tumour characteristics such as histology or EGFR gene copy number (GCN) status. This study examined the role of EGFR GCN as a potential in intestinal-type adenocarcinomas of the stomach, gastro-oesophageal junction and distal oesophagus.
Method: 220 tissue samples were analysed with EGFR and HER2 immunohistochemistry and those with moderate/strong staining intensity with silver in situ hybridisation to quantify GCNs. The results were associated with clinicopathological patient characteristics.
Results: Moderate/strong EGFR protein expression was found in 72/220 (32.7 %), EGFR gene amplification in 31/220 (14.1 %), moderate/strong HER2 protein expression in 31/220 (14.1 %) and HER2 gene amplification in 29/220 (13.2 %) of the tumours. Co-amplification was detected in only eight tumours (3.6 %). EGFR amplification associated with shortened time to cancer recurrence ($p = 0.026$) and cancer specific survival ($p = 0.033$).
Conclusion: The determination of EGFR GCN status together with immunohistochemistry could improve the specificity of patient selection for anti-EGFR therapies in gastric cancer. The rarity of co-amplification suggests that anti-EGFR therapies might be applicable to some patients not eligible for anti-HER2 treatment.

PS-16-083

Intestinal lymphomas, 15 years' experience of a single center

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Objective: The incidence of small intestinal (23–30 %) and colorectal lymphomas (6–23 %) are less than stomach (60–75 %). But their frequency shows geographic variation and they display a broader histological spectrum and clinical presentation.
Method: We reviewed endoscopic biopsy (n = 36) or resection specimens (n = 52) of 75 primary intestinal lymphomas (IL) with available data diagnosed between 2000 and 2015 years and correlated the clinicopathological features by nonparametric tests.
Results: The most common subtypes were diffuse large B-cell lymphoma (DLBCL) (n = 34;45.3 %), and Burkitt lymphoma (BL) (n = 17;22.7 %), followed by MALT Lymphoma, Mantle cell lymphoma, Enteropathy associated T-cell lymphoma (EATL), follicular lymphoma. Rare subtypes as plasmablastic lymphoma were also observed. Almost all BLs were seen in first decade while FL, MCL, EATL were observed in 4th-6th decade. DLBCL has the widest age distribution ($p = 0.003$;chi-square). There was a male predominance (female/male ratio:1.6). The most commonly involved site was small intestine (n = 33;44 %) followed by colorectum (n = 21;17.3 %). Multifocal involvement was seen in 6 cases. (8 %). The complications as perforation (n = 10;13.3 %) and obstructing bulky masses were seen especially in DLBCL. Coeliac disease -like enteropathic changes accompanied EATL.
Conclusion: ILs are histologically more divergent, more frequently occurs in males, and after >50 years of age. (except for BL). Perforation with massive heamorrhage and obstruction are the important complications. DLBCL and BL are the most common ILs. Despite geographic predisposition no immunproliferative small intestinal disease (IPSID) cases were identified in our series.

PS-16-084

Role of EUS-FNA in the diagnosis of intra-abdominal lesions

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Objective: Non palpable intra-abdominal lesions because of poor accessibility is a diagnostic challenge and mandates tissue sampling by guided techniques. We hypothesize that the Endoscopic Ultra Sound (EUS) guided FNA of such lesions yields better tissue samples and aim to evaluate its role in cytodiagnosis.
Method: In this 4 year cross sectional study, EUS FNA was performed using 22 gauge needle through GF-UCT -140 Olympus/ Aloka endoscope. Aspirates obtained by three passes were processed by conventional cytological methods and evaluated statistically.
Results: 96 aspirates (89 %) from 108 patients who underwent EUS guided FNA were evaluated but only 65(87 %) were adequate; 10 (13 %) inadequates were from pancreas. 15 (23 %) from lymph nodes in and around celiac and aortic axis, 4(27 %) were reactive; 4(40 %)were tubercular; 5(33 %) were malignant. 46(71 %) pancreatic aspirates were adequate; 12 cystic; 32 solid—25 neoplastic and the rest inflammatory/benign. 4 from retroperitoneal SOLs were malignant. Two cases of malignancy underwent resection and findings were concurrent.
Conclusion: EUS FNAs, least invasive is the most effective modality for diagnosing deep seated inaccessible lesions. On site pathologist to check for adequacy, patterned aliquoting, correlating with clinical, radiological, serology and good cytology preparations with ancillary techniques facilitate diagnostic accuracy.

PS-16-085

Does total macroscopic examination of the appendectomy specimen change the pathologic diagnosis in pediatric cases?

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Objective: Acute appendicit is the most common cause of abdominal surgery in children. The major objective in dissecting an appendectomy specimen is to document the presence or absence of inflammation and confirm the diagnosis. If the pathology report is as no appendicitis then clinical search for other causes should be performed. In routine practice of macroscopic appendectomy evaluation, one section each from the base, body and tip and additional sections from inflamated or perforated area are performed.
Method: In the present study we first undertaken routine sections in two casette then exampled the rest of appendix totally. The diagnosis of routine exampled sections and total examination were compared.
Results: A total of 87 appendectomies were examined of which 58.6 % male with a mean age of 11.7 (1–18 years). The diagnosis was changed in 14 (16 %) cases. In 8 (9.1 %) cases the diagnosis of reactive lymphoid hyperplasia changed as acute focal appendicitis (early appendicitis), in 4 (4.5 %) cases acute suppurative appendicitis as acute suppurative and perforated appendicitis, in 2 (2.2 %) cases acute perforated appendicitis as acute perforated and gangrenous appendicitis.
Conclusion: Total macroscopic examination of the appendectomy specimen in cases of negative appendicitis would improve the diagnosis and can document early appendicitis cases.

PS-16-086

Clinicopathologic spectrum of malignant gastrointestinal neuroectodermal tumour: A study of 7 cases

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Objective: Gastrointestinal Neuroectodermal tumour (GNET) is a recently described clear cell sarcoma-like tumour of the gastrointestinal tract. Our aim was to study the clinicopathologic spectrum of GNET.
Method: Histopathology and immunohistochemistry slides of all GNET cases diagnosed at our institute were retrieved and diagnosis was confirmed. EWSR1 rearrangement was assessed by fluorescent in-situ hybridisation (FISH) in 5 cases. Clinical details were recorded from patient charts.
Results: Seven cases were studied. Median age was 44 years; male-to-female ratio was 0.4:1. Tumours originated in small intestine (n = 4), stomach (n = 1), rectum (n = 1) and retroperitoneum (n = 1). Histologically an admixture of clear, epithelioid cells in nested pattern with ovoid to spindle cells in fascicles was seen typically. Scattered osteoclastic giant cells were present in 2 cases. Diffuse immunoreactivity for S-100 (6/7) and variable reactivity for CD56 (2/2) & synaptophysin (2/3) was seen. Specific melanocytic, gastrointestinal stromal tumour, epithelial and myoid markers were immunonegative in all. All 5 cases tested by FISH showed split EWSR1 signal. Nodal and distant metastases were seen in 3 patients each.
Conclusion: GNET is a distinctive clinicopathologic entity with aggressive biology. Awareness of its clinicopathologic spectrum is essential in distinguishing it from its mimics.

PS-16-087

Clinicopathologic and evolutive characteristics of digestive neuroendocrine tumour: A retrospective analysis of 40 cases in Tunisian center

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Objective: Digestive neuroendocrine tumours (DNET) are a group of rare tumours with increasing incidence. We propose to study the clinicopathological and prognosis features of DNET.
Method: This is a retrospective study of 40 DNET diagnosed over a period of 5 years (2007–2012). Tumour grade was assessed according to the 2010 WHO classification. Tumours were staged according to the 2009 TNM staging system.
Results: The median age was 58 years and the female–male ratio was 1. The tumour was located in the pancreas in 13 patients (32.5 %), stomach in 13 patients (32.5 %), colon in 5 patients (12.5 %), rectum in 2 patients (5 %), small intestine in 5 patients (12.5 %), liver in 2 patients (5 %). The tumours were identified as grade 1 in 24 patients (60 %), as grade 2 in 10 patients (25 %) and as grade 3 in 6 patients (15 %). All small intestine neoplasms were grade 1. Ten patients had liver metastasis at the time of diagnosis. Eight patients received adjuvant chemotherapy. The overall survival was 34.6 months.
Conclusion: In southern Tunisia, Pancreatic and gastric locations are the most frequent. More than half of DNET are grade 1. However, a quarter of the tumours are revealed at the stage of liver metastasis thus requiring the use of targeted therapies.

PS-16-088

Evaluation of pathological reports quality for management of patients with colorectal cancer: Results of a large observational French cohort

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Objective: In 2009, the French Pathological Society published guidelines for pathological colorectal cancer (CRC) reports allowing optimal patient's management. The aim of this study was to analyze implementation of these guidelines in routine practice from a large territory and to identify obstacles for his application.
Method: This observational survey was conducted in a French region in 2010, among 1593 patients treated for a CRC by a surgical resection. 878 pathological reports have been checked to determine the presence of 11 main criteria and the use of standardized reports.
Results: Histological type (WHO 2010), grade, infiltration, number of analyzed and involved nodes, and pTN (UICC classification, 7th edition) were indicated in over 95 % of cases. Vascular emboli were present in 81 %, state of the surgical margin and perineural invasion in 70 %. The perforation was mentioned in only 35 % and the value of circumferential margin (mm) for rectal tumours in 16 %. These results were improved by the use of the standardized report.
Conclusion: Global quality of CRC pathological reports was high with good guidelines compliance. Better implementation of standardized reports in laboratories should be expected. We pointed out difficulties to correctly apply some criteria which could impact accurate patient's management.

PS-16-089

Dysplasia in Barrett's esophagus: Intraobserver and interobserver concordance in diagnosis and classification

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Objective: Dysplasia is the only clinical validated marker of cancer risk in Barrett's esophagus (BE). This study aims to analyze intraobserver and interobserver agreement in the diagnosis of indefinite for dysplasia (IND) and low-grade dysplasia (LGD) in BE and to evaluate the impact of pathologists' agreement on the progression risk to high-grade dysplasia (HGD) or adenocarcinoma (ADC).
Method: BE's biopsies classified as IND (n = 26), LGD (n = 25), and non-dysplastic (ND) (n = 23), from one institution, were randomly and blindly reviewed by 3 GI pathologists. The strength of interobserver and intraobserver agreement (k values) was classified as: poor <0.21, fair 0.21-0.40, moderate 0.41-0.60, substantial 0.61-0.80 or excellent 0.81-1.00.
Results: Intraobserver agreement was excellent (k = 0.82) for dysplasia (D) vs ND and moderate (k = 0.47) for LG/IND. Interobserver agreement was substantial (k = 0.64) for ND and D, moderate (k = 0.59) for LGD and poor (k = 0.14) for IND. From the patients diagnosed as LGD by 2 or more pathologists, 62,5 % progressed to HGD or ADC.
Conclusion: Intraobserver and interobserver agreement is moderate for LGD diagnosis, and poor for IND, even between GI pathologists. When at least 2 pathologists agree with LGD diagnosis, the risk of progression is high, so ablation in such cases seems justified.

PS-16-090

Telomerase Reverse Transcriptase (TERT) promoter mutational analysis of anorectal melanomas

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Objective: Anorectal melanoma is a rare and highly lethal malignant neoplasm comprising approximately 2 % of all melanomas and 3 % of anal tumours. The prognosis is poor with a 5-year survival rate of 20 %. Underlying genetic alterations are poorly defined, and current data suggest that a significant proportion of

anal melanomas harbor KIT mutations. In human somatic cells, telomeres shorten with each replicative cycle, eventually leading to cellular senescence. Telomerase activity is detected in approximately 90 % of malignancies, allowing tumour cells to bypass senescence and achieve unlimited proliferative potential. Recently, mutations in the TERT promoter region at positions 124 and 146 bp upstream of the ATG start site have been described in tumours from multiple organ systems, including sporadic and familial cutaneous melanomas. These mutations carry a UV-signature and portend a poor prognosis in cutaneous melanoma. The purpose of this study was to investigate the prevalence of hotspot mutations in the TERT promoter region in a cohort of anal melanomas.
Method: 15 cases of anal melanoma were collected from the United States, Canada, and Germany with approval from respective Institutional Review Boards. After microdissection to enrich for lesional tissue, DNA was isolated from FFPE tissue and analyzed for hotspot TERT promoter mutations by real time PCR using allele specific probes.
Results: 13 of 15 cases had sufficient amounts of DNA for analysis. TERT promoter hotspot mutations were absent in 12 cases and indeterminate in one case of primary anorectal melanoma.
Conclusion: TERT promoter mutations are not prevalent in anal melanomas, and likely do not represent a significant oncogenic driver event in this melanoma subtype.

PS-16-091
Poorly differentiated clusters: Are they important in evaluation of colorectal carcinoma?
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Objective: The histological grade based on gland formation is widely used in colorectal carcinoma (CRC), but its prognostic value is limited by interobserver variability. We aimed to assess the clinicopathological significance of poorly differentiated clusters (PDCs), defined as ≥5 cancer cell with no gland formation in CRC.
Method: 50 CRC consecutive resection specimens from Timisoara County Hospital were reviewed. The histological grade based on PDCs counting was assessed on H&E and CD31 immunostained sections. Associations between PDCs and pT1-T2 vs. pT3-T4, nodal status (LNM), distant metastases, peritumoural lymphocytic infiltrate as well as the presence of lymphovascular invasion (LVI) were analyzed using the Chi-square test.
Results: Using conventional histological grade 6 % of all the cases were well-differentiated (G1), 82 % moderately (G2) and 12 % poorly (G3) differentiated CRC, while in the PDCs-based grade 14 % were G1, 48 % G2, 38 % G3, respectively. In multivariate analysis PDCs-based grade was significantly associated with LVI ($p = 0{,}0022$) and LNM ($p = 0{,}0033$). Grading based on glandular differentiation did not significantly correlate with the analyzed parameters.
Conclusion: The novel grading based on PCD counting should be considered as a robust and promising prognostic factor in patients diagnosed with CRC.

PS-16-092
Collagenous colitis, with heterogenous clinical presentation
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Objective: Colloagenus colitis (CC) is characterized by thickened subepithelial collagenous band (>10 μm) containing entrapped red blood and inflammatory cells. Watery diarrhea and a normal endoscopy is also characteristic.
Method: We searched the relationship between collagen band thickness (CBT) and clinicopathological features. CBT was measured by a morphometry programme (AxioVision LE, Rel. 4.6) in the thickest area in 23 cases, diagnosed as CC histopathologically between 2008 and 2014 years, and correlated with nonparametric tests.
Results: Female/male ratio was 0.91. Mean age was 57 ± 16 years-old (Range:27–84). Thirteen percent of the patients were attended by anemia in addition to chronic diarrhea and the endoscopy showed eroded lesions in 26.1 % (n = 6) of the cases while it was normal in 65.2 % (n = 15). Collagen band thickening was focal in 17.4 % of the cases, contained inflammatory cells in 95.7 % (n = 22). Mean CBT was more than 25 μm in 39.1 % of the cases (median: 32.07 ± 22.5 μm) and was more frequent in females (66.7 %), in cases with diffuse involvement (89 %) and in endoscopically normal (55.6 %), cases, although the difference was not statistically significant.
Conclusion: CC is a variant of umbrella term "microscopic colitis", however it is not necessarily present as a uniform disease and can even be associated with endoscopically eroded lesions. Further research is warrented to rule out the histological specificity of incomplete forms of the disease.

PS-16-093
Gall bladder carcinoma: A clinicopathological study of 33 cases
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Objective: Gall bladder carcinoma accounts for 0.3 % of the all new cases in UK, being more common in females than males. This study was conducted to assess the clinicopathological features of gall bladder carcinoma diagnosed in a tertiary cancer centre.
Method: The study included all histologically proven gall bladder carcinoma cases between 01.10.2009 and 31.03.2016, excluding the inoperable cases. These include both the incidental carcinoma and pre operatively diagnosed operable cases. Winpath database, histology slides and medical records were the sources of information.
Results: 33 cases of primary gall bladder carcinoma were identified. Of these, 20 cases were incidental, whereas 13 were operable cases. The M: F ratio was 1:2. Adenocarcinoma was the commonest histological sub type with poor differentiation seen in 15/33 cases (45 %). 8 of 13 operable cases had advanced stage of disease pT3/pT4 (61.5 %) and 7 of these died of disease. 5 of 20 incidental cases (pT2) had subsequent liver bed resection and did not show any residual disease.
Conclusion: Nearly 60 % of the total gall bladder carcinoma cases in our study occurred incidentally (20/33 cases). Even when diagnosed pre-operatively, gall bladder carcinoma presented with advanced stage of disease and showed aggressive behavior with poor prognosis.

PS-16-094
Fluorescence lifetime imaging provides label-free recognition of mucin production in gastrointestinal specimens
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Objective: Fluorescence lifetime imaging (FLIM) permits to gain additional information by measuring the time delay (also called lifetime) between the excitation of tissue molecules and the emission of the fluorescence photons. A virtual fluorescence lifetime image (FLIM) is built by the contrast due to differences of the lifetime values (transformed in pseudo-colors) between the pixels of an image. The lifetime values depend on the molecule structure and their physicochemical environment. For these theoretical reasons, this technique should be able to recognize mucin producing cells in label-free histologic or cytologic preparations.

Method: We collected fresh, formalin-fixed, or paraffin embedded material from 25 cases of gastrointestinal specimens containing normal or tumour tissue. FLIM images of unstained preparations were created by a confocal microscope with a pulsed laser at 405 nm, and a time-correlated single-photon counting equipment.
Results: The FLIM technique showed very precisely morphologic details. Lifetime of mucins was generally much lower than that of the cytoplasm of normal or neoplastic cells, thus permiting easily the recognition of mucin production. Signal intensity was usually higher in fresh material than in histologic sections.
Conclusion: The FLIM technique permits rapid and efficient screening for mucin production in unstained material and reveals new insights into the histology of mucin producing cells.

PS-16-096
Characteristics of colorectal carcinomas with KRAS/NRAS and BRAF mutations: Analysis of 1160 cases from cerrahpasa medical faculty
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Objective: Mutations affecting the KRAS/NRAS/BRAF genes are established predictive markers of outcome with anti-epidermal growth factor receptor (EGFR) antibodies in metastatic colorectal cancer (mCRC). The aim of this study was to analyse the KRAS, NRAS and BRAF mutations in mCRC and associations of their subtypes and clinicopathologic parameters.
Method: We analysed 1160 mCRC cases for KRAS and NRAS mutational status of codon 12, 13, 61, 117 and146 using Real-time PCR based assay with commercial kit. Another commercial kit was used for BRAF V600E mutation in Real-time PCR as well. The tumours histologically were reexamined according to pathology reports. The correlations with KRAS, NRAS and BRAF mutation status and clinicopathological parameters were analysed statistically.
Results: M/F:1.56 and mean age:60.64 (23–81). KRAS 12/13, KRAS 61/146, NRAS, and BRAF mutations were detected in 47.7, 3.0, 4.1, and 6.3 %, respectively. The most common mutation types were 12ASP (36,2 %),13ASP (21,8 %), 12VAL (21,2 %), 12CYS (7,4 %). The tumours with codon 13 (13ASP) mutation have more mucinous secretion than the tumours with codon 12 mutations ($p < 0,05$). All NRAS mutated tumours were in conventional adenocarcinoma morphology. In multivariate analysis indicated that BRAF mutant patients had slightly poorer survive than KRAS/NRAS mutant patients (20.57 versus 28,69 months, respectively). Microsatellite Instability suggesting findings were observed in 34 % of BRAF mutant tumours.
Conclusion: Subtyping of KRAS/NRAS mutations have importance in mCRC. Characteristics and prognosis of CRC with BRAF mutations are different from those with KRAS or NRAS mutations.

PS-16-097
Endoglin and VEGF overexpression in colonic mucosa of patients with ulcerative colitis—possible therapeutical target
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Objective: Endoglin (CD105) is an pro-angiogenic factor involved in inflammation, as well as in tumoural neoangiogenesis. In ulcerative colitis (UC) its actions are correlated with vascular endothelial growth factor (VEGF). There are some anti-VEGF molecules targeted against this pathway, but further studies are nedeed for better understanding their role in UC pathogenesis.
Method: We studied expression of CD105 and VEGF on colonic biopsies from patients with UC at the beginning of the study and 12 months later. The study group included 45 UC patients, who underwent complete clinical and endoscopical evaluation each 12 months.
Results: All patients had incresead stromal expressoion of CD105 and VEGF in colonic mucosa lamina propria, with significant corelation of the two markers (t-test two-tailed $p = 0.0139$). During treatment, expression of these markers decreased concordantly (t-test two-tailed $p = 0.0085$). Patients with severe incresed of stromal CD105 had a higher risk of relapse and unfavorable evolution.
Conclusion: CD105 and VEGF have concordant evolution in colonic mucosa of UC patients, and coorelate with their outcome. These data suggest that they are not only angiogenic factors, but also pro-inflammatory molecules ands promising therapeutical targets.

PS-16-098
EFGR expression in patients with wild type KRAS mutation status: Avoiding unnecessary exposure to anti-EGFR therapies
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Objective: Currently, epidermal growth factor receptor (EGFR) is a therapeutic target in metastatic colorectal cancer (mCRC). The benefit from EGFR inhibitors appears to be limited to a subset of patients with RAS wild type. However, 25 % of patients of this group are resistant to EGFR therapy. Mechanisms of resistance to EGFR inhibitors are still being identified. EGFR expression is a potential mechanism of resistance that requires further researches. Therefore, we aimed to evaluate EGFR expression in mCRC patients with wild type KRAS status.
Method: This study enrolled 27 patients with mCRC, RAS wild type status at the same stage and grade. To evaluate EGFR expression we investigated immunohistochemistry (IHC) on formalin fixed paraffin embedded sections using NCL-EGFR (NCL-EGFR-384, Novocastra) monoclonal antibody. Scoring took into account the percentage of stained tumour cells (0–100 %) as well as staining intensity category (0–3).
Results: Our results showed that among the 27 samples, five had negative staining (18.5 %), seven harbored score 1 (26 %) whereas, 15 had score 2 or 3 (55.5 %).
Conclusion: These results show that 44.5 % (score 0 and 1) of patients receiving EGFR inhibitor therapies had a weak expression of the targeted receptor. This could explain, at least in part, the difference in response observed in treated patients and should be taken into account for the selection of patients to avoid toxicity of an inactive drug.

PS-16-100
KRAS and BRAF mutation and microsatellite status in gastric cancer in the elderly
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Objective: Our previous studies demonstrated that microsatellite instability was significantly related to aging in gastric cancer (GC). Recently, it was reported that KRAS and BRAF mutation status is limited in gastric cancer and has not been compared with various clinicopathological features.
Method: KRAS (codon 12 & 13) and BRAF mutations were examined for 460 consecutive GCs from 415 patients (222 men and 193 women; median age, 78 years, range, 51–96 years) as well as microsatellite status. The relationship among KRAS/BRAF mutation statuses, microsatellite status and clinicopathological variables was analyzed.
Results: KRAS and BRAF mutations were observed in 18 (3.9 %) and 2 (0.43 %) carcinomas, respectively. The proportion (2.4 %) of KRAS mutation in codon 13 was rather frequent than that

(1.7 %) in codon 12. KRAS mutation was significantly related with older age, female, lower third location, histology (solid-type poorly differentiated adenocarcinoma and papillary adenocarcinoma) and microsatellite instability. BRAF mutation showed no significant relation to clinicopathological variables.
Conclusion: These results suggest that KRAS mutation and age-related microsatellite instability have a role in a small subgroup of GC. Unlike colorectal cancer, BRAF mutation have little role in the development of GC.

PS-16-101
PD-L1/PD-1 pathway activation in EBV+ and MSI gastric cancers
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Objective: It is known that in human cancers, several immune system regulatory checkpoints are altered to escape from immune-control. Program death-1 (PD-1) and program death-ligand 1 (PD-L1) interaction leads to down-regulate immune response and it is one of the most promising immunotherapy target. PD-L1 is highly expressed on cancer cells of various malignancies, including gastric carcinoma (GC). Epstein-Barr virus infected (EBV^+) and microsatellite instable (MSI) GCs are characterized by a peculiar morphology, a high T lymphoid infiltration and a better prognosis. Objective: to investigate the activation of PD-L1/PD-1 pathway in GCs.
Method: 119 formalin-fixed paraffin-embedded GCs (19 EBV^+, 49 MSI and 51 EBV^-/microsatellite stable MSS) were analyzed for PD-L1 and PD-1 immunohistochemical expression.
Results: PD-L1 membrane immunoreactivity in more than 5 % of cancer cells was more frequent in EBV^+(58 %) and MSI (26 %) than in MSS/EBV^- (4 %) GCs ($p = 3 \times 10^{-5}$). In MSI GCs PD-L1 expression was associated with a better prognosis ($p = 0.05$). PD-1^+ intra-epithelial lymphocytes mean count was significantly different among the three groups (24 cells/HPF in EBV^+, 7 cells/HPF in MSI and 3 cells/HPF in MSS/EBV^-; $p \leq 0.01$).
Conclusion: PD-L1/PD-1 pathway is selectively activated in a subset of GCs and it could be considered as possible target for therapy.

PS-16-102
CEA monoclonal expression in ampullary cancer
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Objective: Adenocarcinoma of Ampulla of Vater (AMPAC) comprise about 5–6 % of periampullary cancers. We analyzed intestinal and pancreatobiliary AMPAC cell lines for protein expression levels using shotgun proteomics and revealed CEA-monoclonal (CEAM) as a significant marker in a study cohort containing 39 patients.
Method: Five cell lines (AMP7, AVC1, RCB1280, SNU478, SNU869) derived from AMPAC were analyzed using shotgun proteomics. CEAM expression results were confirmed in a study cohort comprising 39 patients. All results were correlated with clinico-pathological parameters.
Results: Proteomic analysis detected CEAM expression (isotypes 1, 5, 6 and 7) only in the cell line SNU478. Cell culture in medium conditioned by cancer associated fibroblasts led to a substantial decrease of CEAM expression. CEAM ($p = 0.016$), lymphnode-ratio ($p = 0.007$) and R-classification ($p = 0.0001$) demonstrated a multivariate significant correlation for OS. Histological subtype classification ($p = 0.018$) was univariate significant, but was lost in multivariate analyses.
Conclusion: Our data suggest that beside lymphnode-ratio and R-classification CEAM is a strong prognostic marker in AMPAC and superior to the histological subtyping. In multivariate analysis traditional parameters as pT classification and Grading lost their prominence as a source of prognosticating survival of AMPAC.

PS-16-103
Mucosal alterations in Helicobacter pylori positive and negative chronic gastritis and their effect on the diagnostic efficiency
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Objective: To investigate the presence of the different mucosal alterations in Helicobacter pylori (H. pylori) positive and negative chronic gastritis cases. To compare three H. pylori detecting methods (Giemsa, Immunohistochemistry (IHC), FISH) and to investigate whether mucosal structural changes influence their diagnostic efficiency.
Method: 2152 chronic gastritis cases were examined (795 H. pylori positive, 1357 negative) over a 3-year period. Statistical correlations between mucosal alterations and Giemsa, IHC and the H. pylori FISH test were evaluated by Chi square, Fisher's exact, McNemar's tests and Holm-Bonferroni Sequential Correction.
Results: Intestinal metaplasia, atrophy, erosion/ulcer, foveolar hyperplasia, hyperplastic polyp, fundic gland polyp, lymphoid follicle, lymphoma, adenoma, dysplasia/carcinoma were identified as mucosal structural alterations. Presence of lymphoid follicles ($p < 0.0001$), erosion/ulcer ($p = 0.035$), moreover, active inflammation ($p < 0.0001$) showed positive correlation with H. pylori positivity. Structural alterations negatively influenced the sensitivity of Giemsa staining (87.1 %- > 75.9 %, $p = 0.0001$). This reduction was also present but not diagnostically significant in the case of FISH (99.2 %- > 95.9 %, $p = 0.0013$). Intestinal metaplasia did not have a statistically significant effect on the sensitivity of these stainings.
Conclusion: Presence of structural alterations of gastric mucosa can significantly reduce diagnostic efficiency of the Giemsa staining. In order to achieve higher diagnostic accuracy, the use of advanced staining techniques like IHC and FISH is recommended.

PS-16-104
HER2 gene amplification and protein overexpression in gastric adenocarcinoma in a Turkish population: A clinicopathologic analysis
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Objective: Recent advances in molecular targeted therapy have identified HER2 as an important target for anti-cancer therapy in gastric carcinoma (GC). Our aims were 1) to detect the prevelance of HER2 positivity in our population, 2) to compare our HER2 immunohistochemistry (IHC) and gene amplification results, and 3) to investigate the correlation of HER2 status with clinicopathological parameters.
Method: GC cases were retrospectively screened from the pathology archives of Marmara University School of Medicine (2013–2016).
Results: The patients ranged from 14 to 89 years, male/female ratio: 2.28. Among 469 primary GC cases a total of 466 were scored for HER2 immunostaining using ASCO/CAP guidelines. HER2 IHC status were 3+ in 88, 2+ in 88, 1+ in 23 and 0 in 263 of the cases. Gene amplification was evaluated by fluorescence in situ hybridization (FISH) in 135 cases: 3+ ($n = 57$), 2+ ($n = 50$), 1+ ($n = 7$), 0 ($n = 7$) . Although IHC 0 and IHC 1+ subgroups showed no amplification or low amplification, the IHC 3+ and IHC 2+ cases showed amplification in 82.4 % and 35 % of the cases, respectively. Proximal localization, intestinal type, papillary and well differentiated GCs had more diffuse immunostaining and high HER2 amplification levels ($p < 0.05$).
Conclusion: The IHC results showed high concordance with dual-FISH results ($k = 0.876$). Fixation/tissue processing problems and section levels

could be the cause of negative FISH results in IHC 3+ cases. In resection specimens with focal 3+ IHC (less than 10 %) FISH must be performed, because even focal HER2 overexpression in GC could point to uniform amplification by FISH.

PS-16-105

The role of mesothelial lining and peritoneal elastic lamina in staging colorectal carcinoma

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Objective: Although serosal involvement is an important parameter in staging colorectal carcinoma(CCa), it is challenging to recognize it in some cases. Mesothelial lining (ML) and peritoneal elastic lamina(PEL) can be useful markers for deep tumour invasion around the serosal surface. In this study we re-evaluated pT3 and pT4a CCa cases to understand the role of ML and PEL in staging.
Method: Among CCa's which were staged as pT3 or pT4a in our department, 46 challenging cases were included. Hematoxylin-eosin(H-E) stained sections were re-evaluated by an experienced gastrointestinal pathologist and 57 tissue blocks were selected for further evaluation with CK7 to demonstrate ML and Elastic Van Gieson (EVG) to outline PEL.
Results: In our pathology reports 13 (28 %) cases were pT3 and 33 (72 %) were pT4a. After re-evaluation, among pT3 cases there was serosal perforation in 5 H-E stained slides. CK7 revealed entrapped mesothelial cells within neoplastic cells in 6 slides. These findings up-staged 9 cases (27 %). On the other hand, in pT4 cases, 3 were re-staged as pT3. Because of background staining with EVG, only in 28 % of the cases we could identify PEL.
Conclusion: CCa staging could be challenging, mainly due to the decision of serosal involvement. In this study, we underlined the difficulty of deciding peritoneal invasion, even with the eyes of an experienced pathologist. CK7 was found as a useful parameter in this study, consistent with the literature. We did not consider the EVG as a helpful stain in this study, in contrast to the previous literature.

PS-16-108

Histomorphologic factors of early gastric carcinoma treated by endoscopic submucosal dissection: relation to effeciency of endoscopic resection

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Objective: Early gastric cancer (EGC) is defined as cancer invasion confined to the mucosa or submucosa, irrespective of lymph node metastasis. ESD is still being developed in Europe and has not gained enough popularity although it has been recommended as the treatment of choice for superficial gastric neoplastic lesions by European Society of Gastrointestinal Endoscopy (ESGE) in 2015.
Method: The aim of the study was to perform a retrospective analysis of clinical, histomorphologic and immunohistochemical features of 58 cases of EGCs removed by ESD in a university hospital in Western Pomerania in Poland and to evaluate factors related to the efficiency of ESD resection.
Results: With univariate analysis, indications for ESD with the highest R0 rate were found in EGCs limited to mucosa (T1a, small mucosal, M), without muscularis mucosa invasion, localised in the lower part of stomach and intestinal type in histological examination. The R0 complete resection rate was significantly ($p < 0.0001$) lower for T1b than that for T1a tumours (21.4 vs. 100 %). Tumours with submucosal involvement were associated with lower efficiency of ESD procedure.
Conclusion: Our data showed that in EGCs with favourable histomorphologic characteristics, ESD seemed to be a totally efficient and safe method of treatment in a European small-volume centre and should be recommended as the main treatment of EGC in other countries of Western Europe.

PS-16-109

Comparison of intratumoural and peritumoural budding in colorectal carcinoma

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Objective: In colorectal carcer, tumour budding (TB) at the invasive front (peritumoural budding -PTB) is associated with poor outcome in multiple studies but clinical relevance of tumour budding within the tumour center (intratumoural budding-ITB) is not yet known. Also there is not an established cut off for high TB. We aimed to compare ITB and PTB in colorectal carcinoma with prognostic parameters.
Method: We retrieved HE stained sections from 70 colorectal carcinoma cases. Tumour grade, tumour infiltrating lymphocytes, Crohn like inflammatory infiltrate, and vascular invasion were recorded. The maximum number of tumour buds was determined at the advancing edge of the tumour in a x20 objective and within the tumour center. Cases with >10 and equal to 10 buds were classified as high budding and those with 0 to 9 buds were classified as low budding. Low and high ITB and PTB are compared also for liver metastasis, T and N stage.
Results: PTB and ITB are highly correlated ($p < 0,001$). High ITB was present in 45,7 % of cases, high PTB was present in 52,9 % of cases. High TB is associted with liver metastasis and vascular invasion in both groups. There was no correlation betweeen TB and histologic grade, Chrohn like lymhoid reaction, T and N stage.
Conclusion: In conclusion, these preliminary results suggest that both intratumoural and peritumoural budding are associated with poor prognostic factors such as liver metastasis and vascular invasion. We suggest a histologic cut off >10 and equal to 10 for high tumour budding. Investigation of larger series of cases are needed to support our findings.

PS-16-110

Spectrum of pathologies detected in appendectomies with clinical suspicion of acute appendicitis: 10-year experience

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Objective: We aimed to evaluate the histopathologic diagnostic spectrum of appendectomy specimens resected for clinical diagnosis of acute appendicitis (AA).
Method: The appendectomies examined in the pathology department of a large university hospital between 2006 and 2016 were retrospectively analysed. The appendectomies having clinical diagnoses other than AA were excluded. Age and gender distributions were evaluated based on pathologic diagnoses.
Results: Out of a total of 3002 cases, histopathologic features of AA were present in 2693 (90 %) patients with a male predominance (1.8/1) and a median age of 25 years which is lower than neoplastic appendicular pathologies. No pathologic features were detected in 221 (7.3 %) appendectomies. Neoplastic and non-neoplastic pathologies (neuroendocrine tumours, mucinous cystic neoplasms, parasites, adenomas, diverticula, endometriosis, mucocele) were detected in the remaining 88 (2.8 %) patients.
Conclusion: Even though AA has very well-recognized clinical features, there are still unnecessary appendectomies without any pathology revealed despite thorough pathological examination. Clinical features can be mimicked by several other non-neoplastic and neoplastic pathologies. Pathologists should be aware of the possibility of other appendicular pathologies which are much less encountered than AA and range of normal histological features of appendix to avoid over- or misdiagnosis of AA.

PS-16-111

Precursor lesions of hereditary diffuse gastric cancer (HDGC) in prophylactic gastrectomies performed in carriers of CDH1 germline mutations. The experience of a reference center

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Objective: To describe the frequency and morphology of precursor lesions of HDGC—in situ carcinoma (ISC) and pagetoid spread (PS) of signet-ring cells - in prophylactic gastrectomies performed in carriers of CDH1 germline mutations.
Method: Overall, 27 prophylactic gastrectomies were studied (7 from our Hospital and 20 consultation cases). Specimens were totally submitted for histology (number of slides observed per case: 32 to 261).
Results: Isolated or multiple foci of ISC (n = 58 in 11 prophylactic gastrectomies) and PS (n = 98 in 17 prophylactic gastrectomies) were identified, both lesions coexisting in 10 cases. Intramucosal carcinoma (pT1) was observed in 25 cases. ISC was frequently observed at the neck zone and PS in the foveolar region. ISC displayed a mono-layer structure (single row of depolarized signet-ring cells) and PS displayed a two-layered structure (typical signet-ring cells spreading beneath the preserved foveolar/glandular epithelium).
Conclusion: To the best of our knowledge, the precursor lesions of HDGC herein described have only been identified in carriers of CDH1 mutations. The practical implications are twofold: whenever diagnosed, the patients should be referred for genetic testing; in difficult cases, a second opinion should be searched for the confirmation of the diagnosis and exclusion of mimickers of HDGC.

PS-16-112

Carbonic Anhydrase IX expression in resected pancreatic ductal adenocarcinoma is a marker of superior prognosis and insensitivity to pyrimidine nucleoside analogs

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Objective: To study CAIX expression as a prognostic and predictive marker in pancreatic ductal adenocarcinoma (PDAC).
Method: A tissue microarray was constructed from 261 patients who underwent a Whipple procedure for resectable PDAC. Sections were stained for CAIX and assessed using a four-tiered scoring system: negative, weak, moderate, and strong. The primary outcome was disease-specific survival (DSS). Sensitivity to adjuvant pyrimidine nucleoside analog-based chemotherapy was assessed.
Results: Thirty-four percent (N = 88) of cases showed negative CAIX expression, 30 % (N = 78) weak, 8 % (N = 47) moderate, and 18 % (N = 48) strong respectively. The strong staining category was associated with an increased median survival of 3.01 years (p = 0.0023) compared to 1.49, 1.32, and 1.17 years for the negative, weak, and moderate categories. In multivariable DSS analysis, CAIX high expression (strong staining) was associated with a RR 0.61 (p = 0.0216) compared to CAIX low expression (negative, weak, and moderate staining). With predictive DSS analysis, CAIX low expression cases were sensitive to adjuvant chemotherapy (p = 0.0015), whereas CAIX high expression had less sensitivity (p = 0.1786).
Conclusion: PDAC with high CAIX expression was associated with better survival. High CAIX expression may be associated with a reduced sensitivity to adjuvant chemotherapy with pyrimidine nucleoside analogs.

PS-16-113

Early gastric cancer — evaluation of endoscopic resection criteria in gastrectomy specimens

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Objective: Evaluate retrospectively 65 Early Gastric Cancers (EGC) treated with gastrectomy, and see if they had been effectively treated with endoscopic resection (ER).
Method: All the gastrectomies preformed for EGC (2001–2010) in our Institution were reviewed and the following information was collected: tumour location; dimension; macroscopy (Paris Classification); histological type (WHO2010); differentiation (G1,G2,G3); depth of invasion: Mucosa, Submucosa: SM1 (<500vm), SM2 (≥500vm); lymphovascular invasion (LI), and lymph node status (N). The lesions were classified in 3 groups: with absolute, expanded or with no indication for ER according to the Japanese Guidelines.
Results: A total of 65 patients treated with gastrectomy (33F/32M), with median age of 65 (32–96). 53 % of the tumours were localized in the antrum, with a median macroscopic tumour size 2,45 cm, 40 % 0-III (Paris Classification); 63 % tubular adenocarcinomas, 41 % G3, 38 % T1a; 62 % T1b (11%SM1 and 51%SM2); 7 % LV+. N+ detected in 11 cases (17 %). Fourty six (70,7 %) patients had no indication for ER, 21,7 % were N1. The eight patients with absolute ER criteria were all N0. One of the 19 (5.26 %) patients with expanded criteria was N1.
Conclusion: Patients with absolute criteria would have been safely managed by ER preventing gastrectomy morbidity and mortality; Patients with expanded criteria have shown lymph node metastasis in 5.26 % of the cases.

PS-16-114

Epithelial to mesenchymal transition of mesothelial cells contributes to the generation of carcinoma associated fibroblasts in locally advanced intestinal carcinoma

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Objective: To determine if epithelial to mesenchymal transition (EMT) of mesothelial cells contributes to the generation of carcinoma associated fibroblasts (CAF) in advanced intestinal adenocarcinoma. Mesothelial cell origin of CAF has been proved in peritoneal metastases but its contribution to primary neoplasms is less known.
Method: We have evaluated 14 surgical specimens corresponding to infiltrative large bowel adenocarcinoma (pT3 and pT4). The immunohistochemical expression of cytokeratin AE1/AE3, calretinin, HBME-1, CK7, CK20, WT1, D2-40, CDX2 and alpha smooth muscle actin (SMA) was evaluated in CAF. Mesothelial to mesenchymal transition is defined "in vivo" by the expression of mesothelial cell markers in cells that show fibroblastic location, morphology and expression of alpha SMA (myofibroblasts).
Results: The immunohistochemical study revealed that a subpopulation of intestinal CAF expressed mesothelial cell markers. Such fibroblasts were seen within the tumour as well as in the vicinity of the peritoneal surface. In addition to alpha-SMA they showed variable expression of cytokeratin AE1/AE3, CK7, calretinin, WT1 and other mesothelial markers. CAF showed no expression of CK20 or CDX2.
Conclusion: EMT of mesothelial cells not only plays a role in the development of peritoneal metastases. It also contributes to the generation of CAF in locally advanced intestinal adenocarcinomas.

PS-16-115

Granulomatous gastritis: A clinicopathologic analysis of 24 biopsy cases

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Objective: To evaluate the clinical fields and to discuss the etiology of gastric granulomatosis in our experience.
Method: 24 cases of ganulomatous gastritis were reviewed. Clinicopathologic findings and associated lesions were analyzed.
Results: Mean age was 44,6 years [24–74] and sex ratio was 0,33 [M/F = 6/18]. Indication of endoscopy was gastric pain (10 cases), chronic diarrhea (4 cases), anemia (2) cases, and vomiting (3 cases). Discovery of gastric granulomatosis was fortuitous in 5 cases. Upper endoscopy was normal in 6 cases, showed antral gastropathy (11 cases). Granuloma was unique in 7 cases and multiple in 17 cases. 6 patients (25 %) had Crohn's disease while 5 had gastric tuberculosis (21 %). In two cases, H Pylori was the retained cause of gastric granulomatosis. In the other patients, the final diagnosis was a foreign body reaction (n = 1), sarcoidosis (n = 2), yersiniosis (n = 1). In our series, seven cases were unclassified.
Conclusion: Although many cases remain unclassified, in most cases of granulomatous gastritis, a diagnosis of Crohn's disease or tuberculosis could be established. If these etiologies are excluded, an association with H. pylori is discussed.

PS-16-116
Recommendations for reporting tumour budding in colorectal cancer based on the International Tumour Budding Consensus Conference (ITBCC) 2016
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Objective: To achieve a consensus for reporting tumour budding in colorectal cancer (CRC).
Method: The ITBCC was organized into 9 sessions with presentations, a pre-meeting survey, and an e-book including the main literature on tumour budding in CRC.
Results: The following statements achieved consensus: Tumour budding is defined as a single tumour cell or a cell cluster consisting of 4 tumour cells or less. Tumour budding is counted on H&E. The hot spot method (in a field measuring 0.785 mm2 at the invasive front) is recommended. A three-tier system should be used along with the budding count in order to facilitate risk stratification in CRC. Tumour budding is an independent predictor of lymph node metastasis in pT1 CRC. Tumour budding is an independent predictor of survival in stage II CRC. Tumour budding should be taken into account along with other clinicopathological features in a multidisciplinary setting. Intratumoural budding exists in CRC and has been shown to be related to lymph node metastasis. Tumour budding and tumour grade are not the same.
Conclusion: The ITBCC proposes to include tumour budding in guidelines/protocols for CRC reporting.

Wednesday, 28 September 2016, 09.30–10.30, Hall 11.3
PS-17 Neuropathology

PS-17-001
Glioblastoma with ependymoma-like perivascular pseudorosettes: An under-recognised variant of glioblastoma with the potential for misdiagnosis as anaplastic ependymoma
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Objective: According to the 2007 WHO classification of central nervous system tumours, perivascular pseudorosettes are a "histological hallmark" of anaplastic ependymoma. However, glioblastomas may also feature perivascular pseudorosettes, and their distinction from anaplastic ependymoma may present a diagnostic challenge.
Method: A 60 year old male presented with a left parieto-temporal brain tumour. Gross total resection showed a high grade glioma with prominent perivascular pseudorosettes, prompting the diagnosis of anaplastic ependymoma. On multidisciplinary review, glioblastoma was favoured. Further to informal discussions with experienced neuropathologists, additional immunohistochemistry for neurofilament protein showed entrapped neurites centrally within the tumour. Olig2 and MAP2, known to stain neoplastic astrocytes of glioblastoma, but not cells of ependymoma were positive. Electron microscopy revealed no ultrastructural features of ependymoma. Review of the H&E stained slides showed an infiltrative tumour border.
Results: A revised diagnosis of glioblastoma with ependymoma-like foci was rendered. The tumour recurred 4 months post-excision and adjuvant radiotherapy.
Conclusion: The distinction between glioblastoma with perivascular pseudorosettes and anaplastic ependymoma is crucial as the former has a relatively poor prognosis, whereas the latter, being circumscribed, may be adequately treated with gross total resection. Clinical and neuroimaging correlation, and appropriate immunohistochemistry are useful in distinguishing glioblastoma with ependymoma-like foci from anaplastic ependymoma.

PS-17-002
Prognostic significance of ALK overexpression in glioblastoma
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Objective: Evaluation of the prognostic significance of ALK immunohistochemical expression and underlying genetic alterations in glioblastoma.
Method: 51 glioblastomas (M/F 33/18, mean age 59.5 (28–84) years, mean follow-up 6.5 (1–40) months were assessed with two different antibodies/ detection systems (5A4/Nichirei Biosciences & D5F3/Ventana) and screened for possible alk gene alterations using fluorescent in situ hybridization (FISH). Results were correlated with IDH1R132H status, cell proliferation (Ki-67 LI), p53 expression, clinicpathological variables and overall survival.
Results: 10/51 (19.6 %) glioblastomas showed intense granular cytoplasmic ALK immunostaining. All 10 were primary (IDH1R132H-) and only 1/10 displayed multiple alk gene signals with FISH, indicative of gene amplification/polyploidy. ALK overexpression was not detected in secondary (IDH1R132H+) glioblastomas (n = 5). The Ventana method showed higher sensitivity (p = 0.000) but was equally specific compared to the Nichirei. Intense ALK immunostaining was correlated with high proliferation index (Ki67 ≥ 50 %) (p = 0,043). There were no statistically significant correlations between ALK overexpression and clinicopathological variables, p53 expression, and patient overall survival.
Conclusion: In glioblastoma, ALK overexpression is infrequent and is rarely the result of underlying alk gene amplification/polyploidy. Although its presence is more frequent in rapidly-growing glioblastomas indicating a more aggressive clinical behavior, ALK overexpression does not appear to affect patients' prognosis.

PS-17-003
Lipoastrocytoma: A rare case report and review of literature
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Objective: Lipoastrocytoma is an extremely rare tumour, with only few cases described. We report a case of a low grade astrocytoma occupying right cortical lobe in parafalcine location.

Method: The patient was admitted with headache, vomiting and altered sensorium for duration of 1 year. MRI revealed a large heterogeneous enhancing mass in right fronto-parieto-temporal lobe with intratumoural fat along with cystic changes and calcification (correlated with CT) showing mass effect on third ventricle. A Gross total excision of the tumour was performed.
Results: Histologically, tumour showed glial cells that contained lipid droplets coalescing into a single large droplet, similar in appearance to adipocytes. Immunohistocemically, tumour cells strongly expressed GFAP and S-100. Ki-67 labelling index was low. A diagnosis of lipoastrocytoma was established.
Conclusion: This case report represents a unique, rare variant of low grade astrocytoma in children which is distinct from diffuse astrocytoma and has been referred to as lipoastrocytoma. It is imperative to report each new case of this rare tumour to produce a better characterization of this lesion and its biologic behaviour.

PS-17-004
A rapidly fatal case of diffuse leptomeningeal melanocytosis with NRAS mutation in a 22-month old boy
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Objective: To narrate the clinical and radiologic findings in a case of leptomeningeal melanocytosis in a 22-month old male and describe the autopsy, histologic, immunohistochemical and molecular studies.
Method: A partial autopsy (limited to the brain) was done.
Results: No abnormal skin pigmentation is noted. The external surface of the brain revealed diffuse dark brown to black discoloration of the leptomeninges over the convexities and base. The cerebellum is macerated. Histological examination show dense mildly pleomorphic cellular infiltrates with pigmentation in the leptomeninges, sparing the ventricles. Tumour cells are immunoreactive to vimentin, S100 and HMB-45. Epithelial, lymphoid and glial markers are non-reactive. Ki-67 labelling is 1–2 %. NRAS mutation (Q61H, 183 A>T) is present. These findings support the diagnosis of diffuse leptomeningeal melanocytosis.
Conclusion: Ante-mortem diagnosis is challenging as it is rarely suspected unless histopathologically proven or there are concurrent skin lesions that help suspect neurocutaneous melanocytosis. Given the rapidity of the course of disease once neurologic symptoms set in, diagnosis is usually confirmed only after autopsy. No treatment strategy has been proven to be effective in controlling this disease but clinical trials are currently underway for a viable cure based on the molecular profile of the tumour, emphasizing the need for molecular diagnostics.

PS-17-005
Glioblastoma with PNET-like components: Case report
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Objective: Glioblastoma is the most common malignant primary brain tumour in adults, known for its wide spectrum of heterogenicity. PNET is an embryonal-type neoplasm reminiscing the developmental stages of the CNS, almost exclusively encountered in children. It has the capacity to differentiate along glial, neuronal, muscular or melanocytic lines. Tumours demonstrating both PNET features and advanced astrocytic differentiation are limited to individual case reports although some authors suspect they are often underdiagnosed.
Method: We report the case of a 25 years old woman, admitted to our hospital accusing headaches. Contrast MRI revealed a right temporal subcortical mass with partially cystic appearance of 56/52/37 mm and a nodular component of 26/20/17 mm. The patient was scheduled for neurosurgery and intraoperative consultation was required. Squash preps and frozen sections revealed a high grade glioma with marked atypia and giant cells.
Results: Due to the young age of the patient and radiologic appearance the possibility of a pleomorphic xantoastrocytoma was considered but was eventually dismissed due to the presence of necrosis and atypical mitoses. The tumour was resected and sent for histologic examination. Light microscopy revealed the biphasic nature of the lesion consisting of a giant cell glioblastoma intermixed with a small blue cell component. The glial and embryonal nature of the tumour was confirmed by immunohistochemistry.
Conclusion: The histogenesis of this lesion is not completely understood. While some consider the embryonal component as part of glioblastoma's known heterogenicity, other suspect a high form of glial differentiation. Concerning treatment, certain studies have demonstrated better response to PNET specific radiotherapy but, at this time, data remains insufficient to make a statement.

PS-17-006
Case report: Intracranial pleomorphic liposarcoma mimicking chordoma
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Objective: We report the case of a 68 year old woman with a tumour located in the sellar region infiltrating the left sinus cavernosus. Initially diagnosed with chordoma in 2010, the patient received proton irradiation. However, she subsequently developed a fast growing recurrence in 2016.
Method: The submitted material was fixed in 4 % buffered formalin and routinely processed. Sections were stained with HE. Immunohistochemistry was performed on an Omnis autostainer with antibodies against S100, keratins, EMA and brachyury (all Dako).
Results: The 2016 sample showed predominantly tumour cells with hyperchromatic nuclei scalloped by cytoplasmic vacuoles. Mitoses were brisk. Tumour cells were negative for antibodies against keratins, EMA and brachyury but stained focally for S100. Reinvestigation of the 2010 material revealed large tumour cells with vacuolated cytoplasm arranged in sheets with moderate atypia. The tumour cells were focally positive for S100 and single cells expressed keratin. Recent brachyury staining on the initial specimen was negative.
Conclusion: Pleomorphic liposarcoma is the rarest subtype of liposarcoma, most commonly occurring in the extremities. To the best of our knowledge, we report the first case of pleomorphic liposarcoma arising in the pituitary region. Despite being exceedingly rare, sarcomas should be considered as differential diagnosis of intracranial neoplasms.

PS-17-007
Cerebellar liponeurocytoma: A novel report from Nigeria
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Objective: We present a 6 year old Nigerian girl with Cerebelar Liponeurocytoma. She presented with complaints of headache and vomiting, of 4/52. Headache was insidious, dull, predominantly left sided, worse in the morning associated with vomiting which relieved it. She had a gait disturbance. She was a fully conscious child with intact high cerebral function. Had truncal ataxia.
Method: Case report.
Results: Cranial CAT and Magnetic Resonance Imaging revealed left cerebellar tumour with obstructive hydrocephalus (Fig 1 and 2). She had an initial right frontal Venticulo-peritoneal shunt for cerebrospinal fluid diversion, and later a left retrosigmoid suboccipital craniectomy with microscope assisted gross total resection of left hemispheric tumour 1 week later which was complete. Intraoperative finding was soft greyish to yellowish mass with

partly cystic consistency and a fairly well defined brain-tumour boundary. There was a leash of tumour vessels that bled briskly. The post-surgery scan is shown in fig 4. She had fever and mild anaemia post-surgery and these were managed. She was discharged from the hospital 2 weeks later with a Karnofsky score of 90 % and is still being followed up in the out-patient. Histology report was cerebellar liponeurocytoma.
Conclusion: The rarity of this tumour and paucity of pertinent information regarding its biological potential and natural history have resulted in the application of various treatments. It is suggested that these lesions have much more favourable prognosis than medulloblastomas, and that adjuvant therapy for liponeurocytoma need not be as extensive as that administered for medulloblastomas. No place exists for radiotherapy. Patient is alive and well 1 year after.

PS-17-008
Anaplastic and meningothelial meningiomas in a single tumour: A "dedifferentiated meningioma"?
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Objective: The coexistence of anaplastic and low-grade components in a single meningeal tumour has been rarely reported. This dimorphic appearance is reminiscent of "dedifferentiation", a phenomenon infrequently seen in various mesenchymal and salivary gland neoplasms. We report here a case of the coexistence of anaplastic and meningothelial meningiomas in a single tumour.
Method: The patient was a 74-year-old man, who developed progressive cognitive impairment and gait instability. Neuroradiological examination demonstrated a large and predominantly extra-axial tumour spreading over the bilateral frontal base, indicative of olfactory groove meningioma. Shortly after the operation, the patient developed a local recurrence of the tumour and multiple metastases to the cerebrum, bone, and skin.
Results: The greater part of the resected tumour consisted of a dense, patternless proliferation of large, round, or polygonal cells and the compactly fascicular growth of spindle cells. Tumour cells showed markedly anaplastic cytological features. In small areas of the tumour, a typical meningothelial meningioma showing no cellular atypism was found. Both tumour components were closely juxtaposed, and no pathological features of an intermediate grade (atypical meningioma) were noted.
Conclusion: We think that the term "dedifferentiated meningioma" can be appropriately applied to tumours such as that reported herein.

PS-17-009
Non-adenomatous tumours of the sella turcica
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Objective: Over 90 % of sellar masses are Pituitary Adenomas (PA) and in most cases a near certain diagnosis is made pre-operatively allowing adequate treatment. However, other rare lesions can involve the sellar region simulating clinically and imagiologically a PA. In those cases the diagnosis relies on histological examination which might be surprising and challenging. To review non-adenomatous sellar tumours that simulated PA focusing on pathologic differential diagnosis and to correlate with imaging studies.
Method: Sellar lesions diagnosed in the pathology department from 1 January 2007 to 31 March 2016 were retrieved. Pure PA, pituitary apoplexy and neoplastic recurrences were excluded. Selected cases were reviewed for clinical and imagiological presentation, and for pathologic features.
Results: 17 out of 22 non-adenomatous lesions were selected as representative. Our series includes 4 non-neoplastic lesions: 2 Hypophysitis, 1 Rathke cleft cyst and 1 post-surgical mucocele and 13 neoplastic lesions: 1 Inflammatory Myofibroblastic Tumour, 3 Gangliocytomas, 1 Lipoma, 1 Hemangioma, 1 Granular Cell Tumour, 1 Pilocytic Astrocytoma, 3 Craniopharyngiomas, 1 Chordoma and 1 metastasis.
Conclusion: In line with other authors, our series encompasses an heterogeneous group of conditions, dominated by benign neoplastic lesions (~75 %) and includes several rare entities. Careful neuro-imaging with MRI can provide important clues for pre-operatory diagnosis.

PS-17-010
Mixed sellar tumour: Pituitary adenoma and hypotalamic gangliocytoma, case report
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Objective: Adenomas are the most common tumours of the pituitary. While their development is still not entierly understood, increased hypotalamic secretion of brain peptides seems to play an important role. While extremely rare, the association of hypothalamic gangliocytoma appears to reflect this relation.
Method: We present the case of a 66 years old woman, recently diagnosed with acromegaly. The patient was admitted to the Bagdasar-Arseni Clinical Emergency Hospital for neurosurgical evaluation. Neuroimaging revealed a large mass occupying the sella turcica, encompassing the hypophyseal portal system and compressing the optic chiasma. The tumour was removed through trans-sphenoidal adenectomy.
Results: Light microscopy revealed two different cell populations. We identified the unremarkable features of a pituitary adenoma intimately associated with a neuronal proliferation of large, sometimes bi or multinucleated polygonal cells, characteristic for a gangliocytoma. Both components were evenly represented.
Conclusion: The exact histogenesis of these combined lesions is not entirely understood. Some authors have suggested pituitary hyperplasia and adenoma may be induced by a primary neuronal neoplasm while others consider that adenohypofisal cells may transform to ganglion cells through the nerve growth factors implicated. Either way, the existence of these mixed lesions should be considered to avoid any possible diagnostic pitfalls.

PS-17-011
Sudden unexpected death from extraventricular neurocytoma: A case report and review of the literature
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Objective: The authors present the case of a 35 year-old male who died suddenly and unexpectedly.
Method: Full autopsy, histology and toxicological analysis were performed in order to diagnose the cause of death.
Results: The only findings related to the cause of death were concerning a spherical tumour of the midbrain, which was pressing on the pons and cerebellum. Histology and immunohistochemistry set the diagnosis of a neurocytoma with positive staining for SY, NF, CD56, and NSE in the cytoplasm, disclosing the neuronal nature of the lesion.
Conclusion: The autopsy, histology and immunohistochemistry revealed a primary extraventricular neurocytoma of the midbrain, which was responsible for causing cardiopulmonary arrest and sudden death, through pressure on the pons and cerebellum. Neurocytomas are unusual neuronal tumours, especially affecting young people, commonly arise in the ventricles and have a benign outcome. Currently, these tumours have been well recognized outside the limits of the cerebral ventricules and, in these instances, have been called "extaventricular neurocytomas" (EVNs).

PS-17-012

Transformation of the histological type of diffuse astrocytoma with IDH-mutation in a patient with Gilber's syndrome

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Objective: Gemistocytic astrocytomas (GA) are astrocytomas where the content of gemistotcytes exceeds 20 %. A number of gemistocytes in fibrillary astrocytomas (FA) may increase after the combined therapy.
Method: MRI detected a homogeneous tumour mass in the left frontal lobe in a 23-year-old male with Gilbert's syndrome and bilirubinemia up to 64 mmol/l in medical history. After removal of the tumour FA with Ki-67 4 % was diagnosed. The patient received radiation and drug therapy. After 6 years, a second operation was performed because of the recurrence. GA (Ki-67 6 %) was diagnosed.
Results: Molecular-genetic testing (quantitative PCR) in the first operation material revealed a high level of expression mRNA gene PDGFRα, β-tubulin III, Ercc1, middle level of MGMT, VEGF, TP and low level of C-Kit and TOP2α. In the second operation material there were high levels of TP, β-tubulin III, VEGF, PDGFRα, average level of Ercc1, MGMT, C-Kit and a low level of TOP2α mRNA expression. Also IDH1 gene mutation (R132H) and the absence of 1p19q codeletion in both materials were found. The most significant is the increase in VEGF and TP gene expression levels, which, along with the growth of Ki-67, shows an increase in the malignancy process.
Conclusion: It's difficult to prove the role of the different treatment options in this transformation. Gilbert's Syndrome may be a concomitant disease or it may play a role in the described phenomenon because of the increase of unconjugated bilirubin which interacts with the phospholipids of cell membranes, particularly in the brain.

PS-17-013

Pathology study of angiomatous meningiomas: A rare variant of brain tumours

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Objective: Angiomatous meningioma (AM) is a rare histological variant (2.1 % of meningiomas) in which it is described an increased peritumoural brain edema. We analyze the clinicopathological features and the mast cells index, reviewing their neuroimaging studies and possible correlation.
Method: From 692 meningiomas altogether, 2,02 % (14) were diagnosed as AM (median: 60 years old). Most of them were located in the frontal lobe and were surgically treated.
Results: Histology of the tumours revealed numerous variable sized blood vessels, hyalinized, in a background of plump spindle cells with oval vesicular nuclei. Vimentin, EMA and GFAP showed positivity, so AM were diagnosed. Using CD117 stain, we observed 0,3 %-3 % of mast cells index depending on the case studied. Peritumoural edema was significative increase on computed tomography. However, we couldn't correlate it with the mast cells index. The majority of the patients had a good prognosis.
Conclusion: Radiologically, angiomatous meningiomas have more frequent peritumoural edema. Histologically, they are rich in blood vessels. Surgery is the treatment of choice, adding radiotherapy if tumour remains. Overall, its prognosis is as good as other benign meningiomas. We need more studies to understand the role of the mast cells in the development of the edema and its importance in the diagnosis.

PS-17-014

Vascular Endothelial Growth Factor (VEGF) and its inhibitory isoform VEGF165b: Dual role in pituitary adenomas

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Objective: To evaluate the expression of vascular endothelial growth factor (VEGF) and its inhibitory isoform VEGF165b in pituitary adenomas.
Method: Our study included 68 specimens of pituitary adenomas immunohistochemically assessed for VEGF and VEGF165b and RNAscope method.
Results: VEGF was positive in 45 % of the cases. GH presented a statistically significant correlation with VEGF expression ($p = 0.02$). Also, for prolactinoams, PRL presented a partial superposition of its expression with that of VEGF (p Kendall = 0.02, p Speaman = 0.04). Particular expression was observed in case of ACTH and TSH positive pituitary adenomas. Areas of VEGF postive cells, with a membraneous intensification and with an islet-like aspect, surrounded by VEGF negative cells were observed on the entire surface of the section of analysed specimens. A percentage of 88.2 % of evaluated cases by means of in situ hibridization were VEGF positive. A percentage of 16.6 % of our cases were positive for VEGF165b, most of them having a low intensity. VEGF165b positive tumour areas were lacking for blood vessels.
Conclusion: GH-secreting pituitary adenomas are the most active regarding VEGF synthesis and release. VEGF can be a potential therapeutic target in pituitary adenomas with high microvascular density. VEGF 165b was found to be downregulated in pituitary adenomas.

PS-17-015

Embryonal tumour with abundant neuropil and true rosettes: A fetal autopsy case

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Objective: To describe a rare embryonal tumour in a fetus.
Method: We present an autopsy case of a female fetus with 19–20 weeks and medical termination pregnancy who showed a central nervous system malformation localized in brain with cystic formations in posterior fossa.

Results: Gross examination demonstrated a tumour mass in brain midline with supra and infratentorial involvement in relation to meningeal cystic formations. Histopathological examination showed hypercellular areas with small cells forming rosettes, with abundant neuropil and frequent mitosis, apparently contiguous with posterior meninges and ventricular space.
Conclusion: ETANTR is a rare subtype of central nervous system PNET which affects children under 4 years, with female predominance and poor prognosis. Neoplasia is constituted by undifferentiated neuroepithelial cells with abundant neuropil and ependymoblastic rosettes, commonly with expansive pattern growth. Ependymoblastoma and ETANTR share 19q13.42 amplification at a frequency about 95 %. This tumour is a childhood neoplasia with scare reported cases and we think that this is the first case with fetal presentation.

PS-17-016
Expression of integrin B4 in relation to decreased invasiveness and increased proliferation in glioblastoma cell lines
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Objective: To identify mechanisms of glioblastoma invasion, we evaluated the expression of integrin subunits in glioblastoma cell lines.
Method: We selected the first 10 % of invading cells (U87-Inv) from U87MG using laminin-2 (merosin) coated Transwell filters. To characterize the super-invasive cells, we used wound assay, proliferation assay, and RT-PCR for integrin receptors. Furthermore, we compared U87MG and U373MG for invasiveness and integrin β4 expression. We transfected U87MG with pRK5 β4 plasmid DNA, and knocked out integrin β4 using integrin β4 shRNA plasmids in U373MG.
Results: Migration rate of U87-Inv increase 20 % compared with relatively lower invasive cells (U87-Non). U87-Inv demonstrated faster wound healing whereas lower proliferative activity. The expression levels of integrin α1, α7, and β1 increased mildly in U87-Inv compared with U87-Non, while the expression of integrin α6 and β4 reduced in U87-Inv. In comparison with U87MG, U373MG showed relatively decreased invasiveness whereas relatively higher proliferative activity. The expression of integrin β4 increased in U373MG compared with U87MG. Integrin β4 transfected U87MG revealed decreased invasiveness and increased proliferation. Integrin β4 knocked out U373MG showed increased invasiveness and decreased proliferation.
Conclusion: Our findings suggest that expression of integrin β4 is related to decreased invasiveness and increased proliferation in glioblastoma.

PS-17-017
A rare case of centronuclear myopathy with DNM2 mutation: Genotype-phenotype correlation and review of articles
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Objective: Centronuclear myopathy (CNM) is a group of rare genetic muscle disorders characterized by muscle fibers with centrally located nuclei. The most common forms of CNM have been attributed to X-linked recessive mutations in the MTM1 gene, autosomal-dominant mutations in the DNM2 gene encoding dynamin-2 and the BIN1 gene, and autosomal-recessive mutations in BIN1, RYR1 and TTN gene.
Method: Dominant CNM due to DNM2 mutations usually follows a mild clinical course with onset in adolescence. Up to now, around 35 mutations of DNM2 gene have been identified in CNM; however, the underlying molecular mechanism of DNM2 mutation in the pathology of CNM remains elusive, and the standard clinical characteristics have not yet been defined.
Results: Here we describe a case of a 17 year old female manifest with proximal muscle weakness along with congenital anomalous pulmonary venus connection (which hasn't been described in previous cases of CNM), scoliosis and lung Disease without any positive family history. Creatine Kinase level was normal. Histology, special stains and electron microscope findings on the muscle biopsy showed CNM with characteristic features of DNM2 mutation which later on confirmed by Next Generation Sequencing.
Conclusion: This case expands the known clinical and pathological findings of CNM with DNM2 gene mutation.

PS-17-018
Motor system neuropathology in progressive supranuclear palsy
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Objective: Progressive supranuclear palsy (PSP) is a neurodegenerative tauopathy. Clinically, PSP presents with extrapyramidal symptoms with variable cognitive deficits. Neuropathologically, PSP features neuronal loss, gliosis and the presence of neuronal and glial tau protein inclusions in the cortical and subcortical regions, brain stem, and cerebellum. The potential involvement of the motor cortex, including the spinal cord with corresponding upper and/or lower motor neuron symptomatology, in PSP is not well understood and under researched.
Method: We analyzed motor system tau pathology in 7 PSP cases. Neuronal, glial, and neuropil tau-immunoreactive inclusions were semi-quantitatively analyzed in the primary motor cortex, internal capsule, crus mesencephali, pons, corticospinal tracts, anterior horns of the spinal cord, and in spinal nerves roots.
Results: Tau-related pathology was seen at all motor levels. The intensity of spinal cord involvement correlated with tau pathology in other areas of the pyramidal system. Six of the cases were found to involve the entire motor system.
Conclusion: The pyramidal system and spinal cord were involved in the majority of PSP cases investigated. This involvement can influence PSP clinical symptomatology and potentially lead to a false diagnosis of motor neuron disease or at least significantly influence the differential diagnosis.

PS-17-019
Embryonal tumour with abundant neuropil and true rosettes: A rare entity
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Objective: Embryonal neoplasms of the central nervous system (CNS) generally arise in the early years of life and behave in a clinically aggressive manner, but vary somewhat in their microscopic appearance. Several groups have reported examples of an embryonal tumour with combined histological features of ependymoblastoma and neuroblastoma, a lesion referred to as "embryonal tumour with abundant neuropil and true rosettes" (ETANTR).
Method: We describe the case of a 7-year-old girl with recurrent acute headache for about 6 months ago, bilateral papilledema and intracranial hypertension. MRI of the brain demonstrated an expansive mass located in both frontal lobes midline.
Results: Histologically, the specimen appearance was variably cellular, with a mixture of hipercellular regions and many paucicellular fields composed largely of a fibrillar, neuropil-like matrix occasionally containing rare ganglion cells and abundant calcifications. The distintive feature of the ETANTR was the presence of ependymoblastic rosettes. It was

treated according to SIOP - PNET protocol 5: chemotherapeutics, radiation therapy and bone marrow transplant.
Conclusion: ETANTR is a unique entity, a subtype of CNS PNET, with female predominance and quite different from that the other CNS embryonal tumours. The prognosis is extremely poor.

PS-17-020
Distribution of iron and calcium deposit in basal ganglia of Huntington Disease: Post mortem study of six patients
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Objective: The neuropathology hallmark of Huntington Disease is the presence of nuclei inclusions of ubucuitin, p62 and Huntingtin protein. Neuronal loss in the striatum classifies the disease in 5 categories. It is known that iron deposition plays an important role in neurodegeneration.
Method: We analized the distribution of iron and calcium deposit in basal ganglia, substantia nigra and dentate nucleus of six brain donors of the brain bank, Navarre, Spain. We also correlated the deposition with the stage of the disease.
Results: From the cases studied, two were in each of Vonsatell category (initial, intermediate and advanced). Iron deposition was observed in all cases, being more prominent in caudate and putamen nucleus compared with globus pallidum and substantia nigra. The density was higher in intermediate and almost negative in advanced stages. The iron deposition was observed in macrophages, astrocites and neurons. Calcium cristaloids were also observed in endotelial walls.
Conclusion: The presence of calcium and iron in intermediate stages of the disease may indicate that oxidative stress occurs in the course of the disease and not the beginning. If iron toxicity is related with the course of the disease, chelating therapies could be considered for application in the different stages of the disease.

PS-17-021
Undiagnosed meningiomas in a Portuguese forensic autopsy population
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Objective: To characterize undiagnosed meningiomas, in a Portuguese forensic autopsy population.
Method: The reports from autopsies performed during a 10-year period (2005–2015) at the Central Branch of the Portuguese Legal Medicine and Forensic Sciences National Institute were reviewed.
Results: Sixteen undiagnosed brain tumours were macroscopically detected and microscopically diagnosed as meningiomas of various types. They were grade I, measuring 15 to 50 mm. Two were in the same person. As for cause/manner of death, 1 tumour contributed to the fatal event (SUDEP). Other 2 were at the frontal lobe of victims committing suicide. Another 3 tumours were in 2 drowning cases, whose victims had psychiatric disease/epilepsy antecedents.
Conclusion: Despite neuroimaging techniques development, Incidental Meningiomas range 2 %. Their diagnosis is of great relevance, since they may underlay epilepsy; location/size may lead to behaviour/cognitive changes; histopathological type may favour brain hemorrhage. These factors may interfere with cause/manner of death (with medical/judicial implications). Furthermore, tumour genotype may correspond to a "hereditary meningioma", needing family counselling.

PS-17-022
Retrospective study of oligoastrocytomas under new diagnostic criteria
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Objective: Oligoastrocytomas (OA) are gliomas with mixed morphology. The discovery of mutations associated to astrocytic lineage (ATRX), together with the classic 1p/19q codeletion allows avoiding the great subjectivity and disagreement between pathologists, reclassifying them into oligodendrogliomas (O) and astrocytomas (DA). The aim of this study is to retrospectively reclassify OA according to these new guidelines.
Method: Twenty-six cases of OA, grade II (19) and III (7) were selected from the pathology files. Immunohistochemistry for IDH1 R132H and ATRX, and FISH for 1p/19q codeletion was performed in all cases.
Results: IDH1 R132H mutation was found in 61,5 % of cases (16/26). OA grade II cases were reclassified into 5 O grade II, 5 DA, 6 grade II gliomas NOS, 2 anaplastic astrocytomas (AA) and one OA grade II. Anaplastic OA were reclassified into 4 glioblastomas, 2 AA and one anaplastic oligodendroglioma. In 6/26 cases the new diagnosis implied a higher tumour grade, even a change from low to high grade.
Conclusion: There is a need to retrospectively review cases of OA in order to offer patients an accurate treatment. However, even if the majority of OA will be reclassified following the new diagnostic criteria, there is a small subset of true morphologically and molecular mixed tumours.

PS-17-023
Alzheimer and Heparanase
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Objective: Heparanase (HPSE) cleaves heparan sulfate and is implicated in diverse physiological and pathological processes. A central pathological event of Alzheimer's disease (AD) is accumulation and deposition of cytotoxic amyloid-beta peptide (AB) in the brain parenchyma. Heparan sulfate proteoglycans are found associated with AB deposits in the brains of AD patients.
Method: 7 different areas of 4 brains (1 control, 1 low AD, 1 moderate AD, and 1 severe AD) were obtained. Transcriptional levels of HPSE using RT-PCR and the expression of the protein using immunohistochemistry were centered on Braak & Braak areas and nucleus basalis of Meyner and cerebellum.
Results: HPSE is expressed in all studied areas of the control and AD brains. AD brains overexpress HPSE except in nucleus basalis of Meyner. HPSE expression is better related with AB deposits rather than tau deposits. Cerebellum, an apparently non-altered structure in AD showed HPSE overexpression in all pathological cases. Immunohistochemically HPSE is observed at extracellular level in neuritic plaques with a fragmented core. In cells, HPSE highlights some neurofibrillary tangles and reactive astrocytes.
Conclusion: Our study has revealed increased expression of HPSE in the brains of AD patients in both extracellular and intracellular levels.

PS-17-024
Diffuse infiltrating gliomas WHO classification may be sustained by routine 1p/19q codeletion search
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Objective: Diffuse infiltrating gliomas (DIG) are currently classified after the criteria defined in the World Health Organization Classification applied on Hematoxylin-Eosin and Imunnohistochemistry cytological features also correlated with prognosis. DIG are subdivided in large categories of astrocytomas, oligodendrogliomas and mixed oligoastrocytomas demanding different therapeutic procedures. Molecular pathology became a tool to be applied in daily routine for DIG classification and molecular characterization of 1p/19q co-deletion was sought.
Method: A series of 30 DIG with heterogeneous morphology was selected from our files: IDH1 (R132H), GFAP, and p53 expression had been determined by immunohistochemistry as routine diagnostic panel and co-deletion 1p/19q was assessed by FISH in paraffin sections.
Results: All these 30 cases had co-deletion of 1p/19q positive, confirming oligodendroglial differentiation in ologodendrogliomas, oligoastrocytomas and glioblastomas with oligodendroglial features.
Conclusion: Due to DIG histopathological heterogeneity, difficult cases may be validated by 1p/19q codeletion to fill one class or define molecular heterogeneity observed in WHO tumour grading and validate prognosis and treatment. As molecular biomarkers will diminish the difficulty of classifying oligodendroglial lineage of tumours, the implementation of this molecular marker in the framework of routine scheme is essential to improve patient treatment, prognosis and clinical decision, avoiding immunohistochemistry in differential diagnosis of other brain tumours, reducing Pathology practice cost.

PS-17-025
A rare case of balloon-cell melanoma brain metastasis
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Objective: In recognition of the rarity of metastatic melanomas in the brain of the morphological variant of the balloon-cell type, we report a new case of balloon cell melanoma (BCM) metastatic to the brain of a 54-year-old male.
Method: The excised tumour tissue was histopathologically and immunohistochemically examined.
Results: There was diffuse infiltration of the brain tissue by large, tightly packed, pale neoplastic cells, occasionally of giant size, with an abundant, clear, foamy cytoplasm and relatively uniform nuclei with minimal to mild atypia and few mitoses. These characteristic balloon cells were amelanotic. The neoplasm was arranged in a solid pattern within the white matter with no connection to the meninges. Immunohistochemically, the tumour cells were positive for vimentin, S100, Melan-A and HMB-45, but negative for cytokeratins AE1/AE3 and 8/18, PAX8, calretinin and synaptophysin.
Conclusion: The clear cell morphology prompted initial differential diagnostic considerations of various cell types of metastatic carcinoma. However, the positive melanocytic immunohistochemical markers as well as a revealed history of cutaneous melanoma helped to establish final diagnosis. To our knowledge this is only the fourth reported case of metastatic BCM to the brain. BCM can be a challenging diagnosis to make in frozen section and pathology in general.

PS-17-026
An extremely rare case of a primary cervical intradural malignant peripheral nerve sheath tumour with multiple cranial and spinal leptomeningeal metastases
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Objective: Cervical intradural malignant peripheral nerve sheath tumour (MPNST) is an extremely rare pathological entity, which can give in uncertain circumstances cranial and spinal leptomeningeal metastasis, making the correct diagnosis extremely difficult.
Method: A 60-year-old female without history of neurofibroma or prior radiotherapy presented with headaches, back pain and rapid onset of tetraplegia. The imaging of the entire neuraxis revealed a cervical (C3-C4) intradural tumour with infiltration of the spine cord and with additional cerebral and spinal leptomeningeal lesions. The patient underwent cervical laminectomy and tumoural debulking without gross tumour resection as the tumour infiltrated the entire cervical spinal cord.
Results: The histopathological examination of the removed tissue revealed tightly packed spindle cells, placed in long, straight fascicles with a herringbone appearance. The tumoural cells were positive for S-100 protein and the proliferation index was more than 10 %. Based on the morphological and immunohistochemical features the diagnosis of MPNST was established.
Conclusion: Primary cervical intradural MPNST is a very rare tumour, with only 7 adult cases described in the literature to our knowledge. Secondary cranial and spinal leptomeningeal metastases from an intradural spinal location is even rarer.

PS-17-027
Benign melanocytic tumour of the brain: Case report
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Objective: Benign melanocytic tumour of the brain is rare finding and diagnostic dilemma for pathologists. We report a case of infratentorial benign melanocytoma in 42 years old female, clinically manifested as a hemorrhagic stroke. MRI reviled infratentorial tumour.
Method: Resected tissue was studied by H&E and immunohistochemistry (with anti- Melan-A, CD117, S100, CD99, GFAP, Synaptophysin, AE1/AE3, 34β/E12 and Ki67 antibodies (Leica)).
Results: Microscopically tumour consisted of slightly spindled, well-differentiated melanocytes, containing high amount of melanin. They formed of tight nests, fascicles and sheets. Cells contained oval or bean-shaped nuclei, small eosinophilic nucleoli, no cytologic atypia. Mitoses - <1/10hpf. Tumour expressed Melan-A and S100 and was negative for CD117, CD99, GFAP, Synaptophysin, AE1/AE3 and 34β/E12. Ki67 labeled <1 % of nuclei.
Conclusion: Based on histopathologic features, differential diagnosis included melanocytoma, melanoma, melanotic schwannoma and meningioma. Unlike our case, melanoma cells are more pleomorphic and has higher mitotic rate. Melanotic schwannoma was excluded by molecular profile (GFAP-, Melan-A+). Tumour also was negative for pan-cytokeratin markers, which excludes meningioma. Tumour was classified as benign melanocytoma. No adjuvant chemotherapy or radiation therapy was performed. After 16 month of follow up, patient has no recurrence and return to normal life with minimal neurologic complication (slightly decreased field of vision).

PS-17-028
Integrated diagnoses of 19 WHO grade II astrocytomas, oligodendrogliomas and oligoastrocytomas diagnosed between 2011 and 2015 using ATRX, IDH1 and p53 immunohistochemistry
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Objective: To apply the International Society of Neuropathology-Haarlem consensus guidelines on WHO grade II astrocytomas, oligodendrogliomas and oligoastrocytomas.
Method: We performed IDH1, ATRX and p53 immunohistochemistry in 19 WHO grade II astrocytomas, oligodendrogliomas and oligoastrocytomas diagnosed from 2011 to 2015.

Results: The median age of the patients was 40 years. The tumours were mainly located in the frontal lobe and 73,7 % presented with seizures. Eight patients underwent complete resection but only seven had no radiological evidence of residual tumour in the follow up. One patient died after the surgery. From the 9 oligodendrogliomas all had ATRX loss of expression, 7 showed mutated IDH1 and 1 overexpressed p53. The 6 diffuse astrocytomas showed ATRX loss of expression, 1 had IDH1 mutated and 5 overexpressed p53. From the 4 oligoastrocytomas 2 had ATRX loss of expression, 2 showed mutated IDH1 and 2 overexpressed p53 being therefore classified as diffuse astrocytomas.
Conclusion: We were unable to test for IDH2 mutations or 1p/19q co-deletion but IDH1 mutation accounts for 90 % of IDH mutations and ATRX loss of expression and p53 overexpression are almost mutually exclusive with 1p/19q co-deletion. Unfortunately we couldn't correlate the outcome with the expression of any these markers due to the short follow up.

PS-17-029
Malignant gliomas with primitive neuroectodermal tumour-like components: Clinicopathological analysis of 5 cases
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Objective: The presence of Primitive Neuroectodermal Tumour-like (PNET) Components in Malignant Gliomas (MG-PNET) is rare with only few series reported. The biological behaviour, molecular alterations, nomenclature in the WHO classification and their clinical evolution remains poorly known.
Method: We review all cases from the Department of Pathology of Hospital Universitari Bellvitge since 2011.
Results: Five patients, 1 female and 4 male ranging from 27 to 76 years (median = 45,4 years). Lesions were predominantly located in more than one lobe. One case had a previous biopsy of grade II Glioma and another was initially diagnosed of PNET and the necropsy revealed the presence of MG-PNET. The glial component resembled Grade III Astrocytoma and Glioblastoma. The PNET areas showed high nuclear/cytoplasmic ratio, hyperchromatic oval shaped nuclei with neuroblastic rosettes and foci of anaplastic cytologic features. Immunohistochemistry confirmed the expression of synaptophysin in PNET areas with focal expression of GFAP. Four patients were followed until dead with a survival from 2 to 26 months (median = 10 months). One patient is alive after 3 months of resection.
Conclusion: The presence of neuroectodermal components in malignant gliomas is rare and supposes a diagnostic challenge. In our series one case was previously diagnosed of lower-grade glioma.

PS-17-030
Colloid cysts of the third ventricle: Clinicopathological review of 57 cases
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Objective: Colloid cysts (CC) of the third ventricle are rare, benign lesions, which may be incidental or present with obstructive hydrocephalus, acute neurological deficits or even sudden death. The purpose of this study is to evaluate clinical and pathological features of CC patients and correlate with outcome.
Method: We retrospectively analyzed CC patients diagnosed in 1992–2016 at the University of California, San Francisco.
Results: 57 patients (33 male) were included in the study. Median age was 36 (14–81) years. Most common clinical presentation was headache (n = 43). Cyst-lining was columnar, cuboidal, pseudostratified epithelium or mixed. 2 cases showed squamous metaplasia and both had acute symptoms. One patient had accompanying diffuse glioma and one had pituitary macroadenoma. Resection was gross-total in 35 cases and subtotal in 15 cases. 3 patients recurred once and 2 patients recurred twice, most often after subtotal resection. Mean cyst size was 1.4+/−0.7 cm. The median follow-up time was 14 months (1–262); 14 patients were free of disease, 4 had residual disease, 39 were lost to follow-up.
Conclusion: Extent of resection appears to be important for the outcome. Type of epithelial lining is not associated with symptoms or outcome in this study.

PS-17-031
Postnatal differentiation of intrauterine neuronal migration defects caused by vitamin C deprivation in guinea pigs
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Objective: With prenatal vitamin C deprivation and the consequential disturbance in collagen synthesis we couse pial basal membrane rupture and the sequential development of dysplastic changes in the cerebellar cortex. In this study we investigated postnatal differentiation of prenatal caused neuronal migration defect.
Method: The experiment included 20 guiena pig 1 year old. First group of animals (10) was control and second was experimental (10) wich was during prenatal life (from 10th to 50th intrauterine day) deprived for vitamin C. We analyse vermal region of cerebellum using neuronal (NeuN, calbindin, synaptophysin), glial (MBP, pTTT, S100 and GFAP) and structural (collagen IV, CD34) immunohistochemical markers.
Results: In analysis of dysplastic cerebellar cortex neronal immunohistochemical marker show high morphological disturbance in final Purkinje cell development (calbindin) and complete maturation in ectopic granule cells (NeuN, synaptophysin). Using glial markers we show alteration in gliogenesis and myelination (pTTT, S100, MBP).
Conclusion: The experiment showed that although the granular cells located in ectopic medium and Purkinje cells lose polarity they can properly differentiate and mature. The fact that neither humans nor guinea pigs are able to synthesize vitamin C, this animal model creates an new view in understanding of pathogenesis of neuronal migration disorder in humans.

PS-17-032
Solitary fibrous tumour of the central nervous system: Two uncommon sites
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Objective: Solitary fibrous tumour (SFT) of the central nervous system (CNS) is a mesenchymal neoplasm composed of fibroblasts, collagen, and hemagiopericytoma (HPC)-like vessels. It is now considered a spectrum of lesions of increasing cellularity ending in tumours previously considered HPC. It is a rare tumour with only 213 cases reported in the literature. Prognosis of SFT is now determined by the Marseille System grading.
Method: We report a first case of a 27-year-old woman with SFT of the lumbar spine. We present a second case of a 72-year-old man with intracranial cellular SFT.
Results: The first patient presented with a six-month history of a cauda equina syndrome. Neuroimaging revealed an extradural mass of the lumbar spine. The second patient presented with a 3-month history of seizures. Neuroimaging revealed a frontal lesion with extension to the frontal sinus and ethmoid bone. Both patients underwent surgical resection. The first histopathological examination showed SFT grade I. The second examination showed cellular SFT grade Iia. Follow-up of patients showed no recurrence.
Conclusion: SFT of the CNS is now considered a wide spectrum. Increasing cellularity, mitotic activity or necrosis are associated with a worse prognosis. This is now established by the Marseille System grading.

PS-17-033

CD34 and MAP2 expression of focal cortical dysplasia associated tumours/ Experience of Cerrahpasa medical faculty

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Objective: Focal cortical dysplasia (FCD) with associated tumours at epileptic surgery, had been offered a new classification by Blumcke et al. with CD34 and MAP2 staining patterns. In our study we aimed to evaluate the morphological findings and immunoexpression pattern for MAP-2 and CD34 of these tumours and to discover the contribution of these findings to classification.
Method: We reviewed tumours associated with FCD recorded between the years 2005–2015. Cases were reexamined histopathologically and immunohistochemical MAP-2 and CD34 stains were performed for each case.
Results: We detected 237 FCD cases, 37 of them associated with tumours. According to ILAE classification was FCD type I (9/37) and type II (29/37). Associated tumours were: Ganglioglioma (19/37), DNT (10/37), gangliocytoma (1/37), isomorphic astrocytoma (2/37), SEGA (1/37), angiocentric glioma (1/37), glioneuronal tumour-low grade (2/37) and oligodendroglioma (1/37). In ganglioglioma cases CD34 immunopositivity was 53 %. For MAP2 we detected increased staining in neuronal component and glial components stained variable.
Conclusion: Ganglioglioma cases displaying CD34 positivity can be considered as a different group of tumours. CD34(-) gangliomas can be appreciated as a group of tumours related with DNT. All neuronal component were positive with MAP2, but glial component was variably stained in.

PS-17-035

Two cases of medulloblastoma. Infrequent onset in local recurrence. Case report and literature review

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Objective: Medulloblastomas are tumours with an increased risk of recurrence and metastasis. In most cases, tumour cell dissemination is located in leptomeningeal space, within the physiologic flow of CSF. We present two cases with supratentorial, respective in choroid plexus recurrence, most probable favorited by the intracranial hypertension.
Method: The clinocopathological data of two patients with posterior fosa tumours were collected from Pathology department database of Bagdasar Arseni Emergency Hospital during 2010–2015. The histopathological exam revealed medulloblastoma. Case 1: Despite surgery, tumour cells disseminated into the choroid plexus, causing severe symptomatology of intracranial hypertension that imposed immediate decompressing surgery. Case 2: The patient presented recurrence of disease after surgery and chemotherapy manifested with generalized seizures. An MRI exam revealed tumoural spread in the Frontal, Temporal and Occipital hemispheres
Results: Tumoural fragments were histopathological examined. The result was that the tumour recurrences were disseminated into the choroid plexus in the first case, respective in the cerebral hemispheres in the second.
Conclusion: Despite the propensity of medulloblastomas to disseminate via leptomeningeal space, few are cases that are spreading ascending, into the hemispheres, respectively into the choroid plexus.

PS-17-036

Intracranial primary squamous cell carcinoma: A diagnostic pitfall

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Objective: Metastasis is the most common type of brain tumour while primary squamous cell carcinoma is exceedingly rare. We present a case of primary squamous cell carcinoma arising from pre-existing dermoid cyst in a 48-year-old lady who has a cystic lesion with "atypical features" in posterior fossa in pre-operative imaging studies.
Method: We examine small biopsy tissue at frozen section and subsequent resection specimen.
Results: Islands of atypical squamous cells with focal "less atypical" squamous epithelium and inconspicuous mitotic activity are seen at frozen section. Over 90 % of the tissue by area shows islands of atypical squamous cells in focal desmoplastic or fibrotic stroma. Rare small foci of benign-looking epidermal lining with associated sebaceous glands and hair in transition to squamous dysplasia and invasive carcinoma are identified after histologic examination of the whole specimen.
Conclusion: Extensive sampling, preoperative imaging and intraoperative findings remain key for the accurate diagnosis and subsequent management.

PS-17-037

Primary central nervous system lymphoma: Pathological and evolutive study of 13 cases

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Objective: We analyzed patients' histological and immunophenotypical characteristics and survival of primary central nervous system lymphoma (PCNSL).
Method: Retrospective review of 13 patients diagnosed with primary brain lymphoma, between 1993 and 2014.
Results: All the patients were immunocompetent. The mean age at diagnosis was 54.1 years. The sex-ratio was 2.5. Ten patients presented with a single lesion and 3 with 2 to 3 lesions. Six tumours (46.2 %) were located in the left hemisphere and 5 (38.5 %) in the right one. The remaining two cases were respectively bilateral and median involving the sella turcica. Diagnosis was performed following craniotomy in 9 cases (76.9 %) and after stereotactic biopsy in 3 cases (23.1 %). Pathological study found 11 diffuse large B-cell lymphoma (DLBCL) (84.6 %), 1 anaplastic large-cell lymphoma, and 1 Burkitt lymphoma. Immunophenotypic profiling revealed 77.8 % of non germinal center B-cell (GCB) subtype and 22.2 % of GCB subtype. All DLBCL were positive for CD20. All cases had high Ki67 and were negative for Epstein-Barr virus. Mean survival time was 2.3 months. Survival outcome was similar between GCB and non-GCB subgroups.
Conclusion: Most PCNSLs fell into the histological category of DLBCL which frequently have a non-GCB immunophenotype and were not associated with EBV.

PS-17-038

pic3ca mutation frequency in glioblastomas

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Objective: Glioblastomas (GBM) which are the most common and highly agressive malignancy amoung in adult primary central nervous tumours. The surgical resection, radiation therapy, and chemotherapy with temozolomide are standart therautic modalities for GBM. Despite the development in the treatment of GBM, the prognosis still remains poor and the majority of the patients relapse soon after the treatment. The phosphoinositide 3-kinase (PI3K) signaling pathway plays an important role in cancer progression. Dysregulation of the PI3K/mammalian target of rapamycin (mTOR) pathway occurs frequently in some cancers, including GBM. In this study, we have aimed to determine the frequency of PIK3CA (codon 540–546 in exon 9 and codon 1042–1049 in exon 20) gene mutations in 25 GBM patients.
Method: In this study 25 GBM patients which were diagnosed histopathologically were studied geneticaly by using pyrosequence method.

Results: Amoung the patients in this study one patient found to have E545K mutation in exon 9 were detected.
Conclusion: Though further investigation is required, therapeutics targeting the PI3K/mTOR pathway may be beneficial for GBMs.

Wednesday, 28 September 2016, 09.30–10.30, Hall 11.3
PS-18 Other Topics 2

PS-18-002
Myocardial ischemia as presenting manifestation of IgG4-related disease: A case-based review
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Objective: Coronary involvement in IgG4-related disease (IgG4-RD) has been scarcely reported, and myocardial ischemia as its presenting feature is even rarer. Here, we describe an additional case with novel and relevant observations.
Method: Patient's clinical, radiological and pathological data were retrievew and gather to present this rara case.
Results: The patient was a previously healthy, middle-aged woman who presented to the clinic with new-onset typical angina. One tumefactive lesion encasing the left anterior descending artery was found during her work-up. The most common underlying malignancies with secondary cardiac involvement were rationally ruled out. Symptoms persisted despite medical treatment and she was therefore referred to surgery. Tumour excision was successfully performed and she received coronary bypass grafting. IgG4-related coronary arteritis with pseudotumour formation was subsequently diagnosed following the comprehensive diagnostic criteria. This condition was clinically classified as active and circulating plasmablasts were found to be increased (5480/mL), even when these were determined 38 days after surgery. A PET/CT revealed an additional hypermetabolic lymph node. She was therefore treated with rituximab as induction therapy (two 1000 mg doses, administered 15 days apart). Three months later, her disease remained clinically inactive. Circulating plasmablasts were repeated and these had dropped to 0/mL.
Conclusion: We lastly suggest that IgG4-RD should be part of the differential diagnosis of any patient with tumefactive lesions surrounding the coronary arteries, since it can initially presented as sudden cardiac death.

PS-18-003
Introducing a 3D software in the educational process at the Department of Pathology
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Objective: Pathology represents a serious challenge for undergraduate students who start learning this subject during the second year of their education. To understand a level of comprehension of the subject we introduced a 3D interactive application that allowed students to 'play' with a pathological process in question.
Method: We introduced a program during a practical session on heart and blood vessel disorders at the AMU. The participants were asked to model transmural myocardial infarction and then to select histological slides that corresponded to the pathology. During the 'modeling' stage, students received an opportunity to assess the surface of the organ, to investigate its cut surface, to look at the organ under different angles. At the end of the task the program evaluated the students. After this session, we asked 32 students and 8 instructors of the AMU to fill in a questionnaire to assess the software and their own interaction with it.
Results: Both instructors and students mentioned that the program could represent an alternative to the written or oral classroom test, as well as a tool that allows to prepare for the pathology seminar. Students found the first part of the test more challenging compared to the second part. According to the students, modeling of the pathological process allows to visualise it.
Conclusion: Diversity of pathological processes allows to individualise and to objectify the system of assessment. Moreover, from our point of view development of such tools allows to work with a new generation of students, who use new technologies in their everyday life.

PS-18-004
Diagnostic pathology service, research and publication through telepathology in an underserved country: The Dhaka basel experience
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Objective: To improve the diagnostic pathology service in a underserved country like Bangladesh and to use it in terms of research and publication.
Method: The 4660 cases (both histopathology and Cytopathology) were submitted to have a second opinion from the expert Pathologists. The opinions were compared with the final diagnosis where available. An analysis was done. A paper was published.
Results: The usefulness of the iPath to get second opinion we showed by the 87.7 and 82.0 % accuracy of the telemedical HCC diagnoses made on the histological and cytological images. The study showed, that most of the false diagnoses occurred in tumours with unusual cytological and histological patterns which need additional immunochemical tests to come to the correct diagnosis.
Conclusion: A welcome side-effect of the consulting via iPath was an improvement of preparation techniques. From this experience we think that in view of the uneven distribution of the medical, especially pathological services in Bangladesh a more general use of the iPath could help to improve the medical care. But that would only work with an increased circle of experts.

PS-18-005
The importance of the autopsy in ascertaining the cause of death as an audit tool in a resource poor setting
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Objective: To determine concordance between ante-mortem Clinical Diagnosis and Post-Mortem causes of death.
Method: All records of autopsies performed between Jan 2009 - Dec 2015 from the files of the Department of Pathology, University College Hospital, Ibadan were retrieved and reviewed. The age, gender, referral pattern to our hospital and time spent in hospital prior to demise, clinical diagnosis, post-mortem causes of death and organ system involved were collated. All the causes of death were classified using the International Classification of Diseases, Version 10 (ICD-10).
Results: 533 cases were identified with a male female ratio of 1.6. Age range was less than 24 h to 86 years. The peak age group was 50–59 years and accounted for 18.4 % of cases. The most common post mortem causes of death were Injuries (20.6 %), Circulatory system (19.7 %), Infections (16.9 %) and Malignant Neoplasms (9.4 %). Only 297 (55.7 %) of the cases showed a concordance between the post-mortem causes of death and the clinical diagnosis.

Conclusion: Clinical diagnosis alone is insufficient in achieving sensitive and accurate diagnosis. The post-mortem autopsy is useful in the audit of contemporary medical practice in low resource settings.

PS-18-007

Immunohistochemical features of inflammatory mechanisms in core and peri-ischemic area after transient focal cerebral ischemia in rat brain

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Objective: The aim of this experimental study was to establish the immunophenotype of inflammatory cells involved in focal cerebral ischemia and reperfusion.
Method: Six adult Wistar male rats were included in our study, divided randomly in two groups, control (n = 3) and ischemic (n = 3). In the ischemic group transient focal cerebral ischemia was induced by intraluminal filament technique, obstruction of the left MCA for 90 min, followed by gently removing the filaments. Subjects were sacrificed after 24 h to assess morphological and molecular changes. The distribution of neuronal damage was evaluated with Nissl stain. Immunohistochemistry was performed using leukocytes markers (MPO, Neutrophil elastase, CD68, CD3,CD4, CD8), their released cytokines (MMP 9 and MMP 8) and FXIII (involved in macrophages activation). Positive cells were quantified using digital morphometry.
Results: Postischemic resident microglial cells are activated after ischemia along with a large number of leukocytes, neutrophils being the first blood-derived leukocytes. CD3 positive T-cells were present in low numbers in peri-ischemic area in association with MMP 9/MMP 8 macrophages, some of them with the expression of FXIII.
Conclusion: The inflammatory responses to ischemia are activation of microglial cells and accumulation of circulatory inflammatory cells.

PS-18-008

Tissue preparation: Does one method fit all?

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Objective: Molecular techniques for detection of genetic and chromosomal abnormalities have become important clinical tools. This study aim to establish a protocol for FFPE tissue that is applicable for molecular assays, FISH and immunohistochemistry (IHC).
Method: Thirteen fresh tissues were each split in sections, which underwent combinations of fixation and decalcification (agent and time) leading to 18 different pre-analytical procedures plus one fresh frozen sample. These 247 tissue samples were paraffin embedded, sectioned and split for IHC-(MLH1, MSH2 staining), FISH - (HER2/CEN17) and RQ-PCR analysis (Quantimize, Qiagen).
Results: Evaluating quality of analyses, fixation time per se does not significantly influence the results of IHC, FISH or RQ-PCR. The decalcification agent, on the other hand, had a significant impact on the analysis quality. In general, decalcifying tissue with microwaves impaired downstream applications. The effect of formic acid as decalcifying agent varied with fixation time. This agent mostly affected DNA quality and the damage increased with exposure time. Treatment with EDTA gave the overall best results.
Conclusion: We demonstrate that the best downstream analysis results are obtained when tissues fixate for 24 h in formalin followed by decalcification with EDTA for 24 h.

PS-18-009

Cerebral hemorrhage produced by ruptured tuberculous aneurysm of the posterior communicating artery: Necropsy feature and histological study

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Objective: Tuberculous aneurysm of the cerebral artery is exceptional and exposes patients to a very high risk of unpredictable rupture.
Method: We report an autopsy case of 33-year-old male who was hospitalized for a therapy of endocarditis associated to pulmonary tuberculosis who dead suddenly.
Results: An autopsy was performed showed endocardiac vegetation, pulmonary abscess, and an edematous brain with fresh massive hemorrhage in the basal ganglia. The dissection of the Willis circle showed a ruptured aneurysm of the posterior communicating artery. A microscopic examination was performed showed tuberculosis lesion of the heart, the lung and the spleen with granulomatous lesion associated to caseation necrosis. The histological study of the brain confirms those found with the unaided eye and show several lacunars infracts in the cerebral parenchyma. The walls of the cerebral arteries are infiltrated by granulation tissue associated to a caseation necrosis and show a discontinuity of the arterial wall compatible with an aneurismal ruptured due to a tuberculosis infiltration.
Conclusion: By our case we illustrate a rare fatal manifestation of tuberculosis and we underline the role of autopsy in explaining such rare threatening mechanism of some well known disease.

PS-18-010

Immunohistochemistry causes colour chages in inked marked resection margins

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Objective: Pathological routine protocols provide resection margin ink marking for orientation during microscopy. Diverse resection margins of one tissue specimen require diverse ink colors. The distinct discrimination between the colours is crucial for subsequent therapeutically regimes. In some cases, for example assessment of tumour residuals close to the resection margin, adjacent immunohistochemistry analyses are necessary. Here we describe color changings in the resection margin ink markings after immunohistological stainings.
Method: Two resection specimen were color ink marked using red, blue, green, black and blue colour and TippEx. Tissue processing was performed using a classical processing system with ascending and descending Ethanol and Xylol sequences, one using a vacuum and one using a microwave based processing system. Next, all series were cut into 2 μm thick slices and routine immunohistochemistry was performed.
Results: Except for the blue color, all markings were equal for paint marking color and intensity, independent from the processing regime and used antibody.
Conclusion: Our results demonstrate an interesting and important pitfall in routine immunohistochemistry based diagnostics.

PS-18-013

Cutaneous-visceral loxoscelism. Presentation of an autopsy case in Bogotá, Colombia

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Objective: To describe the case of a patient who dies from toxic secondary clinical picture spider bite Loxoceles genre.

Method: The arachnid accident secondary to bite by spiders belonging to the Loxosceles genus (brown recluse spider) occurs in 0.2 % of the events related to poisoning by animals. This is characterized by the appearance of dermonecrotic lesions to systemic involvement that can result in death.
Results: an autopsy case of cutaneous and visceral Loxoscelism in a male patient of 16 years in Bogota, Colombia (2640 m.a.s.l.) is reported. It featured irregular necrohemorrhagic generalized skin lesions, disseminated intravascular coagulation, and acute renal failure. Despite the intensive care unit handling, the patient died at 96 h after the bite.
Conclusion: We must take into account the presence of these spiders in urban areas and its association with generalized clinical pictures that can lead to death. It is important to identify the type of spider to guide treatment properly, improving patient prognosis.

Wednesday, 28 September 2016, 09.30–10.30, Hall 11.3
PS-19 Paediatric and Placental Pathology

PS-19-002
Congenital infantile fibrosarcoma: Is there a perycitic origin?
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Objective: In the 2013 WHO classification infantile fibrosarcoma (IF), a rare lesion of infancy with intermediate prognosis and ETV6-NTRK3 gene-fusion, is listed among the fibroblastic/myofibroblastic tumours. However, vascular-pattern and resemblance with cellular myofibroma suggest a relationship with perivascular/pericytic tumours. We analysed the immunohistochemical expression of pericyte-markers (αSMA, PDGFRβ, CD146) in IF in order to investigate its possible pericytic nature.
Method: H&E slides from 24 IF were reviewed for kaposiform hemangioendothelioma-like (KHE-L) or hemangiopericytoma-like (HP-L) vascular-pattern and myofibroma(MI)-like features. Immunostains for αSMA, PDGFRβ and CD146 in 15 cases were compared to 5 infantile IM.
Results: 13/24 IF showed IM-like features, 19 HP-L and 11 KHE-L vascular-pattern (Table 1 summarizes immunohistochemistry/histology in IF/IM).
Conclusion: IF, especially those with myofibroma-like features, display a pericytic immunophenotype similar to classic myofibromas; together with the peculiar vascular-pattern and morphological resemblance to myofibroma the results demand further investigations into the hypothesis of pericytic differentiation/possibile perivascular origin of IF.

PS-19-003
Testicular regression syndrome: A clinicopathological spectrum in 21 cases
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Objective: To study the clinicopathological spectrum of testicular regression syndrome (TRS) and review the literature.
Method: Clinical features and pathologic specimens of patients undergoing surgery for undescended testis (UDT) were analyzed in 5 years (2010–2014). Original diagnosis was studied in context of pathological recognition of TRS. The inclusion criterion was defined as the presence of fibrovascular nodule (FVN) with calcification or hemosiderin; or cord elements (vas deferens and/or epididymis) with residual tubules.
Results: On secondary review, 21 cases of UDT showed features consistent with the diagnosis of TRS. Among these, FVN was observed in 16 (76.2 %), calcification in 3 (14.3 %), hemosiderin in 15 (71.4 %), vas deferens in 13 (61.9 %), epididymis in 11 (52.4 %), prominent vessels in 20 (95.2 %) and seminiferous tubules in 5 (23.8 %) cases. Three of these cases showed sertoli cells while germ cells were demonstrated in two cases.
Conclusion: TRS is a common pediatric surgical problem, which is unrecognized by many pathologists. There is a theoretical risk of malignant transformation in the long term. When blind-ending spermatic cord without viable testis is submitted for tissue analysis, it is imperative to characterize such cases as consistent with regressed testis which obviates further surgical intervention.

PS-19-004
Morphometric analysis of duodenum in human fetus
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Objective: The mucosa of duodenum is lined by finger-like villi. In adults, the villus-to-crypt height ratio is about 4 to 5:1. The aim of this study is to evaluate the villus-to-crypt ratio in human fetus.
Method: This study was carried out 81 human fetuses. Three random villi were measured with the X and Y axis. The statistical analysis was performed by T-Test and One-way Anova test in SPSS 13.0.
Results: There were 29 female and 52 male fetuses and the age range between 12 and 40 weeks of gestation. The mean villus to crypt ratio was 2,75; 3,21; 3,76 in the first, second and third trimesters, respectively. Although the villus to crypt ratio increases with trimesters correspondingly, the correlation of this ratio for trimesters were not statistically significant (p = 0,376).
Conclusion: In our study, we found that villi are blunter and shorter than in adults but not in children regardless of gestational weeks. The villi are elongated gradually after birth. It is concluded that enviromental factors may be affect elongation of villi after birth.

PS-19-006
The possibility of postmortem MRI in the diagnosis of congenital pneumonia
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Objective: To explore the possibilities for postmortem MRI for the detection of congenital pneumonia at died newborns.
Method: Investigated the bodies of 13 dead newborns at the age from 2 h to 28 days. Before the autopsy was carried out postmortem 3T MRI in T2 mode at sagittal projection. We determined the optical density of the right and left lung (DL), pleural fluid (DF) and calculated the airiness indicator of the lung tissue in both lungs (DF/DL). During the autopsy performed macroscopic, microscopic and microbiological examinations of the lungs.
Results: Based on the results of morphological studies in 9 deaths of newborns was diagnosed bilateral focal-drain pneumonia. In 4 cases the causes of death were congenital malformations. At postmortem MRI the development of neonatal pneumonia accompanied by a decrease in the airiness indicator (DF/DL) less than 2.5 in both lungs. Indicators of the diagnostic value of postmortem MRI were as follows: sensitivity—88.9 %, specificity—100 %, overall accuracy—92.3 %.
Conclusion: The development of congenital pneumonia is characterized by signal changes on T2-weighted images at postmortem MRI. The definition of MRI airiness indicator of the lung tissue with high diagnostic efficiency reveals the presence of neonatal pneumonia.

PS-19-007
Inhomogeneity of the placental structural adaptations in cases of circulatory hypoxia
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Objective: It is known that inhomogeneity of the villous tree may cause diagnostic problems for pathologist in cases of complicated pregnancy.

Method: Placentas from pregnancies complicated with circulatory hypoxia due to maternal congenital heart disease (CHD) were studied by naked eye and tissue samples were taken from various regions. Then histological slides, stained with hematoxylin and eosin, were studied microscopically and with computer morphometry. All material was divided into three groups: I–20 cases of CHD without surgical correction; II- 19 placentas with surgical correction of CHD and 15 cases of uncomplicated pregnancy (control group- CG). I. Data were analyzed using statistical methods. Differences between groups were evaluated with the help of non-parametric test of Wald-Wolfowitz. The following format of the description of data was used Me (QR), where Me—median; QR—the interquartile range. Reliability established at $p < 0.05$.
Results: Results have shown that severe hypoxia in group I resulted in increased volume fraction of infarcts, fibrinoid accumulations and calcification predominately in the margin zone of placenta. In the group II the volume fractions of dystrophic alterations and compensatory terminal villi proliferation were closer to the CG parameters. Surgical correction of the CHD resulted in enhanced adaptive morphological remodeling of placental structures with lower level of degenerate changes in the marginal, paracentral and central zones of placentas.
Conclusion: Conclusion Histopathological data in cases of fetomaternal hypoxia should be analyzed on the basis of entire placenta investigation. Meaningful results must represent compensatory and pathological processes in central, paracentral and marginal placental zones.

PS-19-008
Unusual presentation of a peripheral T cell lymphoma: The importance of a liver biopsy
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Objective: Peripheral T cell lymphoma, NOS, is a wide and heterogeneous category of mature T cell lymphomas that is a diagnosis of exclusion. It represents 30 % of peripheral T cell tumours, affecting mostly adults and rare in children.
Method: Five years-old male child, febrile with 2 weeks evolution under antibiotic, presented with pain, abdominal distension, liver cytolysis and failure, without encephalopathy and with hepatomegaly and ascites—clinically a Budd-Chiary syndrome.
Results: Liver biopsy showed massive sinusoidal infiltration with obliteration, and lesser portal involvement, by a lymphoma composed of small and round cells diffusely positive for CD3, CD5, CD2, CD7, CD8, CD56, and CD99; EBER in situ hybridization was negative. The tumour morphologic and immunohistochemical profile does not fit into any of the WHO specific lymphoma categories, allowing the diagnosis of peripheral T-cell lymphoma, NOS (confirmed by two international experts). There was general condition deterioration with evolution for multiple organ failure and death. Autopsy study showed massive organic infiltration by T-cell lymphoma.
Conclusion: The diagnosis of non-Hodgkin lymphoma should be considered in the differential diagnosis of a patient with large hepatomegaly presenting clinically as Budd-Chiary syndrome. Liver biopsy, promptly performed, is a safe and accurate tool to achieve the correct diagnosis and guide patient management.

PS-19-009
Salivary gland anlage tumour: Report of a rare congenital tumour
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Objective: Salivary gland anlage tumour (SGAT) is a rare benign tumour, with only a few cases being reported in literature. This tumour is composed of mixed epithelial and mesenchymal elements and it recapitulates the early stages in the embryology of the salivary gland between the 4th and 8th weeks of development. To report a rare case of salivary gland anlage tumour (SGAT), review the histological features, immunohistochemical studies and review the literature.
Method: Medical records, radiologic studies, and pathologic report were reviewed.
Results: The patient is a 15 day old neonate who presented with nasopharyngeal mass and respiratory distress at birth. CT scan of head was performed which suggested a vascular tumour. MRI revealed a non vascular mass in the nasopharynx. Operative findings showed a huge mass attached to the posterior part of the septum and obstructing both choanae and extending into the right nasal cavity. The mass was removed and histopathology with immunohistochemical studies confirmed a diagnosis of salivary gland anlage tumour.
Conclusion: Salivary gland anlage tumour of the nasopharynx is a rare cause of neonatal airway obstruction. Recognition of SGAT is important because simple excision of the lesion achieves cure.

PS-19-010
Vascularisation of the placental villi at early- and late-onset preeclampsia
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Objective: Comparative morphometric study of terminal villi of the placenta at early- (ePE) and late-onset preeclampsia (lPE).
Method: Complex morphological study of 18 placentas from ePE, 22 placentas from lPE and 10 term placentas from uncomplicated pregnancies (control group) was performed. Morphometric indices of terminal villi vascularization was determined on immunohistochemical preparations with the use of CD31.
Results: Average values of cross-sectional area of the villi less benchmarks by 16,4 and 17,8 % at ePE and lPE respectively. Established a smaller number of blood capillaries by 17,7 % at ePE and by 11,3 % at lPE compared to a control group. The average values of perimeter and area of the capillaries in ePE smaller than the corresponding normal values by 18,6 and 25,7 % respectively, and in lPE is less than 12,9 and 17,5 % respectively. The total cross-sectional area of capillaries at one villus less than the values of the control group by 36,6 % in ePE group and by 28,0 % at lPE, and summary measure of the capillaries perimeters less by 30,3 and 23,2 %.
Conclusion: Development hypoxia of the placenta and fetal in preeclampsia is caused not only by pathology of the spiral arteries, but revealed by us violations of the terminal villi vascularization of the placenta.

PS-19-011
Ultrastructure features of placenta villi in cases of preeclampsia
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Objective: The aim of study is analysis of ultrastructure features of placenta villi in cases of preeclampsia.
Method: Group with PE included 9 women with PE and 8 women with physiological pregnancy (PP) of reproductive age, 26–39 gestation weeks after cesarean section. We performed histological and electron microscopy studies.
Results: By electron microscopy in PP were revealed fusiform cells in intermediate placenta villi with long, thin processes by which were in contact with each other forming network. The latest were characteristic features of telocytes (Tc). In PE stroma cells of intermediate villi were also present signs of fibroblastic differentiation: a greater volume of the

cytoplasm, increased number of granular endoplasmic reticulum cisternae in the cytoplasm, thickness of processes, being collagen deposits in stroma. Moreover, in PE intermediate villi capillaries were smaller, frequently without endothelium, with sludge, stasis, microthrombi formation. All of that leading to disturbance hemato-placental barrier, which increased hypoxia. Syncytiotrophoblast of normal placenta villi had microvilli. Preeclampsia was characterized by damaged apical part, the presence of multiple vacuoles in cytoplasm of syncytiotrophoblast.
Conclusion: Forming debris of syncytiotrophoblast may be trigger of a systemic inflammatory response. Lesions of stroma cells of intermediate placenta villi in PE played a significant role in angiogenesis.

PS-19-012
Histology in paediatric Wilson's disease — a challenge!
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Objective: Wilson's disease (WD) is an autosomal recessive disease with an incidence of 1/30.000, rarely symptomatic in children, that should be excluded in acute or chronic liver disease, of unknown etiology. Histopathology of WD is not specific, especially in early stages, making the differential diagnosis a challenge.
Method: Histopathology review of liver biopsies of paediatric patients diagnosed with WD within 2000–2014—12 biopsies.
Results: 9 cases (7F:2M), with median of age 10 (4–15), median biopsy size 12 mm (10–17 mm) and median number of portal tracts 7 (3–17). Clinically, 5 presented with aminotransferase elevation, 2 as acute liver failure, 1 with portal hypertension and 1 with cholestatic hepatitis. Morphologically the more frequent findings were fibrosis, hepatocellular ballooning and portal tract inflammation (75 %), glicogenated nuclei (58,3 %), interface hepatitis and macrovacuolar steatosis (50 %), billirubinostasis (33 %), mild necrosis and ductular reaction (25 %) and Mallory-Denk bodies (17 %). 5 cases (42 %) were positive for rhodanine/Shikata techniques.
Conclusion: The morphologic spectrum is wide and non-specific in WD and the absence of histochemical staining in more than half of the cases should not invalidate WD diagnosis. A high suspicion is necessary, especially since it is a treatable disease, where delay in the diagnosis may lead to a bad prognosis.

PS-19-013
Extracellular matrix in human placenta
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Objective: The maintenance of uterine placental attachment during pregnancy depends on the adhesive interactions between cytotrophoblasts and the extracellular matrix (ECM). The aim of the study is to localise the ECM components,CollagenIV and Fibronectin(FN) in the placenta of normal and abnormal deliveries.
Method: Formalin fixed and paraffin embedded material from placenta were studied:mothers with intra uterine growth retardation(IUGR baby)20,neonates with congenital anomalies(8)and normal deliveries(14). Haematoxylin and Eosin staining was done. LSABtechnique with two primary antibodies:mouse monoclonal antihuman collagenIV(DAKO) and rabbit antihuman Fibronectin(dako) in dilutions of1:30 and 1:20 were used. Pressure cooking was done to unmask the antigen. AEC was used as chromogen and Gill's hematoxylin was used as nuclear counterstain.
Results: Thickening of BM was seen in placentas of IUGR neonates whose mothers had pregnancy induced hypertension. Fibronectin positivity was observed in the trophoblastic BM, villous stroma,vessels,fibrinoid(intravillous,intervillous and matrix type) and subchorionic fibrin deposits.
Conclusion: Thickening of BM observed points to an altered trophoblastic activity. FN was less in IUGR infants and increased in those with congenital anomalies. . Collagen IV and Fibronectin are a good indicator of disturbances in blood circulation resulting in IUGR and other abnormalities.

PS-19-014
Congenital and childhood nephrotic syndrome diagnosis in renal biopsies from Minas Gerais state: Six cases report
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Objective: To investigate pediatric patients undergoing renal biopsy with clinical and morphological aspects compatible with Congenital and Childhood nephrotic syndromes.
Method: Analysis of renal biopsies of pediatric patients from Nephropathology service of UFTM from 1996 to 2014. We selected those with proteinuria, diffuse mesangial sclerosis morphology, foot process effacement, absence of the slit diaphragm, cyst formation in dilated tubules and mild mesangial hypercellularity.
Results: Six cases with morphologic diagnosis of Congenital/Childhood Nephrotic Syndrome aged from 3 months to 13 years were detected. From these cases, four had diffuse mesangial sclerosis, and two of those had genitourinary abnormalities suggestive of Denys-Drash syndrome. In the other two cases, the findings were consistent with Congenital Nephrotic Syndrome of the Finish type (CNF), since they had foot process effacement, absence of the slit diaphragm, cyst formation and mesangial hypercellularity.
Conclusion: Congenital and Childhood Nephrotic Syndrome are rare diseases with glomerular dysfunction and prominent proteinuria. The main diseases that make up the syndrome are Congenital Nephrotic Syndrome of the Finish type, cortico-resistant NS, Pierson syndrome, Nail-Patella syndrome, Denys-Drash syndrome, Frasier syndrome and autosomal dominant FSGS. This study provides findings that are uncommon in pediatric biopsies and suggests more studies are needed, including genetic ones, to clarify a better diagnosis.

PS-19-015
Fas and FasL expression in placentas complicated with intrauterine growth retardation with and without preeclampsia
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Objective: To compare the level of Fas and FasL immunohistochemical expression in villous trophoblast (VT), extravillous trophoblast (EVT) cells, decidual cells (DC), endothelial cells (EC) of villous blood vessels and spiral arteries between study groups of intrauterine growth retardation (IUGR) placentas with and without preeclampsia (PE).
Method: The study included 17 placentas from pregnancies complicated by IUGR+PE and 17 placentas from pregnancies complicated by idiopathic IUGR (I-IUGR). Seventeen placentas from normal pregnancies served as a control group. CD31 was used to detect endothelial cells (EC). Immunohistochemical expression of Fas and FasL was assessed in all examined parts of placenta using the semi-quantitative HSCORE method.
Results: FasL expression was significantly higher in all examined parts of placenta in I-IUGR as compared to IUGR+PE and control group. Placentas with IUGR+PE had the significantly lowest expression of FasL in VT and EC of villi vessels. Expression of Fas did not differ significantly between study groups.
Conclusion: Different expression of FasL in placentas from I-IUGR and IUGR+PE suggests that FasL probably has a different role in the etiology of these two syndromes.

PS-19-016

Estrogen and androgen receptor expression in Morgagni hydatids in cryptorchidism

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Objective: The expression of androgen receptors (AR) in the Morgagni hydatid has been suggested to play a role in the process of testicular descent. There are controversial reports though, concerning their presence in cryptorchidism, which may also be age- and puberty- related.
Method: Fifty-seven testicular Morgagni hydatids were collected prospectively, 36 from cryptorchid testes (CrT) and 21 from control group/hydrocele cases (CG). All the children were pre-pubertal ranging from 3 months to 9 years of age. The expression of AR and ER was examined by immunohistochemistry and assessed by the Allred score. Statistical analysis was performed using Mann–Whitney test and Spearman's rho.
Results: In CrT, ER expression was lower than in CG ($p = 0.028$), and correlated with AR expression ($p < 0.001$); AR expression, although lower in CrT, did not significantly differ; expression of ER correlates with AR ($p < 0.001$). In CG, but not in CrT, size correlates with AR expression ($p < 0.001$) and marginally with ER expression ($p = 0.054$).
Conclusion: Interestingly in our study, Morgagni hydatid AR expression was not significantly different between CrT and CG but ER expression in the CrT children was significantly lower. This possibly suggests that Morgagni hydatid ER expression, and not only AR expression, may play a role in testicular descent.

PS-19-018

Ciliopathies: Report of six cases of Meckel-Gruber Syndrome and two cases of Bardet-Biedl Syndrome with review of literature

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Objective: The dysfunction of cilia results in a group of severe clinical manifestations, that can be classified based on their phenotypic similarities. In this work we intended to identify the various clinical features characteristic of Meckel-Gruber Syndrome (MKS) and Bardet-Biedl Syndrome (BBS) in our cases.
Method: We analysed fetal autopsies reports, ultrasonographic findings, clinical and genetic data from 2006 to 2015.
Results: We collected 8 cases of termination of pregnancy with gestational age between 13 and 27 weeks, 6M/2F. In the autopsy 8/8 had polycystic kidneys, 6/8 with polydactyly, 4/8 with occipital encephalocele, 4/8 with ductal liver proliferation, and 4/8 with other major and minor anomalies. Ultrasonography has identified 6 of 8 polycystic kidneys present in the autopsy (6/8), 2/6 of polydactyly, 4/4 of occipital encephalocele and 4/7 of other anomalies. Genetics confirmed 2 of 2 presumable cases of BBS and 1 of 6 presumable MKS.
Conclusion: MKS and BBS are congenital conditions, typically inherited in an autossomal recessive manner, with considerable risk of recurrence in affected families. Diagnosis of these conditions is important for early detection in future pregnancies and accurate genetic counseling.

PS-19-019

Diversity of KI67 and P53 expression of different subtypes of medulloblastoma in Latvia

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Objective: The aim of this study was to determine the immunohistochemical expression of Ki67 and p53 and their correlation with histological subtypes of medulloblastoma.
Method: 20 pediatric medulloblastoma cases diagnosed in Latvia from 2000 till 2015 were analyzed immunohistochemically by counting Ki67 and p53 positive tumour cells in the highest staining region (magnification 400). Comparison between the histological subtypes was calculated by the independent sample t-test ($p \leq 0, 05$).
Results: The average Ki67 proliferation index in whole medulloblastoma group was 36,81 %, in classic medulloblastoma group ($n = 15$) 37,43 % in nodular/desmoplastic tumour group-($n = 3$) 23,98 %; SD, in anaplastic tumours- ($n = 2$) 51,4 %. The average of p53 positive cells in whole medulloblastoma group was 11,74 %, in classic medulloblastoma group 12,34 %, in nodular/desmoplastic tumour group 11,80 %; in anaplastic tumours 7,10 %. The diferences of both Ki67 and p53expression between classic and nodular/desmoplastic tumour groups were not statistically significant ($p = 23$; $p = 0,94$). The differences between both markers expression in anaplastic and nodular/desmoplastic tumour and anaplastic and classical tumours were not statistically significant, respectively $p = 0,12$; $p = 0,32$; $p = 0,60$; $p = 0,61$.
Conclusion: As the differences of Ki67 and p53 protein expression of different subtypes of medulloblastoma was not statistically significant, it should not be taken in consideration during the assessment of histological subtypes.

PS-19-020

Diagnostic approach of congenital urinary malformations: Multicentric autopsy cases performed between 2000–2015 in Antalya

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Objective: Renal malformations are traditionally classified as abnormalities of mass, position, paranchymal differentiation. Congenital malformations of urinary system is aproximately %10 of all births.
Method: Between 2000 and 2015 1004 perinatal autopsies was evaluated in two medical centers' of Antalya and urinary malformation cases were selected fort his study.
Results: Among 1004 perinatal autopsy cases 90 (9 %) cases had congenital urinary system malformations. In this group 35 cases (38.9 %) were female and 55 cases (61.1 %) were male. Among these cases with congenital urinary sytem malformation 60 cases (65.9 %) had at least one associated anomaly. Most common associated anomaly was dismorphic findings (47.8 %). And it is followed by skeletal dysplasias and lung malformations with a percentage of 27.8 %. And neural tube defects are also common associated anomaly (10 %).
Conclusion: Congenital urinary malformations are classified as renal abnormalities of renal mass, abnormalities of renal position-form, congenital anomalies of upper urinary tract, abnormal renal differentiation. Renal cystic disease is an important group of congenital urinary system malformations which is included in abnormal renal differentiation. Diagnosis of renal pathology should be given clearly because some may be hereditary or associated with other anomalies and be a component of a syndrome. For genetic counseling and clinical follow-up perinatal autopsy keeps its importance.

PS-19-021

MMPs-2/9 and TIMP-2 expression in infantile hemangiomas on propranolol therapy

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Objective: Propranolol is widely known beta-blocker approved for treating infantile hemangiomas (IHs). The mechanisms of spectacular results of performed propranolol treatment remain unclear. There is suspected that propranolol may influence metalloproteinases (MMPs) expression. The aim of the study was to perform an evaluation of

MMPs-2/9 and TIMP-2 in IHs to find their relation to unusual tumour biology and systemic propranolol treatment.
Method: MMPs-2/9 and TIMP-2 were analyzed in 71 IHs tissues with the use of immunohistochemistry and RT-PCR and in 50 serum samples of IHs' patients by an ELISA assay.
Results: There were significantly lower MMPs-2/9 and higher TIMP-2 levels in IHs' tissues on mRNA level as well as lower serum MMP-2 concentration among the treated individuals.
Conclusion: Obtained results pointed that MMPs-2/9 and TIMP-2 both are involved in natural IHs' biology and propranolol pathways covering its antiangiogenic properties. The most reliable method of IHs examination appears to be direct tissue assessment on molecular level, however MMP-2 evaluation in patients' serum may also benefits in clinical practice in doubtful cases.

PS-19-022
Expressions of neutrophil gelatinase-associated lipocalin and kidney injury molecule-1 in Wilms tumour
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Objective: Neutrophil gelatinase- associated lipocalin (NGAL) and Kidney injury molecule1 (KIM1) play important roles in both immunity and cell proliferation. It was reported previously that they are overexpressed in various human cancers. The present study was undertaken to examine the expressions of NGAL and KIM1 in Wilms Tumours. We also investigated their relevances in clinical and pathological features of Wilms tumours.
Method: Tissue samples of 50 Wilms Tumours were evaluated and underwent immunhistochemical staining for NGAL and KIM1 protein expressions.
Results: Results: NGAL expression was negative in all tumours except the neutrophils within the tumours. KIM1 expression was positive in 37 tumours (74 %), while was absent in 13 tumours (26 %). Using Mann Whitney U Analysis, KIM1 expression was found to be correlated with the stage of the tumour ($p = 0.027$).
Conclusion: The preliminary data indicates that KIM1 expression may be associated with stage in Wilms Tumour. However further studies are needed to validate these pilot observation and to clarify the functional and mechanistic significance of this relevance.

PS-19-023
Tissue expression of AT-rich interacting domain 1 alpha in Wilms tumour
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Objective: AT-rich interacting domain 1 Alpha (ARID-1A) is a subunit of chromatin remodeler Switch/ Sucrose Non-Fermentable (SWI/SNF) complex. It is involved in several important cellular processes such as differentiation, regulation of cell cycle and restoration of DNA damage. Although higher mutation rate of ARID-1A is strongly determined in several human cancers, its significance has not been fully established in Wilms tumour (WT). The aim of this study was to determine the prognostic value of ARID-1A expression in WT.
Method: The nuclear ARID-1A expression in tissue samples of 50 Wilms Tumours and its relationship with prognostic parameters were evaluated.
Results: Twenty-three (46 %) of the cases were male while 27 (54 %) were female. The mean age was found to be 3.26 ± 2 years. The average tumour size was 9.16 ± 2.9 cm in diameter and the average weight of kidney was 478 ± 312 g. Thirteen (26 %) cases were stage I, 18 (36 %) cases were stage II, 7 (14 %) cases were stage III, 6 (12 %) cases were stage IV. Thirty-nine cases were alive (78 %), while 11 cases (22 %) were deceased. Mean overall survival time was 68.2 ± 39.5 (2–148) months. ARID-1A expression was normal in most tumours, while was decreased or negative in 14 tumours (28 %). Statistically, ARID-1A expression was found to be correlated with the weight of the tumour ($p = 0.002$) and survival ($p = 0.021$).
Conclusion: This study indicates that ARID-1A expression may be associated with development of Wilms Tumour. However further studies are needed to clarify the importance of this relevance.

PS-19-024
Sacrococcygeal germ cell tumour—the 38-year experience
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Objective: An analysis of the occurrence of sacrococcygeal germ cell tumours (SC-GCTs) in a large national paediatric institution in a very long period and comparison with the related world studies.
Method: The distribution of SC-GCTs in relation to histological category (mature, immature, malignant), age and sex was analyzed in children aged 0–18 years diagnosed and treated in Mother and Child Health Care Institute of Serbia during 38-year period (1977–2014).
Results: There were 71 SC-GCTs out of 259 GCTs in our series (27.4 %). It was by far the most frequent GCT in extragonadal localizations (71/110; 64.5 %). Fifty percent of SC-GCTs were diagnosed in the first month of life. Only 14 % of SC-GCTs were malignant in the first year of life and the youngest patient with the malignant form being 11-month-old baby. By contrast, 57 % of these tumours were malignant in children older than 1 year. Male to female ratio was 1 : 2.55.
Conclusion: The relative frequency and distribution of SC-GCTs by histologic category, age and sex in our series was in accordance with the relevant summary data from the literature. Our results emphasize the importance of diagnozing and resection of SC-GCTs in the first months of life.

PS-19-025
Molecular characterisation of a disseminated congenital melanoma with unexpected long term survival
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Objective: Congenital malignant melanoma (CMM) is an exceedingly rare diagnosis. These cases arise either from transplacental metastatic melanomas or Giant Congenital Melanocytic Naevus or de novo.
Method: We received slides and blocks from a neonate who presented with a large periorbital ulcertated tumour. CCM was diagnosed on routine histology and confirmed by immunohistochemistry. Furthermore, we received a skin biopsy of a rash, a bone marrow biopsy and ocular contents all showing metastatic disease. We performed molecular testing on paraffin blocks of the primary lesion looking for Braf, cKit, Nras, Kras, Egfr and GNAQ and GNA11 mutations.
Results: Primary lesion revealed an undifferentiated tumour which was positive for the MelanA and HMB45 and S100. It was tested Braf (exons 11,15), cKit (exons 9,11,13,17), Nras (exons 1,2), Kras (codon 12,13), Egfr (exons 18,19,21) and GNAQ and GNA11. Only a mutation in codon 209 of the GNAQ gene was identified.
Conclusion: This boy is now 4 ½ years old and developing well with stable disease. He is treated with a weekly dose of 5 % Diphencyprone. Extensive molecular testing was undertaken. Only a partial deletion of chromosome 3p and a mutation in codon 209 of the GNAQ gene were identified which are typical in uveal melanomas.

PS-19-026

Primitive neuroectodermal tumour in pediatric kidney patient: Case report

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Objective: The primitive neuroectodermal tumours (PNET) are of embryonic origin and are characterized by the presence of poorly differentiated neuroepithelial cells (1). One percent of cases are renal neoplasms (3).
Method: Female patient, 12 years old with a month long history of abdominal pain and mass sensation. The contrasted abdominal CT showed sub-solid ground glass nodules in lung parenchyma. Increased right kidney size due to heterogeneous mass density which presents enhancement with contrast medium. Ganglion clusters are observed. The patient received nephrectomy. Microscopic examination showed renal parenchymal involvement due to tumour lesion consisting of small, atypical, round cells, with hyperchromatic nuclei and scant cytoplasm.
Results: Immunohistochemical studies showed strong and diffuse reactivity for CD99 and FLI1 in the tumour population, focal for synaptophysin and negative for CD45, EMA, WT1 and desmin. Additionally, translocation of the EWSR1 gene was detected, the FISH study is considered positive for rearrangement involving gene EWSR1 (22q12).
Conclusion: This is a primary primitive neuroectodermal tumour of the kidney with ganglionic EWSR1 metastastasis and gene translocation, due to the low incidence it is important to describe the proper handling and include it in the differential diagnosis when the mass of kidney is addressed.

Thursday, 29 September 2016, 09.30–10.30, Hall 11.3
PS-20 History of Pathology

PS-20-001

Illustrated heart & vessels: The collection of a world heritage museum

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Objective: Drawings and paintings of the human body and its anatomical components goes back to primitive civilizations. First as scenes of daily life, after as art and afterwards as science. Through the history of mankind, many are the worldwide renowned illustrations. The authors intend to explore the "Heart & Vessels Illustrations" in a World Heritage Museum.
Method: The XIIIth century Coimbra University was classified World Heritage by UNESCO in 2013 and within it, the Medical School Pathology Museum. FMUC's Pathology Museum dates from the XIXth century; occupies a 500 m2 area and gathers 3000 pieces (fixed and dehydrated pathological specimens, wax models, ancient books and pictures). The authors examined the gross macroscopy and the microscopic old atlas and compendia.
Results: Water-coloured and black- and-white macroscopic and histological illustrations of heart and vessels diseases from the XIXth century were found.
Conclusion: These drawings and paintings not only are a priceless heritage of the combination of "art and science" for future generations, but also an up-to-date teaching tools, due to the similarity to pathology found at the present time.

PS-20-002

Actinic keratosis, historical aspects of an actual but still controversial nosological entity

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Objective: Recapitulate the history of the term actinic keratosis (AK) as mile stone to elucidate the concept of a precancerous lesion.
Method: We review the literature examining the definitions and the clinic-pathological correlation that this entity has received in the past. We also presented the most diffused recently proposed classification of AK.
Results: The first description of AK was formulated by Duheruilh in 1896 (keratosis senilis). He found evidence that keratosis senilis is prone to evolve into invasive squamous carcinoma of the skin. In 1926 W. Freudenthal defined the histological aspects of keratosis senilis (KS), distinguished it from "Verruca senilis" also known as seborrheic keratosis. RI Sutton (1938) believed that this lesion is de facto a cancerous entity and not a pre-neoplasia. This according with Lever (1949): he suggested that KS is a form of squamous cell carcinoma. The first correlation of KS with UV (ultraviolet) rays was made in 1958 by Pinkus. He also first used the term AK.
Conclusion: Although histologically well defined, AK is still source of debate as stated by its several definitions and classification as a premalignant or in situ skin cancer. Four classifications (after 1958 to date) were identified in literature.

PS-20-003

Anatoly Ivanovich Strukov — Russian pathologist, scientist and educator (06.04.1901 - 13.03.1988)

A. Zubritsky*
*Moscow, Russia

Objective: To collect and systematize the biographical information on Professor Strukov. Born in the village Spassky of Novomoskovsky District of Tula Region; graduated from the Medical Faculty, Voronezh State University (1925); doctoral thesis on "Age of tuberculous spondylitis pathology" (1936); preparator (1924–25), assistant (1925–33), Pathology Department, Voronezh University; assistant, ass.prof., Prof., Pathology Department, 1 Moscow Medical Institute (1933–88), and other. Editor in Chief of "Archives of Pathology" (1968–88); Academician of the AMS USSR (1966); Hero of Socialist Labor (1971).); proposed a new clinical and anatomical classification of tuberculosis, described the early signs of pulmonary tuberculosis, followed the dynamics of the disease; creator of the doctrine of the unity of structure and function in the development of biology and medicine; they formulated the new ideas in the field of inflammation, introduced the concept of "immune inflammation," and the study of the microvasculature in various pathologies allowed to understand the pathogenesis of most diseases. Interests: problems of tuberculosis, lung disease, atherosclerosis, hypertension, myocardial infarction, collagen diseases, and others. Author of over 300 scientific papers. Distinctive feature: love of teaching, a brilliant lecturer gift, hard work and sense of responsibility. Hobbies: prose, poetry. Died in Moscow on 87-year life of a brain hemorrhage. He was buried at the cemetery Kuntsevo of Moscow.

PS-20-004

Vladimir Germanovich Shtefko — Known Russian phthisiopathologist and anthropologist (29.11.1893 - 03.10.1945)

A. Zubritsky*
*Moscow, Russia

Objective: To collect and systematize the biographical information on Professor Shtefko. Born in Moscow; graduated from the Medical and

Physical–mathematical faculty, Moscow University with honors (1916); Head, Laboratory of Pathomorphology, Central Institute of Tuberculosis (1926–45) and others; he found that in certain age periods, not all histologic elements develop evenly, that there is a certain predominance in the development of that one, the other entities, the explanation of which lies in the alternation of stages of differentiation and growth stages of histological elements, thus it was established phenomenon diskhroniya development intraorgan structures; his work has shown that humanity in its structure is fragmented, concluded: "The considerations made on basis of experimental data lead us to an extremely important and highly interesting conclusion. Cultural race of mankind, such as Europeans have a more complex structure of protein molecule than inferior races. Thus, biological, or rather, a biochemical point of view, they are more difficult to organize than latter "; he denied almost famous postulate that all men - brothers; developed a classification of types of human constitution, which was reason for his political persecution in connection with which work had to be stopped, however, this did not stop wrath of his enemies; author of over 300 scientific papers, including 24 monographs, related to study of child age morphology and tuberculosis; features: fluent in five languages, unusual diligence, real love for science, almost never used vacation; interest in philosophy and poetry; committed suicide Oct. 3, 1945 in Moscow on 52th year of life.

PS-20-005

The history of textbooks on pathology and pathological anatomy for teaching in Russian Empire, USSR and Russian Federation

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Objective: The formation of textbooks is connected directly with history of the state.
Method: The textbooks of museum of pathologies' chair of Belgorod State National Research university.
Results: In the end of XIX century and in the beginning of XX century textbooks, issued in other countries, were often used in medical institutes in spite of teaching, conducted on Russian language. Books on pathological anatomy, issued on German language were on the first place. Thus, the textbook "Pathologische Anatomia"(1913) by Ludwig Fschaff was recommended in St.Petersburg and in Moscow. In 30s the significant number of books of scientists of Russian school of pathology was published. The book of Nikiforov and Abrikosov "The basis of pathological anatomy" (1928) should be noted. The monopolization of separate schools for issuing of students' manuals and the publishing of uniform textbook on pathological anatomy occurred in USSR in period of 70s-90s of XX century. Nowadays in Russian Federation teaching of pathology and pathological anatomy is carried out in dependence from specialty with extended number of textbooks. The qualitative atlases are issued. Such textbooks as "Anderson's Pathology" are used for teaching.
Conclusion: The usage of specialized textbooks determines further tactics of medical work.

PS-20-006

Pathology: Relationship with clinical and biomedical research in Tunja, Boyacá

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Objective: Digestive cancer, gastric or colonic origin, has been associated with environmental exposure to Helicobacter pylori on contaminated food, waste toxic residues, inappropriate use of pesticides and the habit of cooking too much burned. Early detection in Gastric cancer, could diminished sanitary budget and could improve mortality by preventable degenerative chronic diseases. in Boyaca, Colombia.
Method: Reseach group has focused on three lines oriented by pathologist point of view: 1. Assurance of epidemiological and clinical data based on pathology diagnosis. 2. Relationship with clinical and biomedical research of Gastric cancer. 3. Focusing in Geographic Pathology.
Results: Local research network has begun and It has received support of scientifics groups in Colombia and Spain. MicroRNAs has been selected as potential candidates of neoplastic detection. Soil studies have been made in population near a waste close to the city. ARCGIS maps of cancer have been published to community.
Conclusion: Pathologist proposal have made a rol in medical education and multidisciplinary research with basic sciences: Gastric cancer network has been consolidated, in order to validated MicroRNAs as biomarkers of early gastric cancer in clinical and population studies.

PS-20-007

On philosophical pathology and UNO Agenda 21

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Objective: Philosophy is science of science acc. to Immanuel Kant considering epistemology-ethics-aesthetics. Central-position of pathology in medicine needs foundation of philosophical pathology.
Method: REFERENCES/see Neu-Michailov-et-al. IAP/ESP-2016. DEDICATION to moral support 2015–1980: Austria: E.Busek, E.Gornik, K.Lorenz*, M.Plattner, France: J.Dausset*,J.-M.Lehn*, R.Seve, Germany: M.Eigen*, H.Michel*, E.Neher*, B.Simma, W.Scheel, B.Vogel Japan: L.Esaki*, K.Fukui*, Y.Ikemi, UK: B.Josephson*, Lord A.Todd*, USA-India: H.G.Khorana*, D.Hubel*, E.Wiesel* (Nobel-Laureates*).
Results: CONCEPTION. A. EPISTEMOLOGY. Creation of integrative pathology could include not only pathological physiology-morphology-genetics, but also psycho-pathology. Acc. to axiology-logic-semantic is necessary clarification of notions reflecting volume/limits of pathological-disciplines/incl. functional-pathomorphology. B. MORAL PHILOSOPHY. Independently from various modern ethical-theories/deontology-etc. has to be considered by KANT conc. human obligations to (a)-himself/pathologists, (b)-other humans/patients, (c)-sub-human/e.g. reduction of animal-experiments, (d)-suprahuman beings/philosophical & theological-ethical limits of pathological-practices/biopsy-etc. C. AESTHETICS. Acc. to A-B is necessary paradigm-changes in pathology supporting diagnosis-therapy, e.g. oncological-interventions leading to pathophysiological-morphological & psychopathological-effects of radiochemotherapy/radiocystitis-etc. (primum non nocere).
Conclusion: Establishment of common interdisciplinary congress-sessions of IAP-ESP with philosophical/FISP-ISB-EACME-etc., psychological/IUPsyS-etc., physiological/IUPS-etc., medical societies/ISIM-ICC-FIGO-SIU-etc. could open new scientific&political-dimension in medicine, leading to humanization, higher-efficacy&internationalization of science-medicine-ecology in-context-of UNO-Agenda21 for better health-education-etc. on global level.

PS-20-009

The history of study of pathology in the Belgorod State National University

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Objective: In 2016 the Belgorod State National will celebrate 140 anniversary.
Method: Exploration of university archives.
Results: The history of the Belgorod State National University was connected with era in Russian educational system, what was contributed by reforms of sixties of 19th century. "The regulations of teacher institutes", signed by Alexander II, was published in 1872. The Belgorod Teacher's Institute, which was opened in 1876, had become the ninth in Russian

Empire. Training of teachers in this institute included study of philosophy, anatomy and pathology of human in the course of natural science. The chair of anatomy and physiology with bases of pathology was established in structure of faculty of biology and chemistry in 1971. The chair of pathology was opened in 1998 on medical faculty under direction of professor Pavlova T.V. Scientific works are conducted in next areas: endocrine pathology, gynecological pathology, pathology of soft tissues and bones, haematological pathology, history of pathology, urological pathology and other topics. Methods of raster microscopy, transmission microscopy, atomic power microscopy, confocal microscopy and immunohistochemistry are used. Conferences and trainings for pathologists are conducted on the chair. Five monographs were issued. The 4th All-Russian Congress of Pathologists with international participation was conducted in 2013.
Conclusion: The development of pathology in medical institute of Belgorod State National University contributes to improvement of quality of health care in Belgorod region.

PS-20-010
Questionnaire portrait of the Russian pathologist, pathophysiologist, histologist, scientist, and educator Professor Israil Solomonovich Pentman (09.05.1888 - 29.01.1939)
A. Zubritsky*
*Moscow, Russia

Objective: This work has the purpose to collect and systematize the biographical data according to the questionnaire prepared by me.
Conclusion: Born in Omsk in a family of artisan engaged in trade. Graduated from the first class of Omsk secondary school, after moving to Switzerland of parents—Basel real school, University of Basel, Faculty of Medicine, with the title of doctor of the Swiss Federation; after writing a thesis on the topic «Zur lehre der Splenomegalie» was awarded the title of Doctor of Medicine, University of Basel; after returning to Russia, and of the passing exam, he received the title of doctor, Faculty of Medicine, Tomsk Imperial University, he lectured on general, the private course of general histology and pathology, Head, Department of Pathological Anatomy, Omsk Medical Institute; under his leadership was organized an expedition to the Altai Mountain in Shoria and material collected was the basis for the development of iodine prophylaxis of endemic goitre. Interests: Study of age-related changes of the thyroid gland in the Omsk region, parasitic diseases and diseases of the blood system. Repressed (1937), was arrested by the People's Commissariat of Internal Affairs (1938), he was accused that he was a Jew-Hitler's spy and "prepares the plague in Siberia"; was sentenced to capital punishment—shooting (Novosibirsk); rehabilitated by the Plenum of the Supreme Court of December 11, 1957.

Thursday, 29 September 2016, 09.30–10.30, Hall 11.3
PS-21 IT in Pathology

PS-21-001
Input device research for digital pathology: An ergonomic outlook
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Objective: Digital Pathology (DP) introduces changes in the traditional work of pathologists. An important issue is the image handling from an ergonomic point of view to avoid work-related musculoskeletal disorders (MSD). The aim of this study was to investigate a proper input device (ID) for DP.
Method: Research included two phases: 1. Eight medical students analyzed 11 IDs (figure 1), with the ImageViewer software and the web-based Fitts'-law-test to objectify accuracy. A questionnaire with ergonomic topics was included. 2. Evaluation by two experienced pathologists the best rated ID and comparison with a voice recognition system (VRS), using a headset microphone and rating perceived workload using NASA Task-Load-Index with 28 digitized preparations. Digital-Image-Hub with a 4-MegaPixel-display were used.
Results: Correlation between technical aspects of the evaluated devices and accuracy (Fitts'-law-test), and comfort with overall satisfaction existed ($p < 0.05$). The assessment concluded that vertical mouse was the best rated ID. However, it has a slightly higher perceived workload in comparison with VRS, which was the proper controller for DP in this study.
Conclusion: We describe a methodology that can study and compare IDs for future workstations in DP. VRS can function as a good handsfree device for DP and could be considered in physical disability situations.

PS-21-002
Remote teaching of histopathology using scanned slides via skype® between the UK and Nigeria
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Objective: Web based learning is a major component of distance education. We explore its applications for pathology teaching in resource limited sub-Saharan Africa.
Method: The participants were consultant pathologists and trainees drawn from tertiary institutions in Nigeria. They viewed the digital slides via the Leeds virtual pathology website following which interactive lectures were given via Skype®. Questionnaires were administered via SurveyMonkey® to all participants of 12 sessions between 2014 and 2015.
Results: Nine consultant pathologists and 32 trainees participated in this survey. Twenty-nine (69 %) of the respondents thought it was fairly easy to navigate the system, 11 (26.2 %) thought it was easy while 2 (4.8 %) felt it was difficult. Twenty-six (61.9 %) respondents found it fairly easy to make a make a diagnosis, 13 (31 %) thought it was easy, while three (7.1 %) noted that it was difficult. Twenty-four (57.1 %) respondents had a fairly smooth user experience, 12 (28.6 %) experienced occasional crashes while six (14.3 %) reported a smooth experience. Almost all (97.6 %) of the respondents felt the pathology teaching was beneficial to their local pathology practice and all indicated the need for more of such sessions.
Conclusion: The beneficial applications of internet based lectures make it a viable cheaper, faster and cost effective alternative to face-to-face lectures in delivering education to resource-limited countries.

PS-21-003
Technology enhanced cognitive scaffolding: Unique and innovative pathology teaching in a rural medical school in Australia: One man army!
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Objective: 1. Share experience of unique undergraduate medical curriculum with strong focus on applied pathology in the senior clinical years. 2. Share experience of challenges faced in teaching integrated clinical pathology effectively to large cohart of students in remote clinical rotations. 3. To present several successful innovations in teaching pathology, microscopy through Blended Adaptive Integrated Learning (BAIL). 4. Demonstration of digital microscopy laboratory (First in the world*) 5. Demonstration of student monitoring and support using Technology Enhanced Cognitive Scaffolding.

Method: Oral presentation with multimedia sharing successful innovations in Teaching pathology to senior clinical students developed over two decades, which have improved student satisfaction, participation & learning. All by single academic staff, my colleagues call "ONE MAN ARMY". Presentation will summarise decades of experience in teaching pathology, its challenges and innovations in a humorous way.
Results: Significant improvement in student participation and learning of clinically integrated pathology in their senior years. Also this has resulted in significant improvement in retention and application of basic sciences to clinical case management. Note: Some of these innovations have been recognised by local and Australian national awards for teaching excellence.
Conclusion: We have developed unique innovative, clinically integrated pathology centred undergraduate curriculum. Despite being rural and remote, students have access to teaching resources including microscopy and specimens tutorials. Students have not only participated better, but also performed significantly better in both pathology and clinical learning.

PS-21-004
Turn Around Time Measurement In Anatomical Pathology: Application of Survival Analysis
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Objective: Turn-around time (TAT) in pathology is a key performance indicator, but TAT methodology is rarely a focus in the literature. TAT follows non-normally distributed (right skewed) pattern, requiring transformation or use of a semi-parametric approach;. mean TAT cannot not be used in such settings. The aim of this study is to apply survival analysis (time to event analysis) to TAT monitoring.
Method: We extracted TAT data (2010–2014) for all breast core biopsies processed in our department (n = 4,118), time of accessioning and time of sign-out for each case. There were no censored cases. We built a histogram and ran Kaplan-Meier analysis, using 1-minus-survival (time to task completion) plot, and stratified the data by the calendar year and complexity. Log-rank test was used to compare the differences in TAT between calendar years and complexity codes.
Results: The model fits proportional hazard assumption. The TAT displays non-normal right-skewed distribution. The Kaplan-Meier curves show notable similarity over the years, with a small yet statistically significant difference in TAT over the years (log rank test, $p < 0.0001$, from median 4.3 (95%CI 4.1–4.6) days in 2010 to 3.8 (95%CI 3.4–4.2) days in 2014) and are dependent on case complexity.
Conclusion: Kaplan-Meier (time to event) analysis is a robust method of monitoring TAT in anatomical pathology. It is more informative than point estimates of mean and median TAT. Furthermore, it is potentially applicable to monitoring of individual pathologist turn-around time and allows for multivariate adjustment to case complexity, daily workload, and use of ancillary methods.

PS-21-005
Evaluation of Ki-67 Index in invasive breast cancer: Comparison between visual and automated digital assessment
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Objective: The reliability of the established Ki67 scoring is limited due to lack of standardization of methods used for assessment of the Ki67 value. Digital pathology is currently suggested to be a potential solution to Ki67 assessment problems.
Method: A retrospective & prospective study including 100 patients diagnosed with invasive breast cancer. Three senior pathologists have been asked to estimate the Ki67 proliferative index for each of the 100 cases by examining the glass slides by optical microscope and the virtual slides on the monitor and providing a percentage score of tumour cells with positive staining then a categorical score 'high' and 'low' Ki67 score using 14 & 20 % as threshold indicatives of high ki67 status. Finally, a digital quantitative assessment of Ki67 was performed.
Results: A high inter-observer agreement was found when using optical microscopy slides as well as virtual slides for ki67 assessment, with slightly higher Correlation coefficient values when using optical microscopy. Ki67 values were linearly correlated with automated evaluation of Ki67. When using categorical scores, a statistically significant difference between the overall results of 3 observers on virtual slides and automated assessment of Ki67.
Conclusion: Digital pathology can be considered as a potential easy-to use tool for a robust and standardized fully automated Ki67 scoring.

PS-21-006
GP-HELPER (v1.2): The new medical app about general pathology
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Objective: Smartphone applications (apps) have become increasingly prevalent in medicine. GP-HELPER is a novel app developed as a reference tool in general pathology, developed for Android and iOS platforms.
Method: "GP-HELPER," was created using Mobincube website platform. This tool also integrates "FORUM GP-HELPER," an external website created using Miarroba website (http://forum-gp-helper.mboards.com) and "COMMUNITY GP-HELPER" a multichannel chat created using Chatango website platform.
Results: The application was released in July 2015, and it is been periodically updated since then. The app has permanent information about different pathology and a database with more than 5000 immunohistochemistry results from different tumours. Online data have links to more than 1100 reference pathology video lectures, 250 antibodies information, more than 70 pathology association websites, 46 pathology providers, and 78 outstanding pathology journal websites. The app has two interactive places that let users to stay in touch everywhere and every time. Expert consult section is also available.
Conclusion: "GP-HELPER" pretends to integrate offline and online data about pathology with two interactive external places in order to represent a reference tool for general pathologists and associate members.

PS-21-007
Evaluation of an automated tissue-sectioning system for paraffin blocks towards clinical implementation as a part of digital pathology workflow
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Objective: Slide quality plays an important role in digital pathology and is an important consideration when using whole slide images (WSI) in clinical diagnosis. We have adopted an automated tissue sectioning system (ATSS) for WSI/digital imaging research because of consistency of tissue thickness and quality. Use of ATSS in clinical settings is limited by type of paraffin, inefficient block trimming and facing, and lack of LIS integration. The latest ATSS has attempted to overcome some technical limitations. In this study, we evaluate whether the ATSS can section clinical standard paraffin blocks at a quality sufficient for diagnostic purposes.
Method: 110 paraffin blocks used previously for diagnostic purposes were sectioned using the AS-410 (Dainippon Seiki, Co. LTD., Japan) at 5um thickness. Nine organs were represented. 1500 slides were sectioned and evaluated manually. One-third of slides were stained with H&E and evaluated for section quality by both microscope and digitally.

Results: Satisfactory sections were obtained from most blocks. In particular, sections obtained from lung and breast excisions were of high quality. A moderate number of small biopsies and bone displayed holes or tissue distortions. A small percentage of gastroinstestinal tissue sections showed mild-moderate tissue artifacts.
Conclusion: Sections produced by an ATSS show promise for clinical application.

PS-21-008
Telepathology for rapid turnaround time in malignancy diagnosis in low-middle income settings
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Objective: Delivering cancer care in low-resource settings is dependent on developing efficient and accurate pathology systems. In this study, we analyzed the efficacy of implementing a telepathology system to remotely provide cancer diagnostics to Butaro District Hospital in rural Rwanda.
Method: Our system consisted of static images obtained by histotechnologists using a standard protocol, uploaded to ipathnetwork.com, and reviewed by a team of pathologists with various areas of expertise in common malignancies. Over the 9-month implementation of telepatholgy, we divided the study into three segments—training, technical workflow, and testing segment. In this presentation, we will breakdown the efficacy of the telepathology system in Butaro District Hospital for oncology cases.
Results: For the three implementation phases over the 9-month study period, we will present the turn-around time, from procedure date to result, as well as the volume of cases triaged for pathologist review that were unable to be diagnosed through telepathology.
Conclusion: Over the three implementation phases, the turn-around time of cases drastically decreased, allowing clinicians to receive results and initiate more accurate and timely treatment for cancer patients. Simultaneously, the percentage of cases triaged for pathologist review that could not be properly diagnosed through telepathology significantly decreased through improvements in technical imaging, communication, and workflow management.

PS-21-009
Telepathology in Boyacá, Colombia
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Objective: Telepathology is playing a very important role in the consult and quality control of cancer diagnosis (Kayser, 1999). Global experiences of national programs and international network of the first world have shown that it can be part of the solution to the unequal distribution of human resources in the countries. The agreement in diagnosis can vary from 0 to 59.8 % (Chen J, 2014) However, what is most important is that today, mobile devices have the obviously real potential to support an online network of specialists working together (Corredor G, 2015).
Method: Collaborative research between Europe has supported the building of a patented device in order to scan preparations. Qualitative experiment with scanning liver preparation was performed. Virtual reading of the scanned slide was made in less of one day but scanning and fusing the squares spents a week.
Results: Sensitivity was proper, but the suitability of diagnosis has been different, by the fact of the inherent categorization of the case.
Conclusion: ICTs are improving diagnostic quality and efficiency of clinical work in the world (Rojo, 2014, van den Tweel JG, 2011). In Boyacá, there are efforts to develop telepathology, one of the resources of pathologist in third world.

PS-21-010
The reproducibility of pathological diagnosis: The results of the online diagnostic competition
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Objective: To indicate the importance of collecting rare cases and their expert assessment with the help of digital microscopy.
Method: Fourteen rare cases from different sub-specializations field in pathology were selected by two expert pathologists from the Czech Republic and Italy. The slides were digitized and introduced with clinical information to 250 specialists registered to take part in the competition.
Results: The range of the right answers varies between 3 and 56 %. The most difficult case for the participants was the one with no tumourous pathology: ectopic hamartomatous thymoma. There were 3 % of full match. The biggest number of full match to experts' diagnoses can be seen in the cases with soft tissues tumours. To analyze the disagreements we divided them in two groups: MAYOR Disagreement—potentially wrong histological diagnosis changes the clinical tactics of patient's treatment. Potentially wrong pathological diagnosis leads to wrong course of patient's treatment and wrong chemotherapy, etc. MINOR Disagreement—potentially wrong diagnosis doesn't have any clinical matter. This tactic showed that the case of hyalinized endometrioid adenocarcinoma turned out to be the most difficult one for the participants. The range of MAYOR Disagreement here is 66 %, while the full match is 14 %.
Conclusion: Rare cases show very low reproducibility index. The digital microscopy is a good way not only to spread the information (education and training) but also to collect the data about difficult and rare cases. Compared to rare cases large data samples are better for reproducibility researches.

PS-21-011
Analysis of the impact and value of a specimen tracking and routing system implementation for anatomic pathology
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Objective: Accurate and effective specimen tracking and routing in a surgical pathology laboratory is critical for improving efficiency, reducing error, and improving patient care. Performing specimen tracking and routing in the traditional manner could cost significant time and resources, with minimal to no, real-time workflow monitoring.
Method: Sunquest CoPath, as the laboratory information stystem, integrated with specimen management routing and tracking. Additional hardware requirements include Windows based workstations, 2-D barcode scanners, slide label and cassette printers/etchers, and network.
Results: An automated tracking and routing system was successfully implemented with the necessary hardware and software. Compared to our current laboratory information system, CoPath+SMART provided more accurate routing, detailed tracking, and valuable workflow monitoring functions.
Conclusion: As the major histology lab for a tertiary regional medical center, the lab benefitted from an automated specimen tracking and routing system. Increased work efficiency, reduced error, and better lab management were achieved. This required changes in laboratory culture, workforce adjustment, and a well-tailored plan to increase benefit/cost ratio.

Thursday, 29 September 2016, 09.30–10.30, Hall 11.3
PS-22 Molecular Pathology

PS-22-001
Tumour-associated fibroblasts as generic target of cancer immunotherapy
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Objective: The ideal way to study adaptive immunity involves direct detection of endogenous epitope-specific T cells using methods that distinguish TCR specificity by its binding to cognate peptide—MHC complexes. CTLs expressing a particular TCR are able to recognise not only tumour cells antigen but also microenvironment specific antigens, such as those on TAFs. They can be selected by Streptamers®, subsequently analysed and get infused into tumours of patients.
Method: We used surgically removed fragments of breast cancer to obtain TAFs, which were further cultivated and expanded in vitro in standard culture conditions. Blood samples were obtained from the same patient, and peripheral blood mononuclear cells (PBMC) were obtained by density gradient centrifugation and stored in liquid nitrogen until further use. On the surface of TAFs, we identified by flow-cytometry the presence of a specific antigen—fibroblast activation protein (FAP) and we custom-made MHC I-Strep HLA-A*0201 FAP for isolation of CTLs. Antigen-specific T cell sorting was performed by magnetic nanobeads separation, biotin-binding for removal of magnetic particles, and we performed co-culture of TAFs with positive and negative T cell fractions.
Results: After in vitro expansion of PBMCs for 2 weeks, we were able to isolate using Streptamer® technology a proportion of 20 % of CD8+ T cells, specific for the fibroblast activation protein (FAP) antigen.
Conclusion: Co-culture of cytotoxic T lymphocytes was performed in a ratio of 1:1 with TAFs. TAFs proliferation in vitro was abolished after 3 days of co-culture with FAP-specific CTLs, compared with non-specific T cells, which induced only decrease in TAFs proliferation after 5 days of co-culture. As our ongoing research on TAFs uncovers novel antigenic targets, the flexibility of the Streptamer technology will allow us to select ever more specific CTLs at the same resource expenditure.

PS-22-002
The relevance of BRAF exon 11 testing in melanoma — single center experience
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Objective: Since the availability of targeted therapy, BRAFV600 mutation testing in metastatic melanoma has become obligatory. A second mutational hotspot for high-activity kinase BRAF mutations is in the exon 11.
Method: We performed a retrospective analysis of 145 metastatic melanoma samples that were previously tested for BRAFV600 with next generation sequencing covering the codons 581 to 620 of the BRAF gene (on exon 15). Due to the increasing clinical relevance of mutations in the exon 11 we tested the 145 samples using pyrosequencing covering the codons 464 to 469 of exon 11.
Results: 49 (33.8 %) samples were positive for a mutation in the BRAF gene in exon 15. Additionally, four mutations in the BRAF exon 11 could be identified (G466E; 2x S467L; G469E), all in BRAF exon 15 wild type samples.
Conclusion: In-vitro experiments suggest that mutations in exon 11 of the BRAF gene respond to targeted therapy, such as MEK inhibitors, and are more sensitive to chemotherapy. Therefore, the mutational spectrum in melanoma other than BRAFV600 might be of clinical relevance in the future and should therefore be included in melanoma mutation analysis panels.

PS-22-003
Dysgenetical gonads in Turner syndrome: Morphology and karyotype correlation
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Objective: to study morphological and karyotypical features of dysgenetical gonads (DG) in Turner syndrome (TS).
Method: surgical material from 16 patients 11–24 years old with TS. Immunohistochemistrical detection of Ki-67, Vimentin, Desmin, Inhibin-a, AR, ER. The tissue karyotype (TK) and SRY-gene has been detected by fluorescence in situ hybridization and polymerase chain reaction, the serum karyotype (SK) - cytogenetically. Data processing: Statistica 7.
Results: three groups were detected: streak-gonads (8), DG with ovarian tissue (DGOT-6), DG with gonadoblastoma (DGGB-2). Six patients with streak-gonads: 45X SK and XO TK, the SRY-gene—in one case. Two more patients: 45X/46XY SK and XO/XY, XO/XY/XYY TK, the SRY-gene—in both. Four patients with DGOT: 45X SK with XO TK in the three cases and one—XX. Two others: 45X/46XX SK and XO TK, the SRY-gene—in one case. DGGB: 45X/46XY SK and XO, XY TK, SRY-gene—in both cases. Immunohistochemistrically: streak-gonads—high expression of Vimentin and low of all rest. DGOT—high expression of ER; DGGB—high expression of Inhibin-a, ki-67.
Conclusion: morphology correlates ($p < 0.01$) with SK but not with TK in all cases,especially with Y-chromosome and SRY-genepresence, that may result of SRY-gene translocation to X-chromosome during meiotic recombination.

PS-22-004
The broad variety of next-generation sequencing methodologies and the impact on biomarker testing
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Objective: Next-generation sequencing (NGS) is the next best thing for oncology biomarker testing in molecular diagnostics. A comparative study with different NGS panels and bio-informatics pipelines gives more insight in the efficiency of the panels and the quality control (QC) metrics used in practice.
Method: Twenty-six institutes reported on identified variants in 10 patient samples of the ESP EGFR external quality assessment (EQA) and 2 synthetic DNA samples containing more than 300 variants. The raw data is further analysed and used QC metrics are questioned.
Results: Comparison of performance scores in the ESP EGFR EQA show an advantage for NGS users versus non-NGS users, respectively 91,8 % and 87,1 %. Less false positive and false negative genotyping errors are identified, however, additional SNPs are more often reported as actual variants in NGS using laboratories. Most laboratories were not able to identify all variants in the two synthetic DNA samples. There is a great variety in QC of the NGS analysis, both in number and type. Up to 15 different QC metrics are reported in 1 laboratory.
Conclusion: Even though NGS is a promising technique in molecular diagnostics, laboratories must be aware of the pitfalls when implementing the technique for the first time.

PS-22-006

Four colour, multimarker (12 and up) multiplex immunophenotype of a single FFPE slide

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Objective: To define a pathologic process by multimarker characterization on whole slide images (WSI) from FFPE routine material.
Method: WSI, in transmitted light and quadriband immunofluorescence (IF) are obtained from a slide scanner (Aperio Scanscope-FL and Nanozoomer RS2.0). One single FFPE section, dewaxed and antigen retrieved is sequentially immunostained, stripped (Gendusa R et al., JoHC, 2014; PMID: 24794148; Boi G et al., JoHC, 2016; PMID: 26487185) and re-immunostained several times (five or more). A a multilayered final image composed of 12 or more aligned immunostains is created. Tissue autofluorescence is linearly subtracted pixel-by-pixel from each channel. WSI registration and image cytometry analysis is performed with the AMICO ImageJ software (Furia et al., Cytometry, 2013; PMID: 23463605). The analysis is performed with a PC with at least 32 Gb of RAM.
Results: One single routinely processed section from each of several renal biopsies was immunostained with panels of antibodies identifying all leucocytes (CD45, CD43), T cells (CD3), B cells (CD20, CD79a), histiocytes (CD68, CD163), cDC (CD1c, CD141), pDC (IRF8), proliferating cells (Ki-67), epithelia (cytokeratins).
Conclusion: Multiplex immunostaining of one single FFPE routinely processed section by sequential staining cycles and image cytometry analysis on WSI is a simple, affordable method.

PS-22-007

Error types in external quality assessment schemes and corrective actions to improve laboratory performance

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Objective: Erroneous results in personalized medicine can significantly compromise patient safety. Unfortunately, tumour analyses for metastatic colorectal and non-small cell lung cancer are error-prone. External quality assessment schemes aim to educate laboratories and to monitor their performance. However, no research has yet been conducted on the error distribution, root causes, or the corrections undertaken for molecular diagnostics.
Method: An electronic pilot questionnaire was sent to 62 laboratories from 24 countries, with at least one genotyping error during the 2015 ALK/ROS1 scheme of the European Society of Pathology, or with a suboptimal score for the technical evaluation of ALK immunohistochemical staining.
Results: Twenty-three of 62 laboratories from 11 countries responded, yielding a total of 31 errors. An equal distribution between pre-, post- and analytical errors was observed for ALK, except for the technical assessment (analytical). Causes were mainly methodological and reagent-based. ROS1 errors were mostly post-analytical/unknown of nature (interpretation errors). Most corrections were protocol revisions (ALK) and staff trainings (ROS1). Remarkably, 20 % of the laboratories did not undertake any action.
Conclusion: There seems to be a difference in error distribution and causes between markers. Additional data is required to investigate the variation between techniques or laboratory characteristics in a longitudinal manner.

PS-22-008

STD pathogens determined in semen using PCR and flow-through hybridization technology

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Objective: The aim of this study was to access in health care facilities for diagnosis and common pathogens of STDs, those causing infertility and Chlamydia trachomatis, Neisseria gonorrhoeae and Mycoplasma hominis. Genital wart is a highly contagious sexually transmitted disease caused by some sub-types of human papillomavirus (HPV).
Method: Semen samples were obtained by masturbation into sterile containers after sexual abstinence of 48 to 72 h. Samples were subjected to semen analysis within 1 h of collection and processed for freezing within 2 h of collection. The concentrations of sperm as well as sperm motility were also determined. DNA extraction was extracted of all the samples and the PCR assay was performed. The amplicons are subsequently hybridized to pathogen-specific capturing probes via "Flow-through" hybridization.
Results: During our study we came across with the STI pathogens present in our population and the reason for infertility was the main cause. When Chlamydia trachomatis and Neisseria gonorrhoeae were detected in their wife's were also screened and these STI pathogens were identified.
Conclusion: The main route for the transfer of STI pathogens were the men special those who visited commercial sex workers or hotel-based sex workers as they were working in other cities and the complained for infertility. Screening for bacterial STI pathogens, Mycoplasma hominis, Chlamydia trachomatis and Neisseria gonorrhoeae are strongly recommended because these pathogens can cause serious reproductive complications such as pelvic inflammatory disease, ectopic pregnancy.

PS-22-009

Interlaboratory variation in molecular testing for EGFR, KRAS and ALK in stage IV non-squamous non-small cell lung cancer in The Netherlands in 2013

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Objective: To assess whether Dutch pathology laboratories optimally perform molecular testing for EGFR, KRAS and ALK in metastatic non-small cell lung cancer (NSCLC) patients.
Method: Using the Netherlands Cancer Registry, all stage IV non-squamous NSCLCs from 2013 were identified and matched to the Dutch Pathology Registry (PALGA). Data on molecular testing for EGFR, KRAS and ALK were extracted. Proportions of tested cases were determined and compared between 48 laboratories.
Results: In total, 3393 stage IV non-squamous NSCLCs were identified, and 3193 (94.1 %) were matched to PALGA. Currently, we have assessed 1660 (52.0 %) tumours. Molecular testing for EGFR was performed in 1149 tumours (69.2 %; range between laboratories 28.6–93.1 %), for KRAS in 1191 tumours (71.7 %; range 16.7-93.1 %) and for ALK in 447 tumours (26.9 %; range 4.5–71.4 %). In case of wildtype EGFR and KRAS (n = 628), ALK reflex testing was performed in 345 cases (54.9 %; range 16.1–100 %).
Conclusion: According to these preliminary results, molecular testing for EGFR, KRAS and ALK was suboptimal in The Netherlands. Furthermore, substantial interlaboratory variation was observed, which may have hampered optimal use of and benefit from targeted therapies in a selection of laboratories. To determine whether molecular testing has improved, a more recent cohort will be analyzed as well.

PS-22-010

Carboplatin chemoresistance is associated with MiR-205 and miR-218 expression

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Objective: Identify the molecular mechanism in lung cancer chemoresistance through microRNA expression and immune system regulation.

Method: MiRNA-transfection (MiR-205 and miR-218) of A549 and H1975 lung cancer lines. Ex vivo lung tissue was performed to analyse PARP, cleaved caspase-3, Bax and reduction in Mcl-1 and Survivin protein and mRNA levels.

Results: MiR-205 overexpression in A549 and H1975 lung cancer cells is concurrent with the down regulation of miR-218 and in linked with carboplatin sensitivity and chemoresistance. Interestingly, ectopic miR-218 overexpression reduced cell proliferation, invasion and migration of lung cancer cells, whereas miR-205 rescued the suppressive effect of miR-218 by altering the expression levels of the pro-apoptotic proteins PARP, Caspase 3, Bax and upregulating the anti-apoptotic markers Mcl-1 and Survivin.

Conclusion: Taken together our findings imply that the miRNAs miR-205 and miR-218 play a key role in the development of lung cancer acquired chemoresistance and the tumour suppressor role of miR-218 in inhibiting lung cancer cell tumourigenesis and overcoming platinum chemoresistance is significant for future cancer therapeutic approaches.

PS-22-011

Regulation of TGF-beta/Smad signaling by vanadium species

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Objective: Characterize the role of antitumour vanadium in TGF- beta (β)/Smad signaling, and association with cancer cell proliferation, differentiation, and metastasis.

Method: Vanadium compounds were tested in lung cancer adenocarcinoma A549 and aggressive breast epithelial tumour MDA-231 cells for the period 24, 48 and 72 h, using RT-PCR, immunofluorescence and Western blot methods.

Results: The experiments showed that vanadium down-regulates the TGF-β signaling pathway by reducing the expression of phosphosmad2, smad 1, 4, PAI-1 and activates the apoptotic process thus leading A549, MDA-231 cells to cell death. In addition, the expression levels of the inhibitory smad7 which inhibits TGF-β activation were raised following vanadium treatment in both cell lines. Furthermore, vanadium suppresses the expression of the cell cycle proteins cyclin D1 protein and E1, involved in cell cycle regulation and development of tumour process and plays an important role in the mechanism of differentiation and growth of cancer cells.

Conclusion: Overall, the findings highlight the multifaceted antitumour action of vanadium and its synergistic antitumour efficacy with current chemotherapy drugs, knowledge that could be valuable for targeting cancer cell metabolism and cancer stem cell-mediated metastasis in aggressive chemoresistant tumours.

PS-22-012

Vanadium reduces autophagy and inhibits epithelial-mesenchymal transition by induction of TRAIL-induced apoptosis in cancer cells

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Objective: Identify the molecular mechanism by which vanadium inhibits autophagy and EMT transition through augmentation of TRAIL-induced apoptosis in breast epithelial MCF-7 and lung adenocarcinoma A549 cells.

Method: Inhibition of autophagy by siRNA or 3-MA and study of TRAIL-mediated apoptosis through DR4 and DR5 protein expression in MCF-7 and A549 cancer cells.

Results: Vanadium reduces NF- binding to Becn1 promoter, thereby preventing initiation of autophagy and abnormal proliferation. It was demonstrated that vanadium directly targets autophagosome formation and reduces LC3-I and II expression, both of them important molecules involved in autophagy. The accruing results suggest that inhibition of autophagy by vanadium allows cancer cells to undergo apoptosis, thereby contributing to reduction in cancer cell invasion and metastasis.

Conclusion: Collectively, the work a) identifies a biologically active antitumour novel vanadoform containing peroxido and betaine moieties, and b) reveals a crucial role for vanadium in autophagy inhibition, thereby providing new molecular perspective(s) into finely configuring vanadoforms for cancer drug research and therapy.

PS-22-013

Molecular determination of the clonal relationships between multiple tumours in BRCA1/2-associated breast and/or ovarian cancer patients is clinically relevant

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Objective: BRCA1/2 mutation carriers affected with breast and/or ovarian cancer may develop new tumour deposits over time. It is important to know the clonal relationships between multiple tumour localizations, enabling differentiation between multiple primaries or metastatic disease with consequences for therapy and prognosis. We evaluated the value of targeted Next Generation Sequencing (NGS) for determining tumour relatedness.

Method: Forty-two female BRCA1/2 mutation carriers with ≥2 tumour localizations were selected. Patients with inconclusive tumour origin after histopathological revision (cases) and with certain tumour origin of ≥3 tumours (controls) were analyzed by targeted NGS. Based on identical or different mutations and/or LOH patterns, tumours were classified as 'multiple primaries' or 'one entity'.

Results: Histopathology yielded conclusive results for 38/42 (90 %) patients. Four cases and 10 controls were analyzed by NGS. In 44 tumour samples, 48 mutations were found; 39 (81 %) concerned TP53 mutations. In all 4 cases, the intra-patient clonal relationships between tumour localizations could be unequivocally identified by molecular analysis. In all controls, molecular outcomes matched histopathological results.

Conclusion: In most BRCA1/2 mutation carriers with multiple tumours routine histopathology is sufficient to determine tumour origins and relatedness. In case of inconclusive results, molecular analyses can reliably determine clonal relationships between tumours, enabling optimal patient treatment.

PS-22-014

EGFR mutations in sinonasal Squamous Cell Carcinoma (SCC) and papilloma

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Objective: To describe the spectrum of oncogenic mutations of sinonasal squamous cell carcinoma (SNSCC) arising from inverted sinonasal papilloma (ISP), focusing on EGFR mutations.

Method: Using next generation sequencing (NGS), seven inverted papilloma (ISP)-associated SNSCC and their synchronous associated ISP, six non-SNSCC-associated ISP, ten non-ISP-associated SNSCC and four sinonasal adenocarcinomas were analyzed.
Results: Activating EGFR mutations were detected in 75 % of SNSCC-associated ISP (and corresponding SNSCC) and in 83 % of non-SNSCC-associated ISP. All detected mutations took place in exon 20. We also found in one non-SNSCC-associated ISP a mutation in ERBB2 exon 20, analogous to the EGFR exon 20 mutations. Conversely in none of non-ISP-associated SNSCC and sinonasal adenocarcinoma an EGFR mutation was found. TP53 mutations were detected in 50 % of SNSCC-associated ISP and 80 % of their associated SNSCC but in none of non-SNSCC-associated ISP, indicating that TP53 mutations occur later than EGFR/ERBB2 mutations in ISP-tumourigenesis. Furthermore, mutations of MET, NFE2L2 and PIK3CA were described in ISP-associated SNSCC, mutations of MET, KRAS, PIK3CA and TP53 in sinonasal adenocarcinoma, mutations of TP53, NFE2L2, KRAS, PTEN and PIK3CA in non-ISP-associated SNSCC.
Conclusion: EGFR/ERBB2 exon 20 driver-mutations are defining a specific molecular tumour entity for SNSCC arising from ISP. According to our preliminary data, the mutational profile of sinonasal carcinoma appear analogous to non-small-cell-lung-cancer.

PS-22-016
Mutational load and classical pathology in breast cancer

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Objective: Breast cancer routine diagnosis is based on a small set of well-characterized clinicopathological and molecular variables. We set out to investigate the correlation of these features with the underlying mutation landscape.
Method: We evaluated the quantity and quality of mutations in a cohort of 687 primary breast cancer patients from The Cancer Genome Atlas (TCGA) project.
Results: The number of mutated genes was strongly associated with tumour grade (positive association, $p = 1.4E-14$) and with the molecular subtypes of breast cancer ($p = 1.4E-10$). The number of mutated genes was higher in HR-/HER2-, HR-/HER2+ and HR+/HER2+ breast cancer and compared to HR+/HER2- breast cancer. Furthermore, we detected significant associations of the number of mutated genes with patient age, tumour size and nodal stage. Mutations in specific cancer genes (TP53, NCOR1, NF1, PTPRD and RB1) were significantly associated with high loads of mutated genes. Finally, multivariate analysis of overall survival revealed a worse survival for patients with high numbers (≥22) of mutated genes (hazard ratio = 4.6, 95 % CI: 1.0–20.0, $p = 0.044$).
Conclusion: The study is a step towards genomics-informed breast pathology and provides a basis for future studies in this field bridging the gap between morphology, tumour biology and treatment.

PS-22-018
Simvastatin modulates monocyte chemotaxis in atherosclerosis via down regulating phospholipases (PLA2) signaling

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Objective: Clinical use of Simvastatin is attributed to its lipid lowering effect and considered as potential drug for the management of Atherosclerosis. Previously vascular Monocyte Chemoattractant Protein-1 (MCP-1) expression was downregulated by statins suggesting the beneficial effects in prevention of cardiovascular diseases. Considering the potential role of phospholipases in cell migration, the present findings depicts mechanism of action of simvastatin against MCP-1 dependent cell migration targeting phospholipases (cPLA2 & iPLA2) signaling pathways.
Method: Anti-atherogenic effect of simvastatin in human subjects was validated by quantitative assessment of CCR2 transcript levels using reverse transcriptase-polymerase chain reaction (RT-PCR). Further, in-vitro human monocytes migration was analyzed by using microchamber chemotaxis assay whereas, thioglycolate-induced mouse peritoneal inflammation model and adoptive transfer mouse model was employed to analyzed inhibitory effect of simvastatin against monocyte migration both ex-vivo & in-vivo.
Results: Simvastatin significantly and dose dependently downregulate CCR2 mRNA expressions in circulating human monocytes. In addition, simvastatin (10 mg/kg) substantially reduced the transmigration of murine monocyte upto 70 % after oral treatment. It also displayed >90 % inhibitory effects in adoptive transfer mouse model at concentration of 10 μg/ml. In addition microchamber chemotaxis assay demonstrates, 2.5 μg/ml, 5 μg/ml, 10 μg/ml of simvastatin significantly reduced human monocytes migration in a concentration dependent fashion induced by human recombinant MCP-1.
Conclusion: Simvastatin has potential ability to impair MCP-1 dependent chemotaxis via interfering cPLA2 and iPLA2 signaling pathways. This novel pleiotropic effect of simvastatin on circulating monocytes may prevent the excessive accumulation of monocytes on the arterial wall during the process of atherosclerosis.

PS-22-019
Microsatellite Instability and mutations of BRAF-gene in ampullary carcinoma

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Objective: Ampullary carcinoma (AC) accounts for 0.5 % of all malignant neoplasms of GIT. Many authors refer AC to hereditary non-polypous colorectal cancer (HNPCC) with high incidence of microsatellite instability (MSI). To evaluate frequency and clinical and biological meaning of MSI in patients with AC.
Method: We investigate specimens of 31 patients with AC who underwent surgery in 2003–2015. Detection of MSI in AC patients were made in two steps: first, IHC stains for MLH1, PMS2, MSH2, MSH6 and second, molecular analysis using 5-panel of microsattelite primers (NR21, NR24,BAT25, BAT26, BAT27).
Results: Evaluation of level of DNA reparation system proteins revealed 41,9 % (13 of 30) cases with protein deficiency. In most cases (8 of 13) deficiency of the basis of PMS2 gene was detected. Combination of MLH1/PMS2 was revealed in 2 of 13 cases and combination of MSH2/MSH6—in 3 0f 13 cases. All tumours had intestinal immunephenotype. In two cases MSI-low status was detected and in one case—MSI-high status. There were no hereditary anamnesis or presence of synchronous/metachronous tumours of other localizations. There were no cases with BRAF-gene mutation.
Conclusion: This study shows that MSI was detected in 16.7 % of sporadic AC and characterized tumours with intestine immunophenotype as often as in colorectal cancer. There were no mutations of BRAF-gene in our series. One case with high-level of MSI and loss of DNA-reparation proteins could be regarded as predictive factor of hereditary cancer.

PS-22-020
A mechanistic study to vasodilatory effect of Aegiceras corniculatum in vivo and in vitro models

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Objective: Hypertension causes endothelial dysfunction by impairing vascular relaxation eventually develops pressure on the heart. Endothelial disruption leads to inhibition of the release of vasodilators (nitric oxide) causes alteration in vascular cell functions. Cholinergic/noradrenergic receptors along with voltage-operated channels are involved in control in vascular targets.
Method: In the present investigation hypotensive effect of Aegiceras corniculatum, methanol and ethyl acetate extracts and their mechanism of actions were experimentally evaluated in in vivo and in vitro using normotensive rats and rabbit aortic rings.
Results: Methanol extract has shown tremendous effect at 10 mg/kg i.v. in reducing mean arterial blood pressure (MABP) 79.2 ± 1.8 mmHg as compared to control group of 128.2 ± 0.8 mmHg in rats, which was significantly suppressed (33 %) in the presence of atropine. Furthermore, methanol extract failed to produce vasodilation in endothelium denuded rabbit aorta and in the presence of L-NAME a nitric oxide synthase inhibitor in phenyleprine contracted tissue. Whereas, ethyl acetate extract exhibited inhibition (35–67 %) in % fall in mean arterial blood pressure (MABP) in the presence of nifidipine (0.3–0.9 mg/kg, i.v.). Antihypertensive effect of extracts were further supported by anti-platelet aggregation and eNOS activation.
Conclusion: Methanol and ethyl acetate extracts possess significant hypotensive and vasodilatory activity via muscarinic receptor dependent release of endothelium derived relaxing factor, nitric oxide and calcium channel blocking potential, thus the study validates traditional use of A. corniculatum against cardiovascular disorders.

PS-22-021

The CE-IVD next generation sequencing panel oncomine solid tumour DNA kit in routine clinical practice for non-small cell lung cancers and colorectal adenocarcinomas

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Objective: Target therapies have been effective in EGFR-mutated Non-Small Cell Lung Cancers (NSCLC) and KRAS/NRAS-wild type Colorectal Adenocarcinomas (CADK). Given the increasing number of clinically-relevant gene aberrations, single gene analyses are being outdated. NGS panels allow to simultaneously assess many cancer-related genes. We aim to evaluate the performance of CE-IVD NGS "Oncomine Solid Tumour DNA kit" (OST) in a single-center molecular diagnostic practice.
Method: We evaluated the OST panel (22 genes) on Ion Torrent™ NGS platform in previously analyzed retrospective and prospective cohorts of NSCLC and CADK (n = 90 and n = 100, respectively).
Results: We confirmed all the known gene alterations of the retrospective group and we identified additional gene mutations (range 2–4) in 68 samples (75.6 %). Eighty-five prospective samples displayed adequate DNA quantity for NGS analyses. Clinically-relevant gene mutations were detected in 75 % of these samples. All the mutations were validated with RT-PCR-based techniques.
Conclusion: NGS OST offered a greater numbers of clinically-relevant information with low DNA input and in a single batch, reducing time and costs of single gene evaluations. Although skilled personnel are required, this procedure provided a higher throughput of mutations in potentially actionable genes. CE-IVD mark allows a simple performance verification instead of a full validation.

PS-22-022

Opuntiol coated gold nanoparticles suppress Toll-like receptors (TLR-2/TLR-4) and Dectin-1 in adjuvant induced arthritic rats

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Objective: Rheumatoid arthritis (RA) is a chronic inflammatory disorder that results in severe cartilage damage and bone destruction in synovial joints. In recent years an important role for immune receptor in RA has emerged and Toll like receptors and Dectin-1 modulate adaptive immune responses especially TH17 that control immunopathology of RA. In the present study we set out to target immune receptors therapeutically using Opuntiol coated gold nanoparticles.
Method: Arthritis was induced by intradermal administration of heat killed mycobacterium tuberculosis (Complete Freund's adjuvant 0.1 ml) into the paw of wistar rats for 14 days in the absence and presence of Opuntiol nanoparticles. For the assessment of arthritic damage histology of knee joints and radiographic analysis were performed. The splenocytes cultures were prepared of all control and treatment groups, TLR2/4 and Dectin-1 mRNA expressions were analyzed using RT-PCR and TNF-α and IL-1β were analysed by ELISA.
Results: Opuntiol coated gold nanoparticles (10–30 mg/kg, p.o) decreases the expression of TLR2/4 and Dectin-1 significantly than that of control arthritic group. Lymphoid infiltration of synovium and vacuolization was suppressed along with reformation of joint spaces and reduction in soft tissues volumes and osteolysis.
Conclusion: Our findings suggest that Opuntiol coated gold nanoparticles reduced adjuvant induced arthritis in pleotropic manner, suppressing TLRs/Dectin-1 mediated joint inflammation.

PS-22-023

Comprehensive characterization of ischemia effects on gene expression in human liver

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Objective: Lack of standardization in pre-analytical workflow of tissue samples may induce gene expression changes unrelated to the disease, making biomarker development and validation difficult. A comprehensive gene expression study was performed to identify changes of RNA profiles during and after liver surgery.
Method: For evaluation of warm and cold ischemia effects 150 non-malignant human liver samples from 30 patients of two medical centers were snap-frozen at defined time points at beginning, during and up to 6 h after liver surgery. Expression profiling on Affymetrix-Human-Genome-U219-Array-Plates was performed, selected genes validated by RT-qPCR.
Results: A high patient-to-patient variability in expression levels was observed resulting in unpredictable changes associated with individual reactions to ischemia effects influenced by variables such as patient's biology or underlying disease. A subset of genes was identified with stable gene expression (e.g. FTL, HP) during the ischemia time course in both cohorts and validated by RT-qPCR.
Conclusion: Ischemia during and after surgery until sample preservation leads to gene expression changes in post-surgical samples that do not entirely reflect gene expression profiles in pre-surgical samples. A stable mRNA subset was identified that could serve as reference genes for validation of pre-analytical effects and assay development of new therapeutic target genes.

PS-22-024

Structural and functional impact of mutations in RAS Proteins

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Objective: To explore the impact of mutations on KRAS, HRAS and NRAS structure and their binding with GTP and GDP.
Method: Full length molecular models of wild type RAS proteins were constructed using iterative threading alignment. The models were refined

for the structural parameters and thermodynamic parameters. Subsequently, cavity analysis and molecular docking was conducted between GTP/GDP and RAS proteins.
Results: Superimposition of RAS proteins with its mutants at tertiary structure level did not show any considerable differences with RMSD deviation ranging from 0.06 to 0.10 Å. However, mutant residues superimposition showed noticeable differences in the spatial orientation. For example in KRAS, K5E, K5N, G10GG, G13D, Q22E, I36M, Q61H, Y71H, K117N, K147E, F156I and F156L showed considerable change in the orientation of residues. Similarly, wildtype GTP/GDP binding cavity holds volume and surface area as 680.64 Å3 and 1062.48 Å2. Where volume of G10GG, Y71H and K117N are 1123.71 Å3, 974.59 Å3 and 954.37 Å3 respectively. Similarly, surface area of the GTP/GDP binding region increased to substantial scale compared to wildtype. Subsequent molecular docking analyses verified this notion.
Conclusion: The data showed that certain mutations on KRAS, HRAS and NRAS genes leads to the significant structural changes on the encoded proteins which further entail perturbation in their binding with GDP and/or GTP.

PS-22-025
A multi-center assessment of a next-generation sequencing assay for detection of germline and somatic BRCA1 and BRCA2 gene variants from formalin fixed paraffin embedded samples
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Objective: We designed a new highly multiplexed amplification-based assay which allows detection of BRCA1 and BRCA2 gene variants in somatic and germline samples through semiconductor-based DNA sequencing. The current study summarizes the findings of over 20 research centers situated in 12 countries that were given early access to the new assay for analyses of their samples. The purpose was to evaluate the performance of the assay on a variety of sample types, including formalin fixed paraffin embedded (FFPE) samples, under realistic conditions.
Method: BRCA gene target regions, including all coding exons, were enriched via highly multiplexed amplification reactions. Libraries were prepared by using manual and automated preparation methods, followed by semiconductor-based sequencing on multiple instrument platforms. Single nucleotide and insertion or deletion variants were identified using available software solutions. Participants reported the concordance between the variants detected by the new assay and expected variants, identified by orthologous techniques.
Results: A high degree of coverage uniformity, 98 %, was achieved on both germline and somatic samples. Sensitivity of variant detection was 96.5 %, with positive predicted value of 94.2 %.
Conclusion: Performance of the new BRCA sequencing assay in this collaborative early access study indicates the panel, planned for official release soon, will help advance BRCA gene research.

PS-22-026
New histopathology assessment — do you see what I see?
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Objective: Molecular Pathology testing relies on the expertise of Histopathologists to determine samples are suitable for molecular testing and to provide an accurate estimation of the tumour nuclei content and cellularity within marked areas for DNA extraction. This is critical for high quality molecular testing and accurate interpretation of variants detected. As part of the delivery of the 100,000 Genomes project, NHS England funded an external quality assessment scheme (EQA) to measure the degree of variation and standardise approaches to tumour assessment.
Method: The pilot EQA was provided as an online module for colorectal and lung cancer tissue. Participants estimated the cellularity and percentage of tumour nuclei present on nine H&E slides and annotated regions for macrodissection for molecular testing.
Results: Highly variable results were submitted for both tumour types. Tumour nucleic estimations for the same sample ranged from 21 to 80 % and cellularity estimations were inconsistent. Areas marked for macrodissection were often impractical. Full results will be discussed.
Conclusion: These results demonstrate a need to measure the degree of variation with the aim to educate and standardise approaches to tumour and cellularity estimations and annotation. This will help prevent inaccurate molecular profiling and false negative results and promote high quality molecular pathology testing.

PS-22-027
The importance of independent cell free DNA reference standards to evaluate the performance of circulating tumour DNA assays and workflows
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Objective: Monitoring of circulating tumour DNA (ctDNA) is an emerging technique providing clinicians with a less invasive, faster and cheaper way to evaluate the clinical status and response to therapy of cancer patients. Of utmost importance will be the analysis of resistance mutations in advanced lung cancer patients under treatment with tyrosine kinase inhibitors (TKI). One of the main challenges in the adaptation of ctDNA assays is evaluating technical sensitivity of the specific detection method; because the amount of ctDNA may be underrepresented in a background of cell free DNA (cfDNA) of non-cancer origin.
Method: The genetically defined Horizon Quantitative Multiplex and cfDNA Reference Standards were used in our laboratory to establish the molecular detection workflow and to validate the technical sensitivity for the detection of mutations with low-allelic burden.
Results: The expected allelic frequencies of mutations including EGFR (p.ΔE746-750, p.V769-D770insASV, p.T790M, p.L858R), KRAS (p.G12D), NRAS (p.A59T, p.Q61K) and PIK3CA (p.E545K) were detected reproducibly with a custom-made targeted NGS panel for liquid biopsies which comprises hot-spot regions from 7 genes. The limit of detection of ctDNA assays (5, 1 and 0.1 %) were established.
Conclusion: Reference standards providing an independent control, enabling ongoing measurement of sensitivity and specificity of ctDNA assays.

PS-22-029
Anchored multiplex PCR enables detection of internal tandem duplications in FLT3 by next-generation sequencing
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Objective: Internal tandem duplications (ITDs) in FLT3 have been detected in over 20 % of acute myeloid leukemia (AML) cases and confer an aggressive phenotype. ITD sequences are identical to reference sequences and vary greatly in size and insertion point, rendering them difficult to detect by next-generation sequencing (NGS). We developed an approach using Anchored Multiplex PCR (AMP™) and bioinformatic analysis tools to amplify, detect and size FLT3-ITDs from DNA samples.
Method: We developed the VariantPlex Core AML library preparation kit with AMP probes encompassing the commonly mutated juxtamembrane domain and tyrosine kinase domain 1. Our novel de novo assembly algorithm in Archer Analysis was used to assemble sequenced libraries.

Results: The VariantPlex Core AML kit in conjunction with our novel detection algorithm showed both exceptional sensitivity and specificity in the detection of FLT3-ITDs in >2000 in silico datasets and >20 patient DNA samples extracted from blood. These results were concordant with standard capillary gel electrophoresis results.
Conclusion: Our data show that AMP enables accurate NGS-based detection of FLT3-ITDs from clinical DNA samples. As this approach can detect multiple mutation types from a single sample, our VariantPlex Core AML kit enables simultaneous detection of multiple mutations relevant in AML.

PS-22-030
Comprehensive thyroid and lung cancer profiling by anchored multiplex PCR-based next-generation sequencing
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Objective: Thyroid and lung cancers are driven by multiple types of genetic aberrations, including single nucleotide variants (SNVs), insertions and deletions (indels), copy number variants (CNVs) and fusions. Next generation sequencing (NGS) of target-enriched libraries is a highly sensitive and scalable method to detect these mutations. Anchored Multiplex PCR (AMP™) is a target enrichment strategy that uses unidirectional gene-specific primers and molecular barcoded adapters ligated to DNA ends for amplification. This enables amplification of both known and unknown mutations within target regions and increases coverage of target regions.
Method: We developed AMP-based comprehensive thyroid and lung (CTL) assays, VariantPlex™ and FusionPlex™ CTL, with probes covering relevant genes in thyroid and lung cancers.
Results: Our data show that parallel interrogation of DNA and RNA using VariantPlex and FusionPlex CTL assays, respectively, enables simultaneous detection of known and unknown SNVs, indels, CNVs and fusions from low-input clinical sample types. Furthermore, we show that characterization of gene expression, including detection of splice variants, expression imbalances and whole gene expression levels provides orthogonal verification of detected mutations.
Conclusion: These results demonstrate the utility of CTL assays to simultaneously and sensitively detect all types of mutations in clinically relevant genes in thyroid and lung cancer samples.

PS-22-031
Sensitive detection of copy number variants from FFPE samples by anchored multiplex PCR-based next-generation sequencing
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Objective: Copy number variations (CNVs) impact more of the cancer genome than all other mutation types combined. Next-generation sequencing (NGS) is an invaluable tool to detect CNVs. However, routine formalin-fixed paraffin-embedded (FFPE) storage of clinical specimens severely damages DNA, limiting detection sensitivity. We developed a target enrichment strategy based on Anchored Multiplex PCR (AMP™) to enhance NGS-based detection sensitivity of CNVs.
Method: AMP generates libraries for NGS by amplifying degraded DNA fragments, thereby increasing read coverage of target regions. We developed the Archer™ VariantPlex™ Solid Tumour kit with AMP probes to amplify 43 CNVs associated with a variety of carcinomas. We also developed the PreSeq™ DNA QC Assay to determine the integrity of genomic DNA prior to library preparation.
Results: By screening 139 FFPE samples, we show that NGS-based CNV detection sensitivity is primarily driven by the integrity of the input genomic DNA. Using optimal input amounts of genomic DNA, the VariantPlex Solid Tumour kit enabled detection of CNVs as low as 2-fold in FFPE samples and in samples with as low as 3 % tumour cellularity.
Conclusion: These results demonstrate that AMP-based NGS accurately detects low-level CNVs in genomic DNA from low-input clinical samples and from samples with low tumour cellularity.

PS-22-032
How low can you go? A snapshot of molecular pathology test sensitivity and specificity
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Objective: As an enhancement to the UK NEQAS Molecular Pathology External Quality Assessment (EQA) Scheme a reference sample was provided to enable laboratories to accurately assess the sensitivity and specificity of molecular pathology testing.
Method: The reference sample of formalin fixed paraffin embedded cells was custom manufactured by Thermo Scientific™ (AcroMetrix™) and was distributed a part of the Molecular Pathology EQA run. The sample contained 555 variants in 53 clinically relevant genes at allelic frequencies ranging from 1 to 17.9 % (average 5.3 %). Laboratories were invited to genotype and submit results to the Scheme, provide methodology details, list genes tested and the levels of detected variants.
Results: One-hundred and one laboratories reported 3008 test results on 53 different genes. As expected, testing for mutations with clinical relevance was prevalent. Few false positives were reported (0.7 %), however a number of laboratories did not detect clinically important variants within regions tested. The ability of methods to detect low level variants will be discussed.
Conclusion: The use of a standardized reference sequence has successfully enabled laboratories to measure the test sensitivity and specificity in-house and provided inter-laboratory comparisons of methodologies and limits of detection for the testing of solid tumour variants.

PS-22-033
Enabling PD-L1 IHC standardisation using defined reference standards and digital pathology
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Objective: There is growing concern regarding intra- and inter-laboratory reproducibility of Immunohistochemistry (IHC) assays performed with Formalin-Fixed Paraffin Embedded (FFPE) tissue sections. For new targets such as Program cell Death Ligand-1 (PD-L1) this need is becoming crucial, especially given the breadth of potential variables, including the range of companion diagnostic assays. There is a growing need to have defined, consistent and sustainable reference materials to support reproducibility and methodology transfer.
Method: Using CRISPR gene editing technology, we have developed precisely defined PD-L1 IHC HDx™ Reference Standards.
Results: PD-L1 IHC HDx™ Reference Standards have a range of controlled protein expression to understand the differences in assay performance, establish the practical lower limit of detection, support laboratories with tools to routinely monitor and standardize workflows, from instrumentation to assay to antibody. Cell lines are extensively characterised by molecular and protein assays. In addition, we use quantitative digital pathology to further define positive and negative core.
Conclusion: PD-L1 IHC HDx™ Reference Standards have been successfully used to control the performance of the four PD-L1 IHC assays currently used to support the PD-L1 drugs.

PS-22-034

Oral and esophageal tumourigenesis in conditional Notch1 knockout mouse model

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Objective: Recently, the genomic microarray and next generation sequencing technology have identified many genetic alteration associated with cancers. Among them, Notch1 inactivating mutation is frequently observed in head and neck squamous cell carcinoma. In normal epithelium, NOTCH1 is expressed in basal layer and seems to play an important role in their differentiation. Our previous study showed the reduction of NOTCH1 in the majority of human oral and esophageal cancers and precancerous lesions. In this study, we aimed to investigate the role of Notch1 in oral and esophageal squamous neoplasia.
Method: To study the effect of Notch1 reduction, we generated Notch1 conditional knockout (N1cKO) mice by CRISPR/Cas9 technology. The carcinogenesis assay induced by oral administration of 4-nitroquinoline-1-oxide (4NQO) was performed in the N1cKO mice and wild type littermate. The pathological changes of tongue and esophageal tissue were studied in different time points.
Results: After 4-NQO treatment, the hyperplastic and dysplastic changes of tongue and esophagus were noted in both N1cKO and wild type groups. However, the lesions found in the transgenic group showed higher number and more severity. The lesions exhibited reductions of NOTCH1, Keratin13 and Keratin 15, which were similar features in human lesions.
Conclusion: Our results indicate that inactivation of Notch1 appeared to increase the susceptibility of oro-esophageal squamous neoplasia, which suggests the function of Notch1 as a tumour suppressor in these tissue.

PS-22-035

Clinicopathologic and molecular features of mucosal melanoma: Data from a tertiary care center

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Objective: Mucosal melanomas (MMs) are rare neoplasms which constitute 1–2 % of all melanomas. Our aim was to determine molecular alterations in a large series of MMs, regarding their histopathological findings, and site of origin, along with prognostic parameters.
Method: Seventy-six MMs, diagnosed between 2000 and 2016, were collected. Several histopathological parameters were evaluated. BRAF (exon (ex) 15), KIT (ex 9,11,13,14,17,18), NRAS (ex 2,3), GNAQ&GNA11 (ex 4,5), and TERT promoter region (the positions of C228T and C250T) mutations were analyzed by direct sequencing.
Results: Our study group consisted of 27 sinonasal, 15 oral, 21 anal, 9 vulvar/vaginal and 4 urethral melanomas. The mean age was 64 with 33 males and 43 females. The number of patients with follow-up information was 48 (34 dead, 14 alive) and their mean overall survival time was 30.4 months. Among all patients, analysis concerning the molecular alterations have been completed for 35 cases. Mutations of BRAF, KIT, NRAS and TERT genes were detected in 1,1,1 and 3 cases, respectively.
Conclusion: MMs have poorer clinical outcomes than their dermal counterpart and also differ in their molecular profiles.

PS-22-037

Dysregulation of microRNAs may lead to lymph node metastasis of non-small cell lung cancer

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Objective: Lymph node metastases are a common feature of non-small cell lung carcinomas. It is that the different expression levels of microRNAs could predict the metastases to the lymph nodes and help us to understand the mechanisms of the NSCLC spread.
Method: Total RNA was isolated from FFPE samples of NSCLC patients without lymph node metastasis and of NSCLC patients with lymph node metastasis in operable stages. The RNAmicroarray technology was used to detect the changes in microRNA expressions. The online bioinformatics tools (TargetScan, miRDB, miRmap, DIANA tools and PicTar)were used for the microRNA target genes prediction to select the most deregulated proteins contributing to the metastatic processes.
Results: . We observed significant changes in the microRNA of miR-15a, miR-4749-3p, miR-4505, miR-4651 and miR-4690 between NSCLC patients without lymph node metastases and NSCLC patients with lymph node metastases. The microRNA deregulation may lead to the overexpression of proteins involved in cancer spread.
Conclusion: The expression levels of the miR-15a, miR-4749-3p, miR-4505, miR-4651 and miR-4690 in NSCLC may be used to characterize the patients with high risk of lymph node metastasis.

PS-22-038

Diagnostic and prognostic value of MST1R mRNA and protein expression in renal cell tumours

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Objective: To determine the diagnostic and prognostic significance of MST1R expression in renal cell tumours (RCT).
Method: Fresh-frozen tissue (RNA extraction), FFPE sections (immunohistochemistry) and clinical information from renal oncocytoma (RO) and renal cell carcinoma (RCC): chromophobe (chRCC), papillary (pRCC) and clear cell (ccRCC) (n = 120; 30 each). mRNA expression assessment by RT-PCR. Immunohistochemistry evaluation [score = intensity (0-absent, 1-mild, 2-moderate, 3-intense) × percentage (1- < 25 % 2-25-50 %; 3- > 50 %)] and classification as low (L-IHC, score ≤ 5) and high (H-IHC, score > 5) expression. Statistical analysis: chi-square, Kruskal-Wallis, Kaplan-Meier (log rank test), Cox regression.
Results: Significantly ($p = 0.01$) higher percentage of RO displayed H-IHC (n = 14, 47 %) compared to ccRCC (n = 4, 13 %), whilst the highest transcript levels were observed in ccRCC and pRCC, although without statistical significance ($p = 0.22$). No association between mRNA and IHQ expression was depicted. Shorter cancer specific (CSS) and disease free (DFS) survival were associated with H-IHC ($p = 0.002$; $p = 0.032$) in RCC, in univariable analysis. In multivariable analysis adjusting for stage, subtype, gender and age, only stage ($p = 0.002$) and subtype ($p = 0.037$) retained statistically significant for CSS, and stage ($p = 0.008$) for DFS. mRNA expression was not associated with CSS ($p = 0.089$) nor DFS ($p = 0.096$).
Conclusion: MST1R protein expression in RCT is heterogeneous, limiting its value as a diagnostic biomarker, notwithstanding significant differences between RO and ccRCC. The association between H-IHC and shorter DSS and DFS in RCC, in univariable analysis, entails validation in larger cohorts.

PS-22-039

Targeted next generation sequencing of multiplex PCR enriched hotspot genes in prostate cancer

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Objective: Prostate cancer (PCa) shows marked variability in clinical presentation, morphology and patients' survival. An individual assessment is necessary. New molecular markers are proposed for their ability

to predict outcome and targeted therapy in PCa. Therefore, the objective of this study is to identify the most frequent mutations in PCa using next generation sequencing (NGS).
Method: A total of 159 formalin-fixed, paraffin-embedded samples from primary PCa and distant metastases were obtained and used for tumour macrodissection and DNA extraction. Multiplex PCR was performed generating 1837 amplicons by means of the Qiagen Human Prostate Cancer Panel. NGS was then applied to analyse mutations of diagnostic relevant genes using the Illumina MiSeq platform.
Results: Each of the 32 prostate related genes was covered by 400 to 2000 reads. After filtering known single nucleotide polymorphisms (SNPs), silent mutations, and variants with low frequency (<5 %), we identified frequent mutations in MLL2, ZFHX3, TP53, PTEN, ZNF595, androgen receptor (AR), and MED12 genes.
Conclusion: Our results confirm the involvement of MLL2, ZFHX3, TP53, PTEN, ZNF595, AR, and MED12 mutations in PCa progression and their role as potential therapeutic targets. In particular, the identification of AR mutations is suggested to be an important approach for the recognition of castration resistant PCa.

PS-22-043
Molecular and clinicopathological analysis of myxoid liposarcomas by targeted next-generation sequencing
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Objective: Myxoid liposarcoma (MLS) is the second most common type of liposarcoma, accounting for 30–35 % of all LS cases. Over 90 % are characterized by a reciprocal translocation t(12;16) (q13;p11), resulting in a pathogenic gene fusion. The chimeric FUS-DDIT3 fusion protein is suggested to play a crucial role in MLS pathogenesis, although the specific biological function and the mechanism of action remain to be defined. We analyzed 106 comprehensive MLS samples to identify actionable somatic mutations.
Method: Targeted next-generation sequencing (NGS) was performed (Illumina MiSeq) to examine the mutational status of 31 cancer-related genes known to be frequently mutated across various neoplasms. In addition, we characterized the chromosomal FUS-DDIT3 rearrangements by RT-PCR and/or FISH.
Results: In summary, specific FUS-DDIT3 fusion transcripts were detected in >80 % of the samples and correlated to the clinicopathological data. Several oncogenic mutations were detected which have not been reported in MLS previously.
Conclusion: Our results indicate the occurrence of mutational aberrations besides the chromosomal FUS-DDIT3 hallmark. These appear not to be molecularly related to specific subtypes of fusion transcripts in terms of a molecular pattern. Molecular screening aiming at the detection of actionable mutations might represent a rational tool for the implementation of innovative molecular targeted therapeutic approaches in MLS.

PS-22-044
Targeted next-generation sequencing in extraskeletal myxoid chondrosarcoma: A molecular analysis reveals additional genetic aberrations
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Objective: Extraskeletal myxoid chondrosarcomas (EMCs) are rare mesenchymal tumours comprising <3 % of all soft tissue neoplasms. The molecular hallmarks of EMCs are various cytogenetic NR4A3 rearrangements. Over 75 % harbour a reciprocal translocation t(9;22)(q22;q12), resulting in a specific EWSR1-NR4A3 gene fusion. Despite their cytogenetic homogeneity, EMCs display a significantly heterogeneous clinical behaviour. We therefore analyzed a comprehensive collection of 25 EMCs to identify additional genetic alterations.
Method: We characterized the cytogenetic rearrangements by RT-PCR and/or FISH. Targeted next-generation sequencing (NGS) was performed (Illumina MiSeq) to examine the mutational status of 31 cancer-related genes known to be frequently mutated across various malignancies.
Results: Overall, fusion transcripts were detected in 22 of 25 samples (88 %) and the remaining showed a NR4A3 break-apart pattern. Sixteen were positive for the EWSR1-NR4A3 and six for the TAF15-NR4A3 fusion gene. Several oncogenic mutations were detected which have not been reported previously.
Conclusion: We confirm that cytogenetic NR4A3 rearrangements represent a consistent oncogenic event in EMCs. Our results indicate the occurrence of additional genetic aberrations which appear not to be molecularly related to specific fusion subtypes. Molecular screening aiming at the detection of actionable mutations might represent a rational tool for the implementation of novel molecular targeted therapeutic approaches in EMCs.

PS-22-045
An extremely rare case of concurrent BRAF V600E mutation driven hairy cell leukemia and melanoma: Case report and review of literature
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Objective: BRAF protein is a serine/threonine kinase with 766 amino acids. Approximately 15 % of human cancers harbor BRAF mutations as well as other BRAF anomalies (amplifications, fusions). Somatic mutations mainly occur in the catalytic kinase domain (CR3) and the predominant mutation is V600E which is the substitution of glutamic acid (E) for valine (V) as result of a mutation at codon 600 of the kinase domain. To our knowledge, the vast majority of the cancers have non-germline BRAF mutations.
Method: Here we describe a case of a 60 year old female with history of hairy cell leukemia who presented with aphasia and forgetfulness. A follow up Brain CT scan showed 3 distinct brain lesions which were found to be diagnostic of melanoma (confirmed by immunohistochemistry) with no evidence of a concurrent brain involvement by a B-Cell neoplasm. Molecular studies confirmed the same BRAF V600E mutation in both malignancies (Hairy cell leukemia and melanoma).
Results: Thereafter the patient was started on BRAF inhibitor treatment and is now symptom-free after 1 year of follow up.
Conclusion: Having two concurrent malignancies with a shared BRAF mutation is extremely rare and makes this an excellent example of a genomic marker-driven treatment in two histologically and immunophenotypically distinct tumours.

PS-22-046
BRAFV600 mutation detection in tricky melanoma samples using the new IdyllaTM BRAF Mutation Test
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Objective: The detection of BRAFV600 mutations has been crucial in patients with metastatic melanoma disease since the development of the BRAFV600 inhibitors. Recently, we have published a large series of melanomas analyzed for the BRAF status using the cobas® 4800 BRAFV600 Mutation Test and anti-BRAFV600E immunohistochemistry. In this study, we detected a series of cases where the employed

methods failed to detect the BRAF status, generating both false positive and negative results (Riveiro-Falkenbach et al., 2015). We aim to reanalyze these difficult cases using a new molecular method called IdyllaTM BRAF Mutation Test.
Method: IdyllaTM is a real time PCR that allows the detection of BRAF mutations directly from formalin-fixed, paraffin-embedded tissues.
Results: We were able to reanalyze 20 samples, including 8 primary melanomas and 12 metastases. Interestingly, IdyllaTM detected the BRAFV600 mutation status in 19 (95 %) of 20 difficult cases. The unique case where the BRAF status was not detected by IdyllaTM was a micrometastasis with less than1% of tumoural cells.
Conclusion: IdyllaTM is an efficient method for the detection of BRAFV600 mutation status in melanoma tumours. Further studies using this new molecular method would be of great interest to evaluate its applicability in routine practice.

PS-22-049
Prospective clinical validation of targeted next generation sequencing in molecular diagnostics of lung and colon cancer
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Objective: To validate in the clinical practice the applicability of targeted next generation sequencing (T-NGS) in molecular testing for lung and colon cancer.
Method: Ninety-two consecutive samples (lung: 67, colon: 25) prospectively collected between September and December 2015 were analyzed in parallel using current standard protocols (pyrosequencing for EGFR, KRAS, NRAS, BRAF, PIK3CA, HER2; Diatech; real time PCR for EGFR; Therascreen Qiagen) and T-NGS using Ion Torrent apparatus (Colon&lung panel, 22 genes, ThermoFisher).
Results: The standard and T-NGS approaches gave concordant results in 100 % of cases for the genes analyzed upon clinical request. T-NGS identified additional mutations in 70 cases (14 from colon and 56 from lung), 49 of these harboring mutations in genes of potential clinical interest, including MET, FGFR3 and DDR2. The diagnostic workflow for T-NGS did not impact in the turn-around time (7 days for both approaches) and in the effort for unit of personnel. The overall nude costs slightly increased for T-NGS as compared to standard procedure (38.180 vs 30.186 euros, respectively).
Conclusion: T-NGS is a valuable and feasible tool in molecular testing for lung and colon cancer. The increase in costs is balanced by the increase in the genetic data obtained, most of them of clinical relevance.

PS-22-050
Universal screening for Lynch Syndrome detection
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Objective: Current strategies for detecting Lynch syndrome (LS) include studying microsatellite instability and/or loss of expression of mismatch repair proteins in cases meeting clinical criteria for suspicion. We aimed to determine whether universal screening of patients with colorectal cancer (CRC) and endometrial cancer (EC) increases the detection rate.
Method: We used IHC to study PMS2 and MSH6 expression in 226 cases (n = 194 CRC and n = 32 EC) and then MLH1 and MSH2 in cases without PMS2 or MSH6 expression, followed by BRAF-Study/MLH1 promoter methylation in MLH1-negative cases. We considered candidates for LS: no expression of MSH6 with/without MSH2, PMS2 with/without MLH1, or MLH1, PMS2 and MSH6 when not epigenetic.
Results: We detected 27 (12 %) cases (n = 14 CRC, n = 13 EC) with at least one silenced protein. Of these, 16 (7 %) presented epigenetic silencing: 5 CRC (5/14 = 36 %) and 11 EC (11/13 = 85 %); and 11 (5 %) were candidates for genetic study: 9 CRC (9/14 = 64 %) and 2 EC (2/13 = 15 %). All MLH1-negative cases of EC (n = 11) were MLH1 hypermethylated. Of the 11 suspected LS cases, only 4 had clinical suspicion.
Conclusion: Suspected-LS detection rate: 5 %; 60 % of these cases were not clinically suspected; 7 % showed epigenetic instability; Loss of MLH1 expression in EC was always associated with MLH1 hypermethylation.

PS-22-051
Gene profiling identifies FBXW7/APC as a recurrent alteration in colorectal carcinoma
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Objective: Enormous strides have been made in defining genetic and epigenetic alterations in colorectal cancer (CRC). The discovery of several oncogenes/ tumour suppressor genes has provided key insights into the mechanisms of tumourigenesis. Increasing evidence shows that cancers exhibit unique gene mutation profiles. This study aims to further the understanding of the nature and heterogeneity of CRC and identify new therapeutic targets for the expanding field of personal genomics.
Method: Pathology of 80 prospectively accrued primary/metastatic CRC from Toronto General Hospital were reviewed and material was available for targeted sequencing using Illumina Trusight Tumour Panel of 26 cancer related genes and sequenced on Illumina MiSeq sequencer (read depth coverage = 500×).
Results: Mutations present in 70/80 samples (88 %) and many samples demonstrated combination of mutations(M) (2M = 21 %; 3M = 28 %; 4M = 16 %; 5M = 2.5 %). Frequent mutations identified in: APC (56 %), KRAS (45 %), P53 (43 %), PIK3CA (14 %), BRAF (10 %), SMAD4 (8 %) and FBXW7 (6 %). Combination mutations between KRAS and P53 (41 %) and KRAS, P53 and APC (29 %) identified. Interestingly, all FBXW7 mutations co-existed with APC mutations.
Conclusion: Next generation sequencing is a feasible way of detecting multiple mutations simultaneously. This allows for a better integrated view of genetic/genomic changes in CRC, providing opportunities for combination therapy and better understanding of molecular pathways impacted by these changes.

PS-22-052
The molecular tests in colorectal cancer (KRAS, MSI): Evaluation of practices in a large observational French cohort
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Objective: The pathologist contributes to achieve KRAS mutations analysis for anti-EGFR prescription in metastatic colorectal cancer (CRC) and to determine MSI (microsatellite instability) for Lynch syndrome diagnosis. The objective was to evaluate the real-life practices of these molecular tests in a French region in 2010.
Method: This observational survey was conducted in a population based sample of 2067 patients treated for a CRC. Molecular data were collected on the molecular genetic centers of the region. Indications of these tests and their therapeutic implications were analyzed.
Results: KRAS mutations analysis were performed in 68 % metastatic patients and in 11 % non metastatic. The non-metastatic patients with KRAS analysis often had poor prognostic factor (vascular or peri-neural invasion, higher level of tumour infiltration). Among metastatic patients,

57 % without KRAS mutation were eligible for anti-EGFR treatment. The patients of 60 and less years old had a MSI analysis in 40 % and, in the older, 5 % among those with family history of Lynch Syndrome cancer.
Conclusion: The indications of the molecular tests were in 2010, insufficiently respected particularly for the MSI status. KRAS mutation analysis, could be done prematurely if poor prognostic factors were present. The therapeutic implication of this test was also studied.

PS-22-053
How close are we to standardised extended RAS gene mutation testing? The UK NEQAS experience
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Objective: Since 2008, KRAS mutation status in exon 2, has been used to predict response to anti-EGFR therapies. Over recent years, a growing body of evidence has demonstrated that NRAS status, in addition to KRAS status is predictive of response. Despite this, are we really moving towards such an extended screening practice in reality?
Method: Data was analysed from four consecutive UK NEQAS for Molecular Genetics Colorectal cancer EQA schemes. Laboratories provided genotyping and interpretation results and information on which codons were routinely screened.
Results: At least 85 % of laboratories routinely tested KRAS codons 12, 13 and 61. Over the four runs, there was an increase in the number of laboratories routinely testing KRAS codons 59, 117 and 146. A similar pattern was seen for NRAS testing although fewer laboratories provided an NRAS service. There was a marked introduction of next generation sequencing technologies (NGS). Alarmingly, only 36.1 and 24.1 % of participating laboratories met the ACP Molecular Pathology and Diagnostics Group and ASCO guidelines respectively, for extended RAS testing in the latest scheme run.
Conclusion: Despite recommendations there has clearly been a delay in implementing 'extended testing' in clinical laboratories which could result in patients being subjected to harmful treatment regimens.

PS-22-054
Genetic diversity of HIV and its drug resistance in Karachi, Pakistan
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Objective: To study the current HIV drug resistance in IDUS and MSMs in Karachi, Pakistan.
Method: 100 HIV-1 infected patients who are on treatment were included in the current ongoing study. DNA was extracted from whole blood using DNA extraction kit and the extracted DNA was subjected to nested PCR to amplify the HIV RT region using specific primers. PCR products were sequenced using sequencing primers. Sequences were assembled, blast, cleaned and aligned using MEGA5 to reference sequences on HIV-1 database to ensure the quality of the sequences. RT gene sequences were entered into Stanford HIV drug resistance Database for analysis of drug resistance and mutations.
Results: 60 percent of the patients showed major and minor mutations to NRTI and NNRTI. According to our results virus is showing high level, potential low level, low level and intermediate resistance to both NRTI and NNRTI drugs such as Lamivudine (3TC), Emtricitabine (FTC), Stavudine (D4T), Didanosine (DDI), Abacavir (ABC), Tenofovir (TDF), Zidovudine (AZT) and Etravirine (ETR), Nevirapine (NVP), Tenofovir (TDF), rilpivirine (RPV) respectively.
Conclusion: Majority of patients receiving Anti- Retroviral drugs have shown major or minor mutations resulting in a drug resistant virus in our community. Data indicates that virus is becoming resistant to most of the drugs. Our results are showing High level to Potential low level resistance which indicates that HIV drug resistance is on rise on our part of the world. These results are alarming on contrary to the previous reported data in which hardly any drug resistance has been reported from this area.

PS-22-055
Beyond BRCA—HRD scoring using Affymetrix Oncoscan microarrays
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Objective: BRCA mutations confer sensitivity to platinum compounds and PARP inhibitors in serous ovarian carcinoma through homologous recombinational repair deficiency (HRD). HRD through other repair protein mutations, promoter hypermethylation, etc. lead to a plethora of analysis targets. Luckily, increased genome wide LOH is the common hallmark of HRD and could be used to identify BRCAwt/HR deficient patients suitable for PARP inhibitor treatment.
Method: After tumour DNA purification the BRCA1/2 mutation status was determined by Ion Ampliseq BRCA1/2 panel sequenced on the Ion Torrent Proton sequencer. Genome wide LOH detection and HRD scoring was performed using the Affymetrix Oncoscan FFPE microarray.
Results: HRD scoring is feasible within two working days in a typical molecular pathology laboratory. HRD scores are slightly higher than reported with the previous generation of microarrays. BRCA mutated and a subset of BRCA wild-type ovarian cancers showed high numbers of LOH regions.
Conclusion: At least a subset of BRCA wildtype but HRD high tumours can potentially be targeted by PARP inhibitors. Clinical repsonse rates of HRD low/high tumours need further evaluation in future studies. Reliable determination of the HRD score using freely available tools and workflows is a prerequisite to these studies.

PS-22-056
Detection of all major classes of MET deregulation by anchored multiplex PCR-based next-generation sequencing
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Objective: Deregulation of the proto-oncogene, MET, confers an aggressive phenotype in a variety of cancers. MET deregulation can be driven be gene amplification, overexpression, single nucleotide variants (SNVs), exon 14 skipping and fusions. We developed target enrichment kits for next-generation sequencing (NGS) to sensitively detect all types of MET aberrations from low-input clinical sample types, such as FFPE samples.
Method: VariantPlex™ and FusionPlex™ kits were developed based on Anchored Multiplex PCR (AMP™) to generate NGS libraries from DNA and RNA, respectively. Probes were designed to cover the MET gene and transcript, enabling detection of copy numbers and SNVs by VariantPlex, and fusions, exon skipping and expression by FusionPlex kits.
Results: VariantPlex and FusionPlex kits enabled detection of MET amplifications, confirmed by FISH, and the resulting overexpression in FFPE samples. Exon 14 skipping was also detected in FFPE and in cells, concomitant with splice site SNVs, and verified by RT-PCR. Lastly, we detected a GTF2I:MET fusion in an FFPE sample and a Y1253D activating point mutation in cells.
Conclusion: These results demonstrate the utility of Archer VariantPlex and FusionPlex kits to detect all types of MET mutations by NGS. Enhanced detection sensitivity enabled by AMP technology permits confident detection of mutations from low-input clinical samples.

PS-22-057

Diagnostic algorithm for detection of therapeutic driver mutations in lung adenocarcinomas: Comprehensive analyses of 205 cases with immunohistochemistry, real-time PCR and fluorescence in situ hybridization methods

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Objective: Along with the implementation of highly sensitive and/or mutation-specific antibodies, immunohistochemistry has been considered an alternative method for identifying driver mutations in lung adenocarcinomas. In this study, the feasibility of immunohistochemistry in therapeutic diagnosis in comparison with molecular-based methods was addressed.
Method: A total of 205 lung adenocarcinomas were examined for therapeutic driver mutations, including EGFR mutations and ALK and ROS1 rearrangements using real-time PCR, fluorescence in situ hybridization and immunohistochemistry in parallel. The association between these driver mutations and clinicopathological characteristics was also evaluated.
Results: We found 58.5 % of cases harboring EGFR mutations, 6.3 % with ALK rearrangements and 1.0 % with ROS1 rearrangements. EGFR mutations were more prevalent in female, non-smokers, and positively associated with micropapillary-predominant pattern; ALK rearrangements were significantly associated with adenocarcinomas with cribriform-predominant pattern, extracellular mucin production and signet ring morphology. Immunohistochemistry of EGFR mutations showed an excellent specificity but the sensitivity is suboptimal, while immunohistochemistry of ALK and ROS1 rearrangements demonstrated high sensitivity and specificity. No significant difference regarding the performance of different antibody clones was observed, except clone 43B2 showed a higher sensitivity than SP111 in the detection of EGFR mutations.
Conclusion: An immunohistochemistry-based lung adenocarcinoma testing algorithm in therapeutic diagnoses was proved to be applicable and effective.

PS-22-059

Clinical validation of a next generation sequencing panel for ovarian and endometrial tumours

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Objective: Molecular profiling studies of endometrial or ovarian tumours have identified molecular alterations with diagnostic, prognostic or theranostic value. Next generation sequencing (NGS) is an attractive technology for gene panel sequencing. However, transfer of NGS technology to an ISO15189-certified laboratory requires validation.
Method: We validated an Ion Torrent AmpliSeq custom panel comprising of 78 amplicons targeting hotspots of 16 genes altered in endometrial and ovarian tumours. We analysed specificity, sensitivity and precision using 2 commercial reference standards, 5 non neoplastic tissues, 16 ovarian tumours and 11 endometrial carcinomas. Finally, 10 samples tested in another lab for FOXL2 mutations were analyzed with our NGS panel.
Results: Sensitivity and specificity for detecting variants at an AF >4 % was 96.8 and 100 %, respectively for commercial reference standards. Among the 27 cases, all were successfully sequenced. All expected mutations were detected using our custom panel. The concordance for the detection of FOXL2 mutation was of 100 % with the other lab.
Conclusion: Overall, our NGS panel focused on molecular alterations observed in endometrial and ovarian tumours was specific and sensitive and can be incorporated in an ISO15189-certified laboratory.

PS-22-060

BRAF mutation testing quality in malignant melanoma: Results from a German, observational, multicentre study

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Objective: To assess the simultaneous impact of multiple parameters on routine BRAFV600 testing, we intended to develop a statistical model to predict mutation status at individual patient and testing centre level.
Method: Epidemiological data from routine BRAF diagnostics of 642 melanoma patients including clinical, histological, and mutational findings were collected in 28 institutes of which the majority is certified for BRAF testing (QUiP). We analysed this unique cohort for factors influencing BRAF mutation rates via multiple logistic regression. The resulting factors were integrated in a multivariate model to estimate the probability of BRAFV600 mutation.
Results: Baseline characteristics were typical of the melanoma population. Overall, BRAFV600 mutations were detected in 37.5 % of patients, of which the BRAFV600E being the most common variant (78.0 %). Origin of metastasis ($p = 0.0093$) and patient age ($p = 0.0143$) had the strongest influence in prediction of BRAF mutation status.
Conclusion: The rate of BRAFV600 mutations was highly variable across centres considering that diverse diagnostic assays and novel technologies have been applied. We identified patient age and location of metastasis as factors influencing BRAF testing results. Finally, our data suggest that the developed stats model might be utilized to monitor BRAFV600 mutation rate in local clinical routine. Further validation of this model is needed to confirm reproducibility and broader applicability in clinical routine. High quality BRAF-testing ensures optimal treatment for pts with melanoma in the context of approved and emerging combination therapies.

PS-22-061

Form follows function—morphological and immunohistological insights into tumour architecture

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Objective: In cancer cell biology, the architectural concept "form follows function" is reflected by cell morphology, migration and EMT protein expression pattern. Features of EMT are associated with tumour budding. Hereby, little is known about tumour buds and their migration pattern in 3D. This study aimed to redefine the processes of tumour budding and cell dissemination.
Method: Serial formalin fixed paraffin embedded tissue slices were used for virtual 3D reconstruction of pancreatic, breast, colon and lung adenocarcinoma and stained for PanCK, ZEB1 and E-Cadherin. Tumour cells were characterized for morphology (polarized/rounded/spindle-like) and EMT marker expression (ZEB1/E-Cadherin).
Results: The majority of tumour buds are 2D artifacts. Decreasing individual cell cluster size is the strongest determinant of increasing partial EMT features. Using a regression model, a strong inverse correlation of cancer cell cluster size and EMT features was confirmed. We were able to define a sequence of partial EMT at the invasive front (E-Cadherin loss, ZEB1 expression, rounded cell morphology).
Conclusion: Cancer cell dissemination is accompanied with histomorphological changes suggesting partial EMT in rare cancer cells. The sequence observed was loss of membranous E-Cadherin and shift to cytoplasmic expression, followed by nuclear ZEB1 staining, rounded/amoeboid morphology and finally mesenchymal—like spindle shape.

PS-22-062

A prospective comparison of the method of determining the molecular phenotype of breast cancer on the basis of multigenic panel OncoQuantex and surrogate ICH method

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Objective: Many genetic profiles have been developed to identify the molecular subtypes of breast cancer commonly known as Luminal A, Luminal B, HER2-Enriched (HER2-E) and Basal-like. Prospective studies are needed to determine their effectiveness compared to «surrogate» IHC method.
Method: We used the OncoQuantex BR RT-qPCR assay to investigate expression profile 523 tumours patients of Russian Scientific Center of Roentgenoradiology with breast cancer. OncoQuantex BR RT-qPCR assay—the method was developed by DNA technology and includes analysis of expression of the 24 genes. All samples were scored by IHC for estrogen receptor (ER), progesterone receptor (PR), Ki67 and Her2/neu (HER2) protein expression.
Results: The samples were divided into 5 classes based on analysis of expression level of 24 genes with using the multivariate Ward's method of "blind" clustering. The classification result was verified with the use of methods CHAID, (C&RT) and Discriminant Analysis. The coincidence of the classification results by different methods were more than 96 %. However, the coincidence with the classes defined by the method of ICH were significantly worse and were as follows: Luminal A −66,7 %, Luminal B (HER2/neu plus subtype) −55,8 %, Luminal B (HER2/neu minus subtype), HER2-E-67,5 %, Basal-like −87,5 %.
Conclusion: Comparison of the effectiveness of the classification of gene expression panels and "surrogate" method with the use of the IHC shows the necessity of switching to the RT-gPCR multigenic panel.

PS-22-063

Down-regulation of RUNX3 expression in solid tumours metastatic to the brain

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Objective: Brain metastasis remains a major driver of cancer mortality. The runt-related transcription factor 3 (RUNX3) is a tumour suppressor gene that has a critical role in epithelial-to-mesenchymal transition. We investigated RUNX3 RNA expression in selected solid tumours paired with their brain metastasis.
Method: A retrospective study was performed on archived tissue from cases with both primary tumour and brain metastasis available. RNA was extracted from formalin-fixed-paraffin-embedded tissue using a commercially available kit. RUNX3 RNA levels were tested using gene-specific primers and SYBER Green on tumours as well as control tissues by quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) with beta actin being the internal control.
Results: Forty samples from 20 adult patients with solid tumours (n = 20) and brain metastasis (n = 20) were analyzed. Solid tumours included lung adenocarcinoma (n = 15), invasive breast carcinoma (n = 4) and melanoma (n = 1). Male:female ratio was 3.3 (M = 14; F = 6) and the median age was 61 years (ranging from 39 to 80 years). The RUNX3 expression was significantly lower in the brain metastasis compared to the primary site ($p < 0.0001$).
Conclusion: RUNX3 loss likely has a potential role in solid tumour metastasis to the brain and poses a potential target for treatment. Larger scale studies are warranted to better understand the mechanism of this dysregulation.

Thursday, 29 September 2016, 09.30–10.30, Hall 11.3
PS-23 Ophthalmic Pathology

PS-23-001

Morphologic spectrum of conjunctival neoplasms in Jos, North Central Nigeria

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Objective: To document and describe the morphologic patterns of conjunctival neoplasms at the Jos University Teaching Hospital.
Method: A hospital based, retrospective study, involving retrieval of archival records, paraffin wax blocks and glass slides of neoplasms of the conjunctiva seen at the Histopathology laboratory of Jos University Teaching Hospital between January 2004 and December 2013. Tumour behaviour, histologic subtypes of malignancies, as well as age and sex distribution of lesions were represented using frequency tables, bar and pie charts.
Results: Most neoplasms (86 %) were malignant, with only 14 % being benign. Squamous cell carcinoma was the commonest malignancy, forming 88 % of cases. Malignant melanoma, Kaposi sarcoma, and Mucoepidermoid carcinoma, made up only 12 % of all cases. Conjunctival tumours were commoner in males than females, with a ratio of 2:1. Malignancies were rare before the age of 20 years with 81 % of cases occurring between the ages of 21 and 50 years.
Conclusion: Most neoplasms in this study were malignant, consistent with similar studies in other parts of the country. Few melanocytic tumours were seen in this study, with most being epithelial. This, suggest that pigmented conjunctival tumours mainly affected white patients, while epithelial tumours are more prevalent in countries with larger actinic exposure. Most cases of Squamous Cell Carcinoma in this study were within the ages of 21–50 years. This bracket is the most commercially viable and sexually active group and includes persons likely to be exposed to biological, carcinogenic agents [Human Papilloma and Human Immuno-deficiency Viruses] as well as those present in the environment.

PS-23-003

Neuron-specific enolase, synaptophysin and pRb (RB1) expression in retinoblastomas: Immunohistochemical study on whole tissue sections and tissue microarrays

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Objective: To perform a conventional whole tissue section and a tissue microarray study for neuron-specific enolase, synaptophysin and pRb (RB1) in a series of 22 tumours to test the value of these markers as a tool to confirm the diagnosis of retinoblastomas.
Method: A total of 22 cases were selected from the archives of IOBA Laboratorio de Anatomía Patológica Ocular over a 10-year period. A semi-quantitative assessment of the results of the immunohistochemical study was carried out according to the following scheme: Fraction of stained cells: rare, <25 %, between 25 and 75 %, >75 %. Staining intensity: negative, weak, moderate, strong.
Results: For neuron-specific enolase, 17 retinoblastomas (77 %) showed 75–100 % positive cells. For synaptophysin, 20 tumours (91 %) showed 75–100 % positive cells. For pRb (RB1) one case was positive in more than 75 % of tumour cells. High levels of agreement were achieved between the results found in tissue microarrays and those obtained from standard whole tissue sections for all three markers.
Conclusion: Retinoblastoma cells express neural/neuroendocrine markers (neuron-specific enolase and synaptophysin). Strong and diffuse

pRb (RB1) positivity is not related with a less aggressive behaviour according to the pathologic classification (pT) of retinoblastomas. To the best of our knowledge, this is the first tissue microarray study performed in retinoblastoma samples.

PS-23-004

Morphological spectrum of orbitoocular diseases in a tertiary health centre in Keffi, North Central Nigeria

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Objective: The objective of this study was to carry out a clinicopathological analysis of the ocular lesions requiring biopsy seen in the Department of Histopathology, Federal Medical Centre (FMC), Keffi, in North Central Nigeria.
Method: A retrospective review of the clinicopathologic profile of orbitoocular lesions diagnosed at the FMC, Keffi, was done. Clinical and pathological data were obtained from the patients' clinical records and original biopsy reports, respectively.
Results: Sixty-six cases of orbito-ocular lesions were reviewed for this study. Of the 54 cases investigated, 28 were HIV negative while 26 were HIV positive. There were 30 cases of Ocular Surface Squamous Neoplasia (OSSN) with a male-to-female ratio of 0.9 : 1. Squamous cell carcinoma (SCC) was the most frequent OSSN with 17 cases. The mean age of cases of SCC is 37.1 ± 7.6 SD (years). The mean age of carcinoma in situ is 35.8 ± 11.4 years.
Conclusion: There was no significant difference in the sex distribution of patients with OSSN. It is probable that a diagnosis of squamous cell carcinoma may be encountered in about a year after diagnosis of a carcinoma in situ especially if the in situ carcinoma is left untreated or improperly treated.

PS-23-005

Choroidal pigmented ganglioneuroma in a patient with neurofibromatosis type 1: A case report

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Objective: Ganglioneuroma is a rare benign tumour of the choroid. A few cases of choroidal ganglioneuroma have been reported in association with neurofibromatosis type 1. We present a case of a patient with orbital neurofibroma and choroidal pigmented ganglioneuroma.
Method: A 26-year-old man with facial neurofibromas previously operated on, presented for Left eye blindness, pain along with exophthalmos. An Orbital exenteration was performed.
Results: The globe of the eye was extremely distorted on gross examination. The choroid was remarkably thick. The histological examination showed a choroidal cellular proliferation, consisting of bundles of spindle pigmented cells admixed with clusters of large cells with vesicular nucleus and prominent nucleoli resembling ganglion cells with no atypia or necrosis. Mitoses were absent. Immunohistochemical study revealed positivity of these two populations for S-100 Protein and synaptophysin. Some spindle cells were positive for MART-1 and HMB-45. Ki-67 index was very low (<1 %) The diagnosis of choroidal melanoma was ruled-out. Diffuse and plexiform neurofibromas were found in the periocular and orbital soft tissue.
Conclusion: Choroidal pigmented ganglioneuroma is one of the ocular manifestations of neurofibromatosis type 1. This extremely rare entity should be included in the differential diagnosis of uveal tumours. Careful examination and immunohistochemistry are essential to rule-out choroidal melanoma.

PS-23-006

HEL expression and morphometric design of lacrimal gland in a diabetic rat model

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Objective: Diabetes mellitus is often correlated with alterations of lacrimal gland components, tear film and ocular surface; their pathogenic basis often suggests signaling pathway changes associated with oxidative stress which contributes as major trigger of severe lacrimal gland injury. Our study assess whether the diabetes effects on rat lacrimal gland were mediated by oxidative stress involvement, exploring biomarkers of lipid peroxidation and identifying the diabetic alterations in rat lacrimal gland.
Method: Diabetes was induced in Wistar rats with a single intravenous streptozocin. Oxidant status was determined. The lacrimal gland samples were removed at the end of the experiment, H&E stained and histopathological exam was performed using a Nikon Eclipse 50i light microscope. Immunohistochemistry was used to assess HEL expression in lacrimal glands of normal and diabetic rats.
Results: Lacrimal gland morphology in diabetic rats was altered, acinar and ductal structures presented different degrees of histological changes, glandular epithelial height decreased and lipofuscin deposits were frequently observed. HEL was expressed in lacrimal gland of diabetic rats, more frequently in a periductal and vascular endothelium distribution.
Conclusion: Histological changes and the expression of oxidative markers in lacrimal gland of diabetic rat strongly suggest a correlation between diabetes mellitus, oxidative stress and glandular functional decline; it also provide evidence of a tear film disfunction.

PS-23-007

IgG4-related chorioretinitis: A case report

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Objective: The IgG4-related disease is a specific inflammatory disorder characterized by the presence of elevated serum IgG4, inflammatory infiltrates rich of IgG4-positive plasma cells and fibrosis. Only single cases of uvea and retina involvement in IgG4-related disease were reported. We report a rare case of IgG4-related disease with involvement of the eyes, salivary glands, sphenoid sinus and lymph nodes.
Method: 57 years old female presented with a history of right submandibular gland enlargement. Later exudative retinal detachment of the right eye was diagnosed together with the left submandibular gland enlargement and a lesion within the right sphenoidal sinus. Both glands and a lesion were excised and histology showed lymphoid hyperplasia.
Results: 6 months later decrement in visual acuity of the left eye was diagnosed. Ophtalmoscopy and optical coherence tomography showed proliferation of the pigment epithelium and fibrosis. PET-scan showed enlarged right axillary and right pulmonary lymph nodes. Systemic nature of the disease rise the suspicion of IgG4-related disease.
Conclusion: Histology of the previously excised lesions was reviewed and IHC was performed. Salivary gland lesions showed brisk lymphoid and plasma cell infiltration, storyform fibrosis and obliterative phlebitis. IHC showed many IgG4-positive cells. Also serum IgG4 was elevated up to 454 μg/ml. Systemic corticoids was prescribed.

PS-23-008

Primary orbital leiomyosarcoma: Report of a rare case

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Objective: Primary orbital leiomyosarcoma is an exceedingly rare tumour. To our best knowledge, only 12 cases have been described in literatures.
Method: Herein we present a case of primary leiomyosarcoma arising in intraconal space of an orbit.
Results: A 55-year-old male presented with decreased vision and discomfort of a right orbital area for 3 weeks. On funduscopic examination, huge retrobulbar mass was suspected. Imaging studies revealed a 2.4 cm sized well-defined ovoid mass located in the right orbit, intraconal space. Surgical resection was performed. Histologically, the tumour was consisted entirely of bundles of spindle cells showing narrow, interlacing fascicles. The tumour was characteristic of prominent nuclear palisades reminiscent of Verocay bodies. Individual nuclei showed moderate atypia and plentiful mitotic figures throughout the field, up to 24/10 high power field. Pathologic differential diagnosis included Schwannoma with malignant transformation, cellular variant of Schwannoma, meningioma and other soft tissue tumours, such as leiomyosarcoma and solitary fibrous tumour. Immunohistochemically, the tumour cells were positively stained for smooth muscle actin, smooth muscle myosin heavy chain and negative for desmin, S100 protein, glial fibrillary acidic protein, EMA and CD34. Based on these findings, leiomyosarcoma was diagnosed.
Conclusion: As demonstrated by our case, leiomyosarcoma can arise in orbit and histologically mimic Schwannoma, thus needing careful examination. Moreover, leiomyosarcoma should be considered in the differential diagnosis of orbital tumours.

PS-23-009
Histopathological findings regarding absolute glaucoma
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Objective: The major characteristic of Glaucoma is the elevated intraocular pressure at a level high enough to provoke tissue damage causing optic neuropathy, with a highly specific excavation of the optic disc that leads to a progressive loss of visual field. The loss of sight in absolute glaucoma is also caused by the degeneration of the retinal ganglion cells.
Method: A delicate balance exist between the production of aqueous humor and its outflow from the eye through the trabecular meshwork and the Schlemm canal. Accessory pathways are the iris vessels and the posterior uveoscleral outflow via the ciliary body and the vortex veins. If these routes are affected, the intraocular pressure increases and the patient presents with glaucoma associated symptoms.
Results: We report the case of a 54-year-old male presenting with painful Absolute Glaucoma of the right eye, that required enucleation, associated with cataract and Rubeosis Iridis. A standard Hematoxylin-Eosin stain exposed the following: marked atrophy of the nervous fibers that compose the optic nerve, outward bulging lamina cribrosa, and mixoid degeneration of the optic nerve disc, glaucomatous retinal atrophy and iridocorneal sinechiae.
Conclusion: This case displayed a plethora of histopathological elements in order to safely diagnose end stage glaucoma with buphthalmos and severe degenerative changes.

PS-23-010
Retinoblastoma in Sudanese Patients: A clinicoopathological study in one eye centre
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Objective: To study the histopathological pattern of retinoblastoma in relation to demographic data and clinical presentation.
Method: This is a descriptive retrospective case series study of 54 retinoblastoma patients conducted over 2 years in Makkah Eye hospital (Main Eye Center in Sudan). Data was collected from the hospital records. Paraffin embedded blocks and slides of cases were reviewed.
Results: The patients' ages ranged from 3 months to 10 years, with a peak at 4 years of age. The mean age of 3.4 years (±1.68SD). Half of the cases presented with a mass, followed by leukoria (40.7 %) and proptosis (9.3 %). All our cases underwent removal of eye; 5 of whom had fungating mass with extra-ocular extension that necessitate exentration. All the cases had one or more poor prognostic histologic feature(s) (necrosis, extra-ocular extension, calcification, optic nerve involvement and involvement of the sclera, choroid and ciliary body).
Conclusion: The commonest age of presentation of Retinoblastoma is 1–9 years with a peak at 4 years. All our cases underwent removal of the eye and all have poor histopathologic prognostic features. Our results are in conformity with the African literature, but is different from American and European findings.

PS-23-012
Orbital small B cell lymphoma chronic lymphocytic leukemia like
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Objective: Primary orbital lymphoma is a rare disease and accounts between 8 and 15 % of extranodal presentations. It's the most common malignant orbital tumour in adult (10 %). We aim to describe the epidemiological and clinicopathological caracteristics of this entity.
Method: We report a case of a 31-year-old women who presented exophthalmia since 3 months.
Results: Brain MRI showed a left 5 cm orbital tumour, including the muscles rectus superior, the lateral rectus muscle and the lacrimal gland. The biopsy revealed fibro fatty tissue with diffuse tumour infiltration of small lymphocytic cell, to scant cytoplasm and round hyperchromatic nucleus. Immunohistochemistry showed positivity of tumour cells for CD20, CD23 and CD5. The diagnosis was lymphoma B-small cell chronic lymphocytic leukemia cell type (LLC). The patient had 4 cycles of CHOP chemotherapy with good response and consolidation radiotherapy. The evolution was marked by recurrent proptosis 9 years later. A biopsy with pathologic examination confirmed the lymphoma infiltration type LLC. FCR chemotherapy was prescribed.
Conclusion: The orbital lymphoma is a rare and often indolent disease. The common orbital lymphomas are MALT. LLCs are extremely rare. The diagnosis is made by histological and immunohistochemistry exam. Orbital MRI and or CT reveal tumour extension and guide therapy. The main differential diagnosis is inflammatory pseudotumour.

PS-23-015
The Value of 'en toto' globe submission in the assessment of high risk retinoblastoma cases and subsequent plan for treatment
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Objective: To evaluate the additional value and the importance of "en toto" globe submission in the assessment of choroidal invasion, which is a well-defined pathologic high risk factor in retinoblastoma cases.
Method: Retrospective histopathologic case series of 81 enucleated globes with retinoblastoma, examined between January 2010-December 2013. Inclusion criteria: Retinoblastoma enucleated globes examined "en toto", and had any type of invasion according to the American Joint Cancer Classification (more than pT1). The exclusion criteria: Retinoblastoma globes submitted prior to the implementation of 'en toto" globe submission by the end of year 2009.
Results: 30/81 globes were classified as high-risk cases: 8 cases had massive choroidal invasion in both the PO sections and calottes. 5 cases

have focal choroidal invasion in both. One case had massive choroidal invasion in calottes but not in the PO sections. 2 cases had focal choroidal invasion in the calottes but not in the PO sections. In the last three cases (10 %), the presence of focal/or massive choroidal invasion affected the management plan.
Conclusion: "en toto" retinoblastoma globe examination should be the routine accepted practice universally to avoid missing any choroidal invasion that might not be evident in the routine PO sections consistently submitted for the histopathological examination.

Thursday, 29 September 2016, 09.30–10.30, Hall 11.3
PS-24 Soft Tissue and Bone Pathology

PS-24-002
A clinicopathologic study of nine cases of Composite Hemangioendothelioma (CHE)
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Objective: Clinicopathologic features of nine cases of CHE are analyzed.
Results: The patients were seven females and two males with a median age of 36.0 years. The tumours arose in the foot or lower leg in 6 patients, in the face in two, and as multiple tumours in the left upper extremity in one. The tumours were composed of a complex admixture of histologic components resembling various vascular lesions. The predominant components, present in all cases, resembled retiform HE and epithelioid HE. Angiosarcoma-like areas were observed in three. Two congenital cases exhibiting multiple lesions had angiosarcoma-like components and an angiomatosis-like lesion. One each was associated with Kasabach-Merritt or Maffucci syndrome. Immunohistochemically, all tumours showed expression of at least two endothelial markers (CD31, CD34, factor VIII- related antigen and/or D2-40). Of eight that were followed up (median duration, 8.2 years), one tumour recurred locally. One was a recent case. To date, none of the patients have developed metastases. There was no difference in biologic behavior among cases with various combinations of histology.
Conclusion: CHE should continue to be regarded as a low-grade malignant vascular tumour, with significant potential for local recurrence, but little if any potential for distant metastasis.

PS-24-003
Clinicopathological correlation of tumour-associated macrophages in Ewing sarcoma
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Objective: Tumour-associated macrophages (TAMs) are known markers playing complex roles in tumourigenesis. TAMs can be subclassified into two functional phenotypes: proinflammatory M1 and tumour promoting M2 macrophages. The aim of this study was to determine the density of TAMs in tissue samples of Ewing sarcoma in relation to clinical variables and prognosis.
Method: Immunostaining for CD68 and CD163 was performed in tissues of 24 Ewing sarcomas (13 males, 11 females; age 2.0–27.0 years). The density of CD68 and CD163-positive TAMs were quantitatively assessed using NIS-Elements Software and stratified into three levels. Clinicopathological correlations were statistically analyzed.
Results: CD163-positive TAMs outnumbered CD68-positive cells (median of 130 vs 96, respectively). No statistically significant relationship was found between density of CD68-positive cells and clinical parameters. However, high-levels of CD163-positive TAMs were associated with lower disease stage and M0 status ($p = 0.034$ and 0.008, respectively). Multivariate analysis did not show any significant relationship between density of CD68 or CD163-positive cells and survival.
Conclusion: High-levels of CD163-positive macrophages correlated negatively with stage of Ewing sarcoma. CD163 proved to represent a sensitive marker of macrophages, but based on our results not specific for M2 phenotype, detection of which needs multiple staining using more markers.

PS-24-004
Cell cycle based prognostic model for progression-free survival of giant cell tumour of bone patients
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Objective: Accelerated cell cycle is often associated with aggressive tumour behaviour and poor disease prognosis. Giant cell tumour of bone (GCTB) is a locally aggressive osteolytic lesion, in which neoplastic stromal cells drive osteoclastogenesis and bone destruction. We studied the link between cell cycle progression marker expressions of the mononuclear cell fraction and progression-free survival (PFS) in GCTB.
Method: Duplicate tissue microarray samples of 154 cases (primary/recurrence 100/54) from 139 patients with a total of 40 progression events were immunostained for cell cycle markers and scored in digital slides. DNA index (ploidy) was measured with flow cytometry. Survival analyses were performed using Prentice-Williams-Peterson (PWP) gap-time models.
Results: In univariate analysis, ploidy ($p < 0.0001$) and the proportion of MCM2 ($p = 0.016$), cyclin D1 ($p = 0.022$), cyclin A ($p < 0.001$) and geminin ($p = 0.015$) positive cells showed significant association with PFS. The Akaike information criterion (AIC)-based best prognostic model (AIC = 271.6) included ploidy (HR = 6.20 [2.89–13.30], $p < 0.0001$), cyclin D1 (HR = 2.27 [1.10–4.71], $p = 0.0274$), MCM2 (HR = 2.64 [0.86–8.08], $p = 0.0901$); the second best (AIC = 271.8) also involved cyclin A (HR = 1.62 [0.81–3.23], $p = 0.1732$). Cell cycle phase progression was reflected by the positive association between gradually increasing hazards and elevated post-G1/S-phase cell fractions.
Conclusion: Testing for ploidy and cell cycle progression markers can assist in selecting GCTB patients with high-risk of progression.

PS-24-005
Expression of Emmprin (CD147) in Kaposi sarcoma cases: Relation with biologic behaviour
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Objective: Kaposi sarcoma (KS) is a vascular tumour of low grade malignant potential caused by an oncogenic-herpesvirus, Kaposi sarcoma-associated herpesvirus, also known as human herpesvirus 8. KS has 4 clinical types defined according to epidemiological and clinical features; classical, endemic, epidemic and iatrogenic KS. Classical KS the most common type in our country.
Method: 79 KS cases, diagnosed between January 1982–September 2013 at the Department of Pathology Hacettepe University Faculty of Medicine, were examined in terms of clinical and histopathological features. The expression of Emmprin / CD147, HHV-8 / LNA, CD31 and CD117 proteins was evaluated in these examples using immunohistochemical techniques.
Results: We demonstrated relationship between recurrence, histopathological parameters, disease stage and CD147 expression in this study. CD147 overexpression was found to be associated with advanced stage.

Conclusion: Emmprin / CD147 protein plays a key role in viral pathogenesis, cell migration and in the development of chemoresistance. Overexpression of CD147 protein is thought to be evidence in favor of progression. Significant correlation between nodular growth pattern, presence of solid fibrosarcomatous areas and the expression of CD147 was also seen in our study. Findings in our study can be important for targeted therapies in KS patients.

PS-24-006

The subclonal diversity in Ewing sarcoma exhibit also a different biology

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Objective: Ewing's Sarcoma (ES) belongs to the group of bone cancers defined by the existence of a certain EWS-ETS fusion gene. In this study we use the model cell line CADO-ES1 (EWSR1-ERG fusion gene) to characterize the tumour biology of the versatile ES side-population (SP). We aim to compare SP- and non-SP-cells to identify specific characteristics of the SP which points towards a tumour driving functionality of the SP. Due to some stem cell like properties of the SP fraction a comparison to MSCs is also performed.
Method: The CADO-ES1 cultured cells were FACS sorted to obtain the SP and non-SP fraction and characterized extensively by several assays. The SP fraction and several reference cell types were sequenced mainly on the transcriptomic level. Standard bioinformatics tools were used to conduct various types of analysis.
Results: Expression analysis indicated a significant down regulation of CHN2 expression in SP cells. ID2, a known ES marker is upregulated in SP cells. With a family of further 12 candidates the resulting ES biology is in several aspects supported by Hu-Lieskovan et al. (2005). There is also some evidence that the cells might be susceptible to acquire the additional fusion gene NAIP-OCLN.
Conclusion: The distinctive expression profile of the SP cells give a deep insight into the clonal differences of ES biology.

PS-24-007

High-risk Gastrointestinal Stromal Tumour (GIST) and Synovial Sarcoma (SS) display similar angiogenic profiles: A nude mice xenograft study

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Objective: We studied angiogenic factors and chemokine expression markers in nude mice xenograft models of a high-risk gastrointestinal stromal tumour (GIST) and a monophasic spindle cell synovial sarcoma (SS).

Method: Tumours pieces 3–4 mm were implanted into two sets of 14 nude mice (n = 28). Animals were sacrificed at 24, 48, and 96 h; and 7, 14, 21 and 28 days. We studied the histology, immunohistochemistry (HIF1A, Ki67, VEGF and their receptors), immunofluorescence of ligands CXCL12, CXCL9, CXCL10 and GRO; and their receptors CXCR4, CXCR3 and CXCR2, and other molecular factors.
Results: Histology: at 24, 48, and 96 h, necrosis was associated with a low proliferative index in both tumours. At 7, 14, 21 and 28 days after implantation, Ki67 expression increased inversely to HIF1A in both neoplasms. Angiogenic factors: VEGF family and their receptors were present in both tumours, but with different profiles. Chemokine ligands appeared earlier in GIST than in SS. Chemokine receptors stained more intensely than their ligands. The gene expression profile displayed two different gene clusters in the early and late phase after tumour implantation.
Conclusion: Early angiogenesis profile in a nude mice xenograft model of high risk GIST and SS displayed similar immunohistochemical and molecular profiles. This study was supported by grants of the 6th FP of the EC: EuroBoNeT Network, contract number: 018814, and from the Fundación Instituto Valenciano de Oncología (FIVO), Valencia, Spain.

PS-24-008

Intraosseous synovial sarcoma of the fémur: Morphological and molecular study

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Objective: Synovial sarcoma arising from bone is very uncommon. In the literature there are four cases, the first reported in 1997. We describe a bone Synovial Sarcoma in a young patient with molecular study.
Method: A 16 year old male presented with right thigh pain of 6 months. Osteolytic 14.5 cm tumour occupying the medullary zone with cortical insufflation at its top and cortical thinning and destruction of the distal area were identified. Several biopsies were performed; the histological diagnosis was spindle cell malignant mesenchymal neoplasm.
Results: Tissue samples were sent to the Hospital de la Santa Creu i Sant Pau, to Dra Silvia Bagué Rosell, by the FISH method determined the rearranged gene SS18 (18q11.2), however due to the rarity of the case and a questionable result of hybridization a second sample was submitted, the determination results were positive. The diagnosis was spindle cell sarcoma histological and molecular traits of monophasic Synovial Sarcoma.
Conclusion: Synovial cell sarcoma is one of the most common soft-tissue tumours in adolescents and young patients, however the intraosseous location is very rare and its histogenesis is unclear actually, the diagnosis is complex and include fibrosarcoma, leiomyosarcoma etc. Molecular biological techniques are indispensable for the diagnosis of certain monophasic tumours.

PS-24-009

Classification and diagnostic prediction of sarcoma subtypes using DNA methylation profiling

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Objective: Sarcomas represent a biologically very heterogeneous group of tumours. Methylation array-based profiling has been successfully employed by us to device a classification tool for primary brain tumours. Based on this experience, we expanded our analyses to a set of 600 genetically well-characterized sarcomas.
Method: Genome-wide methylation analysis was performed using the Illumina Infinium HumanMethylation450 BeadChip. Hierarchical cluster analysis identified the CpG probes most highly correlated with distinct sarcoma types. Based a on random forest algorithm, we developed a sarcoma classifier. Genome-wide copy number profiles generated from the raw array data provided additional diagnostic information.
Results: Based on their methylation profile sarcomas could be precisely separated into groups closely matching histopathological entities. All sarcomas with distinctive genetic alterations were assigned to entity-specific clusters, whereas sarcomas with complex genetic alterations clustered to either entity specific (e.g. in MPNSTs or leiomyosarcomas), or entity enriched clusters (e.g. in dedifferentiated liposarcomas). Interestingly, we identified novel methylation subgroups in certain sarcoma entities. Cross validation evaluating the robustness of our classes indicated an accurate prediction for >95 % of our reference cases.

Conclusion: This work illustrates that DNA methylation profiling has the potential to support and improve the classification of bone and soft tissue sarcomas.

PS-24-010

Giant cell fibroblastoma: A rare mesenchymal neoplasm

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Objective: Defined in 1982 by Shmookler and Enzinger, giant cell fibroblastoma (GCF) is a rare recurring but nonmetastasizing subcutaneous mesenchymal neoplasm that occurs predominantly, but not exclusively, in children.
Method: 4 year old male with a tumour in inner thigh, 1 year of evolution. Sonographically measured 70 mm, highly vascularized. Multiple fragments of soft tissue and skin are received.
Results: Microscopically is a poorly defined tumour in the subcutaneous tissue and dermis, epidermis respect. cellular areas alternating with myxoid stroma and dense collagen hypocellular areas. Formed by fusiform cells without pattern. The nucleus cells show slight anisokaryosis and fine chromatin without nucleoli. There are giant cells with hyperchromatic nuclei upholstering sinusoidal pseudovascular spaces. No necrosis or mitosis. The neoplastic cells express vimentin and CD34. Negative markers are: Actin, desmin, CD31, S100, CKAE1/AE3, BCL2, CD99, EMA, Factor XIII A, CD68). The cells lining the pseudovascular spaces are negative for lymphovascular markers (CD31, D2-40). The proliferative index with Ki67 < 10 %.
Conclusion: It is a rare tumour in close relationship with the Dermatofibrosarcoma Protuberans (juvenile form). Both share chromosomal abnormalities: t(17; 22)(q22; q13) with similar effects to PDGFB. It happens in male children, predominantly. A diagnosis clue is the irregular pseudovascular spaces upholstering by hyperchromatic multinucleated cells.

PS-24-011

Morphological, immunohistochemical and molecular profile of Desmoplastic Small Round Cell Tumour (DSRCT): 23 cases from a single institute

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Objective: Desmoplastic small round cell tumour (DSRCT) is a rare, highly aggressive neoplasm, generally located at the peritoneal cavity. In this study, histological, immunhistochemical and molecular profile of DSRCT are reviewed.
Method: We re-examined 23 cases of DSRCT and composed a 0.4 cm diameter tissue microarray. Slides were stained for desmin, AE1/3, cam5.2, EMA, WT-1, CD99, CD56, and calretinin using Leica Bond Autostainer. FISH for EWSR1 gene rearrangement (break-apart) and HER2 amplification were performed in 15 and 11 cases, respectively.
Results: Mean age was 25(6–66) and M:F ratio was 14:9. All cases were located in abdominal/pelvic cavity except one presacral mass. Unusual morphological patterns including epithelioid (3), clear cell (2), cribriform (2), comedo necrosis (5) were encountered. Immunohistochemically, tumour cells expressed desmin (23/23, 100 %), EMA (15/17, 87 %), Cam5.2 (12/15, 80 %), AE1/3 (10/17, 59 %), CD56 (9/17, 53 %), CD99 (3/18, 17 %), WT-1 (2/17, 12 %). All of the studied cases showed EWSR1 rearrangement. No HER2 amplification was present.
Conclusion: Diagnosis of DSRCT is usually straightforward given the clinical presentation, expression of EMA and desmin, and the presence of EWSR1 rearrangement by break-apart FISH. Pathologists should aware of that DSRCT may deviate from the unusual morphology, especially after chemotherapy.

PS-24-012

The GNAS in Ewing sarcoma

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Objective: To determine whether GNAS expression correlates with pathognomonic signs by analyzing mutations, methylation status, and G-protein α subunit (Gsα) expression of GNAS (guanine nucleotide binding protein/α stimulating) gene in Ewing Sarcoma (ES).
Method: Formalin-fixed paraffin-embedded (FFPE) tissue samples from 77 patients with primary ES were obtained, and were studied via methylation chip assay and direct sequencing of the GNAS gene and immunohistochemical analysis of Gsα. The mutation and methylation statuses of the GNAS gene were examined.
Results: We found that GNAS genes in ES tumour samples were less methylated than were normal controls. No mutations were detected at exons 8 or 9 of the GNAS locus complex on chromosome 20q13.3. Gsα expression correlated well with the methylation status of the GNAS gene. Interestingly, high Gsα expression was detected more frequently in samples from living patients than from decedents, although this was not statistically significant ($p = 0.055$).
Conclusion: GNAS mutation is not associated with the pathogenesis of ES tumours. Analysis of the methylation status of the GNAS gene and immunohistochemical Gsα expression suggests that hypermethylated GNAS gene (low Gsα expression) in ES may be related to unfavorable progression with a non-significant trend.

PS-24-013

Aneurysmal cyst of soft tissue: A case report

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Objective: Aneurysmal cyst of soft tissue(ACST) is a very rare benign soft tissue tumour that is histologically identical to aneurysmal bone cyst, but that shows no association with the skeleton. It arises in the deep soft tissues of the extremities of adults. Male and female individuals are affected equally.
Method: A 18-year-old women was admitted with a painless mass of left lateral thigh. Plain radiograhs demonstrated a peripheral calcified mass within muscle. Magnetic resonance imaging revealed 5.5 × 3.5 cm well-circumscribed mass with blood-filled cystic spaces.
Results: Histopathological examination showed multilocular cystic lesion. Blood or serous fluid-filled cystic spaces were divided by nonendothelial lined septae composed of a mixture of mononuclear spindle cells and osteoclast-like giant cells. Hemosiderin-laden macrophages were present. Mitosis and necrosis were not seen. A shell of well-formed bone was also seen at the periphery of the tumour. The spindle cells were positive for smooth muscle actin, vimentin and CD68. Multinucleated giant cells and macrophages were also positive for CD68.
Conclusion: If the surgical excision is incomplete, then local recurrence may develop, but aggressive local growth or metastases do not occur. The differential diagnosis of ACST should include giant cell tumour of soft tissue (GCTST), myositis ossificans(MO) and soft tissue osteosarcoma (STO).

PS-24-014

The evaluation of importance of new immunohistochemical markers for the diagnosis and differential diagnosis of mesenchymal tumours

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Objective: Mesenchymal neoplasms have diagnostic challenges for even the most experienced pathologists due to their rareity and their

morphology. The aim of this study is to re-evaluate the previously reported sarcomas in the light of new knowledge based on the 2013 WHO classification and newly found immunohistochemical markers and to determine of the importance of these new markers for the diagnosis of mesenchymal tumour.
Method: The soft tissue sarcoma cases (183) were diagnosed at the Pathology Department of Cukurova University Medical Faculty. These cases were re-evaluated based on 2013 WHO classification and new markers (TLE1, MUC4, MDM2, CDK4, TFE3, STAT6) that were applied as morphologic features.
Results: The diagnosis of 61 cases out of 183 was changed. Twenty of MFH were re-named as pleomorphic sarcoma and three of MFH cases were re-named as myxofibrosarcoma owing to the new WHO classification 2013. The diagnosis of the 38 cases was changed due to new markers that were mostly leiomyosarcoma and liposarcoma.
Conclusion: New markers have assumed an increasingly important role in diagnosis and differential diagnosis of soft tissue tumours. However, the contribution of all of these markers to the diagnosis depend on careful morphologic evaluation and the choice of proper markers by experienced pathologist.

PS-24-015
Ewing sarcomas highly express mortalin
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Objective: Mortalin (mitochondrial heat-shock protein 70/ mtHsp 70) is a multifunctional protein involved in regulating a wide array of cellular functions with important roles in cellular senescence and immortalisation. We investigated whether mortalin could play a role in the growth of different types of sarcoma.
Method: A tissue microarray constructed from a well-defined series of 80 bone and 401 soft tissue sarcomas of all types linked to a patient database was immunostained for mortalin. Immunohistochemical expression levels were determined using a scoring system based on staining intensity and cellular distribution. 36 separate pre-treatment, post-chemotherapy or metastatic Ewing sarcoma samples from 26 patients were arrayed; mean age 22 years, range 1–59 years old; 14 male: 12 female cases.
Results: High expression of Mortalin was identified in Ewing sarcomas. Seventy-eight percent of primary and secondary Ewing sarcomas displayed either moderate or strong and diffuse positivity. Weak staining was seen in 2 post-chemotherapy cases (5 %).
Conclusion: Our findings suggest that mortalin may be fundamentally involved in Ewing sarcoma tumourigenesis. Since it is known to bind and inactivate wild-type p53 and modulate the Ras-Raf-MAPK pathway, mortalin might provide a specific molecular therapeutic target for this aggressive sarcoma.

PS-24-016
Clinicopathological spectrum of a series of pseudosarcomatous lesions of soft tissues from a single tertiary cancer referral centre in India
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Objective: To analyze clinicopathologic features of a series of soft tissue pseudosarcomatous lesions.
Method: 112 pseudosarcomatous lesions (2004–2014), diagnosed at our institution, were included in this study, after review.In referral cases,initial and final diagnosis were compared to identify discrepancies(major and minor).
Results: The most common lesion was nodular fasciitis(NF)(34)(30.3 %), followed by pigmented villonodular synovitis(PVNS)(33)(29.5 %), myositis ossificans(MO)(16)(14.3 %), spindle cell/pleomorphic lipoma(SCL/PL)(12)(10.7 %), proliferative fasciitis(PF)(5)(4.5 %), ancient neurilemmoma/schwannoma(AN)(5)(4.5 %), proliferative myositis(PM)(4)(3.5 %) and atypical fibroxanthoma(AFX)(3)(2.7) in varying sites and age-groups. The most consistent clinicopathologic features,especially of NF, PF and PM were smaller-sized lesions,focally circumscribed, comprising spindle cells, arranged in fascicles with mild to moderate nuclear enlargement,extravasated RBCs and chronic inflammatory cells. Mucinous areas were seen in NF, ganglion cells in PF and zonation including reactive osteoid in MO. While AFX displayed atypical mitoses, PLs, ANs and AFXs revealed nuclear pleomorphism. Most number of major discrepancies were identified in diagnosis of MO(6/16)(37.5 %) and NF(9/34)(26.4 %); while minor discrepancies were commonly identified in NF(18/34)(52.9 %), followed by SCL(4/12)(33.3 %). Diagnosis of PVNS was 100 % concordant with that of referring laboratories/hospitals.
Conclusion: This study constitutes as the largest clinicopathological series of various pseudosarcomas from our country. NF was the most commonly identified lesion/tumour. NF, PF, PM and MO displayed overlapping histopathological features. MO and NF were commonly associated with diagnostic discrepancies from referring laboratories/hospitals.

PS-24-018
Gastric schwannoma: Report of three cases
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Objective: Mesenchymal tumours, in general, and schwannomas, in particular, are extremely rare among primary gastric neoplasm. We presented here three cases of gastric schwannoma with analysis of histological and immunohistochemical features.
Method: Review of hematoxylin-eosin slides of all gastric "mesenchymal tumours" from pathology files (2005–2015). Immunohistochemical studies for S100, α-SMA, KIT (CD117), desmin, vimentin and CD34.
Results: All patients were women (67-, 54- and 56-year-old) presented with mild abdominal pain duration of 3 and 6 months. Tumour size is as follows 4.0 × 4.5, 2.0 × 2.5 and 6.0 × 7.5 cm. One patient died of colon cancer 4 years later, second and third are free of disease 8 and 7 years. Histologically, spindle cells proliferation of moderate cellularity with diffuse chronic inflammation and peripheral lymphoid cuff typified each tumour. Nuclear palisading was barely visible. Mild cellular atypia, mitotic rate 7/50 HPFs were identified in the one case, mitotic rate of other tumours—5/50 HPFs. Immunohistochemically, in every case tumours represented "schwannoma" phenotype—expressed S100 and vimentin with negativity for CD34, KIT, SMA, and desmin.
Conclusion: The schwannoma differs from other gastric mesenchymal neoplasm and from soft tissue counterpart. The recognition of gastric schwannomas is important to differentiate them from CD117-negative gastrointestinal stromal tumour.

PS-24-019
Tenosynovial aspergillosis of the hand complicating corticosteroid injection: A case report
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Objective: Joint infection by Aspergillus is very rare and occurs usually in immunosuppressed patients. Only several cases of Aspergillus joint infection secondary to intraarticular corticosteroid injection. We report a case of tenosynovial Aspergillus infection associated with corticosteroid injection.
Method: A 79 year-old female was admitted due to swelling and heating sensation on the left third metacarpal area. She had a history of

seropositive rheumatoid arthritis, hypertension and osteoarthritis on both hands. There was no history of trauma. Swelling was developed 1 year before. Three times of arthrocentesis and triamcinolone injections were performed, but symptom was not improved. At that time culture for fungus was negative. She had difficulty in finger extension. MRI study showed a T1 low and T2 low abscess lesion on the dorsum of third metacarpal bone. Rupture of EDC tendon was found during operation. Synovectomy was done.
Results: Histologic examination revealed necrotizing granulomatous inflammation in the tenosynovium with acute angle-branched septate Aspergillus species, confirmed by PAS and GMS staining. Medication with voriconazole and itraconazole was tried for 6 months. She responded well her treatment.
Conclusion: We report a case of tenosynovial aspergillosis because of its rarity and relation to steroid injection.

PS-24-020
Kaposiform hemagioendothelioma arising in retroperitoneum: Case report and review of the literature
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Objective: Kaposiform Hemagioendothelioma is a rera vascular tumour of childhood that is locally aggressive but has little metastatic potential. The tumour is often associated with Kasabach-Merritt syndrome. We present a case of a kaposiform hemagioendothelioma that arose in retroperitoneum in an adult.
Method: Material: A 69-year old woman presented with a 6-months abdominal pain. A CT scan showed an abnormal soft tissue mass paralleling the lumbar spine measured 5 × 5 × 3.8 cm. The patients underwent surgical resection.
Results: Histologically the neoplasmatic mass composed of irregular, infiltrating nodules of compressed vessels, which modulate between areas resembling capillary hemagioma and Kaposi sarcoma. Mitoses were scarce. The neoplastic cells were positive for Vimentin, CD34, CD31 and S-100 protein while they were negative for SMA, D2-40 and HHV-8.
Conclusion: The absence of HHV-8 in kaposiform hemagioedothelioma underscores a different pathogenesis from Kaposi sarcoma, but because of its locally aggressive behavior operative excision if feasible would offer the best chance of cure.

PS-24-021
Myoepithelial carcinoma of the vertebrae: A case report and review of the literature
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Objective: Primary myoepithelial neoplasms of bone are rare entities. Although similar to salivary gland counterparts, they differ in immunophenotypic features, histologic criteria for malignancy and genetics.
Method: We report the case of a 48-year-old woman presenting with 1-month history of dorso-lombar pain. Magnetic resonance showed an L1 vertebral corpus mass with soft tissue extension. With no evidence of metastatic disease, she underwent complete L1 vertebrectomy.
Results: Surgical specimen showed an exophytic 5 × 4 × 3,5 cm tumour, protruding from the vertebral corpus. On microscopy, the neoplasm was composed of sheets of epithelioid and fusiform cells with clear cytoplasm and marked nuclear pleomorphism, convincing immunoreactivity for S-100 protein, epithelial membrane antigen (EMA), p63, smooth muscle actin and calponin. High mitotic count and extensive necrosis were identified. Considering the morphologic aspects and multifocal positivity for EMA, positivity for myoepithelial markers and absence of an extraskeletal lesion, the tumour was classified as a high-grade myoepithelial carcinoma arising in bone. Six months after surgery, local recurrence and lung metastasis were identified. Patient is currently under palliative chemotherapy.
Conclusion: Being exceedingly rare tumours, the possibility of metastasis from an extraskeletal myoepithelial carcinoma must always be considered. To our knowledge, this is the second primary vertebral bone myoepithelial carcinoma documented in scientific literature.

PS-24-022
Histiocytic sarcoma involving the central nervous system: A case report
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Objective: Histiocytic sarcoma is a rare, malign neoplasm of the lymphohematopoietic system that usually occurs in the skin, lymph node and intestinal tract. We describe more less common entity that; histiocytic sarcoma involving the central nervous system.
Method: 27 year-old young man was found unconscious at home, who uses cannabis. The lesion was located in the left parietoposterior meningeal area, measuring 19 × 17 mm. Total resection was applied to the tumour. On histologic examination showed numerous large pleomorphic malignant cells with areas of necrosis, numerous neutrophils and phagocytosis by tumour cells.
Results: Immunhistochemically, the tumour stained positively with antibodies directed against CD68, CD163, CD45, S-100 and did not stain with antibodies directed against CD3, CD20, CD15, CD30, CD56, CD7, CD79a, GFAP, VIMENTIN, PAX-5, CK, CAM 5.2.
Conclusion: We present a rare entity case of central nervous system histiocytic sarcoma has very aggressive behaviour.

PS-24-023
Synovial sarcoma: A case report of rare localization
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Objective: Synovial sarcoma (SS) commonly arises in the paraarticular regions. It usually located around knee and ankle joint, hip, shoulder and elbow. But SS has been described in various other locations. In such cases the correct diagnosis is often difficult. We report a case of primary SS revealed in the spermatic cord, since we found only a few descriptions of this tumour in an inguinal area.
Method: A 54-year-old man was presented with a slow growing slightly painful focal thickening of the left spermatic cord for the past 4 months. This lesion clinically was diagnosed as a cyst and surgically excised. It measured up to 3 cm in diameter. Cut surface was yellow-white with focal hemorrhages and firm. Histological and immunohistochemical studies were performed.
Results: Microscopically the tumour was biphasic and resembled SS. It had spindle cells arranged in fascicles and plump epithelial cells forming poorly differentiated glandular structures, cords and solid sheets. Immunohistochemical analysis showed that tumour cells were positive for panCK (particularly in the epithelial component), bcl-2, CD99 (more in the spindle cell component), CD57, Vimentin, S-100. At the same time, they were negative for CK20, CEA, Mesothelin, SMA, Desmin, AFP, CD45, Inhibin, WT1. Ki-67 was estimated at 60 %. Metastatic process was excluded.
Conclusion: Primary SS of the spermatic cord is extremely rare tumour, but it is necessary to aware of the possibility of its development in this area. Application of an immunohistochemical marker panel helps to avoid diagnostic mistakes.

PS-24-025

Gastrointestinal stromal tumours: Analysis of tle3 expression

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Objective: Spectrum of gastrointestinal stromal tumours (GISTs) varies from benign indolent neoplasms to frank sarcomas. The aim of this study is to estimate the expression of TLE3 in GISTs and to evaluate immunohistochemical correlations with clinicopathological parameters.
Method: Review of hematoxylin-eosin slides of 27 cases GIST followed by stratification into risk groups based on the grading scheme proposed by Miettinen and Lasota 2006. Immunohistochemical studies for TLE3 (DAKO).
Results: Tumours were located as follows stomach 14/51.9 %, small intestine 4/14.8 % and different location 9/33.3 %; according to the grading scheme tumours distributed as follows low-risk grade (LR) 9/33.3 %, intermediate risk (IR) 6/22.2 %, high-risk (HR) 12/44.4 %. TLE3 expression was identified in 3/33.3 % of LR GISTs, in 1/16.7 % of IR and in 4/33.3 % of HR GISTs. TLE3 expression ranged from 25 % in intestinal GISTs to 28.6 to 33.3 % in gastric and the third group GISTs. Gamma's correlation analysis did not reveal the associations either between TLE3 expression and tumour grade ($r = -0.017$, $p = 0.934$), as TLE3 expression and tumour location ($r = -0.04$, $p = 0.842$).
Conclusion: This study showed that TLE3 expression by tumour cells is not helpful for routine histopathology practice to predict the behavior of GISTs.

PS-24-026

Denosumab related histopathological or morphological changes can mimic malignancy

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Objective: Giant cell tumour is benign but local aggressive tumour seen as lytic lesion in epiphyseometaphyseal region of the long bones. Receptor activator of nuclear factor kappa-B ligand (RANKL), expressed by mononuclear stromal cells, is held responsible for the aggressive osteolytic nature. Recurrence in %15-50 and malign transformation in less than %1 of cases has been reported. Standart treatment ranges from surgical curettage to radical resection and denosumab treatment is recently introduced in unresectable, recurrent GCTs. Denosumab is human monoclonal antibody against the RANKL, which acts by blocking the interaction between osteoclastic and mononuclear cells and this results in a decrease in bone resorption.
Method: Four cases of denosumab-treated GCT were here presented. Pre- and posttreatment biopsies were evaluated and the therapy related histopathological changes were discussed.
Results: Histopathological changes included pseudosarcomatous atypia, giant cell loss and osteoid production.
Conclusion: Denosumab related morphological changes in GCTs can be sometimes very challenging and great care should be taken to avoid overdiagnosis of malignancy.

PS-24-027

Diagnostic approach to metastatic carcinomas of bone: Review of 426 cases

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Objective: Bone is the third common site for metastasis, with an unknown primary origin in 25–30 % of cases. Histopathological evaluation is crucial for differentiating from sarcomas, subclassification and for further molecular analysis.
Method: We reviewed 426 bone metastasizing cases diagnosed between 2000 and 2015 years.
Results: The most commonly involved bones were vertebra (n = 136;31.9 %), femur (n = 110;25.8 %), and pelvic bones (n = 76;17.8 %) while fibula (n = 1), mandible, clavicle and ulna localizations (n = 2, each) were rare. In 175 (41 %) cases, the primary site was confirmed either histopathologically (n = 113;26.5 %) or radiologically (n = 62;14.5 %). Breast (n = 36;20.6 %), lung (n = 19;10.8 %), kidney (n = 15;8.6 %) were the most common primaries. No statistical correlation was found between primary and metastatic site, although vertebra and femur were the most common sites for breast and lung cancers while prostate carcinoma metastasized to rare sites (as sternum, ulna). A comment addressing the primary site could be made by histology alone in 87 (20.4 %) cases (particularly in thyroid, renal cell, and squamous cell carcinomas) or by the aid of immunohistochemistry (n = 326;76.0 %).
Conclusion: Breast and lung cancers are the most common metastasizing tumours. Vertebra and femur are the predilection sites irrespective of primary tumour origin. An immunohistochemical panel consisting of cytokeratin-7, cytokeratin-20 and TTF-1 may be useful as a first step in diagnostic algorithm.

PS-24-028

PD-L1 expression in malignant mesenchymal tumours

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Objective: Programmed death ligand 1 (PD-L1) found on tumour cells has recently been introduced to have a key role in development and dissemination of many tumours, such as lung and breast carcinomas. In this study, we retrospectively analyzed PD-L1 expression among different types of sarcomas.
Method: After review of diagnoses of 222 cases of various sarcomas, representative areas were selected and 3–4 mm diameter tissue microarrays were composed from paraffin blocks. Slides prepared from microarrays were stained for PD-L1 antibody (Cell Signaling, E1L3N®) using Leica Bond Autostainer. Any membranous staining over %5 of the cells was regarded as positive.
Results: PD-L1 expression was present in 34 of 222 (15 %) sarcomas. 5/13(39 %) undifferentiated pleomorphic sarcomas, 6/18(33 %) malignant peripheral nerve sheath tumours, 5/16(31 %), dedifferentiated liposarcomas, 4/19(21 %) rabdomyosarcomas, 2/6(13 %) epithelioid sarcomas, 2/15(13 %) leiomyosarcomas, 3/26(12 %) synovial sarcomas, 1/18(6 %) myxoid liposarcoma, 1/2(50 %) extraskeletal myxoid chondrosarcoma, 1/3(33 %) alveolar soft part sarcoma, 1/3(33 %) parachordoma/myoepihelioma, 1/5(20 %) pleomorphic liposarcoma, 1/6(14 %) angiosarcoma, 1/8(13 %) Ewing sarcoma showed PD-L1 expression. Solitary fibrous tumour/hemangiopericytoma(18), Ewing-like sarcoma(6), epitelioid hemangioendothelioma(5), clear cell sarcoma(4), myxofibrosarcoma(4), low grade fibromyxoid sarcoma(2) were all negative.
Conclusion: We have shown PD-L1 expression in a subset of sarcomas. Clinical trials are necessary to further assess the effect of anti-PD-L1 drugs on sarcomas showing PD-L1 expression.

PS-24-029

Intravertebral benign notochordal cell tumour: A case report and differential diagnosis

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Objective: Intraosseous benign notochordal cell tumours are rare and the likely precursors of chordoma. A benign notochordal lesion is presented and the differential diagnosis between benign and malign notochordal lesions is discussed.

Method: A case of the intravertebral benign notochordal cell tumour is presented with clinical, radiological and histopathological features.
Results: A 42 year-old woman, was examined for lumbago and right leg pain with loss of bladder control. In MRI, a posterior corporeal lesion on L4 of 20 mm in diameter was in hypersignal T2, hyposignal T1, non-enhanced. The patient underwent tumour resection. The dura was compressed via the tumour. Histologically, the lesion consist of sheets of vacuolated or less vacuolated eosinophilic tumour cells with round nuclei. The immunochemical techniques revealed diffuse positivity of the cells with anti-AE1/AE3, LMWCK, protein S100 and vimentin.
Conclusion: The striking histologic similarity of the embryonal notochordal vestiges of intervertebral disks, and ecchordosis physaliphoras, benign notochord cell tumours, giant notochordal hamartoma, and chordomas render their various diagnosis difficult, especially on biopsy. Correlation of clinical, radiologic, and histopathologic studies is needed for accurate diagnosis and management of all lesions of notochordal origin.

PS-24-030
Clinical and histopathological difficulties in differential diagnosis of alveolar soft part sarcoma in a three-year-old patient: A case report
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Objective: Alveolar soft part sarcoma(ASPS) is an extremely rare tumour, with an enigmatic histogenesis, without a totally specific immunohistochemical profile, accounting for less than 1 % of soft tissue tumours overall.
Method: We present a case of a paediatric patient with a slow-growing supraorbital mass first catalogued as hemangioma; based on this assumption, laser therapy was performed in a dermatology clinic from another country, but the tumour growth accelerated. Surgical excision was decided with complete tumour removal. A first morphologic suspicion of ASPS was formulated and the case was sent to our department in consultation.
Results: Microscopic examination revealed large polygonal cells arranged in nests separated by slender fibrous septa, demonstrating a discohesive nature. The tumour cells have rounded nuclei with small distinct nucleolus, minimal pleomorphism and rare mitoses. The cytoplasm is finely granular with PAS+ vacuoles. The Gomori stain revealed a reticulin framework surrounding the tumour nests. Tumour cells were positive for INI1. Vimentin, desmin, SMA, MyoD1,AE1/AE3,CK8/18,EMA, Hepatocyte CD34,S100,HMB45,T311,CD30,GFAP, Chromogranin,Synaptophysin,CD56 were negative. Based on this findings, diagnoses like carcinoma, melanoma, paraganglioma and granular cell tumour were excluded.
Conclusion: Infrequently, ASPS diagnosis may be one of exclusion. Immunohistochemistry role in this process consists in invalidating entities with similar morphology.

PS-24-032
Diagnosis of inflammatory myofibroblastic tumour: Importance of histological features in the absence of ALK alterations
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Objective: Inflammatory myofibroblastic tumour (IMT) occurs primarily in soft tissue and viscera of children and young adults. In children ALK immunoreactivity is detectable in approximately 50 % of IMTs and correlates well with the presence of ALK rearrangements, whereas in adults ALK changes are much less frequent. Our aim is to highlight the importance of histological features unaccompanied by ALK alterations in IMT diagnosis.
Method: Two IMT cases (from a 60-year-old male and a 27-year-old female) were retrieved from our department's files by means of a parametric research (years 2011 to 2016). In addition to routine histological and immunohistochemical studies, we performed FISH to evaluate ALK rearrangements.
Results: IMT diagnosis was based on the presence of spindled myofibroblastic and inflammatory cells on an oedematous myxoid and collagenized background. Myofibroblastic cells exhibited immunoreactivity for actin and vimentin but failed to show either ALK cytoplasmic immunostaining or ALK rearrangements.
Conclusion: IMT is an uncommon neoplasm with a peculiar histological pattern and immunohistochemical profile that may or may not show ALK immunoreactivity and rearrangements. In the presence of characteristic histological and immunohistochemical features, the lack of ALK changes does not exclude the diagnosis of IMT in adults.

PS-24-033
Osteoarticular and soft tissue tuberculosis: An attempt of assessing of the main clinical morphological aspects
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Objective: The authors assessed retrospectively the main clinical and morphological aspects of osteoarticular (OATB) and soft tissue (STTB) tuberculosis (TB) discovered during the last 25 years in their pathology laboratory.
Method: The studied material consisted of bone, muscle, joint and ST samples obtained by biopsy or surgical excision from 99 patients confirmed with TB usually histologically, by Ziehl-Neelsen staining but, sometimes, by immunohistochemistry or PCR techniques.
Results: Patients with OATB were usually adults or elderly men, hospitalized mainly in orthopedics and rheumatology clinics whereas patients with STTB were rather women, in adulthood, hospitalized especially in general or thoracic surgery clinics. Granulomatous reaction was in both groups usually of well differentiated type, active, with epithelioid and Langhans cells, classical acidophilic caseous necrosis, centrally located and rarely with perifocal fibrosis. There was, however, a significant contingent of poorly differentiated or disorganized type granulomas in the STTB group. The morphological picture revealed in very rare cases the active and destructive profile of the bacillary aggression.
Conclusion: OATB and SSTB are a certitude, even the cases are rare. Therefore, one should pay attention to patients around 50 years aged, with swelling accompanied by local inflammatory symptoms of joints regions or ST structures accesssible to clinical examination.

PS-24-034
Diagnostics of chronic systemic inflammation (CSI) in patients with inflammatory joint diseases
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Objective: CSI is pathological process characterised by such indicators as the systemic nature of the damaging factor, generation of inflammatory mechanisms, persistent balance between alteration and resistance factors. Objectives. To evaluate the SCI occurrence rate in inflammatory diseases and to assess the possibility of SCI monitoring using individual homeostasis indicators.
Method: Patients gruops: rheumatoid arthritis (RA) (n = 26), ankylosing spondylitis (AS) (n = 27) and reactive arthritis (ReA) (n = 30) were examined. The levels of interleukins-6,8,10, TNFα, CRP, cortisol, myoglobin, troponin I and D-dimers in blood plasma samples were evaluated using CLIA (Immulite). Basing on these markers and applying an in-house procedure, an integrated criterion—a SCI Scale ranging from 0 to 8—was developed. The value of above 3 points indicated SCI.

Results: SCI was identified in 38.5 % patients with RA, in 20 % patients with ReA and in 11.1 % patients with AS. SIR is considered to be a key SCI feature, the applicability of individual SIR criteria for SCI monitoring was assessed. Table 1 shows the average SIR criteria values (excluding IL-10) to exceed those of the control group. However, the ROC analysis found the SCI diagnostic performances of individual indicators to be different for each nosology. Thus, the maximum AUC of 0.944 was observed for TNFα in RA, with that of 0.903 and 0.854 being observed for IL-6 in AS and for CRP in ReA, respectively.
Conclusion: SCI manifestations were found to be unstable. This, therefore, justifies the use of the suggested integrated CSI-Scale, rather than reliance on individual indicators, for CSI diagnostics.

PS-24-035
Prognostic relevance of myogenic differentiation, FNCLCC grading and MDM2 amplification levels in well-differentiated and dedifferentiated liposarcoma: A study of 70 cases
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Objective: We investigate the prognostic value of MDM2 gene amplification level, FNCLCC grade and myogenic differentiation in well-differentiated (WDLS) and dedifferentiated (DDLS) liposarcomas, in terms of local recurrence (LR), distant metastasis (DM) and overall survival (OS).
Method: 70 primary WDLS and DDLS cases were retrospectively re-evaluated and graded. Tumours were immunostained with 5 myogenic markers. MDM2 gene amplification level was assessed by fluorescence-in-situ-hybridization (FISH) analysis. Follow-up data and data on clinical variables were obtained by chart review. Univariate and multivariate analyses were performed.
Results: 49.2 % of all cases showed myogenic differentiation. 71.4 % of DDLS were FNCLCC grade 2, and 28.6 % grade 3. Average MDM2 amplification levels for WDLS and DDLS were 5.95 and 14.10 respectively. Univariate analysis demonstrated a significant correlation between FNCLCC grade and OS, LR and DM, and between MDM2 amplification level and both OS and LR. However, p-values were no longer significant after correction for confounding variables.
Conclusion: Univariate analyses were promising. Multivariate tests could not confirm prognostic impact of FNCLCC grade, MDM2 gene amplification level or myogenic differentiation. However, the limited numbers in our series preclude any robust conclusion. Therefore, we set up a multicentric collaboration with 2 sarcoma referral centers. Results from the extended cohort are pending.

PS-24-036
Correlation of microvessel density with proliferation index and clinico-pathological parameters in primary malignant bone tumours: A pilot study
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Objective: Bone tumours constitute 0.5 % of the total world cancer incidence, and remain a daunting challenge. A better disease free survival rate has been observed with the current multimodality treatment; however prognosis of patients with unresectable primary tumour, clinically evident metastasis or refractory to treatment remains dismal. In this regard, more beneficial prognostic factors and more effective therapeutic modalities are needed. Proliferation index is suggested as an important prognostic marker for bone tumours. Tumour growth and metastasis have been shown to strongly depend on angiogenesis, however, data regarding the relevance of angiogenesis and prognosis in malignant bone tumours are scarce and controversial. With this background in mind, objectives of present study were: 1. Assessment of intratumoural microvessel density (MVD) in primary malignant bone tumours 2. Correlation of MVD with tumour proliferation index (PI) and clinico-pathological parameters
Method: In this 2 year retrospective study; pre-treatment, archival paraffin embedded blocks of patients diagnosed with primary malignant bone tumours on histopathology (including osteosarcoma, chondrosarcoma and Ewing's sarcoma) were reviewed & clinico-pathological data was collected. Immuno-histochemical staining for CD34 (microvascular endothelial cells) and Ki 67 (proliferation marker) was performed. MVD assessment was done using Weidner's method.
Results: Out of total 22 cases, 10 were of osteosarcoma, 08 were chondrosarcoma and 04 were Ewing's sarcoma. MVD values for osteosarcoma and Ewing's sarcoma were higher than chondrosarcoma. In osteosarcoma, higher MVD values significantly correlated with higher PI as well as grade. No statistical significance could be elucidated in chondrosarcoma and Ewing's sarcoma.
Conclusion: Intrtumoural MVD has potential role as a prognostic marker in malignant bone tumours. Further studies comprising of larger sample size are required to explore the prognostic and therapeutic significance of angiogenesis in bone tumours

PS-24-037
Problems in the diagnosis of soft tissue tumours in resource-limited countries
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Objective: The diagnosis of soft tissue tumours (STT), particularly sarcomas, in under-served countries can be difficult due to several factors. These include lack of proper training in STT pathology; lack of properly equipped labs, unavailability of immunohistochemical (IHC) stains and lack of molecular techniques. The author conducted a survey among several pathologists from developing countries to investigate these difficulties.
Method: A questionnaire was sent to pathologists in Jordan, Lebanon, Egypt, Saudi Arabia, Libya, Sudan, Morocco, Algeria, Pakistan, Malaysia, and Indonesia. Questions were directed to the participants included inquiry about the number of STT they encounter annually; whether they have facilities for IHC, molecular techniques and electron microscopy; and if they have multidisciplinary meetings to discuss STT cases; and whether they have fellowship program for STT.
Results: 1. Many centers have relatively few number of cases (less than 30 per year), thus depriving the pathologists from the needed experience. 2. Most labs have IHC stains available, but the panels are limited. Some countries have erratic delivery of the reagents. 3. Most hospitals lack molecular techniques or EM facilities. 4. About half of the hospitals have "tumour boards" that discuss STT and other tumours. 5. No hospitals have fellowship in STT pathology except in Saudi Arabia. 6. Malaysia is the only country that centralizes all bone and STT treatment at one major referral hospital.
Conclusion: IAP and ESP have a responsibility to conduct educational workshops on STT in under-served countries. The speakers can teach the pathologists in these countries pitfalls in the diagnosis of STT, and the best utilization of IHC.

PS-24-038
The effects of intratendinous injections of corticosteroid into achilles tendon: An experimental randomized study in a rabbit model
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Objective: Controversies regarding the benefits and complications of the injection of corticosteroids (CE) for the treatment of tendinopathies. Our

aim was to evaluate the histological, biomechanical effects, and expression of metalloproteinases and interleukins on Achilles tendons of rabbits treated with CE.
Method: The Test Group with 37 rabbits underwent to injection of CE (1.4 mg of betamethasone) in the Achilles tendon of the right pelvic limb. Control Group 36 animals with one injection of saline solution (CP-Placebo Control) and the left Achilles tendon received no procedure (CN- Normal Control). Forty-eight hours after, the tendons were dissected and extracted at an extension of 4 cm from its insertion in the calcaneus bones. The expressions of metalloproteinases (MMP-1/MMP-2) and interleukins(IL-1/IL-6), biomechanical resistance (load x elongation parameters) and histomorphometric(HE, Picrosirius red) analysis, were all performed by observers unaware of the groups.
Results: Test Group had significant reduction MMP-2 expression compared to the both controls ($p = 0.027$). CP was an increase of thick collagen fibers in comparison with CN ($p = 0.041$). There was no additional significant statistical difference between the groups when comparing variables.
Conclusion: Decrease of MMP-2 expression after a single intratendinous injection of CE in the Aquilles Tendon of rabbits, suggesting a potential minor collagen degradation.

PS-24-039
Cigarette smoke exposure leads to bone resorption, matrix remodeling and a worsening in bone mineralization
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Objective: Since it has been described the adverse effects of cigarette smoking on bone healing, we aimed to evaluate the effects of cigarette smoke (CS) exposure on osteogenesis.
Method: C57Bl/6 male mice were exposed to CS for 45 days, for 30 min (12 ± 1 cigarettes), 2 times/day, 5 days/week. The Control group was exposed to ambient air at the same times. At 46th day, animals were anesthetized for euthanasia and the right tibae were surgically extracted for analysis and part of them were included in methyl-methacrylate and stained with toluidine blue for measuring structural parameters, bone resorption and mineralization and the others were decalcified and stained with Picrosirius for evaluation of collagen amounts.
Results: Animals exposed to CS showed a higher amount of signals of bone remodeling, trabecular narrow-ing ($p = 0.0004$), smaller number of osteoblasts and osteocytes, larger number of osteoclasts and more vascular and cellular infiltration in the bone marrow ($p = 0.03$). Also, there was an increase in bone resorption with a concomitant delay in bone mineralization ($p = 0.01$). The collagen percentage analysis revealed an increase significantly in collagen amounts suggesting a bone remodeling process ($p < 0.001$).
Conclusion: The CS exposure promoted a delay in osteogenesis characterized by increase in bone resorption, decreased mineralization and an important collagen remodeling, compromising the turn over and density of bone.

PS-24-040
Synovial biopsy in etiological diagnosis of mono and oligoarthritis: A clinicopathological correlation
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Objective: Synovial biopsy was fist described by Forestier in 1932 when he obtained synovial tissue by introducing a dental nerve extractor in the joint through a large calibre needle. Nowadays, histological examination of synovial tissue, provided by closed needle or arthroscopic biopsy, can help to determine specific etiological diagnosis of arthritis. Our aim is to evaluate the efficiency of synovial biopsy as a diagnostic aid and determine the clinicopathological correlation.
Method: A retrospective study was performed including 146 cases of monoarticular/oligoarticular arthritis from 2005 to 2015. Clinical criteria for diagnosis of various joint diseases were followed.
Results: Degenerative (29.5 %) and rheumatoid (22.6 %) arthritis are the most common etiologies. Clinicopathological correlation was seen in 123 out of 146 cases, 100 % in infectious arthritis, 78.8 % in rheumatoid arthritis, 81.3 % in mechanic arthritis, 100 % in synovial amyloidosis and 100 % in synovitis of Behcet disease.
Conclusion: Synovial biopsy is a useful investigative tool that may give conclusive diagnosis with a good reliability.

PS-24-042
An unusual malignant tumour of the spermatic cord: Dedifferentiated liposarcoma with a large rhabdomyosarcomatous component
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Objective: Primary malignant tumours of the spermatic cord are rare entities presenting as painless scrotal or inguinal masses. The preoperative diagnosis is very difficult. Most of these tumours are sarcomas. We present a case of spermatic cord tumour that represented a real challenge for the pathologist, radiologist, orthopaedic surgeon and oncologist.
Method: A 72 year old patient underwent surgery in 2007 for varicose veins of the left calf. At the same time an inguinal, 3/3 cm, mass was discovered and resected.
Results: On initial morphological examination, based on a limited number of antibodies (CK, vim, S100, NSE), the tumour was diagnosed as biphasic, epithelial-mesenchymal malignant tumour. Two subsequent evaluations of the same tumour, abroad, diagnosed it as metastatic carcinoma and seminoma respectively, which prompted orchiectomy and radiation therapy. Two years later (2009), the patient was admitted to the hospital for a supra-subclavicular compressive mass, left upper limb oedema, which was suspected to be an infected hematoma. Histopathological diagnosis was high grade sarcoma. The case was reassessed by IHC and FISH and diagnosed as dedifferentiated liposarcoma with features of rhabdomyosarcoma (2010). The patient died 4 years after the first diagnosis.
Conclusion: We present a clinically and morphologically challenging case of spermatic cord liposarcoma. Rhabdomyosarcomatous component in a dedifferentiated liposarcoma is quite unusual. The particular IHC profile and the inadequate panel of antibodies used led to diagnostic errors followed by inadequate therapeutic management.

PS-24-045
C-Kit, CD34 & Alpha-SMA immunohistochemical features in classic Kaposi sarcoma and Kaposiform hemangioendothelioma
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Objective: This work aims to study the clinicopathological features of Kaposi sarcoma (KS) & kaposiform hemangioendothelioma (KHE) and analyze their immunohistochemical expression of c-Kit, CD34, α-SMA to differentiate between them, elucidate their histogenesis and discover molecules that can be targeted in treatment.
Method: Immunohistochemical staining of c-Kit, CD34, α-SMA was performed on cutaneous 10 classic KS & 8 KHE.
Results: KHE shows several dilated lymphatic channels, focal capillary formation, lack of nuclear atypia and mitosis within tumour cells. These

features help to exclude Kaposi sarcoma in spite of the kaposiform pattern of tumour cells. C-Kit was expressed by tumour cells in all KHE cases and in 60 % only of KS. All elements within both tumour groups expressed CD34 antibody. α-SMA was expressed by tumour cells in 70 % of KS cases and none of KHE.
Conclusion: C-Kit and CD34 seem to be reliable at labeling KS and KHE as they can help in diagnosis of these tumours in routinely processed tissue but they don't differentiate between them. If α-SMA also labeled the tumour, then KHE diagnosis can be ruled out. KS & KHE exemplify stem cell tumours that could give smooth muscle cell-like phenotype in KS. Anti C-kit therapy should be tested in KS & KHE to prevent recurrence.

PS-24-047
Superficial (cutaneous and subcutaneous) malignant neoplasms with EWSR1 rearrangement
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Objective: Primary cutaneous or subcutaneous extraskeletal Ewing's sarcomas-like tumours are extremely rare malignant neoplasms; current literature reports only a few isolated cases or small series. Although lower extremity is a relatively frequent site, a limited number of such cases of the foot have been reported.
Method: In the present study, we examined the clinicopathologic, immunohistochemical, molecular, and follow-up characteristics of 3 cases of superficial Ewing sarcoma-like tumours of the foot. One case was restricted to the dermis, two were located in both the dermis and subcutaneous adipose tissue.
Results: All studied tumours composed of cohesive sheets and trabeculae of small blue round cells with a vague rosetting pattern, slightly overlapping nuclei, finely stippled chromatin, and scanty cytoplasm with indistinct cytoplasmic borders. The tumours were strongly and diffusely positive for CD99 with a characteristic membranous staining pattern and negative for muscular and lymphoid markers. Two of three cases contained scarce cytokeratin-positive cells. One tumour showed focal reactivity for EMA and S100 protein. The diagnosis of extraskeletal Ewing sarcoma family tumour was based on histology, immunohistochemistry and molecular cytogenetics (FISH study using EWSR1 break apart probe). Differential diagnoses (carcinoma, melanoma, lymphoma, Merkel cell carcinoma, poorly differentiated synovial sarcoma, and rhabdomyosarcoma) were ruled out on the basis of morphology and immunohistochemical staining. The differential diagnosis with EWSR1-related myoepithelial neoplasms were discussed separately.
Conclusion: Cutaneous or subcutaneous Ewing sarcoma-like malignant tumours remain exceedingly rare neoplasms and they should taken in consideration in differential diagnosis of superficial located small blue round cel tumours.

PS-24-048
Histopathological features of four rare forms of chordoma
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Objective: Chordoma is an uncommon malignant bone tumour of notochordal origin, mostly in axial bones with characteristic histopathological features. Herein, 4 cases of rare forms of chordoma are presented.
Method: Case 1: A 58 year-old-male presented with pain in his sacral region. Imaging disclosed sacral mass. Histopathologic sections from resected specimen showed physaliphorous cells with, markedly atypical tumour cells, including pleomorphic giant cells, spindle cells and atypical mitoses with focal necrosis. By immunohistochemistry, tumour cells were positive for CK, S-100P and brachyury. INI1/SMARCB1 was retained. Diagnosis -pleomorphic chordoma. This patient died-of disease after 18 months. Cases 2 and 3: Two tumours were identified in the spine of a 34-year-old lady and in a 44 year-old male, respectively. Histopathologic sections showed areas of conventional chordoma juxtaposed to a high-grade spindle cell sarcoma. By IHC, differentiated chordomatous components in both tumours were diffusely positive for CK, EMA, S-100P and brachyury/T, whereas sarcomatous component was negative for these markers. Both cases were diagnosed as dedifferentiated chordomas. The latter patient, post-resection, received adjuvant RT, but died-of-disease after 14 months. Case 4: Another, 58-year-old-male patient presented with a soft tissue lesion in his left leg. Biopsy showed tumour cells, including eosinophilic and physaliphorous cells. By IHC, tumour cells were positive for GFAP, S100P brachyury and EMA (focally). INI1 was retained. Diagnosis of an extra axial, soft tissue chordoma was offered.
Conclusion: These 4 unusual cases expand the clinicopathological spectrum of chordomas. An index of suspicion with necessary IHC stains, including brachyury/T is essential to identify these rare tumours.

PS-24-049
High prevalence of autoimmune disease in the rare inflammatory bone disorder sternocostoclavicular hyperostosis
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Objective: Sternocostoclavicular hyperostosis (SCCH) is a rare inflammatory disorder of the axial skeleton, characterised by chronic sterile osteomyelitis associated with sclerosis and hyperostosis. We addressed the potential association with autoimmune processes by evaluating the lifetime prevalence of autoimmune disease in 70 Dutch patients with adult-onset SCCH and their first degree relatives (parents, siblings and children).
Method: Survey data were collected through structured telephone interviews with patients and matched with available medical records. Danish hospital registry data for autoimmune diseases (ICD8/10) were used as reference data.
Results: A diagnosis of at least one autoimmune disease was reported in 20 SCCH patients (29 %) and in 47/518 relatives (9.1 %), compared to an estimated 3.9 % prevalence in the Danish reference population. A diversity of autoimmune diseases was reported in SCCH patients and relatives, most frequently psoriasis vulgaris (14 % of patients). Palmoplantar pustulosis was reported by 28 patients (40 %)—its inclusion as a putative autoimmune disease increased the overall prevalence of autoimmune disease to 54 %.
Conclusion: The high prevalence of autoimmune disease in patients with SCCH and their first degree relatives suggests that autoimmunity may be linked to the still elusive pathophysiology of the intriguing osteogenic response to inflammation observed in this rare bone disorder.

Thursday, 29 September 2016, 09.30–10.30, Hall 11.3
PS-25 Uropathology

PS-25-001
Necdin overexpression is an independent poor prognostic factor for patients with urothelial carcinomas
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Objective: Oncogenesis is a multistep process, resulting from the accumulations of multiple mutations. Of these mutations, disruption of cell growth regulation is the first episode. Nonetheless, the genes associated with cell growth dysregulation have seldom been systematically evaluated in either urothelial carcinomas of upper urinary tract (UTUC) or of urinary baldder (UBUC). By data mining a published transcriptomic

dataset of UBUCs (GSE31684), we identified NDN as one of the most significantly upregulated gene associated with advanced tumour status and metastatic disease among those associated with the regulation of cell growth (GO:0001558).
Method: We used real time RT-PCR to detect NDN transcript levels in 27 UTUCs and 27 UBUCs, respectively. Immunohistochemical study was performed to determine NDN protein (a.k.a. Necdin) expression in 340 UTUCs and 295 UBUCs. Necdin expression was further correlated with clinicopathological features and disease-specific survival (DSS) and metastasis-free survival (MeFS).
Results: NDN transcriptional level was significantly higher in UCs of both sites with stepwise more advanced pT statuses. Through immunohistochemistry, we found Necdin expression was significantly associated with adverse clinicopathological parameters, e.g., advanced pT status, nodal metastasis, high grade histological patterns, and frequent mitotses. (all $P < 0.05$). In univariate analysis, Necdin overexpression not only predicted worse DSS and MeFS in both the UTUC and UBUC groups, it also served as an independent prognostic factor for DSS and MeFS in multivariate analysis (all $P < 0.05$).
Conclusion: NDN may play an important role in tumour progression in UC and could serve as a prognostic biomarker and a potential novel therapeutic target in UC.

PS-25-002
The prognostic impact of C1s expression on patients with urothelial carcinomas of upper urinary tracts and bladders
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Objective: By subjecting a documented transcriptome dataset of urothelial carcinoma of bladder (GSE31684) to data mining and focusing on genes linked to peptidase activity (GO:0008233), we recognized C1S as the most significantly upregulated gene related to more aggressive disease. We subsequently analyzed the association of both C1S mRNA and protein expression with the clinical and pathological significance.
Method: We used real-time RT-PCR to detect C1S transcriptional levels in 20 cases each of urothelial carcinoma of bladder and upper tract. An immunohistochemical stain was conducted to determine C1s protein expression in urothelial carcinoma of upper tract ($n = 340$) and urinary bladder ($n = 295$). Furthermore, we examined the correlation of C1s expression with clinicopathological characteristics, disease-specific survival, and metastasis-free survival.
Results: C1S transcriptional levels were significantly high in patients with advanced-stage tumours of both groups (all $P < 0.05$). By immunohistochemistry, C1s overexpression was not only significantly associated with adverse clinicopathological parameters, but also predictive of poor disease-specific and metastasis-free survival rates for both urothelial carcinoma groups (all $P < 0.05$). It was also an independent prognostic factor in the multivariate analysis (all $P < 0.05$).
Conclusion: C1s may play a pivotal role in urothelial carcinoma progress and can represent a vital prognostic marker and a promising new therapeutic target in urothelial carcinoma.

PS-25-003
Expression of BRCA2 protein in prostatectomy and its correlation with needle core biopsy in patients with prostate cancer
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Objective: Prostate cancer is the most frequent malignant tumour in the masculine population worldwide. BRCA2 tumour suppressor gene is one of the few genetic biomarkers that are associated with increased prostate cancer risk, although its influence in cancer progression after the initial diagnosis is still debatable. Our study aims to verify the BRCA2 protein expression in prostatic adenocarcinomas with Gleason's score ≤7 in needle core biopsies that, after prostatectomy, were reclassified with Gleason's score ≥7.
Method: Immunohistochemistry for BRCA2 was performed in 125-paired samples of biopsy and prostatectomy with the diagnosis of prostate cancer.
Results: BRCA2 was overexpressed in all tumours that were reclassified as Gleason's score ≥7 after prostatectomy. In these tumours, BRCA2 overexpression also correlated with angiolymphatic invasion, bilateral tumour and staging.
Conclusion: Our data suggest that BRCA2 can predict a higher Gleason score as well as a more aggressive behavior in prostatectomy specimens.

PS-25-004
Histopathological pattern of bladder cancer in Kano: A ten year retrospective study and update
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Objective: Bladder cancer is the 6th most frequent malignancy in Kano, Nigeria and 9th in the world. The objective is to describe the pattern of bladder cancer diagnosed at the Pathology department of Aminu Kano Teaching Hospital, Kano, Nigeria in terms of the relative frequency of the histologic types, their age and sex distribution as well update the data on bladder cancers in the Centre.
Method: The materials consisted of glass slides, paraffin embedded tissue blocks and duplicate histopathology request forms of all bladder biopsies received at the Pathology department of Aminu Kano Teaching Hospital, Kano. Clinical data such as age, sex and diagnoses were extracted from the request forms. The corresponding haematoxylin and eosin (H & E) stained slides were retrieved from the archives and re-evaluated to confirm and/ or modified the diagnoses were appropriate. Classification and grading were based on WHO histological typing of tumours.
Results: Bladder cancer represented 6.2 % of all the cancers in the period under review. The male to female ratio was 6.5:1. The ages of affected patients ranged from 10 months to 75 years with a mean age of 46.5 years. Urothelial carcinoma (117/49.8 %) was the most predominant cancer, followed by squamous cell carcinoma (102/43.4 %). The others were adenocarcinoma (13/5.5 %), rhabdomyosarcoma (2/0.8 %) and angiosarcoma (1/0.4 %).
Conclusion: Bladder cancer is a common malignancy in Kano with a marked male preponderance. The predominance of urothelial carcinoma over squamous cell carcinoma is a reverse of the findings of an earlier study on bladder cancers in Kano.

PS-25-005
The members of Wnt pathway SFRP1, SFRP3, and DVL1 are down-regulated in testicular germ cell tumours
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Objective: Wnt signaling pathway components have been shown to be actively involved in normal and malignant germ cell differentiation and progression. In the present study, we aimed to explore the expression patterns of two of the Wnt pathway members, the secreted frizzled-related protein (SFRP) and Dishevelled protein family (DVL) in a subset of testicular germ cell tumours.
Method: Eighty-five formalin-fixed paraffin-embedded tissue samples of the primary germ cell tumours of the testis were stained against SFRP1, SFRP3, DVL1, and DVL2 proteins using immunohistochemistry.
Results: SFRP1 and SFRP3 exhibited lower expression in both seminomas and mixed/non-seminomatous tumours, compared with

normal tissue ($p < 0.001$). SFRP3 expression was lower than SFRP1 expression within the seminoma group ($p = 0.004$), but not within the mixed/non-seminomatous group ($p = 0.409$). The majority of the tested cases (27/28, 96 %) exhibited low DVL1 protein expression (mean 9.6 %). In contrast, 20 out of 22 tested cases (91 %) exhibited a strong overexpression of DVL2 protein (mean 68.6 %, range 0–100 %).
Conclusion: The secreted frizzled-related protein and dishevelled protein family members show different expression profiles in tumours, compared to normal tissue, suggesting their role in the pathogenesis of testicular germ cell tumours. Further molecular and clinical studies should confirm the relevance of our findings.

PS-25-006
Clinicopathological findings, outcome following radical prostatectomies, and location of index tumour: Are different comparing younger vs older patients?
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Objective: It is controversial whether prostate cancer in younger men have less favorable outcome than older men.
Method: From a total of 499 consecutive patients submitted to radical prostatectomy (RP), 430/499 (86.2 %) were >55-year-old and 69/499 (13.83 %) were <55-year-old. Tumour extent was evaluated by a semi-quantitative point count method and index tumour located as predominantly anterior, posterior, basal, apical, at left, and at right. Time to biochemical recurrence (BR) was analyzed by Kaplan-Meier analysis and prediction of shorter time to BR using univariate and multivariate Cox model. BR was considered as PSA > 0.2 ng/mL.
Results: There was no significant difference between younger and older patients comparing the location of the index tumour. Only preoperative PSA, prostate weight, nodular hyperplasia, and surgical specimen Gleason score were significantly higher in older patients. No other clinicopathologic findings were statistically significant. Only seminal vesicle invasion and positive surgical margin were independent predictors of shorter time to BR in multivariate analysis.
Conclusion: Our study did not show any significant difference in location of the index tumour and outcome following RP comparing younger vs older patients. Only preoperative PSA, prostate weight, nodular hyperplasia and surgical specimen Gleason score were higher in older patients.

PS-25-007
Juxtaglomerular cell tumour of kidney with CD34 and Bcl-2 immunoreactivity: A diagnostic pitfall
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Objective: Juxtaglomerular cell tumour of kidney is a rare neoplasm with only about 100 cases reported. It is characterized by the production of renin, with a clinical picture of hypertension, hyperaldosteronism, and hypokalemia. We report a case with unusual immunoprofile.
Method: A 37-year-old female patient was admitted to our hospital for investigation of a refractory hypertension. CT scans identified a renal tumour with 25 × 22mm that was biopsed. Histologically the tumour was a spindle cell neoplasm with fascicular growth pattern; neoplastic cells were bland. Immunostains were positive for actin, CD34 and Bcl-2 (negative for cytokeratins and desmin).
Results: A diagnosis of solitary fibrous tumour was made. The patient abandoned medical follow-up and returned 1 year after, when a partial nephrectomy was performed. In the nephrectomy specimen, histologic features were similar and complementary immunohistochemistry revealed positivity for CD117 and beta-catenin (cytoplasmic). Electron microscopy showed dense rhomboid cytoplasmic crystals, allowing the diagnosis of juxtaglomerular cell tumour of kidney.
Conclusion: Although the literature refers that juxtaglomerular cell tumour is a CD34-positive and Bcl-2-negative neoplasm, we report a case that was both CD34 and Bcl-2-positive. This is the first case reported in the literature with this immunohistochemical profile, which constitutes a considerable diagnostic pitfall, mainly with solitary fibrous tumour.

PS-25-008
Prognostic impact of thrombospodin-2 (THBS2) overexpression on patients with urothelial carcinomas of upper urinary tracts and bladders
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Objective: Urothelial carcinoma (UC) is a type of tumour, especially of the urinary bladder, that affects people worldwide. Clarification of its detailed tumour biology and discovery of potential targets for developing treatment strategies are imperative because of frequent recurrences and poor prognosis of advanced UCs. By data mining a published dataset of UC of bladder (UCB) transcriptome (GSE31684) from Gene Expression Omnibus, we identified that THBS2 was the most significantly upregulated gene among those related to structural molecule activity (GO:0005198).
Method: THBS2 immunostaining was performed in 340 UCs of upper urinary tract (UC-UUTs) and 295 UCBs; subsequently, both groups were dichotomized into high- and low-expression subgroups. Moreover, statistical analyses were performed to correlate the association between THBS2 expression and clinicopathological parameters with two survival indexes: disease-specific survival (DSS) and metastasis-free survival (MeFS).
Results: High THBS2 immunoexpression was significantly associated with advanced primary tumour status, nodal metastasis, and vascular invasion in both UC-UUT and UCB groups (all $P \leq .001$). In addition, THBS2 overexpression was linked to adverse DSS and MeFS in univariate analyses and served as an independent prognosticator indicating poor outcomes in both groups in multivariate analyses.
Conclusion: THBS2 may play a crucial role in UC progression and may be a novel prognostic marker.

PS-25-009
ERG immunohistochemistry in ASAP: Predictive value for Prostatic Adneocarcinoma (PCa)
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Objective: 70 % of PCas in our patient population are positive by ERG immunohistochemistry(IH). In this study, we examine whether ERG-IH in ASAP has predictive value for PCa in this population.
Method: 68 prostate biopsies with a diagnosis of ASAP and a subsequent follow-up biopsies (FU-Bx) were identified. ERG IH was performed on the ASAP focus. PSA values were also reviewed.
Results: 65 cases were evaluable by ERG-IH. 25/65 (38.4 %) had a diagnosis of PCa on FU-Bx. ERG was positive in ASAP in 13/65 at initial biopsy: 6/13 (46 %) had a FU-Bx diagnosis of PCa. In the ERG-negative cohort, 19/52 (36.6 %) had a FU-Bx of PCa. In cases with a final diagnosis of PCa, 5/7 (71 %) of those with ERG-positive ASAP, and 8/8 (50 %) of those with ERG-negative ASAP experienced a rise in PSA by the time of follow-up biopsy.
Conclusion: In our population, ERG-positive ASAP is associated with a 46 % risk of subsequent PCa vs. 36.6 % in ERG-negative ASAP. ERG positivity in ASAP plus a subsequent rise in PSA is associated with a 71 % risk of PCa. ERG-IH in ASAP, plus PSA, may triage patients for prompt rebiopsy.

PS-25-010

Complex approaches at study of prostate pathology

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Objective: The prostate cancer occupies a leading position in structure of morbidity by malignant tumours in men in different countries. In the Belgorod region over the past 10 years this pathology progressively increased almost threefold.
Method: The exploration of prostate tissues of 60 patients with prostate cancer and 25 patients with benign prostatic hyperplasia was carried out with help of light, confocal and raster electronic microscopy with usage of console for dot study of macro- and microelements and immunohistochemistry (PSA, p63, Ki-6, K5 и K18).
Results: The polymorphic cells with thin "bridges" between them, which exceed sizes of cells in some sites and form branched structures, located inside ducts of glands were revealed at prostate cancer with help of scanning microscopy. The reliable increasing of some microelements was traced in case of adenocarcinoma in comparison with benign prostatic hyperplasia: sodium(4,10 ± 0,06; 2,35 ± 0,05), magnesium(12,10 ± 0,82; 1,29 ± 0,04), phosphorus(3,85 ± 0,43; 1,42 ± 0,31). The expression of K5 and K 18 was revealed, what testifies about high proliferative activity of cells. The reaction at usage of Ki-6 was insignificant.
Conclusion: The complex approach at study of tumour growth makes an establishing of more accurate diagnosis possible, what creates premises for further research of pathogenesis and morphogenesis.

PS-25-011

A study of HER-2/neu expression in urothelial carcinoma of the urinary bladder

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Objective: The aim of this study was to investigate HER-2/neu oncogene expression in urothelial bladder cancer (UCB) and its correlation with tumour clinicopathological parameters.
Method: 80 formalin-fixed paraffin-embedded specimens of primary UCB were processed. The specimens were analyzed for HER-2/neu protein overexpression by immunohistochemistry.
Results: Tumour specimens belonged to 52 men (65 %) and 28 women (35 %) with a mean age of 59 years. Tumour grades were 1, 2, and 3 in 12 (15 %), 44 (55 %), and 24 (30 %) specimens, respectively. A total of 48 (60 %) patients were positive for overexpression of HER-2/neu. Two cases of HER-2/neu-positive (4.16 %) were grade 1 tumours, 14 (29.16 %) grade 2, and 32 (66.66 %) grade 3. HER-2/neu was positive in 28 (58.33 %) superficial and 20 (41.66 %) muscle invasive tumours as well as in 31 (64.5 %) recurrent tumours, and 9 (18.75 %) with positive lymph nodes.
Conclusion: HER-2/neu overexpression was not correlated with tumour stage, lymph node metastasis or recurrence of the disease. However, a significant relationship between HER-2/neu overexpression and grade of the bladder TCC tumours was found (P = .002). Further studies with longer follow-up period and a larger sample size can determine the probable role of HER-2/neu expression as a prognostic factor in UCB.

PS-25-012

Persistent müllerian duct syndrome

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Objective: We describe the histopathologic findings of a case of persistent müllerian duct syndrome (PMDS).
Method: A 78-year-old man with histological finding of muscle-invasive urothelial carcinoma undergoes cystoprostatectomy.
Results: Macroscopically, a rudimentary uterus was discovered along the posterior wall of the bladder. Microscopically, in addition to an urothelial carcinoma, endometrial glands embedded in a compact stroma, next to a vas deferens, were noted.
Conclusion: Anti-Müllerian hormone (AMH) produced by fetal Sertoli cells is responsible for regression of Müllerian ducts. Mutation in AMH gene on chromosome 19p13.3 or abnormality of receptor gene on chromosome 12q13 leads to persistence of the uterus and Fallopian tubes in males. It is transmitted with autosomal recessive or X linked pattern. Patients usually present in childhood with cryptorchidism or with inguinal hernia. These gonads have 15 % risk of germ cell tumours. Treatment of PMDS is surgical and aims to correct cryptorchidism. Careful dissection is required to avoid harming the excretory ducts because frequently the vasa deferentia are embedded in the mesosalpynx, uterine wall and cervix. Removal of the uterus is not recommended. Lack of communication between the testis and excretory ducts and lesions at orchidopexy explain why fertility is rare (11 %).

PS-25-013

Vessel malformation in children with Congenital Hydronephrosis (CH)

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Objective: reveal correlations between vessel malformation and dysnephrogenesis markers in CH.
Method: removed kidneys, incision renal biopsies obtained from 63 children from 2 days to 15 years old. We used hematoxylin&eosin, picrofuchsin. Immunohistochemistry: streptavidin-biotin method was made with monoclonal antibodies against VEGF, TGFβ1, TGFβ1 R1 and R2, CD 34, α-SMA.
Results: vessel malformation markers were found in all cases: kinking of arteries, defective vessel branching associated with abnormal topography. There were "budding vessels"—arteries with disproportionate small branches. The artery wall thickness was variable, bundles of SMC were oriented chaotically. The closer distances between arteries and veins were often present, these veins had sinusoid-like appearance. Vessel malformation was always associated with parenchymal hypoplasia—closely spaced glomeruli with capillary deficiency and dilated extracapillary spaces, glomerular and tubular cysts, undifferentiated tubules lined with cuboid immature epithelium. We found TGFβ1 and receptor overexpression in immature tubular epithelium and in cytoplasm of hypoplastic longitudinally oriented SMC of UPJ. VEGF expression were present in glomerular endothelium and in nephrocytes.
Conclusion: the most severe morphological changes in renal parenchyma were found in children first weeks of life. Vessel malformation is directly connected with dysnephrogenesis

PS-25-014

Isolated retroperitoneal hydatid cyst

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Objective: Hydatid disease (HD) is a rare entity that mostly affects the liver and lung, but almost any organ, forming cysts. We present an unusual case of hydatid cyst found in the retroperitoneum without hepatic or any other involvement.
Method: A 33-year-old farmer man presented with right flank pain, nausea and vomiting. Imaging studies revealed a heterogene cystic mass with a diameter of 80 × 70 mm neighbored the superior pole of right kidney. His serology for HD was negative. Total cystectomy was performed.

Results: Histological examination revealed cyst wall composed of fibrous and reactive membrane. Reactive membrane showed hyalinized collagen, erosion, degeneration, coagulation necrosis, calcification and focal lymphocyte infiltration. In the necrotic foci, scolices of the cyst were seen and histology confirmed the diagnosis of late stage HD.
Conclusion: The diagnosis of HD in an atypical location can be difficult. Histopathological evaluation of the excised specimen usually leads to the diagnosis. As our case, for young patients, symptomatic, solitary, large hydatid peritoneal cysts, surgery is the principal method of treatment. Especially in endemic areas such as Turkey, HD should be suspected in the cases of intraabdominal and retroperitoneal cystic masses.

PS-25-015
Immunohistochemical expression of markers Ki67 and Her2neu in urothelial carcinoma and its correlation with clinicopathological parameters in Indian subcontinents
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Objective: The expression of immunohistochemical markers Ki67 and Her2neu and its correlation with clinicopathological parameters in urothelial tumours.
Method: Study included 40 cases of urothelial tumours of urinary bladder. Immunohistochemical evaluation of Ki67 and Her2neu was done using streptavidin biotin immunoperoxidase method. Staining and evaluation using specific polyclonal antibody to Ki67 and Her2neu was done.
Results: The Ki67 expression had significant association with tumour histological grade ($p = 0.024$) and muscle invasion ($p = 0.021$). The association of Her2neu expression had significant association with tumour histological grade ($p = 0.001$) and muscle invasion($p = 0.001$). Muscle invasive tumours showed high expression of Ki67 (70.6 %) as compared to non-muscle invasive tumours (30 %). Her2neu over expression was in accordance with grade, 31.3, 60 and 93 % of low, intermediate and high grade respectively. Co-expression of both markers was demonstrated in 25 % of low, 40 % of intermediate and 78.8 % of high grade.In muscle invasive tumours 70.6 % showed co-expression as compared to non muscle invasive tumours(30.4 %).
Conclusion: Ki67 and Her2neu expression correlated well with tumour grade and progression. Evaluation of both Ki67 and Her2neu co-expression was more accurate in predicting the clinical outcome and had therapeutic implications.

PS-25-016
Prostate cancer outcomes of men with biopsy gleason score 6 and 7 without cribriform or intraductal carcinoma
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Objective: To compare the clinico-pathologic characteristics and patient outcomes of men with biopsy GS $3+4=7$ without cribriform or intraductal carcinoma (7-) to those with GS $3+3=6$.
Method: We included all patients from the first screening round of the European Randomized Study of Screening for Prostate Cancer (1993–2000) with a revised GS $\leq 3+4=7$ ($n=796$) following the 2014 ISUP criteria. Relations with biochemical recurrence after radical prostatectomy or radiotherapy were analyzed using log-rank testing and multivariable Cox regression analysis.
Results: In total 486 patients had GS 6 and 310 had GS 7, 54 of whom had GS 7+ (17 %). During a median follow-up of 15 years, biochemical recurrence was seen in 61 (20 %) GS 6, 54 (21 %) GS 7- and 22 GS 7+ patients (41 %). Both biopsy GS 7- and 7+ patients had significantly higher PSA levels, mean tumour percentage, percentage of positive cores and $\geq$ cT3 than those with GS 6 (all $P < .001$). GS 7 patients did not have a poorer biochemical-recurrence-free-survival (BCRFS) after radical prostatectomy than GS 6 patients (log rank $P = .13$), whereas those with GS 7+ had (log rank $P = .05$). In multivariable analyses, biopsy GS 7- was not associated with poorer BCRFS after radical prostatectomy ($P = .47$) or radiotherapy ($P = .63$). GS 7+ was independently associated with poorer BCRFS after radical prostatectomy ($P = .03$), but not after radiotherapy ($P = .67$).
Conclusion: Men with biopsy GS 7- prostate cancer have similar BCRFS after radical prostatectomy or radiotherapy to those with GS 6 and may be candidates for active surveillance.

PS-25-017
Expanding histologic spectrum of melanotic Xp11 translocation renal cancer
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Objective: Melanotic Xp11 translocation renal cancer (MTRC) is a very rare tumour that belongs to the family of MITF/transcription factor E (TFE) neoplasms. It is a distinctive tumour showing overlapping features between Xp11 translocation renal cell carcinoma, melanoma, and PEComa. Here, we present another case of MTRC, however without melanin production. To our knowledge, this is the first reported case of MTRC that lacks melanin.
Method: The patient was a 25 year-old female presented with flank pain. A mass at lower-pole of right kidney was identified.
Results: Histologically, the tumour was characterized by nests of epithelioid cells which had abundant clear to eosinophilic granular cytoplasm, vesicular nuclei, and prominent nucleoli. TFE3 expression was identified by immunohistochemistry. There was additional immunoreactivity for HMB45. Actin, desmin, cytokeratins, EMA, CD10, PAX2, PAX-8, S100, melan-A were negative. Findings were consistent with diagnosis of MTRC. But in contrast to formerly described cases, no melanin pigment could be identified in the current tumour.
Conclusion: Herein we report a case of MTRC, showing identical features that were described previously except lack of melanin. This report further expands the morphological spectrum of MTRC by showing that it can be amelanotic. The recognition of this histologic presentation should allow for improved diagnosis of this entity.

PS-25-018
Evaluation of CXCR4 expression as a putative cancer stem cell marker in Renal Cell Carcinoma (RCC): A study using tissue microarrays
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Objective: Cancer stem cells (CSC) represent a population with tumour-initiating, self-renewal, and differentiation potential. The aim of this study was to evaluate CXCR4 expression as a putative CSC marker in Renal Cell Carcinoma (RCC).
Method: The expression of CXCR4 in specimens from RCC patients was evaluated by immunohistochemistry on a tissue microarray(TMA). One hundred and seventy-three consecutive patients treated surgically for renal cell carcinoma (RCC) between 2010 and 2015 including 106 (61.3 %) Clear Cell Renal Cell Carcinoma (ccRCC), 35(20.2 %) Papillary and 32 (18.5 %) Chromophobe were selected. The association between expression of this marker and tumour characteristics was then analyzed.
Results: The mean expression of CXCR4 is significantly different in RCC subtypes ($P < 0.000$). Increased expression of CXCR4 was significantly correlated with higher grade tumours ($P < 0.000$) and increase of

stage (P = 0.01). The statistically significant association was not found between expression of CXCR4, age and sex and clinicopathologic features of patients including invasion to pelvis, vein, lymph node and tumour size.
Conclusion: These findings suggest that CXCR4 can be considered as a valuable tool for the study of renal CSCs and provide a therapeutic target for treatment of the patients with renal cell carcinoma in combination with conventional therapy.

PS-25-020
Acinar adenocarcinoma of the prostate: Gleason pattern 4 quantification and morphology in needle biopsy and their relationship with findings in radical prostatectomy specimens
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Objective: The 2005-Gleason consensus restricted the acceptable morphology for Gleason pattern 3 (GP3) and expanded the spectrum of Gleason pattern 4 (GP4). As a consequence, 3 + 3 tumours are more uniform regarding clinical behavior and those with GP4 are more heterogeneous. We compared different forms of quantifications of GP4 in needle biopsies, and the presence of predominant cribriform morphology in GP4, with subsequent findings in prostatectomy specimens.
Method: Seventy-three of needle biopsies with higher Gleason score 6 or 7 were reviewed.
Results: The presence of any amount of GP4 (score >6) was associated with higher tumour volumes, higher volume of high grade component (GP4 or 5), positive margins and extraprostatic extensions at prostatectomy specimens. The findings of predominant cribriform morphology in GP4, total linear extension of GP4 > 5 mm, linear extension of GP4 > 2 mm in a single core, more than 2 cores with GP4 or >30 % of involvement by GP4 in a single core were not associated with any relevant finding at prostatectomy.
Conclusion: The presence of any amount of GP4 is associated with morphologic features of cancer progression at radical prostatectomies. Decisions for active surveillance based on subclassification of GP4 findings at needle biopsy would be temerarious in our experience.

PS-25-021
Primary testicular lymphoma: A clinicopathologic study of 33 cases
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Objective: Testicular lymphomas (TL) are the most frequent testicular tumours in men older then 50. This study aimed to describe clinicopathologic parameters in a series of 33 patients with TL.
Method: A retrospective review (2011–2015) of clinical, ultrasound, ICH-staining dates of 33 TL was carried.
Results: These cases were MALT-lymphomas in 7 (bilateral in 6), 24 DLBC, centroblastic variant, including 8 showed areas of MALT-TL, 2—plasmablastic B-cell TL. In 13 of 33 cases TL was primary bilateral. A 67-year-old patient underwent unilateral orchidectomy in 2012 for MALT-TL. He was treated for DLBC-TL in 2014. Median of average age was 71,4 (47 to 82), and 2 (28- and 32-years-old men) with HIV-associated plasmablastic B-cell TL. 2 patients suffered from prostate cancer. The spread to the adjacent epididymis (19) or spermatic cord (14) was revealed, involving retroperitoneal lymph nodes (9) or inguinal (5) lymph nodes. 4 patients underwent prostate adenomectomy during 2 years before diagnosis of TL, 2 patient had nephrostoma, 1 patient underwent nephrectomy, 1-with hydronephrosis, 3-with ureteropyeloectasis, 1- with chronic pyelonephritis, 5—with renal cysts, 7—with urolithiasis.
Conclusion: In spite of the fact that specific clinical and ultrasound features are absent, pre-treatment diagnostic results are not good.

PS-25-022
The histopathologic spectrum of renal neoplasms seen at the Nairobi hospital over a three year period
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Objective: To determine the relative frequencies of renal tumours and to analyze their histopathological characteristics in the population studied.
Method: This was a retrospective study looking at renal tumours diagnosed in the Pathology department at the Nairobi Hospital over a 3 year period. Surgical specimens from patients who underwent radical nephrectomy/diagnostic-core biopsies provided the tissue samples. Patients' demographic and clinical data was obtained from clinical charts. Two pathologists agreed on the histologic classification.
Results: The male-to-female ratio was 1.2:1. The mean age was 49.5 years. Malignant tumours were 85 % of the total. Renal Cell Carcinoma (RCC) comprised 73 % of the malignant tumours. The other malignant tumours were urothelial carcinoma (18 %) and metastasis (9 %). The subtypes of RCC included; clear-cell RCC, 50 %; papillary-RCC, 25 %; chromophobe-RCC, 12.5 % and RCC-unclassified, 12.5 %.
Conclusion: The spectrum of adult renal tumours in this study is consistent with that of previously reported literature. However, RCC presentation is delayed with advanced disease stage.

PS-25-023
Quantifying subepithelial connective tissue infiltration in bladder urothelial carcinoma in pT1 staging as risk factor of progression and/or relapse
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Objective: The purpose is to determine whether the quantification of the invasion of subepithelial tissue is a significant predictor of progression and/or relapse and witch method is better to quantify.
Method: We present a retrospective study result, in which 214 cases of bladder urothelial carcinoma stage pT1 gotten by TUR were selected. Three methods were used: 1. Rating focal invasion (a single focus to one mm2) vs extensive invasion (more number of focus or major focus larger than one mm2) 2. Quantification in all areas in mm2 3. Determination of the number of foci of invasion.
Results: All methods showed no statistically significant differences in the occurrence of relapse but for the occurrence of progression comparing. Focal vs extensive infiltration ($p < 0.001$, chi-square test), extent of infiltration in mm2 ($p < 0.001$ Mann–Whitney U-test) and counting invasive foci ($p = 0.0009$ Mann–Whitney U-test).
Conclusion: 1. Quantification of the subepithelial connective tissue invasion by the urothelial carcinoma is an important prognostic factor regarding the progression. 2.As for the onset of relapse, statistically significant differences were not observed. 3. All methods have been proved to be valid for such quantification.

PS-25-024
Small Cell Carcinoma (SCC) of the bladder: A rare and aggresive neoplasm
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Objective: SmCC of the bladder is a malignant neuroendocrine neoplasm of the urothelium that accounts for approximately the 0,5 % of all the malignant bladder tumours. Clinical features (such as haematuria, dysuria

and obstructive symptoms) are similar to those of conventional urothelial carcinoma. Majority of patients are men, age of presentation in the sixth or seventh decade of the life and a story of smoking. The differential diagnosis includes poorly differentiated urothelial carcinoma, small cell carcinoma of another site and lymphoma.
Method: Our study is based on an observational retrospective study of 7 patients diagnosed, treated and followed for SmCC of the bladder at the University Hospital Miguel Servet, Zaragoza, Spain, between 2011 and 2016.
Results: All of our patients were men, with an average age of 75,5 years (range 51–94) at the moment of diagnostic. T4 was the most common T stage. The survival average was 2 years after diagnostic. Only two patients are still alive.
Conclusion: SmCC of the urinary bladder is an extremely rare malignant neoplasm with neuroendocrine differentiation and an aggresive clinical course. There are no differences in management of SmCC and conventional urothelial carcinoma in our hospital except in metastatic cases.

PS-25-025
Raman-fluorescence spectroscopy: Applications in diagnostics of prostate cancer
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Objective: To evaluate the ability of Raman- fluorescence spectroscopy (RFS) to detect benign prostatic hyperplasia (BPH) and prostate cancer.
Method: We analyzed preoperative result of RFS examination of prostate tissue samples from 62 patients, who later underwent radical prostatectomy. Spectra correlated with histological features and were used to construct diagnostic algorithms. These algorithms were tested to verify their ability to find pathologic regions using Raman-fluorescence spectrum. Results were analyzed according to Gleason grading system and RSA levels.
Results: It was established that there is inverse relation between intensity of fluorescence and grade of cancer. Important distinctions between spectra in BPH and prostatic cancer were found in regions with specific vibrations of glycogen molecules, phospholipids, carotenoids and NADH.
Conclusion: The results of this study have shown that Raman-fluorescence spectroscopy can be used as accurate and early method of prostate cancer detection. Being safe and inexpensive, RFS is used online and takes only several minutes. It allows to interactively identify tumourous regions pre- and intraoperative and to define volume of surgical intervention with maximum precision.

PS-25-026
TERT promoter mutation ratio of the urothelial carcinoma in Korean is lower than other ethnic groups
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Objective: Telomerase reverse transcriptase (TERT) promoter has been found to be a target of cancer specific mutations in urinary bladder carcinoma. The mutation hot spots are positions −124 and −146 bp from ATG start site, which affected 64.5 % of the 327 bladder cancer. The purpose of this study was to test the ratio of TERT promoter mutations of urothelial carcinoma in Korean patients.
Method: Direct sequencing was done in 142 paraffin-embedded urothelial carcinoma tissues and 69 cases of urine cytology samples. The tissues of urothelial carcinoma were 51 low grade papillary urothelial carcinoma (LGPUC), 39 high grade papillary urothelial carcinoma (HGPUC), and 52 invasive urothelial carcinoma (IUC). The cytology samples were 28 benign atypia or borderline, and 41 malignancy.
Results: The tissue revealed mutation in 21.6 % of LGPUC, 23.1 % of HGPUC, and 3.1 % of IUC. None of the 28 negative or benign atypia cytology samples revealed mutation. The 41 cytology samples of malignancy showed mutation ratio of 26.8 %. The overall mutation ratio of urothelial carcinoma was 18.0 %.
Conclusion: The TERT promoter mutation ratio of the urothelial carcinoma in Korean was lower than other ethnic groups.

PS-25-027
Evaluation of Muc1 and P53 expressions in noninvasive papillary urothelial neoplasms of bladder, their relationship with tumour grade and role in the differential diagnosis
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Objective: The aim of this study was to investigate the usability of MUC1 and p53 for differential diagnosis of noninvasive papillary urothelial neoplasias, especially for distinguishing papillary urothelial neoplasm of low malignant potential (PUNLMP) from non- invasive papillary urothelial carcinomalow grade (LgPUC) when the histologic signs are not obvious.
Method: Seventeen biopsy specimens of the patients with PUNLMP, 20 with LgPUC and 13 with non- invasive papillary urothelial carcinoma, hıgh grdae (HgPUC) were stained for MUC1 and p53 protein by immunohistochemical methods. Histological grading was performed according to an algorithm, which allows histological parameters used in 2016 WHO classification.
Results: We had obvious statistical difference for aberrant expression pattern of MUC1 between PUNLMP and LgPUC-HgPUC ($p = 0.007$). Positivity of MUC1 expression in cytoplasm of basal cells was more observed in HgPUC and LgPUC while PUNLMP was more often showing apical and superficial positivity of MUC1 expression ($p = 0.001$ and 0.011). Nuclear p53 protein in HgPUC was obviously more frequent than that in LgPUC and PUNLMP ($p < 0.001$). Measures showed statistical difference among aberrant MUC1 expression, p53 overexpression and tumour grade ($p < 0.001$).
Conclusion: MUC1 and p53 may be helpful immunohistochemical markers for distinguishing PUNLMP from LgPUC and HgPUC, when the histologic signs are not obvious.

PS-25-028
Prognostic significance and biopsy characteristics of seminal vesicle invasion of prostate cancer: A nationwide registry study
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Objective: To evaluate the prognostic significance of seminal vesicle invasion (SVI) or extraprostatic extension (EPE) alone after radical prostatectomy, and to correlate preoperative biopsy pathology with SVI and EPE.
Method: The National Prostate Cancer Register includes all prostate cancers diagnosed in Sweden. We analysed 31,415 cases diagnosed between 2000 and 2012 and treated with radical prostatectomy. Associations between pT3a and pT3b and progression were evaluated and adjusted for year, age, biopsy grade and serum PSA. Needle biopsy findings in these stages were compared.
Results: Patients with pT3b ($n = 1274$) had a higher risk of death from any cause [HR 1.54 (95 % CI 1.22–1.95), $P = 0.001$] than those with pT3a ($n = 4097$) and were more likely to be treated with postoperative radiotherapy [HR 1.57 (95 % CI 1.39-1.77), $P < 0.001$] or androgen deprivation therapy [HR 2.94 (95 % CI 2.46-3.50), $P < 0.001$], indicating clinical progression. Median cancer extent in preoperative biopsies of pT3a and pT3b was 14 and 24 mm ($p < 0.001$) and Gleason score 8–10 occurred in 11 and 28 % ($p < 0.001$).
Conclusion: SVI of prostate cancer is associated with worse outcome after radical prostatectomy than EPE alone. Needle biopsy findings help to predict SVI, which has major implications in treatment planning.

PS-25-029

Unusual renal cancer resembling Warthin's tumour

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Objective: Current classification of renal tumours includes 15 entities, however pathologist may encounter cases which do not fit well into known categories. We present one such case, with surprising morphology.
Method: The material was routinely processed and paraffin embedded. Immunohistochemistry was done by routine manual method.
Results: A 66-years old male has been admitted to Urology Department because of tumour of the left kidney, incidentally detected on US. Patient's and family history was non-contributory. Nephrectomy was performed by laparoscopic approach. The post operatory period was uneventful and patient was discharged in good general conditions. On gross examination, a 5 cm tumour was found. Histologically, the tumour was composed of tubules lined by a single layer of epithelial cells with eosinophilic cytoplasm and monomorphic nuclei. In most of the tumour stroma, abundant small lymphoid cells were present. This pattern resembled closely Warthin's tumour of the salivary gland. The tumour was limited to the kidney, didn't infiltrate renal sinus, great vessels or renal capsule, and was completely removed. On immunohistochemistry, tumour cells were CK7+, AMACR+, PAX2+, CD56-, WT-, CA9-.
Conclusion: To best of our knowledge, this is the first report of tumour with this peculiar morphology and immunophenotype similar to papillary or tubulocystic carcinoma.

PS-25-030

Prostatic polyp of the ureter: An uncommon location

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Objective: Benign prostatic polyps are rare and unusual lesions of the lower urinary tract. They are more commonly observed in the prostatic urethra and less commonly in the urinary bladder, with only a few cases reported in the ureteric orifice. We report a case of a 77-year-old male presented to our hospital with dysuria.
Method: Ultrasound revealed hydronephrosis of the right kidney. Ureteroscopy showed a polypoid lesion, 6 cm from the ureteric orifice, protruding into the lumen of the right ureter. Above this lesion the ureter was narrowed, having hard consistency. The polyp was removed. Patient's further image examination thickness of the ureteric wall with indistinct boundaries to the adjacent tissues.
Results: The polypoid lesion, measuring 1,5 × 0,2 × 0,1 cm, contained benign glands within a loose stroma and the surface was covered by columnar epithelium and urothelium. The glandular epithelium was PSA immunopositive, confirming the prostatic nature of the polyp. The samples from the ureter and its surrounding soft tissue were negative for malignancy.
Conclusion: To our knowledge prostatic polyps presenting in the ureter have not been previously reported in the literature. Prostatic polyps are a common source of hematuria and have been thought to arise from ectopic prostatic tissue but are more likely of hyperplastic-metaplastic nature.

PS-25-031

Application of Raman-fluorescence spectroscopy for diagnosis of kidney cancer

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Objective: To study laser spectroscopy as a perspective method for distinguishing tumour from intact tissue for early diagnosis of kidney cancer under histological control.

Method: Tissue samples from kidney were obtained during radical nephrectomy or partial nephrectomy from 50 patients with kidney cancer. Before the histological examination of tissue the Raman fluorescence spectroscopy images were obtained. The study was conducted using a Raman analyzer consisting of Olympus microscope combined with a spectrometer InSpectr R532. The samples with high intensity in fingerprint regions: carotenoids (1157 cm-1, 1517 cm-1), aminoacid phenylalanine (1003 cm-1) and methionine (2655 cm-1) were interpreted as suspicious for cancer, and underwent the histological examination which revealed clear cell renal cell carcinoma (CCRCC) in all samples. Malignancy grade was determined according to classification of S. Fuhrman et al.
Results: The results of histologic examination of kidney tissue correlated with the data obtained with Raman fluorescence spectroscopy in 42 cases (84 %) from 50, however, it showed no correlation between the degree of tumour differentiation and the intensity of Raman-fluorescence.
Conclusion: Raman-fluorescence spectroscopy has high sensitivity for early detection of malignancies but it needs to be studied more to evaluate its ability for different types of tumours.

PS-25-032

Papillary adenoma of the kidney

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Objective: To study small neoplasms of the epithelium of the renal tubules.
Method: Kidneys from 402 unselected autopsies were sectioned at 1 to 2 mm intervals and all lesions were examined histologically.
Results: 232 papillary adenomas were found in 76 patients (19 %), ranging from 1 to 35 tumours/patient (mean 3, median 2). Patients with papillary adenomas were older (range 27–90 years) ($p < 0.0001$), more commonly smokers ($p = 0.01$) and associated with glomerulosclerosis ($p = 0.0001$) than those without. Papillary adenomas ranged in size from 0.5 to 5 mm (mean 1.4, median 1) and were morphologically classified in four subtypes. Adenomas consisting of papillae and/or tubules covered by cells with scant cytoplasm, often with psammoma bodies were the most common (149 tumours), 16 were composed of large eosinophilic cells with pseudostratified nuclei, occasionally near to the apical membrane, in 30 the papillae were broad with lymphocytes in the core, and 30 were more cystic lined by columnar cells and containing macrophages and psamomma bodies. Four were unclassified. Mixtures of types within the same tumour were rare (3 in 1 patient).
Conclusion: The first type corresponds well to papillary renal cell carcinoma, type 1 and the second to type 2; the others do not correspond to known carcinomas.

PS-25-033

Renomedullary interstitial cell tumours

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Objective: To elucidate the morphology and clinical correlations of renomedullary interstitial cell tumours (RMICTs).
Method: Kidneys from 402 unselected autopsies were sectioned at 1 to 2 mm intervals and all lesions were examined histologically.
Results: 421 RMICTs were found in 150 patients, ranging from 1 to 23 tumours/patient (mean 3). There was no significant difference in age, gender, hypertension, heart weight, smoking, diabetes, or renal function between patients with RMICTs and without. Fifty-two percent of patients with RMICTs were older than 60 years (range 18–92). Forty-one percent had bilateral tumours and they were older than patients with unilateral tumours ($p = 0.0007$). The tumours ranged in size from 0.5 to 6 mm (mean 1.7). Renal tubules throughout the tumour was found in younger

patients and smaller tumours while the absence of entrapped tubules or their location at the periphery was common in older patients and larger tumours ($p = 0.02$ and $p < 0.0001$). Amyloid-like material was common in older patients ($p < 0.0001$) and in larger tumours ($p < 0.0001$) and correlated with higher heart weight ($p = 0.003$) but not with hypertension ($p = 0.11$).
Conclusion: RMICTs appear to originate as a proliferation of renomedullary interstitial cells entrapping renal tubules. As size increases, cellularity decreases, amyloid-like material is deposited and tubules disappear.

PS-25-034
Primary Squamous Cell Carcinoma (SCC) of the renal pelvis: A retrospective study of 14 cases
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Objective: Primary squamous cell carcinoma of the renal pelvis (PSCCRP) is a rare entity representing 0.5–0.8 % of malignant renal tumours. Our objective is to recall the clinico-pathologic, therapeutic and prognostic features of this entity.
Method: Between 1984 and 2015, we collected 92 cases of upper urinary tract tumours. Fourteen cases of them were diagnosed as squamous cell carcinoma (SCC).
Results: PSCCRP represented 15.22 % of all upper urinary tract tumours. Ten patients were males and four were females with a mean age of 57.28 years. Ten patients had radical nephrectomy, three had nephroureterectomy and only one had partial nephrectomy. Microscopic examination confirmed the diagnosis of verrucous SCC in three cases and classic SCC in 11 of them. The latter type was well differentiated in seven cases and moderately differentiated in only two. Seven tumours showed necrosis. Invasion of the renal vein existed in two cases. Chronic pyelonephritis was found in all cases. According to the WHO classification system, eight tumours were staged as pT4, three as pT3, two as pT1 and one as pTis. Five patients had metastasis. The death rate was 1OO% after 5 years.
Conclusion: The prognosis of PSCCRP is generally poor. Early diagnosis and monitoring of patients with long-standing nephrolithiasis is needed to improve patient outcomes.

PS-25-035
Glomerulocystic kidney presenting as a unilateral kidney mass in an infant with tuberous sclerosis: Report of a case and review of the literature
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Objective: The association between cystic kidney disease and the tuberous sclerosis complex (TSC) is well known, but its presentation as a unilateral mass with glomerulocystic pattern is rare. We describe a case of an infant with a prenatal diagnosis of TSC, with a renal mass that was believed to be a renal tumour.
Method: The clinical, radiological and histopathological findings of a case of TSC associated glomerulocystic kidney (GCK) are described, with a review of the literature.
Results: A 4-month-old infant with maternal history of TSC and prenatally diagnosed subependymal nodules and a right renal mass underwent nephrectomy. Histopathology revealed a segmental GCK with epithelial hyperplasia of the tubules and cysts. A diagnosis of TSC associated GCK was rendered. Eight other cases with similar histopathological findings were found in the literature, two of which presented as a localized mass.
Conclusion: We've described a case of a rare TSC associated cystic kidney lesion. Awareness of the entity and its presentation as a localized mass may aid in the differential diagnosis of renal masses in infants. The hyperplastic tubular epithelium found in ours and other reported cases seems so characteristic that may serve as a major clue for the diagnosis of TSC.

PS-25-036
Renal tuberculosis: A retrospective study of 100 cases
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Objective: Renal tuberculosis (RT) is the most frequent extra pulmonary TB disease and continues to be a major health problem in Tunisia. We propose in this study to review the clinical and histological characteristics of RT.
Method: This is a retrospective study over a period of 26 years from January 1990 to December 2015. Clinical data were reviewed for each patient and the following parameters were evaluated: gender, age at diagnosis, initial clinical symptoms and site of onset and histological features of the lesion.
Results: A total of 100 patients with histologically proven cases of RT were included. The majority were females 54 %, with a mean age of 48 years (ranges from 18 to 83). Symptoms were polymorphic: chronic renal failure 80 %; chronic pyelonephritis 15 %; urinary tract infections 3 %; renal mass 3 %. Twenty percent of patients had a history of extrarenal tuberculosis. The left kidney was the most affected site 60 %. We assessed an association to a clear cell carcinoma, an oncocytoma and an urothelial carcinoma.
Conclusion: RT is characterized, in our country, by the importance of its frequency and the polymorphism of its clinical manifestations. Pathologists must be aware of this pathology that must be suspected in every renal specimen.

PS-25-037
Clear cell papillary renal cell carcinoma: Distinct histopathologic and molecular genetic new entity
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Objective: Clear cell papillary renal cell carcinoma (CCPRCC) is a novel tumour entity that was recently recognized as a new distinct epithelial tumour within the current classification system. It is composed of cells with clear cytoplasm lining cystic, tubular, and papillary structures. The aim is to elucidate the spectrum of morphologic and immunohistochemical findings of a new recent entity.
Method: A 67-year-old man with no history of End stage renal disease was admitted to our medical center with right flank pain. An ultrasound scan revealed a mass in the right kidney. His subsequent computed tomography scan revealed a mass on right kidney, measured 4.5 cm diameter. Patient underwent right nephrectomy. He was discharged at postoperative third day, without any complication.
Results: On macroscopic examination, the tumour was solid and yellow-brown color. On microscopy examination, the tumour showed mixed areas of tubular and papillary structures. The papillae are covered with a single layer of clear cells with low-grade nuclei. The nuclei exhibit a characteristic linear arrangement away from the basal aspect of cells. Foamy macrophages, tumour necrosis, and vascular invasion are not seen. The tumour cells were positive for CK7 and negative for P504 and CD10. The diagnosis of CCPRCC was retained.
Conclusion: CCPRCC may pose diagnostic difficulties, where it may be mistaken for RCC with clear cell and papillary features. Attention to gross and histologic features, and appropriate immunohistochemical and molecular studies, should help distinguish CCPRCC from its mimickers.

PS-25-038

Useful immunohistochemical panel for differentiating renal cell carcinoma with papillary pattern

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Objective: This study aims to highlight the helpful histological and immunohistochemical features of different diagnoses of renal cell carcinoma with papillary pattern to enable reproducible classification.
Method: Thirty one RCC cases papillary architecture were selected then stained for CK7, CD10, Alpha methylacyl-CoA-racemase (AMACR) and TFE3.
Results: Tumour cell can be either clear or eosinophilic in clear RCC, Xp 11 translocation carcinoma. They are eosinophilic in papillary RCC type II and Acquired cystic disease associated carcinoma. The cytoplasm is clear in clear cell papillary RCC. Tumour cell are fusiform with clear cytoplasm in mucinous tubular and spindle cell carcinoma. The characteristic immunoprofile of Clear RCC is CK7−, AMACR−, CD10+ and TFE3−, papillary RCC is CK7+, AMACR+, CD10—and TFE3−, while for clear cell papillary RCC it is CK7+, AMACR−, CD10± and TFE3−, Xp11 translocation RCC is CK7−, AMACR+, CD10± and TFE3+ and lastly Acquired cystic disease associated carcinoma is CK7 -, AMACR+, CD10± and TFE3-. Mucinous, tubular and spindle cell carcinoma is diagnosed essentially on morphologic features.
Conclusion: To conclude, immunohistochemical staining for CD10, CK7, AMACR and TFE3 is a clear advancement in terms of immunohistochemistry application for RCC subtype differentiation when papillary is the predominant architecture as this is very crucial for further prognosis and targeted therapy because of the different behavior of each type.

PS-25-039

Metastasizing pleomorphic adenoma: Report of one case and literature review

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Objective: Pleomorphic adenoma (PA) is the most common benign neoplasm of the salivary gland, which can rarely metastasize without malignant transformation. Metastasizing pleomorphic adenoma (MPA) is indistinguishable from PA, yet produces secondary tumours in distant sites. Here we report a case of a MPA of the kidney 13 years after lateral parotidectomy for pleomorphic adenoma.
Method: A 43-years-old woman presented with haematuria. Subsequent abdominal computed tomography revealed a solitary cystic lesion in left kidney. A renal carcinoma was suspected and a radical nephrectomy was performed.
Results: Surgical specimen showed a grey-white cystic lesion located in the upper pole of the kidney. The lesion protruded from the cortical surface. Microscopically showed a mixed cell composition with epithelial component consisting of sheets and duct-like structures, as well as mesenchymal elements with chondroid differentiation.
Conclusion: Metastasizing pleomorphic adenoma to the kidney is a rare and poorly understood neoplasm and requires a careful patient history. Metastatic disease should be treated surgically when feasible, but the best therapy still remains unresolved. It appears worthwhile to look for any peculiar histology or molecular features to help predict its metastases.

PS-25-040

Genomic analysis of pure yolk sac tumours of testicular origin

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Objective: Pure adult yolk sac tumours (YST) of the testis are rare. In this study, we analyzed 5 pure adult YST and 3 pediatric YST using a 397-gene analysis panel to identify putative pathways in tumour development.
Method: DNA sequences were enriched with custom Agilent hybrid capture probe set, then sequenced on an Illumina HiSeq 2500 using 101 bp reads. A custom bioinformatics pipeline was used to identify variants and query the 1000 Genomes database to aid in the identification of germline variants and the COSMIC and cBioportal databases for known cancer association(s). SIFT and PolyPhen-2 predictions were used to evaluate variants of uncertain significance (VUS).
Results: Adult YST showed a total of 246 genomic variants. Somatic variants were filtered for known or likely deleterious effects; 15 genes harbored clinically significant (CS) mutations or variants of unknown significance (VUS) in a subset of cases. These genes and associated pathway members also showed germline variation in the remaining patients, with protein prediction suggesting a putative effect on protein function. Frequently altered genes include those involved in histone modification and DNA mismatch repair. Alterations in adherens junction/Wnt/APC pathway, splicing factor changes, and voltage-gated ion channel genes were also observed. Two known oncogenic mutations were identified: KRAS p.K117N, a signal transduction GTPase and CTNNB1 p.D32V, a transcription factor. The 3 pediatric YST showed a total of 101 variants, which were distinct from adult YST.
Conclusion: Our data suggests that unique defects in DNA repair and altered histone modification are common in adult pure YST and may contribute to the pathogenesis of this unusual tumour.

PS-25-041

Serous carcinoma involving the bladder wall: A mimicker of urothelial carcinoma

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Objective: Serous carcinoma can occasionally involve the bladder wall. We analyzed 21 patients with bladder wall involvement by serous carcinoma and highlight a subset of cases that lacked typical features and mimicked urothelial carcinoma (UCa).
Method: H&E slides were reviewed and immunohistochemical stains for CK7, WT-1, PAX-8, GATA-3, CK 7, p63 and p53 were performed.
Results: Patients age ranged from 44 to 80 year (average 62 years). Genitourinary symptoms included hematuria, hydronephrosis, and urinary retention; a bladder mass was the initial presentation in 4 patients (19 %). CA-125 was increased in 14 patients. In 16 cases imaging confirmed the presence of a pelvic mass. A concurrent or recent history of serous carcinoma involving the ovary (n = 16), endometrium (n = 3), or fallopian tube (n = 2) was reported and these cases showed classic histological features of high grade serous carcinoma. Psammomatous calcification was seen in 8 cases. Stromal reaction including desmoplasia and fibrosis was seen in 16 cases. However, a subset of cases lacked classic features of serous carcinoma and showed morphologic overlap with UCa, including nested architecture (n = 5), squamous differentiation (n = 2), spindle cell features (n = 2), poorly differentiated adenocarcinoma (n = 3), and lymphoepithelioma-like features (n = 1). Four cases showed full thickness involvement of the bladder wall, including colonization of the urothelial lining.
Conclusion: Serous carcinoma of the gynecologic tract rarely presents a diagnostic challenge. However, occasional cases with full thickness and involvement of the bladder wall, a remote history of gynecologic cancer, or colonization of the urothelial surface can mimic UCa.

PS-25-042

Performance evaluation of a novel rabbit monoclonal antibody to P504S in IHC staining of FFPE tissue

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Objective: A method comparison study for the performance (staining intensity) of rabbit monoclonal anti-P504S antibody (clone SP116) relative to widely used on-market clone (13H4).
Method: A total of 180 tissues were stained for this study (58 normal and 122 neoplastic), including a mix of prostate (81) and non-prostate (99). The list of tissues to be stained for the study was derived from multiple published sources to include normal and neoplastic tissues with various expected levels of expression. Tissues were qualified by a pathologist using H&E. As this was a study to characterize the rate of positivity in the tissues being tested, there were no overall acceptance criteria as an outcome for this study. The stained P504S slides for both clones were blinded and scored independently by two pathologists.
Results: The scoring data for staining intensity and background were analyzed by paired p-test analysis for each pathologist separately and combined across all tissues stained. All p-values are significant (<0.05) and in each case, the SP116 has higher mean staining intensity than the 13H4 clone used in this study, both by pathologist overall and by tissue category. The paired p-test analysis for background staining between the two clones was statistically equivocal in this study.
Conclusion: Rabbit monoclonal antibody to P504S, clone SP116, demonstrated staining that was equivalent or better across the tissues stained.

PS-25-043

GATA-3 expression in normal and neoplastic prostate: A comparative analysis with regard to 34βE12 cytokeratin

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Objective: Immunohistochemical expression of GATA-3 is characteristic of breast and urothelial carcinomas. We have analysed GATA-2 expression in normal and neoplastic prostate and compared it with 34βE12 cytokeratin staining.
Method: 68 samples of needle prostate biopsies (32 benign and 36 adenocarcinomas) were studied. One section of each simple was doublestained for GATA-3 and 34βE12, using an automatic stainer (Ventana). Another section was stained with GATA-3 duplicating the heating epitope retrieval time.
Results: Both GATA-3 and 34βE12 stained basal cells (3+), except in 5 cases (7,3 %) that showed foci only positive for GATA-3. In 48,95 % of our cases, GATA-3 also stained secretory cells. 1 of the 36 adenocarcinomas was GATA-3 positive (10 % of the cells) while all of them were negative for 34βE12 as expected. The two different antigen retrieval protocols for GATA-3 yielded similar results.
Conclusion: GATA-3 is strongly expressed by the basal cells of the prostate. There is no significant difference in the extent and the intensity of staining of GATA-3 compared to 34βE12 staining. GATA-3 may also stain secretory cells, and in very rare cases of prostate adenocarcinomas there be focal positive immunoreactivity. The application of two different antigen retrieval protocols did not produce differences in the staining.

PS-25-044

Profile of cancer of the prostate in Rwanda: Demographics, diagnosis, gleason score and prognostic grading

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Objective: To determine the profile of cancer of the prostate in Rwanda in regard to demographics, diagnosis, Gleason score and prognostic grading.
Method: A total of 120 cases of prostate cancer diagnosed at King Faisal Hospital (KFH), from 2010 to 2015, were retrieved together with clinical data. All cases were reviewed on H&E stain and Gleason score and grading were given using the criteria of the International Society of Urological Pathology (ISUP), 2014.
Results: Age range: 55–96 years; mean age: 70.95 years. Age groups; 61–70 years (42 %) and 71–80 years (33 %) were predominating. About 60 % of patients presented with LUTS/BOO. Only 14 % consulted because of raised PSA. About 50 % had hard nodular prostate on DRE. PSA was raised in 95 % of the cases before sample collection. Gleason score 9–10 (prognostic grade group V); Gleason score 4 + 3 = 7 (prognostic grade group III); Gleason score 4 + 4 = 8 (prognostic grade group (IV) were 40, 26 and 23 % respectively.
Conclusion: The majority of our patients presented with advanced disease. There is need to increase awareness on prostate cancer screening.

PS-25-045

Uncommon variants of urothelial carcinoma: A twelve years study in a Romanian county hospital

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Objective: The aim of this study is to outline the pathological features of uncommon variants of urothelial carcinoma (UC) in a retrospective study. These variants have diagnostic, therapeutic, and prognostic significance.
Method: All bladder transurethral resections (BTUR) performed for bladder cancer suspicion in the pathology department of Tîrgu-Mureş county hospital between 2004 and 2015 were reviewed. UCs were classified according to the 2004 WHO classification. Detailed morphological descriptions were used to diagnose uncommon histological UC variants; sometimes immunohistochemical profile was sought to refine the diagnosis. The corresponding pathological results on cystectomy were also available.
Results: Of 2432 UCs, 151 had divergent differentiation. In descending order, the uncommon variants of UCs were: micropapillary (18), sarcomatoid (12), plasmacitoid (3), inverted UC (2), microcystic (2), nested (2), UC with synciotrophoblastic-cells (1), with villo-glandular differentiation (1), or with osteoclast-type giant cells (1). With only one exception, all these variants were associated with high grade and/or invasive UCs. Unlike other variants, the micropapillary variant had a higher pathological stage at presentation and was more frequently associated with lymphovascular invasion.
Conclusion: Awareness of uncommon variants of UC is critical in avoiding misdiagnosis. Their presence should be mentioned in pathological reports because they may have different clinical outcomes or therapeutic approaches.

PS-25-046

Expression of putative cancer stem cell markers CD44 and CD133 in prostate carcinomas: A tissue microarray study of Iranian patients

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Objective: Cancer stem cells (CSCs) are the main players of prostate tumourigenesis and characterization of CSCs can pave the way for understanding the early detection, drug resistance, metastasis and relapse. Therefore, the current study was conducted to evaluate the expression level and clinical significance of the potential CSC markers CD44 and CD133 in a series of prostate tissues.
Method: One hundred and forty-eight prostate tissues composed of prostate cancer (PCa), high-grade prostatic intraepithelial neoplasia (HGPIN),

and benign prostate hyperplasia (BPH) immunostained for the putative CSC markers CD44 and CD133. Then the correlation between the expression of these markers and the clinicopathological variables was examined.
Results: Higher level of CD44 expression was observed in 42 % of PCa, 57 % of HGPIN, and 44 % BPH tissues. In the case of CD133 expression PCa, HGPIN, and BPH samples demonstrated high immunoreactivity in 46, 43, and 42 % of cells, respectively. There was an inverse significant correlation between CD44 expression with a Gleason score of ($P = 0.02$), while there was no significant correlation between CD133 expression and clinicopathological parameters.
Conclusion: Our results showed higher expression of both putative cancer stem cell markers, CD44 and CD133, almost in half of the prostate cases, while higher level of CD44 expression was observed significantly in PCa cases with lower Gleason score. Considering controversial findings regarding expression of CD44 and CD133 and their clinical significance, these markers still could not be counted as definite markers of CSCs for the development of new therapeutic strategies for PCs.

PS-25-047
Langerhans cell histiocytosis within a clear cell renal cell carcinoma
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Objective: Langerhans cell histiocytosis (LCH) is a rare proliferative disorder that is seldom found in the kidney.
Method: Herein, we report of a 54 year old asymptomatic woman treated for a small renal mass with a partial nephrectomy that was found to have LCH within a clear cell renal cell carcinoma (CCRCC).
Results: The CCRCC had a classical histomorphology (clear cells, chicken-wire like vessels, solid with some cystic and tubular areas) and this was supported by immunostains (positive: CD10, RCC, E-cadherin; negative: CD117, CK7, CK34betaE12, colloidal iron, CD68, S-100, CD1a and CD207). Likewise, the LCH also had a classic histomorphology (cerebri from nuclei, intermixed with eosinophils) and had characteristic immunostaining (positive: CD68, S-100, CD1a and CD207). Molecular testing of the LCH cells demonstrated the presence of a BRAF p.V600E missense mutation.
Conclusion: The surgical margins were clear and on follow-up the patient is well 6 months post-surgery without evidence of recurrence on cross-sectional imaging. Our patient did not have a history of LCH and is a short duration (7.5 years) ex-smoker. To our knowledge this is the third reported case of LCH in the kidney in association with RCC, and the second without a prior history of LCH.

PS-25-048
Is immediately repeat biopsy necessary for Atypical Small Acinar Proliferation (ASAP)?
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Objective: Atypical small acinar proliferation (ASAP) is a diagnoses that occurs in about 1–2 % of prostate biopsies. Within a 5-year period, approximately 30–40 % of patients with ASAP may develop cancer. Guidelines recommend a repeat biopsy within 3–6 months after the initial diagnosis. Our objective was to examine if there is an association between ASAP and high grade prostate cancer, challenge the need for immediate repeat biopsy.
Method: A retrospective multi-institutional review identified 83 patients who underwent prostate biopsy between 2007 and 2016 and were diagnosed with ASAP. Clinicopathologic features were analyzed.
Results: All 83 patients had a repeat biopsy. 18/83 were subsequently diagnosed with prostate cancer. 2 were high grade prostate cancer. 7 was Gleason 3 + 3, 7 was Gleason 3 + 4, 2 was Gleason 4 + 3, 1 was Gleason 4 + 4, 1 was Gleason 5 + 4. Radical prostatectomy was performed on 10 patients, 1 had TUR-P. Preoperative tPSA is significantly higher than the following one.
Conclusion: Only 4 patients have high grade ($8 \geq$ Gleason grade, 83 were ASAP on initial diagnosis. İmmediate repeat biopsy may be safely delayed.

PS-25-049
What is the significance of rete testis invasion by malign germ cell tumour and does hilum predicts metastasis?
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Objective: The significance of rete testis, hiler soft tissue invasion in malign germ cell tumours is stil controversial on current guidelines. We investigated the predictors of metastatic disease at presentation on malign germ cell tumours.
Method: Methods: 59 radical orchiectomy specimens were re-evaluated at Umraniye Training and Research Hospital and Uskudar State Hospital between 2007 and 2015.
Results: From 59 malign germ cell tumours; 26 patients were seminomatous, 33 were nonseminomatous. Mean patients age was 38,54 years (range, 17–89 years). Follow-up in formation was available in 50 patients with known rete testis and vascular invasions tatus. Mean follow-up duration was 39,84 months (range 3–96). Serum tumour marker levels are associated with rete testis invasion (p:0,035). Hiler soft tissue is significantly associated with vascular invaison (p0,001). Vascular invasion is significantly associated with metastasis as expected (p0,024).
Conclusion: We conclude that, there is a strong association between hiler soft tissue and vascular invasion. Hiler soft tissue should be reported on routine pathology reporting. Although we could not exhibit the significance of rete invasion, more information is needed.

PS-25-050
Comparative morphology analysis of kidneys at different kinds of implants in nephropexy: Experimental study
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Objective: Experimental evaluate the structural changes different types of implants with rats' kidney.
Method: 84 rats were divided into 3 groups. The first groups were rats with decellularized xenoperitoneum. Two control groups -partially absorbable lightweight mesh"UltraPro" and fascia-peritoneum graft were used. The kidney was resected on the 7th, 14th, 30th days and processed for histological analysis. Criterias were neovasculasitation, lymphoid infiltration and formation of sclerotic tissue. For morphological assessment was done using heamatoxyline-eosin.
Results: The first group, on 7th day there were vascularization, lymphoid infiltration and formation of granulation tissue. At 14 day infiltration by lymphocytes were observed; on 30th days have been identified of reactive changes and the development of sclerotic processes.In both control groups on the 7th day there were diffuse lymphoid reaction.On14th day formation of granulation tissue were marked. On 30th day growth of fiber connective tissue,adhesions, reactive inflammation were registered.

Conclusion: The performed investigation could recommend decellularized xenoperitoneum, which are most adequate for tissue in nephropexy. Biomaterial are characterized by less progressive fiber connective process, reactive inflammation compared to controls group.

PS-25-051

A grading dilemma; Gleason scoring system: Are we sufficiently compatible? Multi-center study from Turkey

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Objective: Gleason scoring is the grading system which strongly predicts the prognosis of prostate cancer. However; even being one of the most commonly used systems, the presence of different interobserver agreement rates push the uropathologists update the definitions of the Gleason patterns. In this study, we aimed to determine the interobserver agreement variability among 7 general pathologists and 1 expert uropathologist from 6 different centers.
Method: A set of 50 HE stained slides from 41 patients diagnosed as prostate cancer were revised by 8 different pathologists. The pathologists were also grouped according to being students in the same institute or working in the same center. All pathologists' and the subgroups' Gleason scores were then compared for interobserver variability by Fleiss' and Cohen's kappa tests using R V3.2.4. This study was supported by a project from the Scientific Research Projects Management Unit of Mugla Sıtkı Kocman University (Grant number: 15/086).
Results: Eight pathologists from 6 different centers revised all the slides. One of them was an expert uropathologist with experience of 18 years. Among 7 general pathologists 4 were working over 5 years whilst 3 were under 5 years. The Fleiss' kappa was found as 0,4828 for primary pattern; 0,3597 for secondary pattern and 0,4929 for total Gleason score which means moderate agreement.
Conclusion: Assigning Gleason score is a problematic system causing different interobserver agreement rates among pathologists even though the patterns were accepted as well-defined.

PS-25-052

Evaluation of prognostic sub-classifications T1a/b and T1m/e in T1 bladder cancer

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Objective: Several predictors of recurrence and progression of T1 bladder cancer have been proposed including the sub-staging of T1 stage. The aim was to assess sub-stadifications in a single-center patient's series.
Method: One hundred and seventy two T1 bladder tumours were classified according to the two sub-stadifications systems, T1a/T1b (superficial /deep lamina propria invasion) and T1m/e (invasion in a single focus within one HPF/other T1). Uni- and multivariable analyses were performed in order to assess the association of these classifications with disease recurrence/progression.
Results: A modification of the m/e system was proposed : T1M (invasion in one or multiples focus within one HPF each) and T1E (invasion above one HPF). Median follow-up was 5years. Of the 109 T1a tumours (63 %), 66 tumours were reclassified T1M (60 %) and 43 (40 %) T1E. During follow-up, 81 patients recurred (47 %) : 12 had tumours T1M (15 %) and 69 T1E (85 %); 44 patients progressed (25 %) : 6 had tumours T1M (14 %) and 38 T1E (86 %). In multivariable analyses, T1b and T1E stages were predictive of disease recurrence and progression.
Conclusion: This study confirms the reliable use of recent T1 subclassifications systems and the interest of this new reproductive and user-friendly classification M/E.

PS-25-053

Clinicopathological presentation of neuroendocrine tumours of the prostate: A study of 20 cases

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Objective: Neuroendocrine tumours (NET) of the prostate represent a multivarious group of tumours that exist both in pure forms and associated with prostatic adenocarcinoma. Our aim is to evaluate pathological features of NET of the prostate.
Method: Twenty cases of NET of the prostate diagnosed in the pathology department of university hospital Sfax (TUNISIA), were collected from January 2003 to December 2015.
Results: Prostatic adenocarcinoma with neuroendocrine differentiation (ANED) accounted for 70 % of cases. Small cells neuroendocrine carcinoma (SNEC) accounted for 25 %. Large cell neuroendocrine carcinoma (LNEC) was diagnosed in one patient aged 76 years. The Mean age at diagnosis was 62.7 years (range: 18–83) for ANED and 76.75 years (range: 70–81) for SNEC. Serum levels of prostate-specific antigen (PSA) were higher than10 ng/ml in all cases. Histologically, the proportion of neuroendocrine differentiation ranged from 20 to 90 % in ANED and from 5 to 70 % in 2 cases of mixed SNEC. Chromogranin and/or synaptophysin immunostaining were positive in all cases. PSA immunostaining was positive in 66 % of SNEC, 100 % of ANED and LNEC.
Conclusion: It is important to continue to study NET of the prostate to either validate or dispute their predictive clinical significance and therapeutic implications.

PS-25-054

Prognostic significance of lymphatic vessel density detected by D2-40 and its relation to Claudin-4 expressionin prostatic adenocarcinoma

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Objective: To evaluate intra- and peritumoural LVD through immunohistochemical expression of D2-40 in relation to claudin-4 expression and clinicopathological parameters in prostatic adenocarcinoma.
Method: Immunohistochemical staining procedure was performed on 53 paraffin-embedded blocks of radical prostatectomy specimens for prostatic adenocarcinoma using anti D2-40 and claudin-4 antibodies. Sections were evaluated for mean LVD in intratumoural and peritumoural tissues assessed by D2-40 expression.
Results: LVD in intratumoural tissues was significantly lower compared with peritumoural areas (P = .0001). Peritumoural mean LVD was significantly higher in cases with lymphovascular invasion (P = .041) and in cases with positive lymph node metastasis (P = .003) than intratumoural mean LVD. High claudin-4 expression was significantly correlated with high tumour grade (P = .0001), lymphovascular invasion (P = .006), and positive lymph node metastasis (P = .004). High claudin-4 expression was significantly associated with increased mean LVD in peritumoural tissues.
Conclusion: Increased peritumoural mean LVD in prostatic adenocarcinoma is associated with lymphovascular invasion and positive lymph node metastasis. High claudin-4 expression is associated with high tumour grade, lymphocascular invasion, positive lymph node metastasis, and high mean peritumoural LVD suggesting that D2-40 and claudin-4 may represent different mechanisms of lymphatic vessel invasion with both biomarkers is related to poor prognosis.

PS-25-055

Histopathological examination of 554 transurethral resection speciemens of urinary bladder tumours

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Objective: Underlying aims of this study was decumanting the histopathological and clinical features, recurrence and progression of the bladder urothelial carcinoma(UC).
Method: In our study 554 diagnosed transurethral resection material were analyzed retrospectively in the pathology laboratory of two university hospitals, between 2006 and 2014 years.
Results: 554 patients were followed median 17.5 months (minimum 1 month, maximum 162 months). Their estimated mean survival was 121.7 months. According to log rank analysis, gender ($p = 0.955$) presence of differentiation($p = 0.523$), primer ($p = 0.351$) did not show statistically significant effect on survival but age (estimated mean is 138.9 months in 65 and younger, 110.1 months over 65 years old, $p = 0.018$), grade, microscobic tumour infiltration, configuration were statistically significant, ($p < 0.001$). According to Cox regression analysis, age ($p = 0.009$) and grade are most important determinants of survival. Invasive tumours into muscularis propria have significantly bad prognosis compared to non-infiltrative tumours ($p < 0.001$).
Conclusion: Early dignosis can reduce the morbidity and mortality in urothelial carcinomas. Standard urologic evaluation, urinary cytology, ultrasound scanning, contrast urography and cystoscopy, in addition to coordinated efforts between pathologists and urologists should aid early detection and diagnosis of precursor lesions.

PS-25-056

Mucinous tubular and spindle cell carcinoma: Morphological heterogeneity and diagnostic pitfalls

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Objective: Characterize the morphological spectrum of mucinous tubular and spindle cell carcinoma (MTSCC) and underline some diagnostic pitfalls.
Method: Clinicopathological re-evaluation of MTSCC cases diagnosed at Portuguese Oncology Institute-Porto (IPO-P) and literature review. Demographics, morphology, immunohistochemical study and main differential diagnosis were noted.
Results: Two MTSCC were retrieved. Both were from women, with 59 and 73 years, within the reported gender predominance and age range (13–81). One tumour presented classic morphology, low nuclear grade and only focal papillations; differential diagnosis included papillary (solid variant) renal cell carcinoma (RCC) and sarcomatoid change in RCC. Conversely, the other tumour was predominanty composed by spindled cell component; presented a higher nuclear grade and numerous cells with clear or vacuolated cytoplasm; differential diagnosis included mainly clear cell RCC with sarcomatoid change. Indeed, a clear cell RCC diagnosis was rendered in pre-surgery core-biopsy. Sarcomatoid change, seldom described in MTSCC reported cases (<10 %), was absent in our cases. Both tumours were kidney confined and displayed CK7 (multifocal) and vimentin immunostaining.
Conclusion: MTSCC is a rare renal tumour that might present a broad spectrum of morphologic appearances. Awareness of these uncommon morphologies might be determinant to achieve correct diagnosis and immunohistochemistry might be helpful in difficult cases.

PS-25-057

Papillary renal cell carcinoma: Clinicopathological and immunohistochemical study of 15 cases

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Objective: Papillary renal cell carcinoma (PRCC) is the second most common type of renal cell carcinoma and is morphologically separated into 2 subtypes. We reviewed the clinicopathological and immunohistochemical features of 15 cases.
Method: Clinical records, histopathological and immunohistochemical slides of PRCC from our archive from 2003 to 2016.
Results: Of a total of 188 cases, 15 PRCC cases were identified (6 type 1, 8 type 2, and 1 mixed), 11 male and 4 female. Mean age was 59.8 years for type 1 and 58.6 years for type 2. Mean tumour size was 3.1 cm for type 1 and 3.3 cm for type 2. Type 2 tumours had higher nuclear grade than type 1 tumours. Mean follow-up was 36 months (1–151). Based on follow-up data, both subtypes have an excellent prognosis when diagnosed at an early stage. One patient with locally advanced type 2 PRCC died of disease after 22 months. Immunohistochemical profiles of both subtypes were similar.
Conclusion: There is a significant overlap in the clinicopathological and immunohistochemical features of both subtypes of PRCC. The presence of mixed histology suggests that there is a continuum between these 2 types. The follow-up data in this study suggests that mortality from the tumour is low.

PS-25-058

Temporal trends in pathologic carcinoma staging in a 23-year cohort of men treated with radical prostatectomy

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Objective: This retrospective study examined a cohort of 1870 men treated by radical prostatectomy (RP) for CaP between 1993 through 2016 to analyze trends in stage and grade migration at diagnosis over time.
Method: CaP pathologic stage and grade were determined on whole mount prostate specimens in an ongoing, prospective, longitudinal cohort study military patients, a participating center in the Center for Prostate Disease. Grading was re-evaluated retrospectively using the 2016 ISUP revised grade group score (GG).
Results: From 1993 to 2008, the largest tumour dimension (LTD) decreased from $2.5 \pm 0.9 \pm$ to 1.8 ± 0.8 cm ($p < 0.0001$), while the proportions of extraprostatic extension (EPE) decreased from 50 to 28 % ($p < 0.0001$), seminal vesicle invasion (SVI) from 20 to 3 % ($p < 0.0001$) and pT4 spread from 3 to 0.2 % ($p < 0.0001$). After a plateau, the LTD rose between 2012 to 2016 from 1.2 ± 0.8 to 2.1 ± 0.8 ($p < 0.0001$), EPE from 23 to 34 % ($p = 0.005$), and SVI from 5 and 13 % ($v = 0.001$). The mean GG declined from 3.1 ± 1.3 in 1993 to 2.5 ± 1.4 in 2005 ($p < 0.0001$) and then, after a plateau, rose from 2009 to 2016 from $2.3 \pm .07$ to $3.1 \pm .08$ ($p = 0.01$).
Conclusion: In this large prospective cohort of patients with comparable health care access, there were significant time-dependent CaP pathologic stage and grade migrations, which followed somewhat different time courses. A possible link between these trends and changes in PSA screening or treatment interventions with curative intent warrants further examination.

PS-25-059

Predicting the BCG response in bladder urothelial carcinoma: Utility of the Th2/Th1 ratio in peritumoural lymphocytes

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Objective: The mechanism of bladder carcinoma control after treatment with intravesical BCG is unknown and no reliable predictor of response is available. BCG is a potent immunomodulator that polarizes the immune reaction towards a Th1 response. Our aim is to determine the type of immune response (Th1 or Th2) in peritumoural stromal lymphocytes of patients with high grade urothelial carcinoma, non-muscle invasive, before treatment and to establish if immune response type pre-treatment conditions the subsequent clinical response.
Method: We evaluated tumour tissue obtained by diagnostic transurethral resection from 19 patients who subsequently received treatment with BCG, classified as responders (n = 11) and non-responders (n = 8). We determined the number of Th1 lymphocytes (T-bet+) and Th2 lymphocytes (GATA-3+) by immunohistochemistry.
Results: Responders (Rs) to BCG treatment showed more Th2 lymphocytes and fewer Th1 lymphocytes (average: 151 and 28 cells/field, respectively) than non-responders (NRs) (average: 93 and 46, respectively). The Th2/Th1 ratio was significantly higher in Rs compared with NRs.
Conclusion: The presence of Th1 lymphocytes in peritumoural stroma before BCG therapy is associated with a lack of response to BCG. Determination of the Th2/Th1 ratio could be used as a predictive marker of BCG treatment response.

PS-25-060
Non-urothelial bladder tumours: A morphological study
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Objective: Non-urothelial bladder tumours are rare and still diagnostic challenging entities. We aim to make a judgeful correlation between morphologic types and age groups, that can guide towards a better understanding of this pathology.
Method: We analysed 110 cases of non-urothelial bladder neoplasias out of 756 bladder tumours diagnosed in our unit between 2006 and 2015. We received the material as 29 cistectomy specimens and 81 transurethral resection fragments (TURs). The patients were 23 females and 87 males with a mean age of 67 years (ranging from 24 to 89 years old). Imunostains were used in 29 cases to complete the diagnose.
Results: In the younger age group (24–60 years old) we diagnosed 15 secondary tumours (50 %) and 15 (50 %) primary tumours represented by 4 adenocarcinomas, 3 sarcomatoid, 3 undifferentiated and 2 squamous carcinomas, a PEC-oma, a paraganglioma and an atypical leiomyoma. In the older age group (60–89 years old), we diagnosed 51 secondary tumours (63.7 %) and 29 primary tumours (56.3 %) represented by 9 undifferentiated/unelucidated, 8 squamous and 6 sarcomatoid carcinomas, 3 adenocarcinomas, 2 neuroendocrine and a lymphoepithelial carcinoma.
Conclusion: Younger patients could be prone to developing non-urothelial primary tumours that should be carefully taken into consideration in the differential diagnosis.

PS-25-061
Retrospective analysis of urothelial bladder carcinoma in the age group of 45 years and under
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Objective: Urothelial bladder carcinoma (UBC) is a cause of significant morbidity and mortality in the Western world and an illness mostly diagnosed in elderly patients. The aim of the study is to evaluate pathological characteristics of UBC in young patients diagnosed and treated in our centre.
Method: We performed a retrospective study to identify patients ≤45 years of age on initial diagnosis of UBC. Our review covers the clinicopathological data for a period of 5 years. The exclusion criteria for the study was a diagnosis of non-urothelial tumours.
Results: From a total number of 748 patients with UBC, we have selected a number (n = 18) that met our selection criteria (age). The cohort consisted of 17 males and 1 female, with a mean age of 40.8 years, with the youngest patient being 29 years of age. Out of 18 UBCs, 3 cases were PUNLMP (16.6 %), 6 cases low-grade papillary urothelial carcinoma (33.3 %) and 9 cases high-grade papillary urothelial carcinoma (50 %). Initial staging of the lesions showed: 9 pTa cases, 7 pT1 cases, 1 pT2 case and 1 pT3 case. On follow-up, 4 patients presented with local recurrences and progression of the tumour.
Conclusion: UBC in young patients presented histopathological features similar to the one found in the elderly population. Our results showed a male predominance and therefore we suggest the necessity for implementing screening guidelines for the atrisk young population.

PS-25-062
Genetic alteration in urothelial carcinoma: Comparison between upper tract and bladder origin
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Objective: Urothelial carcinoma of the upper tract (UTUC) or the bladder (UCB) share common risks associated factor. We investigated and compared genomic aberration (GA) in urothelial carcinoma in both localisations in order to find specific alteration.
Method: Frozen tissues from 13 UCB (4 pTa, 5 pT1 and 4 pT2) and 16 UTUC (5 pTa, 6 pT1 and 5 pT2) were subject to comparative genomic hybridisation (CGH) with the BCA-1 assay design for urothelial carcinoma.
Results: pTa UCB have more frequent GA than UTUC (16 vs 13 %) and show any amplification (0 vs 6 %). In both origins GA were more frequent in T2 carcinoma (UBC 17 % and UTUC 23 %). Some specifics GA were found: 16q deletion for UCB, 21q amplification for UTUC, 4pq alteration in pT2, 5q amplification in pT2 UCB.
Conclusion: With a specific CGH array for urothelial carcinoma we found GA presents only in UCB or UTUC and also others only in muscle invasive carcinoma. This can be an ancillary test for the origin of urothelial carcinoma specialy on cytology specimen.

PS-25-063
PTEN loss in noninvasive low-grade papillary urothelial carcinoma
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Objective: We investigated the clinical and pathologic significance of PTEN loss in noninvasive low-grade papillary urothelial carcinoma (NI-LGPUC).
Method: Tissue-microarrays were constructed from biopsies of 82 patients with NI-LGPUC of bladder. A Total of 291 transurethral biopsies were included in the array comprising 82 initial and 209 follow-up biopsies. Every biopsy was represented with three cores, two from tumour and one from neighboring benign urothelium. Immunohistochemical staining was performed for PTEN. PTEN expression was scored semi-quantitatively by generating an H-score (intensity x percentage of staining) (range between 0 and 300). Tumours with an H-score of 20 or below were accepted as loss of PTEN expression.
Results: Mean patient follow-up was 64 months (14–285 months). 10 out of 82 tumours (12.2 %) had grade and/or stage progression. We were able to evaluate PTEN expression of 75 cases. Among those, 5 cases (all males) displayed PTEN loss. Three patients with negative PTEN showed grade and/or stage progression in their follow-up. Fourth case developed PTEN loss in its recurrence where tumour transformed to invasive cancer.

Conclusion: Our findings suggest that PTEN loss may have a role in tumour progression in NI-LGPUC. Further studies are needed to investigate the biology and clinical implication of PTEN in NI-LGPUC.

PS-25-064

Sclerosing Sertoli cell tumour. Pitfalls in the diagnosis of a rare neoplasm

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Objective: Sertoli cell tumour is a rare type of sex-cord stromal tumours of the testis. It accounts for less than 1 % of all testicular neoplasms. It is classified into three main variants by WHO. These are Sertoli cell tumour, not otherwise specified; large cell calcifying Sertoli cell tumour; and sclerosing Sertoli cell tumour (SSCT). The later being an exceedingly rare variant.
Method: Case report: A 48-year old Saudi man presented with infertility. On physical examination, he had a left scrotal mass without any nodal or distant metastases. Orchiectomy was done, and a rubbery white tan nodule about 2 CM in diameter was found within the left testis.
Results: Microscopic examination revealed a tumour with areas of sclerosis and hyalinization, composed of cords, nests and trabeculae of uniform cells with small rounded nuclei, finely granular chromatin, small nucleoli, and modest amount of pale or slightly eosinophilic cytoplasm. No mitotic figures, nuclear atypia or necrosis were noted. The differential diagnosis included seminoma, neuro-endocrine tumour, lymphoma, Leydig cell tumour and other sex cord tumours. Immunohistochemical markers for germ cell tumours, neuroendocrine tumours, lymphoma, and sex cord tumours were all negative. The tumour stained positive only for vimentin.
Conclusion: This unusual and rare tumour posed a diagnostic dilemma. The vimentin positive only staining added to the difficulty in diagnosing it. Review of recent literature, and finding that several similar tumours stained only for vimentin, and the sclerotic nature of the tumour made it possible to reach the diagnosis.

PS-25-065

Characteristics of PIN associated with the presence of prostate cancer

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Objective: To describe a set of morphological and immunophenotypic features of PIN, located in close proximity to the glands of prostate cancer (PCa).
Method: Material of 630 multifocal needle biopsies (including 62 repeat biopsies) and 218 radical prostatectomies was analyzed.
Results: It was found that PIN located near the PCa glands had significantly increased frequency ($p < 0,05$) of inverted or cribriform histologic variants when compared with the isolated PIN and characterized by the presence of intraluminal crystalloids, a higher frequency and level of AMACR expression ($p < 0,05$) and do not differ from PCa based on this parameter ($p > 0,05$). ERG-positive nuclear staining of PIN cells occurs in 15 % of the 60 % ERG-positive PCa. To assess the predictive value of features that were significantly more often detected in PIN located in the vicinity of the PCa, 62 cases of repeat biopsies which were diagnosed previously with PIN were analyzed. PCa was detected in 30.6 % of patients in repeat biopsy group. 15 cases were referred to the group with high level of AMACR expression, 47—with the absence of AMACR expression. ERG expression was detected in only 2 patients of this group. Two-sided lesion, PIN multifocality and cribriform PIN occurred significantly more often in the first biopsy in patients who were subsequently diagnosed with cancer. In multivariate analysis, multifocal lesions, cribriform PIN, PIN with high expression of AMACR were independent predictors of PCa detection in consecutive biopsies.
Conclusion: Morphological and immunophenotypical features of PIN associated with prostate cancer were determined, which may help in making a decision on whether to perform repeat biopsy or not.

PS-25-066

Immunohistochemical characteristics of prostate cancer in patients with age-related androgen deficiency and metabolic syndrome

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Objective: To to determine the pattern of expression of androgen (AR) and estrogens (ERa and Erß) receptors, aromatase (Arom), growth factors (TGF-ß, EGFR and VEGF), proliferation (Ki-67, CyclinD1, TopoIIα) and apoptotic (Bax, Bcl-2) markers in prostate cancer (PCa) in patients with age-related androgen deficiency and metabolic syndrome.
Method: Multifocal needle biopsies and radical prostatectomy specimens of patients with prostate cancer in the settings of age-related androgen deficiency and metabolic syndrome, and without aforementioned settings (16 and 30 patients, respectively), were analyzed.
Results: It was found that in patients with age-related disorders of androgen status and metabolic syndrome, prostate cancer has a higher proliferative activity of tumour cells according to the expression of Ki-67, CyclinD1, TopoIIα, more frequent expression of EGFR, absence of VEGF expression, more infrequent decrease in Bax expression, more frequent decrease in AR expression, ERß, an increased frequency of ERa expression and Arom expression. It was found that the presence of inflammation in PCa patients with androgen deficiency and metabolic syndrome was accompanied by increased expression of TGF-ß, without changing the ($p > 0,05$) expression level of EGFR, VEGF and sex hormone receptors (AR, ERa and Erß).
Conclusion: In prostate cancer of patients with age-related androgen deficiency and metabolic syndrome there were increased tumour cell proliferative activity, expression of epidermal growth factor receptor, estrogen receptor A and aromatase, decreased level of expression of androgen receptor, ß estrogen receptor, absence of vascular endothelial growth factor expression.

PS-25-067

Clinical significance of putative stemness marker Nanog in different histological subtypes of renal cell carcinoma. A study using tissue microarrays (TMA)

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Objective: The expression of Nanog in RCC specimens was evaluated by immunohistochemistry on a tissue microarray(TMA). One hundred and fifthy-three consecutive patients treated surgically for renal cell carcinoma (RCC) between 2010 and 2015 including 97(63.4 %) Clear Cell Renal Cell Carcinoma (ccRCC), 28(18.3 %) Papillary and 28(18.3 %) Chromophobe were selected. The association between expression of this marker and tumour characteristics was then analyzed.
Method: The expression of Nanog in RCC specimens was evaluated by immunohistochemistry on a tissue microarray(TMA). One hundred and fifthy-three consecutive patients treated surgically for renal cell carcinoma (RCC) between 2010 and 2015 including 97(63.4 %) Clear Cell Renal Cell Carcinoma (ccRCC), 28(18.3 %) Papillary and 28(18.3 %) Chromophobe were selected. The association between expression of this marker and tumour characteristics was then analyzed.
Results: The mean nuclear expression of Nanog is not significantly different in RCC subtypes ($P = 0.07$). A significant correlation was observed

between H-Score of Nanog and RCC subtypes (P = 0.005). The highest mean H-Score of Nanog (96.8) was observed in ccRCC. The statistically significant association was not found between expression of Nanog and other patients, clinicopathologic features.
Conclusion: These findings suggest that nuclear staining of Nanog cannot be considered as a valuable tool for the study of renal CSCs. Because of its expression in cytoplasm and nucleous in RCC subtypes, more data are needed to confirm the correlation of Nanog with the clinicopathological characteristics of RCC.

PS-25-068
Bilateral testicular germ cell tumours: 3 case reports and review of the literature
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Objective: About 95 % of testicular neoplasms are of germ cell origin. They develop as bilateral in 1–5 % of cases, mostly metachronously.
Method: We report on three cases with bilateral testicular germ cell tumours treated by orchiectomy. Two of the patients underwent bilateral radical orchiectomy. One of them was diagnosed with seminoma in left testis and embryonal carcinoma in right testis, other one was diagnosed with bilateral seminoma. Bilateral partial orchiectomy was performed for the third patient and histopathologic evaluation revealed bilateral embryonal carcinomas. Also, intratubular germ cell neoplasia was detected surrounding testicle parenchyma in each patient.
Results: The patient who underwent bilateral partial orchiectomy for bilateral embryonal carcinomas developed seminoma in right testis after one and half year after the operation.
Conclusion: Bilateral radical orchiectomy is considered as standart treatment for bilateral germ cell tumours of the testicles. However long term effects are not yet known, testis-sparing surgery could be an alternative for the selected patients to improve quality of life and fertility. Here, we discuss the age distribution, interval and histological classification of these cases and reviewed previous reports of bilateral germ cell testicular tumours.

PS-25-069
Synchronous bilateral testicular tumours with different histopathology: Dermoid and epidermoid cyst
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Objective: We report a unique case of epidermoid cyst(EC) in one testicle and dermoid cyst(DC) in other side synchronously.
Method: A 24 year-old man, presented with left painless testicular mass. Laboratory investigations, including tumour markers were normal. Ultrasonography revealed a well-circumscribed, nonvascular mass in left testis and another cyst in right one. Patient underwent left radical orchiectomy, right partial orchiectomy and frozen storage of sperm. Grossly similar looking, one each cyst filled with keratin was seen on both testiscles. Histopathological evaluation of left testis revealed a cyst lined by keratinizing squamous epithelium and filled with keratin debris without dermal appendages or teratomatous elements. Right testis had a cyst lined by keratinizing squamous epithelium and sebaceous glands without noncutaneous teratomatous elements. On both testicles intratubular germ cell neoplasia (IGCNU) was not present. Diagnose was EC in left testis and DC in right one.
Results: No testicular tumours developed during clinical follow-up.
Conclusion: Testicular EC and DC are seen quite rare. They do not require any additional therapy after orchiectomy. Examining surrounding testis for teratomatous components and IGCNU is essential, because these would lead diagnosis to teratoma. This report could be a guide for diagnosis and management of young patients with bilateral benign testicular tumours.

PS-25-070
Cytologic diagnosis of plasmocytoid and small cell neuroendocrine carcinoma of the bladder in urine samples
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Objective: To review the diagnosis in urinary cytology of two rare and aggressive variants of urothelial carcinomas (UC) diagnosed by biopsy.
Method: We looked for bladder "plasmacytoid urothelial carcinoma" (PUC) and "small cell neuroendocrine urothelial carcinoma" (SCNUC) since 1965 to 2015. Only cases with both cytology and biopsy studies and more than 50 % of the variant component were included.
Results: We found 4 cases of PUC (2 were positive and 1 was now identidied as plasmacytoid). Eighteen SCNUC were divided into 3 groups: 1) pure neuroendocrine (9 cases); 2) mixed with urothelial carcinoma in situ (CIS) (6 cases) and 3) mixed with infiltrating UC (3 cases). The positive results in the three groups were 3, 5 and 1 respectively. In review 2, 5 and none were detected as having neuroendocrine morphology. Neuroendocrine differentiation was overlooked in 1 negative cytology (group 1) and 2 suspicious for malignancy (group 3).
Conclusion: Specific characteristics distinguish these variants from conventional UC in urine cytology. PUC is a high grade carcinoma with peculiar round to oval nuclei with a particular smooth nuclear membrane and less irregular chromatin. SCNUC is similar to lung counterpart. The frequent inflammatory background hinders the diagnosis. They are more easily identified when mixed with CIS.

PS-25-071
Clear cell adenocarcinoma of the remnant uterus in a male patient with persistent Mullerian duct syndrome: A case report
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Objective: Persistent Mullerian duct syndrome (PMDS) is a rare genetic disorder characterized by the persistence of Mullerian duct derivatives, including uterus, cervix, fallopian tubes and upper vagina, in otherwise normally differentiated males. We report an extremely rare case of clear cell adenocarcinoma arising from the remnant uterus in a male patient with PMDS.
Method: A 45-year-old male presented with a large pelvic lesion measuring 13 cm in maximum diameter. An exploratory laparotomy was performed.
Results: Unexpectedly the pelvic lesion proved to be a uterus, dissection of which revealed a large tumour in the endometrial cavity measuring 7 cm in length. Morphological and immunohistochemical features of the tumour were consistent with clear cell adenocarcinoma, which infiltrated the uterine wall, the adjacent vas deferens and the seminal vesicle. An undescended testis focally infiltrated by the above tumour was also found.
Conclusion: A variety of germ cell tumours of the testis have been reported in association with PMDS. As regards management of Mullerian remnants, most authors suggest leaving these structures in situ, because of the difficulty in dissection and the presumed absence of risk of malignancy. However, considering the current evidence of malignancies arising from Mullerian remnants, surgical removal or long-term follow-up is necessary.

PS-25-072
DNA repair gene polymorphisms and risk of clear cell renal cell carcinoma
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Objective: Association between DNA repair gene polymorphisms and several types of cancer was widely studied, but their role in development of clear cell renal cell carcinoma (CCRCC) has not been established. The purpose of the present study was to investigate the association of XRCC3Thr241Met, XPDLys751Gln XRCC1Arg194Trp, and XRCC1Arg399Gln gene polymorphism with the risk of CCRCC.
Method: 73 patients with CCRCC and 100 healthy individuals without cancer were included in this study. XRCC3, XPD and XRCC1 genotypes were determined with polymerase chain reaction—restriction fragment length polymorphism (PCR-RFLP).
Results: No association was found between variant genotypes of XRCC3Thr241Met, XRCC1Arg194Trp, and XRCC1Arg399Gln gene polymorphisms and risk of CCRCC in investigated cohorts. A significant difference between patients and controls was noticed for XPDLys751Gln variant genotype (OR = 2.92, 95%CI:1.47-5.79,p-0.001). For the combined genotipes XRCC3Thr241Met/XPDLys751Gln/XRCC1Arg194Trp/XXRC1Arg399 a significant difference between patients versus controls was observed for Thr/Thr+Lys/Gln+Arg/Arg+Arg/Gln (OR = 2.56, 95%CI:1.36-5.62, p-0.002), and for Thr/Met+Lys/Gln+Arg/Trp+Arg/Arg (OR = 3.82 95%CI:1.31–4.25, p-0.01). Also a significant difference between patients versus controls was observed for Thr/Met+Gln/Gln+Gln/Gln (OR = 3.17, 95%CI:1.05-7.54, p-0.04).
Conclusion: The presence of at least two variant genotype (heterozygous or homozygous) of investigated gene polymorphisms may represent a risk factor for developing CCRCC.

PS-25-073
Diagnostic value of percutaneous biopsy for renal masses: A study of 138 cases
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Objective: We report the efficacy and diagnostic accuracy of a percutaneous biopsy for kidney masses.
Method: Clinicopathological data for patients who underwent percutaneous biopsy for a renal mass have been retrieved from the hospital's database.
Results: A total of 138 biopsies of renal masses was performed for the last 8 years in our institution. The biopsy was diagnostic in 107 cases (77.5 %) and non-diagnostic in 31 (22.5 %). Ten were for pediatric patients, 4 of which were diagnosed as a neuroblastic tumour. Sixty-five masses of RCC and 3 cases of urothelial carcinoma have been proven by biopsy. Biopsy proved the metastases of a germ cell tumour in 2, prostatic adenocarcinoma in 1, squamous cell carcinoma in 3, mucinous adenocarcinoma in 1, neuroendocrine carcinoma in 1, lung adenocarcinoma in 1 and serous adenocarcinoma in 1 patient. Two of 5 patients with a diagnosis of mesenchymal tumour was malignant on biopsy. Six patients had benign renal masses including oncocytoma, angiomyolipoma, ganglioneuroma. Six patients have been referred to oncology/hematology clinics with the diagnoses of lymphoma and plasmacytoma. Concordance rates between biopsy and final surgical pathology were > %95.
Conclusion: Percutaneous biopsy is an effective method for providing correct diagnosis of a renal mass and guides treatment decision.

PS-25-076
Extragastrointestinal stromal tumour (EGIST) of the bladder — a case report
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Objective: EGISTs are very rare mesenchymal neoplasms, accounting for less than 5 % of soft tissue tumours. They occur outside the digestive tract and have similar histological and immunohistochemical characteristics with gastrointestinal stromal tumours.
Method: We report the case of a 52 years old man presenting with gross hematuria.
Results: Transabdominal ultrasonography revealed inside the urinary bladder, a pedunculated 5 cm mass, with 1 cm insertion base, which was removed by TUR-B. The tumour was composed of sheets of elongated and polygonal cells, with abundant acidophilic, vacuolar cytoplasm, atypical nuclei, and a mitotic count of 15/ 50 high power fields (HPFs). Tumour cells were positive for DOG 1 and CD34, and negative for CD117.
Conclusion: There are less than 10 bladder EGISTs described to date, and there are insufficient data about their risk of progression. DOG 1 is the most sensitive marker for the diagnosis of EGISTs since they are frequently CD 117 negative.

PS-25-077
pT1 Urothelial carcinomas: A molecular subclassification and correlation with other immunohistochemical features
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Objective: Stage pT1 urothelial carcinomas constitute a heterogeneous group with a different risk of progression. We have applied the recently developed molecular classification of high-grade urothelial carcinoma (two types: basal and luminal) to a group of pT1 urothelial carcinomas.
Method: Immunohistochemistry was performed on sections from tissue arrays (85 samples from 45 different pT1 high grade urothelial carcinomas). A multimer-based method was applied in an automatic stainer (Ventana) using antibodies against CK5, CD44, CK20, p53 and ERBB2.
Results: 29 (64,4 %) cases were categorized as luminal (CK 5-, CD44-, CK20+) and 3 (6.7 %) as basal (CK5+, CD44+, CK20-) subtypes. 13 cases (28.9 %) had overlapping results or no immunoexpression, and were not classifiable. P53 was positive in 18 (62,1 %) luminal and 1 of the 3 basal cases. ERBB2 was 3+ in 10 (34,5 %) luminal and 2 of the 3 basal cases.
Conclusion: Immunohistochemistry aids to classify urothelial carcinomas as basal or luminal types although it is not conclusive in some cases. Most of the pT1 carcinomas are of luminal type, with a large proportion of p53+, and only one third ERBB2 3+. Larger studies are needed to elucidate a possible relevance of classification of pT1 carcinomas as basal type for treatment or follow up.

PS-25-078
Metachronus bilateral testicular germ cell tumours — report of two cases
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Objective: Testicular cancer is the most common cancer of young men and its incidence continues to rise. The developement of bilateral testis cancer is exceedingly rare.
Method: We report the case of two men.
Results: One had stage 1 mixed embryonal carcinoma and teratoma at the age of 17 in 2000. He developed stage 2 contralateral seminoma testis 16 years later. Another patient had right orhidectomy in 2003 for stage 2 embryonal carcinoma, had adjuvant chemotherapy and developed stage 3 contralateral testicular tumour, 13 years later, wich was also seminoma. There is a small but definite risk for development of a second testicular malignancy and chemotherapy for the first testicular tumour does not eliminate the risk of developing a contralateral tumour.
Conclusion: The focal nature of intratubular germ cell neoplasia in the second testis questions the value of biopsy of the contralateral testis. Despite careful follow-up, the second primary tumour was not diagnosed

early enough to avoid chemotherapy. Adelina Birceanu and Monica Hortopan have equal rights.

PS-25-079

Prognostic value of the proliferative index determined by Ki-67 (Bmi-1) in primary papillary urothelial tumours of the bladder (stage Ta/T1): Algerian prospective study about 117 cases

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Objective: To evaluate whether ki-67 index has independent prognostic value for survival of patients with bladder papillary urothelial tumours.
Method: Ki-67 was evaluated in 117 cases. Non-invasive (stage Ta, n = 61) tumours were: papilloma (n = 2), papillary urothelial neoplasia of low malignant potential (PUNLMP; n = 5), low grade (LG; n = 44) and high grade (HG; n = 10) papillary urothelial carcinoma. Invasive (stage T1, n = 56) tumours were: LG (n = 6) and HG (n = 50) carcinoma. Statistical analysis included Fisher and x2 tests, univariate and multivariate survival analyses were performed according to the Kaplan-Meier method with log rank test and Cox's proportional hazard method.
Results: The Ki-67 index increases with the grade; the difference is significant between the LGTa and HGTa (p <10-6). The proliferation index is also correlated with the tumour stage (p < 10–5). In univariate analysis, the Ki-67 is not correlated with recurrence or disease-free survival (DFS) (p = 0.752). However it is a predictor of progression (p < 10–4) and is correlated with progression-free survival (PFS) (p < 0.0001). In multivariate analysis, the Ki −67 emerges as factor independent of tumour progression.
Conclusion: The Ki-67 appears as a predictive marker of tumour progression bladder urothelial cellcarcinoma in multivariate analysis.

PS-25-080

Prognostic significance of contemporary prostate cancer grading system in tumours with positive surgical margins

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Objective: Pre-operative serum PSA, Gleason pathological grade, positive surgical margins and capsular incision are significant in predicting clinical and biochemical recurrence of the disease treated with prostatectomy. The modified Gleason classification uses prognostic groups that better reflect the true biological nature of disease.
Method: 121 patients with acinar type prostate adenocarcinoma were selected following radical prostatectomy with acompaning clinical and histopathological data. Patient groups were divided according to the stage and the positive surgical margins and Ki67 index of proliferation. The outcome was based on the data of biochemical recurrence. We compared the prognostic impact of old and new Gleason classification using standard statistical methods.
Results: By analyzing both Gleason systems (an average score and prognostic groups) comparing groups with a positive and negative margin, a significantly larger Gleason score was found in group with a positive margin (p = 0.003). The significant correlation of biochemical recurrence with new Gleason prognostic groups was also found (p = 0,048) but not in patients with tumours with positive margins after prostatectomy. Ki67 proliferation index significantly correlated with prognostic Gleason group system, also in tumours with positive margins (p = 0,0012 and p = 0,0028; respectively).
Conclusion: The new Gleason prognostic groups in combination with other prognostic markers could provide better characterization of tumours with positive surgical margins in patients treated with radical prostatectomy.

PS-25-081

HLA-G expresion and its prognostic value in renal cell carcinoma

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Objective: HLA-G expression has been associated with an increased tumourigenicity in some solid tumours and has been detected in variable percentages in renal cell carcinoma (RCC) and rarely in nonneoplastic kidney. The aim of the study is to determine HLA-G expression percentage in RCC as well as its prognostic value.
Method: HLA-G expression was prospectively analysed by immunochemistry in neoplastic and nonneoplastic tissue of 85 nephrectomies of patients operated in our hospital between 2003 and 2011. HLA-G quantification was divided into four groups according to the expression. Likewise, a systematic collection of clinical data was performed to evaluate the role of HLA-G expression in the prognosis of RCC.
Results: There is a positive correlation in HLA-G expression between neoplastic and nonneoplastic tissue (p < 0,001). There are no significant differences in HLA-G expression according to histologic type (p = 0,407) or to the stage at diagnosis (p = 0,509). It does not exit significant correlation between HLA-G expression and time to progression.
Conclusion: HLA-G expression is present in RCC regardless histologic type and tumour stage. There is a positive correlation between HLA-G expression in neoplastic and nonneoplastic tissue, so this can not be used as a diagnostic marker. Additionally it is not useful as an independent prognostic marker of RCC.

PS-25-083

Down-regulation of protein arginine methyltransferase 1 (PRMT1) gene expression in renal cell carcinomas

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Objective: Protein arginine methyltransferase 1 (PRMT1) methylate a variety of histones, RNA-binding proteins, enzymes, small molecules, and has been linked to several malignancies.
Method: Real-time RT-PCR (qRT-PCR) analysis of PRMT1 mRNA level was analyzed in 15 clear cell, 6 papillary and 3 chromophobe renal cell carcinomas (RCC), and compared to its expression in normal kidney tissue adjacent to the tumour. Furthermore, PRMT1 mRNA level was correlated to tumour stage, nuclear grade and tumour dimension. Survival analysis was also performed to define predictors of cancer-related death.
Results: PRMT1 mRNA level was almost three times lower in all tumours compared to its expression in non-tumour kidney tissues (p < 0.001). There was tendency of decline in PRMT1 mRNA level by each increase in tumour stage (T1:0.45; T2:0.36; T3:0.34). Moreover, tumours with higher nuclear grades (III-IV) had highly down-regulated PRMT1 mRNA level (0.29) that was lower than those observed in nuclear grade I-II (0.42). Correlation of PRMT1 mRNA levels and tumour dimensions was not statistically confirmed, despite detection of clear negative trend. Nuclear stage, tumour grade and renal vein invasion were predictors of cancer-related death, while mRNA PRMT1 level did not influence patients' survival.
Conclusion: PRMT1 became down-regulated during RCCs pathogenesis and significantly decreased in more advanced carcinomas.

PS-25-085

GLO1 protein expression is strongly linked to adverse tumour phenotype and early PSA recurrence in prostate cancer

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Objective: Glyoxalase 1 (GLO1) is an enzyme involved in glycolysis and removal of toxic metabolites from the cell. In functional analysis using cancer cell line models GLO1 has been shown to be involved in apoptosis inhibition by modification of NFkB signaling. In line with a antiapopototic function GLO1 has been found to be up regulated in a large variety of cancer types. But little is known about the role of GLO1 in prostate cancer.

Method: To analyze the relevance of GLO1 expression in prostate cancer, we utilized our pre-existing tissue microarray containing >11,000 prostate cancer specimens with clinical follow up and attached molecular database.

Results: GLO1 staining was predominantly stained in the cytoplasm of invasive prostate cancers, no GLO1 staining was detectable in normal prostate epithelium. Increased GLO1 staining was associated with adverse tumour phenotype and PSA-recurrence ($p < 0.0001$,each). Furthermore PTEN (10q23) and FOXP1 (3p13) deletions were significantly linked to at least weak GLO1 expression ($p < 0.0001$).

Conclusion: Our data demonstrate that high levels of GLO1 protein expression are strongly linked to adverse phenotype and early PSA recurrence in prostate cancer. They also suggest that these associations might be driven by a strong link of high GLO1 protein expression with molecular features of chromosomal instability.

PS-25-086

Loss of Kallikrein related peptidase 2 expression in prostate cancer is linked to adverse tumour stage and early biochemical recurrence in prostate cancer

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Objective: Kallikrein-related peptidase 2 (KLK2) is one family member of serine proteases (KLK1-15) with a wide spectrum of functions. In general KLKs function relies on the control of steroid hormones through trypsin-like activities. KLK2 has a sequence homology of 78 % with PSA (KLK3) and seems to activate it. In prostate cancer cell culture experiments evidence was given that KLK2 enhances cell proliferation. Only few KLK2 expression pattern analyses in prostate cancer have been performed. To prove the clinical relevance of KLK2 expression in prostate cancer, we took advantage of our pre-existing tissue microarray (TMA) containing >11,000 prostate cancer specimens connected with extensive follow up and molecular data.

Method: For immunohistochemistry, freshly cut TMA sections were immunostained in one day and one experiment.

Results: In statistical analysis we found high-level immunostaining of KLK2 linked to ERG negativity in prostate cancers. Low KLK2 immunostaining was significantly linked to adverse pathological findings. Analyzing associations to PSA recurrence, we found significant association between low KLK2 immunostaining and early PSA recurrence ($p < 0.0001$, each).

Conclusion: High-level immunostaining of KLK2 is linked to ERG negativity in prostate cancer. Deficiency of KLK2 expression in prostate cancer specimens is significantly linked to advanced clinical tumour stage and early PSA recurrence.

PS-25-087

Nephrogenic adenoma of the urinary tract: A 6-year single center experience

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Objective: Nephrogenic adenoma is an uncommon benign lesion of the urinary tract. The aim of this study was to evaluate the clinicopathological features of this lesion and review the literature.

Method: A retrospective series of 17 cases of nephrogenic adenoma diagnosed in our department between 2010 and 2016 was analyzed. The clinical parameters were obtained from the clinical records. All histological slides were reviewed and the diagnoses were confirmed.

Results: Study population consisted of 14 men and 3 women, aged 3–80 years (mean 58.5). The most common location of the lesion was the urinary bladder (13 cases) followed by the renal pelvis (2 cases), ureter (1 case) and urethra (1 case). A history of urothelial carcinoma and repeated TUR procedures were observed in 11 cases. There was 2 pediatric patients aged 3 years. Both of them had undergone previous urosurgery because of megaureter in one and bladder exstrophy in the other. Recurrence of lesion was observed in two patients. Histologically, the lesions exhibited, singly or in combination, tubular, cystic, papillary, polypoid and flat growth patterns.

Conclusion: Nephrogenic adenoma displays a broad spectrum of architectural and cytological features. Recognition of its characteristic histopathological features is needed in distinguishing this lesion from its mimickers.

PS-25-089

Spermatocytic seminoma: Report of three cases

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Objective: Spermatocytic seminoma is a rare tumour of testis composed of germ cells, not associated with intratubular germ cell neoplasia. Spermatocytic seminoma affects more frequently males with descended testis.

Method: We retrospectively explored our archival material searching for the diagnosis of seminoma and/or spermatocytic seminoma during the 10-years period (2005–2015).

Results: We found three cases of spermatocytic seminoma during the 10-years period (rate ~0.04 %). One tumour was diagnosed in older male (60 years old) while the other two spermatocytic seminoma cases were diagnosed in young males (29 and 33 years old, respectively). None of the patients had previous history of cryptorchidism. Two patients were clinically suspicious of testicular cancer while the third one (29yo) had clinical diagnosis of purulent orchitis and semitorsion. Histopathologic examination revealed morphologic features of spermatocytic seminoma confirmed by immunohistochemistry. All three patients received no adjuvant treatment and did well at last check-up.

Conclusion: Spermatocytic seminoma is a rare variant of testicular seminoma that also may be seen in young adults. Surgical treatment appears to be optimal with an excellent clinical outcome.

PS-25-090

Histologic evaluation of the remnant associated with testicular regression syndrome: Groin exploration may be no longer indicated!

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Objective: There is controversy surrounding the optimal management of the testicular remnant associated with the testicular regression syndrome (TRS). Some authors advocate the need for surgical exploration, whereas others believe this unnecessary. These differing opinions are based on the variable reports of viable germ cell elements found within the testicular remnants. This study aimed to quantify the cardinal features of the disease and to determine the incidence of viable germ cells.

Method: This study is a retrospective review of all excised testicular remnants in patients with impalpable testis over a 10-year-period.
Results: A total of 60 cases of TRS were submitted for histopathological examination. Patient age ranged from 1 to 62 years (median: 6 years). Microscopic evaluation showed haemosiderin-laden macrophages in 5 cases (8.5 %), dystrophic calcification in 7 cases (11.7 %), vas deferens in 50 cases (83.3 %), epididymal tissue in 34 cases (56.7 %) and Leydig cells in 16 cases (26.7 %). Seminiferous tubules were noted in 21 cases (35 %) and germ cells were only identified in 2 cases (3.3 %). No atypical germ cells were seen.
Conclusion: Viable germ cells were only found in 3.3 % of examined remnants implying a negligible risk of future germ-cell cancerisation and minimizing the need for their systematic removal.

PS-25-091
TOMM34 expression and clinicopathological correlations in urothelial carcinoma of the urinary bladder
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Objective: While the currently used clinical and pathological variables provide prognostic information on Urothelial carcinoma of the bladder (UCB); they still have a limited ability to predict tumour progression. Cancer cells exhibit a wide range of mitochondrial dysfunctions that could provide a possibility to preferentially target cancer cell mitochondria and improve therapeutic selectivity. TOMM34 is one of the translocases of the outer membrane of mitochondria (Tom) components that was identified a crucial factor for the protein import. The aim is to investigate the expression pattern of TOMM34 in bladder cancer and its correlation with the clinico-pathological parameters of those cases.
Method: Sixty patients with non-invasive (high grade and low grade) and invasive urothelial carcinoma (high grade and low grade) were included in the study in. The immunohistochemical expression was performed using the TOMM34 antibody (Novus Biologicals, USA).
Results: TOMM34 immunohistochemical expression was significantly higher in muscle invasive tumours ($p < 0.01$) and in WHO- ISUP high grade tumours ($p < 0.01$). Higher TOMM34 protein levels were associated with decreased overall survival of patients with UCB (Chi- square 27.9 and $p < 0.01$).
Conclusion: TOMM34 is a potential poor prognostic factor in UCB, and further functional studies could unravel its possible role as a therapeutic target in UCB.

PS-25-092
Nuclear grade predicts prostate cancer outcomes among radical prostatectomy patients
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Objective: Nuclear grading (NG) is not routinely applied to prostatic carcinoma (PCa). This study evaluated NG as a predictor of PCa outcomes in a cohort of radical prostatectomy (RP) patients.
Method: 1579 patients with PCa treated by RP were enrolled in a multicenter national database. Whole-mount specimens were graded by the 2014 modification of ISUP/Gleason and nuclear grade as defined by Mostofi. Outcomes data were obtained as part of ongoing data collection. Unadjusted Kaplan Meier (KM) estimation curves and multivariable Cox Proportional Hazards analyses were used to evaluate two time-to-event endpoints: biochemical recurrence (BCR) and distant metastasis (MET).
Results: Higher NG was significantly associated with higher D'Amico risk stratum ($p < 0.0001$), worse biopsy Gleason sum (GS) ($p < 0.0001$), worse prostatectomy ISUP/Gleason score ($p < 0.0001$), higher cT-Stage ($p = 0.0356$), higher pT stage ($p < 0.0001$), positive margin status ($p = 0.0002$), presence of extra-capsular extension ($p < 0.0001$), and seminal vesicle involvement ($p < 0.0001$). KM curves showed a significant difference in odds of BCR ($p < 0.0001$) and MET ($p < 0.0001$) with poorer outcomes for highest versus lowest NG. Multivariable analysis showed higher risk of MET for highest versus lowest NG category: (HR 3 vs. 1 = 21.39, $p = 0.0049$). In Gleason grade 7 tumours, NG3 had a significant association with BCR ($p < .0001$) and metastasis-free survival ($p = .01$), compared to NG1-2 tumours.
Conclusion: NG is useful in predicting worse PCa outcomes, especially in Gleason grade 7 tumours.

E-Posters

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-01 Breast Pathology

E-PS-01-001
Analysis of clinical-pathological features and Body Index Mass (BMI) in patients with invasive Breast Carcinoma (BC)
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Objective: The aim is to evaluate clinical-pathological parameters in correlation to BMI in patients with invasive BC, since the relation between host-related factors (obesity) and tumour-related factors may have important clinical and prognostic implications.
Method: We retrospectively reviewed invasive BC (2012–2015). Parameters analyzed included age, clinical and pathological tumour size, histological tumour type and grade, presence of axillary lymph node metastases, tumour emboli, inflammatory infiltrate. Patients were divided into normal weight (NW), overweight (OW) and obesity (OB) group based on the WHO criteria.
Results: 245 consecutive patients with invasive BC were identified: 84 (33.07 %) OW, 72 (29.38 %) OB and 91 (37.14) NW. Most of the OW and OB women were aged >40 (0.0092). Also, OW patients had higher rates of grade 1 tumour (0.0138). NW patients had significantly less lymph nodes metastases ($p = 0.0165$) comparing to OW/OB group. There were no statistically significant differences between these three groups and tumour size, histological type, inflammatory cell infiltration and the presence of emboli.
Conclusion: In our series, BC patients had a high prevalence of OB/OW, mostly over the age of 40. OB group is associated with poor prognostic factors (lymph node metastasis). However, most of the tumours in the OW group were of grade 1 histologically.

E-PS-01-002
Livin gene expression in breast carcinoma: Correlation with prognostic factors and patient outcome
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Objective: Breast cancer is the most common malignancy in women. Livin, the most recently identified IAP, is one the most tumour-specific genes in the human genome. Its role in breast cancer progression remains unknown, the expression pattern of livin gene in human breast cancer tissues and its correlation with the prognostic factors including patient outcome was evaluated.
Method: The surgically resected 34 breast cancer tissue specimens were analyzed and examined by immunostaining to evaluate the expression pattern of livin protein. All patients were followed up for disease- free and overall survival.
Results: Livin protein was expressed predominantly in the cytoplasm of tumour cells. The positive expression was observed in 88.2 % (30 out of

34) cases of breast carcinoma specimens analyzed. Livin gene expression was significantly correlated with tumour size. ($P \leq 0.05$) No statistical significant correlation was detected between livin gene expression and patient's age, menstrual status, tumour grade, axillary lymph node metastasis, ER, PR hormonal status and HER-2 receptor status. (P 0.05) There was a statistical significant correlation between livin gene expression and TNM tumour stage. ($P \leq 0.05$) Patients with livin positive breast cancer tumours had a poor disease-free survival and a shorter overall survival in comparison with livin negative tumours, although the difference was not statistically significant. (P 0.05)

Conclusion: We conclude that, the high expression pattern of livin gene in breast carcinoma may play a prominent role for disease progression. Livin expression may help predict the poor clinical outcome and could be useful as a molecular biomarker and therapeutic target for effective breast cancer therapy.

E-PS-01-003

Invasive lobular carcinoma with an initial presentation of metastases to uterus and both adnexa

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Objective: Invasive lobular carcinoma (ILC) is second most common breast carcinoma. ILC is also famous for distinctive metastatic sites which are different from those of the other carcinomas of the breast. We report a case of ILC in a 57-year-old woman who visited the hospital with increased postmenopausal vaginal bleeding for 1 month.

Method: Total hysterectomy and bilateral salpingo-oophorectomy was performed. The uterus and both adnexa were grossly normal except an increased myometrial thickness and hemorrhagic foci within myometrium which are the most common features of adenomyosis.

Results: Microscopically, dyscohesive cells with mild nuclear pleomorphism infiltrated uterine cervix, endometrial stroma, myometrium, and both adnexa. Adenomyosis was found in the myometrium and was also infiltrated by the tumour cells. Immunohistochemically, the tumour cells were positive for estrogen receptor and cytokeratin 7, and negative for CD10, vimentin, and E-cadherin. Ki-67 index was approximately 10 %. Examination of her breasts was done after the tumour was diagnosed as metastatic ILC. Needle biopsies of the breasts revealed ILC in both breasts.

Conclusion: Immunohistochemistry for cytokeratins, E-cadherin, and CD10 should be concerned when atypical dyscohesive cells are found in the endometrial specimen to rule out ILC.

E-PS-01-004

A study of claudins 1, 3 and 4 in pre-cancerous lesions and non-invasive cancers of the breast

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Objective: The claudins are a family of small transmembrane proteins that elicit homo and heterophilic interactions in order to mediate tight junction formation between epithelial cells; maintaining cellular polarity, and mediating permeability. Studies have identified the differential expression patterns of claudins in normal breast tissue and in invasive breast carcinoma. This study was aimed at elucidating the point at which claudin expression began to change during tumourigenesis.

Method: We utilised immunohistochemistry to study claudin 1, 3 and 4 in 80 tissue samples including examples of normal, hyperplastic, atypical and malignant in situ lesions. Six cases of invasive apocrine carcinomas were also studied.

Results: Apocrine breast lesions maintained their expression pattern from benign through to DCIS and invasive carcinoma. In non-apocrine lesions, weak positive expression of claudins 3 and 4 seemed to be acquired once the lesion has progressed to ductal carcinoma in situ. Toker cells of the nipple had a claudin expression vastly different from that of Paget's disease.

Conclusion: Claudin expression in breast lesions is determinant on the expression of cells from which they are derived. Apocrine lesions have a consistent expression pattern from benign to invasive carcinoma. Toker cells may not be the cells of origin for Paget's disease.

E-PS-01-006

High CD105 protein expression is related to phyllodes tumours malignancy: Report of a borderline phyllodes tumour with rapid lung metastases and study of 54 breast phyllodes tumours

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Objective: Phyllodes tumours (PTs) are rare types of breast fibroepithelial tumours which can be further classified into begin, borderline and malignant PTs based on their pathological features. Local recurrence and even distant metastases are big challenges for the clinical treatment of PTs.

Method: To better understand their clinical behavior, we retro-studied a case of borderline phyllodes tumour which caused rapid lung metastases with focus on the morphological transition between the primary tumour and the metastatic lung lesions. CD105 expressions were detected by immunohistochemistry in 54 breast PTs including 33 begin, 11 borderline and 10 malignant tumours.

Results: For the case study, in the primary breast tumour we found only a small tumour area showed increased stromal cellularity and atypia with borderline PT features, while the lung metastatic lesions transformed into highly malignant PT with undifferentiated sarcomatous appearances. We frequently observed tumour heterogeneity in the borderline and malignant PTs which were more likely to have larger tumour size comparing to benign PTs. Moreover, borderline and malignant PTs exhibited higher expression of CD105, suggesting its role in driving PTs development.

Conclusion: This study emphasized on tumour heterogeneity and CD105 expression relating to tumour malignancy and metastases especially for borderline PTs with giant tumour size.

E-PS-01-007

Intra-tumour genetic heterogeneity in breast cancer: A case report

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Objective: Although the majority of Her2-positive breast cancers show homogeneous distribution of Her2 protein expression, intra-tumour heterogeneity sometimes can be observed. In our experience this is a rare phenomenon in breast cancer (approx. 1 per 1000 cases). A case of clear-cut intra-tumour Her2 heterogeneity is presented.

Method: We determined Her2 immunohistochemical (IHC) expression in a breast cancer specimen of 63-year-old woman. In order to distinguish true heterogeneity from staining artifact FISH analysis was performed. In addition, ER, PR and Ki67 were also assessed.

Results: The results clearly showed coexistence of two clones with different Her2 status in one tumour. Her2-amplified and non-amplified regions were closely adjacent to each other and matched corresponded IHC-positive (IHC3+) and negative areas. However, uniform expression of ER and PR was observed. Ki67 rate was high (35 %). So in this case the tumour cells harbored luminal B phenotype with two different Her2 patterns.

Conclusion: We report a case of luminal B breast carcinoma with intra-tumour Her2 heterogeneity. Clinical follow-up for this patient was

limited. However, it emphasizes the possibility of individual tumour variation at a molecular level. Heterogeneous tumours potentially present a challenge for clinicians, as may have impact on treatment response, prognosis and disease outcome.

E-PS-01-008

Intratumoural heterogeneity in breast cancer

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Objective: In this study we observed intratumoural heterogeneity in breast cancer. The study included 160 patients with breast cancer of T1-4N0-2M0-1 stage at the age from 21 to 73 years.
Method: Immunohistochemistry: ER, PgR, Ki-67, Bcl-2, Her2, p63, SMA, a general cytokeratin,cytokeratin 7,vimentin, E-cadherin.
Results: In all cases, histological form of BC was presented by infiltrating ductal carcinoma. Demonstrated variable expression of Her2, ER and PgR within the tumour.IC NST makes up to 75 % of all cases. Intratumoural morphological heterogeneity of IC NST is represented by the presence of five different types of components including tubular, solid, trabecular, alveolar. All tumour cells have necessary set of molecules for intercellular connections (cadherin-catenin complex) and integrin receptors. The majority of tumour cells, which are connected to each other and have no connection with the stroma, defines the second subtype, which includes solid and alveolar structures. An exception are cells, which are in contact with the connective tissue. Most tumour cells of such structures express cadherin-catenin complex, but lose the integrin receptors.
Conclusion: We discovered the connection between the morphological intratumoural heterogeneity and molecular subtypes. It turned out that triple-negative tumours are more frequently characterized by the presence of one type of morphological structure, while in the luminal BC there are tumours with five different types of structures. However, not in all patients basal-like breast tumours show significant intratumoural heterogeneity and triple-negative BC is not always a clonally homogeneous tumour. Thus, the analysis of morphological and molecular heterogeneity of BC is the basis for a better understanding of carcinogenesis and tumour progression mechanisms.

E-PS-01-009

Expression of epithelial-mesenchymal transition markers in breast cancer tumours

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Objective: Our objective was to study structural and functional state of stroma and epithelium in ductal breast cancer (DBC).
Method: Immunohistochemistry, light and electron microscopy
Results: We performed an analysis of surgical specimens from 118 patients with ductal breast cancer between 2009 and 2015. In the test series anaplastic component was present in 21.2 % (25/118) of the cases. Tumours with anaplastic component have not only a difference in the histological structure, but also in their malignant potential, as well as in the expression of epithelial, mesenchymal and immunohistochemical myoepithelial markers. Histologically,desmoplasia of the stroma, which is typical of DBC, is completely absent in anaplastic areas. Tumour cells create a semblance of stromal framework from themselves. Revealed cases of diffuse expression of vimentin, SMA and p63 in anaplastic cells confirm that in the process of differentiation loss, tumour cells acquire myoepithelial and/or mesenchymal phenotype. This fact is associated with epithelial-mesenchymal transition in tumours. This results in the destruction of dense adhesion contacts (reduction and change in polarity of expression of E-cadherin) and the restructure of complexes, which provide the attachment of cells to the substrate.
Conclusion: Heterogeneity of ductal carcinoma is manifested by the anaplastic (sarcomatoid) component, where we can trace the ability of epithelial tumour cells to acquire a properties of mesenchymal cells, which do not require the stroma and have an aggressive malignant potential, affecting the survival of patients.

E-PS-01-011

Homogenous solid lesion, right upper outer quadrant: A histological red herring

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Objective: In this case report we describe what we believe to be the first reported case of primary mediastinal choriocarcinoma presenting with a breast lump.
Method: Our patient is an 18 year old female who presented to hospital with chest pain. On examination, a palpable breast lump was noted. This was biopsied and initially found to be oestrogen receptor negative, progesterone receptor negative and Her-2 negative with a proliferation index of 80–90 %. Further immunohistochemical testing showed the tumour cells to be positive for β-hCG, PLAP and AE1/AE3 and negative for CD30 and AFP. Imaging showed bilateral hilar masses, multiple lung nodules and a lesion in the right breast. There was no history of pregnancy and the uterus appeared normal on ultrasound scan. The patient was treated with four cycles of bleomycin, etoposide and cisplatin (BEP) and follow up scans have shown a partial response to therapy.
Results: While there are reports in the literature of choriocarcinoma metastasising to breast as well as breast carcinomas with choriocarcinomatous features, we could find no reports of patients with mediastinal masses presenting with choriocarcinoma of the breast.
Conclusion: We therefore believe this to be the first reported case of primary mediastinal choriocarcinoma presenting with a breast lump.

E-PS-01-012

Application of immunohistochemistry in diagnosis of the microinvasive carcinoma of the breast

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Objective: To explore the value of cytokeratin, myoepithelial markers and c-erbB-2 in the diagnosis of microinvasive carcinoma.
Method: The expression of CKpan, p63,SMMHC, Calponin and c-erbB-2 were examined by immunohistochemistry on those DCIS cases with suspicious area of microinvasion by H&E, during the period from Jul. 2014 to Mar. 2016. The pathologic-histology diagnosis was made combining with immunostains.
Results: Fifty-seven cases with MIC were distinguished from pure DCIS. The small angulated epithelial clusters were displayed distinctly in the stroma adjacent ducts by CKpan expression, with p63, SMMHC and Calponin negative. These clearly separated microscopic foci were one or more, with the maximum diameter 0.1~1.0 mm. Most of MIC was histological grade-II. The DCIS component ranged from 4 ducts to extensive distribution, 27 cases were high nuclear grade and 30 cases were moderate. The morphological subtypes of DCIS were mainly comedo and solid, others were cribriform and papillary. C-erbB-2 in 31 cases with MIC expressed 3+ or 2+, however, the intensity of 33 cases were lower than or equal to DCIS.
Conclusion: Immunohistochemistry of CKpan, myoepithelial markers and c-erbB-2 could improve the detection rate of MIC, which highlighted more objectively the MIC ranges and benefited to precise individual therapy.

E-PS-01-013

The occurrence of relapses in the breast cancer immunophenotypes

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Objective: Breast cancer (BC) is the most commonly diagnosed cancer in women worldwide characterized by molecular and clinical heterogeneity that results with multiple intrinsic tumour subtypes. The aim of this study was to evaluate the occurrence of relapses in the different immunophenotypes of BC associated with different histological parameters.
Method: The retrospective population study included 173 BC patients diagnosed between 2007 and 2010 in our hospital. Molecular subtype classification was performed on immunohistochemical surrogates for estrogen and progesterone receptor, as well as for proliferation index (Ki-67) and Human Epidermal Growth Factor receptor-2 (HER-2), according to St. Gallen International Expert Consensus recommendations from 2013.
Results: Proportions of BC immunophenotypes were: Luminal A-26,56 %; Luminal B-41.67 %; HER2+ 18,75 % and Triple-negative-13,02 %. In the Univariate analyses there was a significant difference in the distribution of age, tumour diameter, mitotic index, lympho-nodal ratio, Nottingham Prognostic Index, stage of the disease, Ki67 PI and the bcl-2 overexpression among the four BC immunophenotypes. In the multivariate analyses, the age, tumour diameter and the stage of the disease were represented as independent prognostic factors of recurrent disease in different BC immunophenotypes.
Conclusion: The prognostic value of BC immunophenotypes persists when adjusting the age, the tumour diameter and the stage of the disease and this "morphologic-molecular" model was robust in relapse prediction and recurrence risk stratified by traditional prognostic parameters.

E-PS-01-015

Spindle cell lesions of the breast: Report of three cases with emphasis on differential diagnosis

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Objective: Spindle cell lesions of the breast constitute a heterogenous group ranging from reactive to neoplastic, highly malignant disorders and their accurate diagnosis can be quite challenging. We report 3 cases of spindle cell lesions of the breast with emphasis on differential diagnosis.
Method: All three patients were females, aged 24, 60 and 70 years, and presented with palpable masses in the left breast measuring 2, 5.3 and 3 cm in maximum diameter respectively.
Results: The first lesion was a desmoid-type fibromatosis composed of intersecting fascicles of bland spindle cells, positive for SMA and β-catenin and negative for keratins. Histological diagnosis of the second lesion was nodular fasciitis. It was composed of short fascicles of plump fibroblastic/myofibroblastic cells (SMA+, Desmin-, β-catenin-, keratin-), with frequent mitoses, set in a loose, myxoid stroma containing lymphocytes, erythrocytes and thin-walled vessels. The third lesion was a metaplastic myoepithelial carcinoma composed mainly of atypical spindle cells, positive for keratins 5/6, p63 and CD10, with focal squamous and mesenchymal differentiation.
Conclusion: Spindle cell lesions of the breast represent a diverse group of diseases with overlapping histological features. Careful histologic examination in conjunction with immunohistochemistry and clinical history will lead to the correct diagnosis in morphologically challenging cases.

E-PS-01-016

Mucocele like tumour of the breast: Associated with ductal carcinoma in situ and focal ductal carcinoma. Should we operate these patients?

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Objective: Mucocele like tumours (MLT) of the breast are quite rare neoplasms displaying an broad spectrum. These lesions were considered benign initially. But now, they are believed to be related to atypical ductal hyperplasia, ductal carcinoma, or mucinous carcinoma. Preoperative diagnosis in fine needle aspiration and core biopsy is difficult.
Method: We are reporting a case of mucocele like tumour with ductal carcinoma in situ and ductal carcinoma in a 71-year old Turkish woman. The patient had a palpable mass in her left breast. Mammograpy showed ill defined and lobulated mass with widespread tiny microcalcifications. Histopathologic findings were consistent with MLT and microscopic focus of ductal carcinoma was also noted in mastectomy specimen. And she is currently disease-free in the 116th month.
Results: We believe that our case will the first patient from Turkey and will be added to the database as one of the longest term follow-up MLT cases reported in pubmed.
Conclusion: If a mucocele-like tumour is suspected in fine needle biopsy, surgical excision should be recommended and the specimen should be carefully evaluated to exclude the presence of ductal carcinoma in situ or carcinoma.

E-PS-01-017

Desmoid tumour of the breast: A case report

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Objective: Desmoid tumours of the breast are rare. Although benign, they can clinically mimic breast cancer. Their treatment is challenging. We describe a case of a desmoid tumour of the breast and discuss briefly its pathological diagnosis and treatment modalities.
Method: An 18-year-old healthy female presented with a left breast lump that appeared in the prebubertal period and has been progressively growing. Physical examination showed a 6 cm hard mass on the left breast. MRI confirmed the presence of an ill defined of 64 × 60 mm, invading the pectoral muscle. Needle core biopsy was performed; pathological examination was in favor of a desmoid tumour. The patient underwent a wide local excision of the external portion of her left breast.
Results: Gross pathologic evaluation of the specimen received in our laboratory revealed a gray-white firm mass. Microscopic examination showed a proliferation of bland spindle cells arranged in fascicles with variable amounts of intervening collagen. Deep surgical margins were positive. Tumour cells were positive with βcatenin. A diagnosis of desmoids tumour of the breast was made.
Conclusion: Fibromatosis is a rare, locally aggressive breast tumour. Complete surgical excision is the proven method of treatment; frozen section pathology could be used to check surgical margins.

E-PS-01-018

Molecular classification of pure ductal carcinoma in situ of the breast: A study of 21 cases

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Objective: Different molecular subtypes of breast cancer have been identified based on gene expression profiling. Treatment suggestions based on an approximation of these subtypes by immunohistochemical criteria

have been published by the St Gallen international expert consensus panel. Ductal carcinoma in situ (DCIS) can be classified into the same molecular subtypes. Our aim was to study the relation between these newly defined subtypes and prognosis in DCIS.
Method: Retrospective study of 21 cases of breast pure DCIS collected over a 13 year period (1998–2010). The cases were classified into four molecular subtypes according to the recommendations of St. Gallen.
Results: The DCIS were Luminal A in (33 %), Luminal B in (15 %), HER2 in (37 %) and triple negative in (15 %). Mean period of follow-up was 5.2 years (1–14 years). Invasive local recurrence with bone metastases were noted in 2 cases, and 5 to 6 years, respectively: a case Luminal phenotype A and a case of luminal phenotype B.
Conclusion: Our results have demonstrated the prognostic value of molecular classification of DCIS.

E-PS-01-019
Metaplastic carcinoma of the breast: A case report
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Objective: Metaplastic breast cancer (MBC) is a rare subtype of breast carcinoma.
Method: We report a case of a 42 year-old female who presented with a lump in the upper outer quadrant of her right breast since 6 months. Physical examination revealed a palpable mass that was painless, firm and mobile. Lumpectomy was performed. Gross examination of specimen revealed a firm 2.2 cm greyish-white mass, of firm consistency.
Results: Microscopic examination revealed that the tumour was biphasic and contained both epithelial and mesenchymal component. Epithelial component was made of cells arranged in glands,clusters and nests. Tumoural cells were round to oval with a moderate amount of eosinophilic cytoplasm. Nuclei were enlarged with occasional prominent nucleoli. The cells were surrounded by interlacing bundles of pleomorphic, spindle shaped cells, with large hyperchromatic nuclei. Sheets of cartilaginous matrix and chondroid metaplasia were seen. Many mitotic figures were present. Based on these histological features, diagnosis of metaplastic carcinoma was made. Immunophenotype of tumour was estrogen negative, progesterone positive, Her-2/neu positive. Proliferation index Ki-67 was high (90 %).
Conclusion: When pathologist encounters a malignant breast tumour with chondroid elements, metaplastic carcinoma with chondroid differentiation should be considered, due to its rarity and different prognosis.

E-PS-01-021
Pathological response to neoadjuvant chemotherapy in young breast cancer: Correlation between age and treatment response
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Objective: The aim of this study is to identify the potential of neoadjuvant chemotherapy (NCT) on stratified patient's age groups, allowing a better understanding about how each subgroup responds distinctly to NCT.
Method: From January 2008 to June 2014, a retrospective analysis was made on response data of 84 women with operable breast cancer treated by NCT in the oncology department of Sidi Bel Abbes (Algeria). Patients were stratified into two age groups (group1, ≤39 years; group2, >39 years). Pathological node involvement, Tumour grade, conservative treatment, 5-year recurrence and death were analysed according to age at diagnosis. The significance of associations was tested by the chi-squared test.
Results: The death and the recurrence in those < =39 years of age being significantly greater than that in the other age group (50 and 57 % versus 23 and 27 %, $P < 0.03$). There was a trend for patients' group1 to have positive node involvement and tumour grade G > 2 (71 %, 50 %) compared with those of group2 (57 %, 41 %), but without statistical significance.
Conclusion: During the study period, in the youngest subgroup age, the 5-year recurrence and death rates were higher than in older premenopausal patients. The relationship between age and treatment response was not directly correlated.

E-PS-01-022
Prognosis model of young breast cancer in women of western Algeria who underwent neoadjuvant chemotherapy
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Objective: This study aimed to analysis the relative risk (RR) of breast cancer-related recurrence on disease-free survival (DFS) in patients of less than 39 years of age.
Method: Between January 2008 and June 2014, 84 women with operable breast cancer were admitted to the oncology department, for cures of neoadjuvant chemotherapy, followed by surgery and adjuvant treatments. Patients were stratified into two age groups (group 1, ≤39 years; group 2, >39 years). In a forward stepwise procedure, the following four selected parameters were entered in a Cox regression model: age (≤39 years), tumour grade (G > 2), clinical stage and progesterone receptor (PR) status.
Results: The median follow up was 30.5 months. In the youngest patients, a median 5-year DFS of 48 years (95 % CI 8.316–87.684) was noted. Parameters associated with poor prognosis of 5-year DFS by order of entry into the model were clinical stage (stageIII, RR = 3.6, 95%CI [1.4–9.4], P = 0.008), tumour grade (G > 2, RR = 2.3, 95%CI [1.029–5.284], P = 0.043) and young age (RR = 1.2, 95%CI [0.125–0.768], P = 0.011). However, PR expression improved significantly DFS (RR = 0.3, 95%CI [0.157–0.929], P = 0.033).
Conclusion: In this prognosis model, the young age remained at a high risk for recurrence and a worse 5-year DFS, while PR expression showed a significant improvement of DFS.

E-PS-01-023
Benign phyllodes tumour with extensive squamous metaplasia: Case report
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Objective: Phyllodes tumours are uncommon fibroepithelial neoplasms of breast, comprising of <1 % of all breast neoplasms. Metaplastic changes are uncommon in the stromal and epithelial components.
Method: We present a case of 43 year old female patient with palpabl mass in right breast. The excised specimen measured 7 × 3.9 × 2.9 cm, had smooth borders and the cut surface showed millimetric cysts, leaf like structures and whorled appearence. After histopathological examination, it was diagnosed as benign phyllodes tumour with extensive squamous metaplasia.
Results: Extensive squamous metaplasia within phyllodes tumour is rare and there are only a few cases reported in the literature.
Conclusion: In this report we present this uncommon neoplasm and review the literature.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-02 Cardiovascular Pathology

E-PS-02-001
Cardiac metastatic tumours: A rare entity in the spotlight
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Objective: Metastatic tumours involving the myocardium and endocardium are uncommonly encountered. It was our aim to evaluate the prevalence of these rare tumours and study their presentation in order to increase awareness to their existence.
Method: Pathological reports from Sheba Medical Center (Israel) and medical records from Institute for Cardiovascular Diseases (Serbia) were screened for cases of metastatic cardiac tumours. Medical, radiological and pathological data of the identified cases was retrieved and reviewed.
Results: We found less than a dozen cases of metastatic cardiac tumours out of thousands of registered cardiac surgeries. The metastatic tumours identified were melanoma, carcinomas of lung, colon and kidney and sarcomas of uterine origin. We found that metastatic cardiac tumours comprised 15.8 % of all the cardiac tumours. Imaging studies played a central role in the identification of cardiac masses. However, as differential diagnosis exists, primarily with thrombi, histopathological evaluation was required for definite diagnosis of metastatic cardiac disease.
Conclusion: Metastatic cardiac tumours are extremely rare. As new diagnostic technologies and improved survival of oncological patients may increase the incidence of cardiac metastatic tumours in the future, awareness to their existence and knowledge of their presentation are key factors in their timely recognition.

E-PS-02-002
Extensively metastasized cardiac angiosarcoma mimicking systemic sarcoidosis
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Objective: Primary cardiac angiosarcoma is an extremely rare entity with a dismal prognosis. Like other primary cardiac malignancies these tumours present with unspecific symptoms that may mimic other, more common cardiac conditions, thus making the diagnosis extremely challenging.
Method: 46-year-old man, initial presentation with symptoms of a non-ST segment elevation myocardial infarction. A week before his death the patient was referred to our institution with decreasing respiratory function. CT scans showed multiple disseminated cerebral and pulmonal foci, in the transesophageal echocardiography a mass was observed. Miliary tuberculosis, endocarditis with septic emboli, possible metastatic tumour of unknown primary as well as an acute exacerbation of the patient's coexisting sarcoidosis were considered in the differential diagnosis. The patient's condition deteriorated rapidly and he died within days.
Results: Clinical autopsy revealed numerous tumourous foci in nearly every organ and a tumour arising from the right atrium of the heart. Histomorphology and immunohistochemical profile were consistent with angiosarcoma. A previously not described KRAS mutation was detected in the molecularpathological analysis.
Conclusion: Although the prognosis is devastating and ultimately fatal, early diagnosis followed by multimodal therapy improves the survival of primary cardiac angiosarcomas.

E-PS-02-003
Targeting exome sequences in congenital heart diseases: Are we there yet?
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Objective: A model to investigate the protein coding variants during early embryogenesis of the most severe forms of congenital heart defects.
Method: We reviewed the anatomy of ventriculoarterial cardiac anomalies looking for a common denominator on the theoretical concept of teratological continuum in malformations (Schwalbe 1906).
Results: We found evidence of sequential malrotation on the ventricular base-apex axis of the Trabecula Septomarginalis (TSM) in specimens from Dextroposition of the Aorta to Tetralogy of Fallot, Double and Single Outlet Ventricles, Univentricular Hearts, Transpositions. The TSM on the V shape or variants follows the development of the right ventricle.
Conclusion: 1- The abnormal ventriculoarterial connections are distinct manifestations of a similar pathogenetic process during cardiac looping: the TSM malrotation. 2- We present a developmental model based on malrotation of the TSM (Leonardo's cord). 3- Investigating the exome variants in each pathological phenotype will let to interfere on the early embryogenesis (molecular cardiac surgery). - 10th Symposium on Advances in Perinatal Cardiology, St. Petersburg USA, James Henry Keynote Communication, 2014. - 27th European Congress of Pathology, Belgrade, 2015. - 27th Annual Meeting of the Arab Division of the International Academy of Pathology, 2nd Emirates Surgical Pathology Conference, Dubai, 2015.

E-PS-02-004
An unsuspected case of primary inferior vena cava sarcoma
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Objective: Primary leiomyosarcoma (LMS) of the inferior vena cava (IVC) is a rare tumour characterized by clinical latency and a non-specific presentation which result in diagnostic delay, high stage at presentation and poor outcome.
Method: We present the case of a 38 year old woman with a 3-week history of abdominal pain and low-grade fever. An initial diagnosis of abdominal tuberculosis was made and anti-tuberculous therapy (ATT) was started in a private hospital. A week later, the patient developed breathlessness, abdominal distention and jaundice. ATT-induced hepatitis was considered and the patient was referred to our hospital. A Color Doppler and Computed Tomography revealed dilatation and occlusion of the IVC by possibly a thrombus, extending from proximal common iliac vein up to right atrium along with extension into right renal vein and right hepatic vein. A diagnosis of Budd-Chiari syndrome was entertained and the patient underwent thrombolytic therapy. However, her dyspnea continued to progress and she died after 12 days of admission.
Results: A complete autopsy showed marked dilation and luminal occlusion of the IVC due to the presence of a firm, greyish brown tumour with para-caval, right renal and hepatic venous and right atrial extensions. Microscopy revealed a pleomorphic tumour arising from the venous wall, composed of irregular fascicles of plump spindle cells, and multinucleate bizarre cells in a loose fibromyxoid background. Large areas of hemorrhage and necrosis and brisk mitoses were seen. Immunohistochemistry confirmed the diagnosis of leiomyosarcoma.
Conclusion: Awareness and strong clinical suspicion are important for the diagnosis of this rare tumour.

E-PS-02-005
Fabry disease in herat: Clinical-pathological correlation
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Objective: Fabry disease (FD) is a rare disorder by mutation in gene encoding α-galactosidase enzyme wich metabolizes ceramidetrijexoside (Gb3); its alteration produces accumulation of Gb3 in lysosomes kidney, endothelial, myocardial, neurons and smooth muscle cells. We present a patient with severe heart failure wich the early diagnosis through a myocardial biopsy (MB) could improve his evolution.
Method: 54 year old male with myopericarditis 4 years ago, chronic renal failure and hypertrophic non-obstructive cardiomyopathy (HNC), without skin or corneal lesions. The diagnostic study included MB after 1 year.
Results: The optical microscopy presented cells with abundant vacuoles, PAS negative and something positive with oil-red. In ultrastructural study

(US) lipid inclusions, frequent electron-laminated or solid myocyte predominant type level, more isolated in endothelial cells were observed. The diagnosis was suggestive of FD.
Conclusion: FD is inhered disorder with irreversible tissular accumulation of Gb3, despite replacement therapy, so the diagnosis through MB should be early. Gb3 deposits found in this biopsy were diffuse, altering all cell structures. In this sense, our patient, 5 years ago, presented myopericarditis with incipient ventricular hypertrophy, probably, as the beginning of FD. In conclusion, we emphasize the value of MB with US in MNC and to consider starting early enzyme replacement therapy.

E-PS-02-006
Angiosarcoma of the heart with a rapid metastatic progression: A case report
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Objective: Primary cardiac neoplasms are rare. Metastases to the heart are more frequent than primary lesions. We described here the case of the primary cardiac angiosarcoma of the young man firstly presented as metastatic brain tumour.
Method: Light microscopic and immunohistochemical study.
Results: A 19-year-old previously healthy man with rapidly progressing severe headache, nausea and vomiting and multiple painful spots in the spine and extremities was admitted to the neurosurgery department. Left temporal brain metastatic tumour and multiple lytic bone and bilateral lungs metastases were established. Ventricular tachycardia and atrial flutter were documented. In spite of intensive care patient died. An autopsy was performed. It reveled polypoid, multilobar tumour with hemorrhagic surface that was protruding inside the right atrium. It was 9,0 × 1,6 × 1,1 cm in size and occupied the entire chamber. Histologically, the cardiac neoplasm was typified by proliferation of highly atypical cells, somewhere with intracytoplasmic vacuoles. Multiple irregular anastomosing vascular spaces and foci of necrosis and hemorrhages were seen. Tumour cells demonstrated strong expression of CD34, CD31, Flu1, FVIII, and were negative for SMA, calponin, caldesmon, desmin, EMA, Myog and panCK.
Conclusion: In view of the presented case, primary heart sarcomas possess diverse clinical presentation, which predisposes to the high rate of false diagnoses and inappropriate therapy. At the same time, correct and prompt diagnosis of malignant tumours of the heart is extremely important.

E-PS-02-007
Interruption of Aortic Arch in an adult
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Objective: Interrupted aortic arch (IAA) is a rare anomaly representing approximately 1 % of congenital heart disease. It is characterised by luminal obliteration in the arch thereby leading to discontinuity between ascending and descending aortic segments. It may occur in isolation or be associated with other cardiac anomalies. Survival into adulthood is extremely rare.
Method: We present the case of a 38 year old male with history of hypertension, diabetes and left hemiparesis 2 years ago. He had sudden unconsciousness and expired within 2 h of admission to the Emergency Services.
Results: A complete autopsy was performed. The aorta was interrupted distal to the origin of the left subclavian artery (Type A interruption) and also showed an atherosclerotic aneurysm proximal to the interruption. The aorta distal to the interruption was supplied by a bunch of collaterals. The heart in addition showed bicuspid aortic valve and closed muscular ventricular septal defect. Cause of death was related to atherosclerotic critical coronary stenosis.
Conclusion: Although it is extremely rare, IAA must be considered along with aortic coarctation in the differential diagnosis of an adult patient with hypertension refractory to medical management.

E-PS-02-008
Allergic myocarditis: Rare cause of sudden death
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Objective: We studied myocardial changes in cases of sudden death by anaphylactic shock.
Method: We analyzed sudden deaths due to anaphylactic shock triggered by various allergens (insects, microorganisms, drugs, proteins).
Results: Although they were autopsied only 7 cases diagnosed with death from anaphylactic shock, we found that cardiac changes were major. We observed inflammatory reactions, cardiac edema which dissecting myocardial fiber, undulation and myocardial fiber rupture, leukocyte influx. There were microgranulomas composed of eosinophils, macrophage and lymphocytes. In some cases there was necrosis of myocytes, small focal lymphocyte infiltrate, interfibrillar edema, fibroblasts and interstitial collagen. History of allergic reactions contributed to the diagnosis of anaphylactic shock.
Conclusion: The cases of sudden death with anaphylactic trigger require careful observation of changes in myocardial area, which can be considered as belonging to allergic myocarditis, direct cause of sudden death.

E-PS-02-010
Metaplastic bone formation with extramedullary hematopoiesis on the aortic valve: An unexpected discovery in case of a sudden death
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Objective: Metaplastic bone formation or heterotopic ossification on cardiac valves is a rare condition, which appears in one tenth of all calcified aortic valves. However, the association with extramedullary hematopoiesis is uncommon. We present an interesting case of sudden death in which the autopsy revealed only a calcific aortic stenosis.
Method: A 52 year-old male without any prior known medical history was found dead at home. A full autopsy was performed at Institute of Forensic Medicine of Tirgu Mures. Both external and internal autopsy observations were evaluated.
Results: Autopsy examination identified advanced decompositional changes in all organs and calcified masses within the aortic cusps with protrusion through the outflow surface. Routine histopathological examination of the aortic valves revealed metaplastic lamellar bone and complete extramedullary hematopoiesis, consisting of erythroid cells, myeloid cells, megakaryocytes and adipose tissue.
Conclusion: The pathways in the mechanism of the heterotopic calcification on cardiac valves could be related to some inflammatory, metabolic or genetic causes, but the presence of extramedullary hematopoiesis and extent of this condition on clinical status is poorly understood.

E-PS-02-011
Cardiac myxoma: Four cases with evaluation of immunohistochemically by neuroendocrin differantiation markers
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Objective: Cardiac tumours are very rare with an autopsy incidence; 0.001–0.03 % and cardiac myxoma is the most common primary cardiac tumour. They are usually seen in female and in adult people, but rarely in

children. Myxomas may be sporadic or part of genetic conditions. The cell origin of cardiac myxoma is still controversial and its histogenesis is making a sensation.
Method: We evaluate four cardiac myxomas histologically and with immunohistochemistry methods. There was no evidence that they were part of genetic condition; Carney complex. In histologic examination all of the tumours were charachterized by the presence of stellate, polygonal (lepidic) cells in an amorphous, basophilic, afibrillar myxoid stroma containing mucopolysaccharides. Four cardiac myxomas were examined by immunohistochemical analysis with PGP 9.5, S100 and NSE.
Results: In histologic examination all of the tumours were charachterized by the presence of stellate, polygonal (lepidic) cells in an amorphous, basophilic, afibrillar myxoid stroma containing mucopolysaccharides. All four myxoma showed positive immunohistochemically staining with PGP 9.5, NSE and S100.
Conclusion: Altough the histogenesis of the cardiac myxoma is not obvious, it is postulated that they develop from multipotent mesenchymal stem. Herein we aimed to show the neuroectodermal origin of myxoma by immunohistochemically staining with neuroendocrine differentiation markers.

E-PS-02-012
Expression of matrix metalloproteinase-9 in ischemic myocardium
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Objective: The aim of the study was to evaluate the expression of matrix metalloproteinase-9 (MMP-9, gelatinase B) in left ventricular myocardium in the presence of chronic myocardial ischemia.
Method: Heart specimens with persistent ischemia (n = 20, pre-infarction ischemic heart disease (IHD) group) and post-infarction scar (n = 20, post-infarction IHD group) from dissected males who had died suddenly (within 6 h) during the first or repeated acute attack of IHD (without congestive heart failure) and heart explants (n = 17, end-stage ischemic heart failure group) were analyzed. Heart specimens (n = 20) selected at the autopsy from the individuals who died from accidents were used as controls. The slides of myocardium were incubated with monoclonal antibody against the MMP-9 (clone 15 W2, Novocastra). Dako Real Envision visualisation system was employed to stain the samples.
Results: Expression of MMP-9 in the cardiomyocytes of pre-infarction IHD group did not differ from that of control group. It was higher in the post-infarction IHD group ($p < 0.05$) as compared to controls and pre-infarction IHD group, while the cardiomyocytes in the group of end-stage ischemic heart failure had higher expression of MMP-9 in comparison to the post-infarction IHD group ($p < 0.05$). A number of myocardial interstitial cells expressing MMP-9 increased already in the pre-infarction IHD group ($p < 0.05$) as compared to controls. It was higher ($p < 0.05$) in the myocardium of post-infarction IHD group and the highest in the myocardium of patients with the end-stage ischemic heart failure.
Conclusion: Expression of collagen-degrading MMP-9 is increasing in progression of ischemia-induced myocardial dysfunction.

E-PS-02-013
Lessons from autopsies: An unusual cause of massive upper digestive bleeding
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Objective: We present a rare case of aortic aneurysm fistulized into the esophagus and right pleural cavity.
Method: A 64-year-old man without significant personal history excepting biliary lithiasis, presented with right upper abdominal pain radiating to the back and dyspnea, which was the dominant symptom. Soon after admission the patient presented a bleeding episode interpreted as hemoptysis. He died suddenly, before being investigated. The autopsy was performed 10 h later, at the department of pathology.
Results: Postmortem examination revealed an extremely pale skin. The right pleural cavity contained 1200 ml hemorrhagic fluid. There was no blood within the respiratory tree. A longitudinal tear in the lower third of the esophagus with a fresh blood clot was found, communicating with an thoracic aorta aneurysm of 20 cm diameter. An old laminated thrombus was filling the aneurysm, which was adherent to the esophageal wall. The stomach contained a cast of coagulated blood, weighting 1000 g; the same content was found within the duodenum and jejunum. The abdominal aorta showed many complicated atherosclerotic plaques and saccular aneurysms.
Conclusion: Although rare, fistulized aortic aneurysms must be considered in the differential diagnosis of upper gastrointestinal bleeding. Performing autopsies in hospital practice is still useful, at least for teaching purposes.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-03 Cytopathology

E-PS-03-001
Cyto-morphology of malignant melanoma on conventional cervical cytology: Case report & review of literature
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Objective: To study the cellular morphology of malignant melanoma on conventional cervical cytology. To identify the differentiating features from other benign & malignant cells. To review the literature on malignant melanoma of female genital tract.
Method: A 42 year old lady presented to gynaecology outpatient department with complaints of brownish vaginal discharge. Per speculum examination showed a mass in upper vagina. A screening conventional cervical cytology smear was taken, stained with papanicolaou stain and observed under microscope.
Results: The microscopy showed loose aggregates as well as dispersed population of intermediate to large sized cells with nuclear pleomorphism, prominent nucleoli and abnormal mitoses. Few cells showed brownish cytoplasmic pigment. The squamous and endocervical cells appeared benign along with dense neutrophilic infiltration and a dirty background. A suspicion of malignant melanoma was given. Biopsy from the mass supported the diagnosis. The cells were positive for S-100 and HMB-45, and a final diagnosis of vaginal malignant melanoma was rendered.
Conclusion: The eyes see what the mind knows. The possibility of malignant melanoma should be considered if the cyto-morphology is suggestive. Diagnosis on cytology is especially difficult for amelanotic melanoma. In low resource countries like India, cervical screening programmes are an important means to identify such malignant lesions.

E-PS-03-002
Urine analysis of school age children of Dharan Municipality, Nepal
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Objective: To assess the prevalence of urinary abnormalities in school-aged children of Dharan Municipality. To provide the report of the urine analysis to the students which may help for their further health consciousness.
Method: Cross sectional, purposive sampling study of 200 urine samples of school age children (less than or equal to 10 years) was done.

Results: 54 and 46 % were male and female subjects among which the lowest and highest age was 5 and 10 years respectively. Most common pH finding was 6.0,yellow color followed by straw color and clear white respectively. Highest specific gravity of urine was 1.015 (80 %) followed by 1.020 (44 %). Ketone bodies and bilirubin positivity were found in single sample each. 7 % of urine samples had bacteriuria along with 13 cases showed nitrite positivity. Two urine samples had trace amount, while one showed 1+ amount of glucose. The frequency of leukocyteuria showed trace, 1+ and plenty amount in nine, three and in one individuals respectively. Hematuria was found to be seen in 8 % cases with 2+ in one individual Eight students had positive protein value, of which seven had trace and one had 1+ in amount. One student had plenty of epithelial cells followed by 1+ and trace amount of epithelial cells by two and five students respectively. One had dumble shaped crystals followed by two having each of amorphous, phosphate, calcium oxalate and uric acid crystals respectively. The cross tabulations between the gender with presence of RBCs, WBCs, occurrence of heamaturia and bacteriuria showed significant p-values.
Conclusion: Mass urinary screening proved to be an useful tool to identify children with asymptomatic progressive renal diseases. Furthermore, the delivery of the report and counseling them for further preventive measures may also help in improving their condition.

E-PS-03-003
Breast cancer metastasis to the pancreas: A case report
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Objective: The pancreas is a site of metastatic spread from a multitude of different primary neoplasms. Breast cancer metastases to the pancreas are part of this rare spectrum. We present a case of breast cancer metastasis to the pancreas.
Method: A 75-year-old female patient, with a medical history of breast cancer 15-years-ago, was admitted to the hospital with complaints of upper abdominal pain. Abdominal CT imaging revealed a solid nodular mass on the pancreatic body with 32 × 22.3 mm.
Results: Fine needle aspiration guided by endoscopic ultrasound of the pancreatic mass was performed. Conventional smears and cell block cytology revealed small groups and isolated pleomorphic cells with abundant cytoplasm. Immunohistochemistry showed positivity for Ca15.3, p53 (75 %) and HER-2, with negativity for Ca19.9, estrogen receptor and progesterone receptor.
Conclusion: We discuss all aspects of the case management, emphasizing the importance of a careful evaluation of the clinical history and the importance of a multi-disciplinary approach. These aspects are important for a correct diagnostic process and an appropriate therapeutic choice when a pancreatic lesion develops in a patient with prior neoplasm.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-04 Dermatopathology

E-PS-04-001
Evaluation of skin excisional biopsy, one annual period
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Objective: The skin of the head and face is habitually exposed to sunlight. Consequently, this exposure may cause of cutaneous squamous cell carcinoma, cutaneous basal cell carcinoma and cutaneous melanoma.
Method: Total of 64 cases (33 male,31 female) were included in the study. The oldest age was 95 and the youngest age was 23. 25 cases were diagnosed as BCC. 24 cases were diagnosed as SCC. 6 cases were diagnosed as seborheic keratosis. There were 2 melanoma in situ cases and they were both localized at face. Also there was 1 patient who were diagnosed as atypical spitz nevus which had been localized at gluteal region.
Results: BCC was more common in women (56 %). Nose localization (36 %) and nodular subtypes (60 %) were commenest among others. SCC was more common in men (66 %). It was tend to be in ear and lower lip localizations (29 %). Well and moderately differentiated tumours were of equal amounts (50 %). 4 cases of SCC had been developed from keratoacanthoma. Patients who were diagnosed as BCC were younger than patients who were diagnosed as SCC (90-45/95-69).
Conclusion: This study, premalign and malign tumours were determined in the face localization mostly. Nose, lower lip and ear localization were frequency in malign tumours. Premalign and malign tumours were determined in the eyelid localization mostly.

E-PS-04-002
Clinicopathological features of pilomatricoma cases: Review of 65 cases
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Objective: Pilomatricoma is a slow-growing, asymptomatic tumour that arises from outer sheath cells of hair follicle. In this study, we review the clinical presentation and histopathological findings of pilomatricoma.
Method: Retrospective review of 65 cases of pilomatricoma, reported at Ahi Evran University Hospital from 2010 to 2015.
Results: A total of 65 cases of pilomatricoma were reported with age range of 6–80 years (mean age, 30.3) and male to female ratio of 34:31. There were 24 patients younger than 18 years (36.9 %). The most common site of occurrence was upper extremity and second most common site was face. The main presenting symptom was a hard, subcutaneous, slowly growing mass. The size of the tumour ranged from 0.4 to 5 cm in diameter. Multiple occurrences were seen in 3 cases. All cases more or less showed the same histopathologic features of pilomatricoma such as shadow cells, basophilic cells, calcification, ossification and inflammatory cells.
Conclusion: Pilomatricoma is a benign skin neoplasm of hair follicle matrix cells. It is often misdiagnosed with other skin conditions. The treatment of option is surgical excision and the recurrence rate is low. Histopathological study gives the certain diagnosis as clinical impression and fine needle aspiration cytology may be misleading.

E-PS-04-003
Thyroid carcinoma with cutaneous metastasis
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Objective: Cutaneous metastases occur in approximatively 2 to 9 % of patients with a malignancy. Skin metastases from carcinoma of the thyroid gland are rarely observed. We present a case of an incidentally thyroid carcinoma discovered on cutaneous metastasis.
Method: A 63 year-old woman was diagnosed with a mediastinal mass and enlarged cutaneous lesion of the sternum. A skin biopsy was performed.
Results: Histological examination of the lesion identified an infiltrating and poorly differentiated carcinoma. It was composed of nests and cords of epithelial cells with prominent hyperchromatic and atypical nuclei. Immunohistochemical studies revealed strong positivity for TTF1 and thyroglobulin. Chromogranin and synaptophysin were negative.

Conclusion: In this case, subsequent investigations identified primary thyroid lesions. Although cutaneous metastases of thyroid carcinoma are very rare, they could be the only presenting feature of the underlying malignancy.

E-PS-04-004

Scrotal calcinosis: Analysis of 5 cases

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Objective: Idiopathic scrotal calcinosis(ISC) is an uncommon benign process,characterized by solitary or multiple,painless,strict scrotal nodules in the lack of systemic metabolic disorder. Its nature and reason have remained unknown and theories of origin contain idiopathic calcification arrising within normal scrotal collagen,dystrophic calcification of inflamed scrotal epidermoid cysts,eccrine duct milia or dartoic muscle,and secondary to minor trauma.
Method: A total of 5 cases were found for ISC during the period 2010–2014 in our department of pathology. All patients underwent surgical excision of the lesions with overlying skin.
Results: Age range was from 25 to 49 years with a mean age of 31.4 years. Three of the patients with multiple lesions (3/5). The common appearance of the masses were hard, slowly growing,semi-mobile,lobulated, and well-circumscribed subcutaneous nodules. Diameter of the lesions ranged 0.7 to 3 cm. Grossly,there were firm,white with chalky and gritty areas. H&E stains revealed basophilic masses in dermis with foreign body giant cell reaction in 4 cases.No recurrences were noted.
Conclusion: ISC is a rare,benign,disease of the scrotal skin that characterized by calcium depositions of various sizes surrounded by a granulomatous reaction. In spite of the debate about the origin of this entity,surgery still seems to be the treatment of option and provides a good clinical outcome.

E-PS-04-005

Collision tumour: Primary Merckel Cell Carcinoma (MCC) and chronic lymphocytic lymphoma

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Objective: We report an extremely rare case of skin collision tumour between primary Merkel cell carcinoma (MCC) and chronic lymphocytic leukemia (CLL) This association has been established, although the cause is still unclear. A 76-year-old man with a history of CLL presented with a non-ulcerated, 1.2 cm, asymptomatic, pink skin nodule on the left frontal region.
Method: A 6 mm punch biopsy was performed.
Results: Microscopically, the punch biopsy showed a dense, diffuse proliferation of uniform, medium-sized cells infiltrating the dermis. Neoplastic cells had scant cytoplasm and round nuclei with finely dispersed chromatin, and inconspicuous nucleoli. Abundant mitosis were found. A second population of neoplastic cells was observed, which was composed of small cells with round nuclei, condensed chromatin, and a small amount of cytoplasm. Mitotic figures were absent in this component. Immunohistochemical stains were performed and supported the diagnosis of both CLL and MCC.
Conclusion: Until now, only five cases of collision between MCC and CLL in the same skin lesion have been documented. The case herein described underlines the importance of a histopathological diagnosis on every skin lesion arising in the course of CLL, as the development of MCC is a possible event in this condition.

E-PS-04-007

Interobserver variability of distinguishing between polyarteritis nodosa and superficial thrombophlebitis by histopathologic features

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Objective: To evaluate interobserver reliability of distinguishing between polyarteritis nodosa (PAN) and superficial thrombophlebitis (ST) by assessing interrater agreement of seven histologic features.
Method: All skin biopsies of PAN and ST diagnosed in Siriraj Hospital were re-evaluated independently by three dermatopathologists and a resident of pathology. Seven histopathologic criteria including; elastic fiber distribution in vessel wall, fibrinoid necrosis, internal elastic lamina, smooth muscle pattern, luminal thrombosis, small vessel vasculitis and plasma protein accumulation were determined. Agreement analysis was performed by kappa coefficient.
Results: All 63 biopsies; 28 cases were PAN and 35 cases were ST. The reproducibility between four observers was substantial agreement ($\kappa = 0.73$). The features with moderate agreement were elastic fiber distribution in vessel wall ($\kappa = 0.68$), fibrinoid necrosis ($\kappa = 0.63$), while internal elastic lamina ($\kappa = 0.51$), smooth muscle pattern ($\kappa = 0.46$) and luminal thrombosis ($\kappa = 0.45$) were fair to moderate agreement. Small vessel vasculitis ($\kappa = 0.28$) and plasma protein accumulation ($\kappa = 0.1$) showed poor agreement.
Conclusion: Overall agreement of distinguishing between polyarteritis nodosa and superficial thrombophlebitis was good. Elastic fiber distribution in vessel wall, fibrinoid necrosis, internal elastic lamina, smooth muscle pattern and luminal thrombosis were useful histopathologic features.

E-PS-04-008

Cutaneous melanoacanthoma

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Objective: We present a case of a rare entity, Cutaneous melanoacanthoma (CM), traditionally considered to be a pigmented variant of seborrheic keratosis.CM is presented as a benign proliferation of melanocytes and keratinocytes usually existing over the head, neck and trunk of elderly people.
Method: A 77 years old man presented with a polychrome pigmented patch of the left flank. The lesion was asymmetric measuring 2.3 cm. Melanoma and seborrheic keratosis were first suspected.
Results: Microscopic analysis revealed acanthosis with proliferation including epithelial and melanocytic hyperplasia. There is no evidence of cytological atypia, pleomorphism or nuclear hyperchromasia. The dendritic melanocytes exhibit diffuse cytoplasmic expression of S100 and MelanA.
Conclusion: Melanoacanthoma is a rare, pigmented, benign, mixed neoplasm, composed of dendritic melanocytes and proliferating epidermal keratinocytes.It usually occurs in elderly individuals, with no sex predilection and may be multiple. Clinically, it presents as an asymptomatic, slowly-growing, hyperkeratotic papule, plaque or nodular lesions with a diameter ranging from a few millimeters to several centimeters and are most frequently found on the head, particularly the lips. In our case, the lesion was cutaneous situated at the trunk. Histopathologically, melanoacanthoma is characterized by numerous large dendritic melanocytes spread throughout the hyperplastic epidermis. Immunohistochemistry may be useful if there is a diagnostical doubt.

E-PS-04-009

Histopathological and immunological evaluation of canine amniotic membrane implantation in rabbits

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Objective: The present study was designed to evaluate the Canine amniotic membrane (AM) as biological dressing for deep cutaneous wound artificially induced in rabbits.
Method: Full term pregnant bitch was used to harvest canine amniotic membrane. Twenty seven New Zealand white male rabbits, were distributed into three groups of nine animals each. Then wound induction was done in all groups. The rabbits were divided into three main groups as follow: group I, wound area was covered by canine amniotic membrane, group II, wound area was dressed by Pividon Iodine and group III, wound area was not subjected to any type of dressing materials. Three animals from each group were sacrificed at 7,14 and 21 days P.W serum and wound granulation tissue samples were collected for estimation of oxidative stress indicators and hydroxyl proline content. Tissue specimens were fixed in formalin for histopathological, immunohistochemical examination.
Results: The results revealed increase in serum and tissue antioxidant levels while reduction in oxidative radicals in AM dressed wound compared with other groups while the hydroxyproline content was higher in AM dressed wound than other group. The histopathological examination revealed that reduction in inflammatory reaction in AM dressed wound with enhanced epithelization and fibroblast proliferation and collagen deposition that was confirmed by masson's trichrom.
Conclusion: It was concluded that amniotic membrane is a useful and effective biological dressing that enhance wound healing.

E-PS-04-010

Immunohistochemical expression of Serotonin in psoriasis and eczema

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Objective: Serotonin, through its serotonin transporter protein (SERT), may play a role in connection with different types of skin inflammation, including psoriasis and eczema. The authors propose to study the role of serotonin in the pathogenesis of psoriasis and eczema.
Method: Immunohistochemical study was performed to study the expression of serotonin in the lesions of 15 patients with psoriasis, 12 patient with eczema and 10 normal skin specimens.
Results: Sex ratio was 1.31 and the mean age at the time of diagnosis was 40 (6–86). Serotonin expression was negative in all normal skin biopsies. Expression of serotonin was significantly strong in the prickle cells, basal cells sweat gland cells and sebaceous gland cells of the lesions of psoriasis in 14 patients. In eczema, strong positivity was found in the prickle cells, basal cells and hair roots for 12 patients. There was no positive expression in the mast cells, collagen fiber, nerve, muscle, Langerhans cells, or epithelial cells of vessels in all of the specimens.
Conclusion: Serotonin probably plays an important role in the pathogenesis and activity of skin inflammatory diseases. Immunohistochemestry may be of great interest to guide the treatment of such pathologies.

E-PS-04-011

Primary PEComa of the skin: A case report

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Objective: Primary perivascular epithelioid cell tumour (PEComa) rarely occurs in the skin. It shows distinct histological features and co-expression of melanocytic and muscle markers.
Method: A 51-year old female presented with a firm nodule on the upper arm. Lesion was excised, histologically and immunohistochemicaly analyzed.
Results: On histology, mostly nodular tumour in dermis and superficial subcutaneous fat tissue was observed. It was composed of polygonal clear cells with vacuolated cytoplasm, round nuclei with conspicuous nucleoli. Multinucleated cells with eosinophilic cytoplasm ("spider cells") were present in multiple foci. Necrosis and mitosis were absent. Differential diagnosis included PEComa, balloon-cell nevus or melanoma, and metastatic renal cell carcinoma. On immunohistochemistry, tumour was diffusely positive for HMB-45, MITF, CD10, and INI 1, and focally for vimentin. CD68 was positive in multinucleated cells. p53 and Ki-67 were expressed in 10 and 1 % of cells, respectively. Epithelial and smooth muscle cell markers, Melan A, Sox10, TFE-3 and RCC were negative. Diagnosis of PEComa was made.
Conclusion: Cutaneous PEComas can show absence of smooth muscle markers and some melanocytic markers. In tumour with typical histology, which is MiTF positive, and cytokeratin, SOX10 and S100 negative diagnosis of PEComa can be made.

E-PS-04-012

Diagnostic histopathological criteria of folliculotropic mycosis fungoides: A study of 3 cases

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Objective: Folliculotropic mycosis fungoides (FMF) is a distinct variant of mycosis fungoides (MF) with its own clinical manifestations, histological features and biological behavior. Histological diagnosis is usually delayed due to subtle morphological alterations. The aim of the study is to highlight the typical microscopic skin changes that allow a correct diagnosis.
Method: We present 3 cases of FMF followed by multiple clinical diagnoses. In each case among them there were lymphoma of the skin and others. Two patents were males aged 18 and 65 years and one was a 53-year-old woman.
Results: The histological hallmarks (n = 3) included perifollicular and intrafollicular infiltration with atypical T-cells, infundibulocystic structures (sometimes resembling milia), basaloid follicular hyperplasia, follicular mucinosis, syringotropism, numerous eosinophils around hair follicles and rare epidermotropism involving nonfollicular epithelium. There were also (n = 1) foci of hair follicles destruction revealed due to entrapped squamous cells and horn masses within dermal neutrophilic pustular lesions. A frequent feature (n = 3) was prominent Langerhans cell hyperplasia. Multinucleated giant cells were found within some hair follicles without evident adnexal distruction. Invariably, the atypical T-cells displayed a CD3+, CD4+ immunophenotype with only scattered CD8+ cells. In all cases a pronounced mixture of reactive T- and B-lymphocytes and CD1a+ cells was found.
Conclusion: The originality of follicle cystic lesions, weak nonfollicular epidermotropism, cellular composition of the infiltrate with immunohistochemical specification help to make the correct diagnosis of FMF and to distinguish it from another kind of follicular injury which can be seen in nontumour folliculitis, acne and secondary involvement of skin adnexa.

E-PS-04-013

Primary penile kaposi sarcoma: An exceptional tumour in HIV negative patient

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Objective: Kaposi's sarcoma (KS) is a connective tissue cancer caused by human herpes virus 8—now called Kaposi's sarcoma-associated

herpesvirus (KSHV). It is a rare angioproliferative disorder of the vascular endothelium, usually associated with HIV infection. Isolated penile KS has rarely been reported, especially in immunocompetent patient. The aim is to attract the attention of pathologists on the exceptional penile location of Kaposi sarcoma especially in HIV negative patient.
Method: The patient was 71 years old male, suffered from itchy penile nodule. He didn't have unprotected extra marital sex. His wife was free from Sexually Transmitted Diseases (STDs). In his past medical history, there was no report of any kind of disease or surgery. On examination, we noted a unique nodular, itchy and well circumscribed lesion on the glans penis.
Results: The histological examination showed showed an infiltration composed of spindle cells scattered between collagen bundles and small vascular proliferation. Slit-like spaces containing red cells were observed. Immunohistochemical investigations revealed a vascular tumour because of reasonable positivity for vascular marker such CD34, and immunohistochemical staining confirmed KS by diffuse nuclear staining of human herpesvirus type 8 (HHV-8).
Conclusion: Our case appears to be noteworthy because of the exclusive penile involvement, HIV seronegativity, and indolent course with complete response to surgical excision.

E-PS-04-014
Synovial metastasis: Exceptional location of metastatic melanoma

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Objective: The synovial is a rare site of tumour metastases with less than 40 cases reported in the literature. Although melanoma is a highly metastatic cancer, only two cases of synovial metastases have been reported. The aim of this case is to attract the attention of clinicians and pathologists on the importance of intra-articular metastatic localization including synovium.
Method: The patient was 73 years old with no notable medical history. She complained of joint pain mimicking a knee sprain. Physical examination showed a swollen knee, red and painful. Radiological examination revealed a filling the joint space. A biopsy of synovium was practiced.
Results: Microscopic examination showed a malignant tumour proliferation largely necrotic arranged in clumps or small nests within an inflammatory stroma. Tumour cells had eosinophilic cytoplasm without pigment melanin. The nuclei were large and highly mitotic with a prominent nucleolus. The immunohistochemical study objectified positivity of tumour cells for HMB45, vimentin and CD99. They were in contrast negative for CK, EMA and desmin. The diagnosis of synovial locating of cutaneous melanoma was retained.
Conclusion: Metastasis of melanoma at the synovium is very rare. They generally occur at the stage of disseminated disease. The treatment is palliative.

E-PS-04-015
Chondroid Syringoma: Report of eight cases and review of the literature

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Objective: We herein present 8 cases diagnosed as chondroid syringoma (CS) in our department to investigate the incidence, determine the spectrum of histomorphologic patterns and clinicopathological characteristics of chondroid syringoma.
Method: The differential diagnosis of CS is made with other benign tumours of appendages such as dermoid or sebaceous cyst, neurofibroma, dermatofibroma, basal cell carcinoma, pilomatricoma, histiocytoma, and seborrheic keratosis. Although chondroid syringomas are predominantly benign, malignant forms have been reported.
Results: It is histologically similar to salivary gland mixed tumours where, proliferation of epithelial and myoepithelial cells set in a myxomatous, chondromatous, or hyalined stroma. Mixed tumours composed of five histological criteria for diagnosis: 1) cuboidal or polygonal cell nests 2) tubuloalveolar structures lined with two or more rows of cuboidal cells 3) ductal structures with one or two rows of cuboidal cells 4) keratinous cysts 5) a matrix of varying composition. CS may have all five characteristics or manifest only some.
Conclusion: The CS, or mixed tumour of the skin, was first described by Hirsch and Helwig, as a benign neoplasm of sweat gland origin and a rare clinical entity. The incidence of CS is <0.01 % of all primary skin tumours. It is usually located in the skin of the head and neck. Rare localization areas are the axilla, abdomen, trunk, genitalia and extremities in patients between the age of 20 and 60 years with a male predominance. CS lesions usually are not clinically distinctive and the diagnosis is made on microscopic examination.

E-PS-04-016
Metastasis of skin melanoma in Warthin tumour of salivary gland-case report

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Objective: We report a cas of metastasis of skin melanoma in Warthin tumour of salivary gland.
Method: 62 year old man had skin melanoma on the right side of temporal region and enlarged lymphatic nodes on the right side of the neck, as well. Patohystological analysis confirmed that it was the case of skin melanoma and metastasis of melanoma in two lymphatic nodes. One year later the patient had the second operation because of the lymphadenoopaty on the right side of the neck, once more. This time patohystological analysis confirmed that it was the case of metastasis melanoma in Warthin tumour of salivary gland. Lymph nodes were not detected.
Results: Patohystological analysis of hematoxylin-eosin staining and also imunohystological staining as well (Melan A,HMB-45, CK7,AE1/AE3) confirmed metastasis of melanoma in Wartin tumour of salivary gland.
Conclusion: To our knowledge this is the unique case of metastasis of skin melanoma in Wartin tumour of salivary gland.

E-PS-04-017
Syringocystadenocarcinoma papilliferum in situ: Report of a case with recurrence

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Objective: Syringocystadenocarcinoma papilliferum (SCACP) is a very rare cutaneous neoplasm, representing the malignant counterpart of syringocystadenoma papilliferum (SCAP). Only 28 cases have been reported, 9 of them as carcinoma in situ.
Method: We present a case of a 64-year-old woman with a nodular mass on scalp that recurred 2 years after excision of the primary tumour.
Results: Microscopically, the lesion composed of cystic duct-like structures that extend as invaginations from the surface epithelium into the underlying dermis. Cyst wall showed papillary projections lined by two-layered epithelium with nuclear atypia. Multilayering, increased mitotic activity and comedo necrosis were detected. Immunohistochemical study with p63, cytokeratin 14 and calponin showed continuous layer of myoepithelial cells throughout the lesion. A pathological diagnosis of SCACP in situ was rendered.
Conclusion: SCACP has favorable prognosis, only 2 cases with local recurrence, 1 case with late recurrence and 3 cases with regional lymph node metastases have been reported up-to-date.

The presented case is the second case with late recurrence in the literature and emphasizes the need of a long-term follow-up in patients with this tumour.

E-PS-04-018

Unusual localisation of primary cutaneous adenoid cystic carcinoma: Case report

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Objective: Primary cutaneous adenoid cystic carcinoma (PCACC) is rare tumour of elderly, often localized on scalp. It often recurs, but metastases are exceedingly rare.
Method: We present a case of primary cutaneous adenoid cystic carcinoma (PCACC) with unusual localization on the forearm in a 46-year-old woman. Clinically, tumour was suspicious for lipoma. Tumour was excised and examined histologically and immunohistochemically.
Results: On histology a dermal based tumour was composed of solid areas with small adenoid and cystic spaces filled with mucin, and multiple adenoid spaces with cribriform pattern. Foci of hyalinized fibrous tissue were also present. Mild to moderate cellular atypia was present. Differential diagnoses included metastatic adenoid cystic carcinoma, spiradenocarcinoma, and adenoid basal cell carcinoma. On immunohistochemistry tumour was positive for cytokeratin, CK7, EMA, calponin, alfa SMA, focally for CK5/6, CK15, CEA, p63 and S-100, but negative for nestin and CK20. Clinical studies showed no presence of tumours elsewhere. Diagnosis of PCACC was made. Tumour was incompletely excised, thus surgical re-excision was advised.
Conclusion: Forearm is unusual localization of PCACC. Because of high local recurrence rate, wide and complete surgical excision of PCACC is recommended.

E-PS-04-019

Digital papillary adenocarcinoma with bone invasion: A case report

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Objective: Digital papillary adenocarcinoma (DPAC) is rare adnexal skin tumour with uncommon bone invasion and high recurrence rate.
Method: We present a case of 32 year old female with history of multiple operations of ingrown nail in the past 12 years, and painful nail deformation of the toe. Clinical suspicion of osteomyelitis was made. Amputation was preformed and specimen was examined histologically.
Results: On histology, tumour was composed of glands, solid sheets of epithelioid and spindle cells, and cystic spaces with micropapillae. Focally, clear cells, and apocrine and squamous differentiation were noted. Focal necroses, high mitotic rate (30 mitoses per 10 HPF) and bone invasion were present. SMA, calponin and vimentin were positive in solid areas, GCDFP-15, mCEA and EMA in glands, while S-100, cytokeratin and CK7 were positive in both areas. p63 was positive in solid sheets and around glands. Diagnosis of DPAC was made. Re-amputation and long-term follow up were suggested due to positive margins and bone invasion.
Conclusion: DPAC should be included as differential diagnosis of tumours on acral site and with bone invasion. It can behave in aggressive manner, and long-term follow up is advised.

E-PS-04-021

Squamous Cell Carcinoma (SCC) on the abdominal wall of a young patient with Werner syndrome: Case report

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Objective: Werner Syndrome is a rare, autosomal recessive genetic disorder. Loss of functional mutations in WNR gene causes classical Werner Syndrome. This syndrome is associated with premature aging.
Method: Age related diseases are seen in early decades of life. Skin malignancies, cataracts, atherosclerosis, osteoporosis are most common disorders.
Results: We are reporting Werner Syndrome associated squamous cell carcinoma in a 25 year old woman. She had persistent wound on periumblicalregion. A punch biopsy was performed. On histological examination well differentiated squamous cell carsinoma was observed on H&E sections.
Conclusion: Werner Syndrome can cause early deaths due to cancers and we present this case because of its rarity.

E-PS-04-023

Freezing skin tissue in Mohs Micrographic Surgery using PrestoCHILL®

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Objective: Mohs micrographic surgery is distinguished by histologic examination of the complete surgical margin prepared from fresh frozen tissue. The purpose is to achieve the examination in one section of the undersurface, the sidewall, and the epidermal margin. To do so, the specimen must be manipulated before freezing, flattening it.
Method: We compare 34 cases frozen by traditional method over a year, with 9 cases frozen by PrestoCHILL® over 3 months.
Results: Traditional method required a mean of 15 slides while the new one only 10. Also the number of frozen blocks needed downgraded from 1.9 to 1. Freezing quality was also improved, and holes and tears seen in fat were also reduced.
Conclusion: The manipulation of the skin while freezing is one of the pitfalls of this technique, since the flattening of tissue is done against gravity, and epidermal margins usually "fall". The solution to this particular problem requires several serial sections or cutting the specimen in more than 1 frozen block to solve. We tested PrestoCHILL® device to freeze the tissue, since the freezing is made faster and in contact of a flat metal surface, facing the margin (favored by gravity).

E-PS-04-024

Combination of rare skin carcinomas in one affected area in the recipient with the cadaveric kidney allotransplant

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Objective: Neuroendocrine Merkel cell carcinoma is a more frequent type of tumour in organ transplant recipients, and it can coexist with other types of skin carcinomas.
Method: We have a rare case of coexistence of Merkel cell carcinoma and high-grade porocarcinoma from the 63-year-old patient with cadaveric kidney allotransplant. A fungoides skin tumour, 3 cm in diameter was

found on the frontal part of the sternal jugular incisure. Complete tumour excision was made.
Results: Histologic examination revealed two closely located dermal tumours. The first one consists of round cells with solid and diffuse types of growth and high mitotic rate. The necrotic areas and karyorrhexis are conspicuous. The tumour cells express CD56, synaptophysin, chromogranin, with aberrant expression of cytokeratin 20. The tumour has a histological appearance and immunophenotype of Merkel cell carcinoma. The second tumour consists of large polymorphous cells with eosinophilic cytoplasm, vesicular nuclei and conspicuous nucleoli. It attaches epithelium of dilated follicular ostium and invades dermis with solid and papillary structures formation. Some cells show sebaceous differentiation. Mitoses are frequent, with pathological ones. The tumour cells express p63, cytokeratins AE1/AE3, 7, some cells—CK5/6. On the base of morphological and immunophenotypical features the diagnosis of high-grade porocarcinoma was suggested.

E-PS-04-026
Primary cutaneous perivascular epithelioid cell tumour: A case report
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Objective: Perivascular epithelioid cell tumours(PEComas) are rare mesenchymal neoplasms of uncertain lineage that characteristically show an epithelioid morphology and a variable expression of both melanocytic and myogenic markers. They usually involve the thorax, the gastrointestinal or genitourinary tracts. Only 34 cases of PEComas arising in the skin were described in the literature. This are apparently benign tumours, although a few malignant cases were reported. Here, we report a case of primary cutaneous PEComa.
Method: A 49-year-old women presented with a painless cutaneous nodule arising in the left thigh. Histopathological and immunohistochemical examinations of resected specimen were performed.
Results: Microscopic evaluation revealed a dermo-hypodermal proliferation of epithelioid cells with clear or granular pale-eosinophilic cytoplasm and centrally located round/oval nuclei and proeminent nucleoli. Architecturally, the tumour presented a nested and focally trabecular growth pattern; tumour stroma contained numerous thin-walled capillaries with a lace-like pattern. Mitoses and necrosis were absent. There was no epidermal involvement. Immunohistochemically, tumour cells were positive for HMB-45, CD10, CD34, CD44 and negative for S-100, Melan-A, alfa-SMA and various cytokeratins.
Conclusion: Diagnosis of PEComa could be a challenge and both histopathological and immunohistochemical examinations of this entity are essential because of potential misdiagnosis as malignant tumours (malignant melanoma, sarcoma, metastatic renal cell carcinoma).

E-PS-04-027
Primary subcutaneous hydatid cyst: A case report
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Objective: Hydatidosis is a parasitic disease that occurs commonly in the liver and the lungs. Primary subcutaneous localizations are really rare. The authors report one case of subcutaneous hydatid cyst.
Method: A 49 year old woman with no particular medical or surgical history presented with a painless swelling of the right thigh. Ultrasonography imaging showed a sub-cutaneous hypoechoic well limited non vascularised mass. a surgical excision was performed. Intraoperative findings were suggestive of an abscess. Pathological examination found inner germinal and lamellated layers of cyst wall that stains with PAS. Serology was performed and was positive. The patient has been followed for 3 months, and no findings associated with local or systemic hydatid cyst recurrence were detected.
Results: In this case the histological findings were suggestive of hydatid cyst, and the final diagnosis was made after clinical, biological, radiological and histological confrontation.
Conclusion: Subcutaneous hydatid cyst may be primary or secondary. The primary cysts are exceptional, however, it should be included in the differential diagnosis of any subcutaneous cystic mass, especially in endemic regions. Their diagnosis is based on the clinico-radiological findings and confirmation is histological. The treatment is surgical and the evolution is marked by fistulisation and recurrence.

E-PS-04-028
Malignant spiradenocarcinoma mimicking a breast carcinoma
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Objective: The malignant counterpart of spiradenoma, known as spiradenocarcinoma, or "carcinoma ex spiradenoma", is a very rare adnexal neoplasm of the skin. The low number of diagnosed cases, problematic classification and naming, the variability of the microscopic features represent reasons for the scarcity and fragmentation of the data regarding their evolution and prognosis. The aim of the present paper is to present a case of spiradenocarcinoma with axillary lymph node metastasis.
Method: A 62-year-old woman presented with a 5/3 cm painful, firm, axillary tumour, fixed to the subjacent planes, which developed in 3 months and raised the suspicion of tumour originating in an ectopic breast tissue. The tumour and axillary lymph nodes were resected. A second tumour, previously diagnosed clinically as dermatofibroma, located on the external aspect of the upper third part of the arm, 3/2 cm in size, firm, with a fluctuant central area was resected and submitted to pathology department next day.
Results: The axillary tumour was diagnosed as metastatic poorly differentiated adenocarcinoma of unknown origin. The arm tumour showed the features of a poorly differentiated adenocarcinoma. The continuity between areas with malignant appearance and remnants of pre-existing spiradenoma facilitated the diagnosis of spiradenocarcinoma.
Conclusion: The present case illustrates the difficulties of clinical and morphological diagnosis of primary and metastatic spiradenocarcinoma and the possible aggressive behavior of some of the tumours in this category.

E-PS-04-029
Periungual human papillomavirus type 16 associated with digital squamous cell carcinoma in situ in patient's immunocompromised. A report of 2 cases and review of the literature
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Objective: Human Papillomavirus (HPV) associated squamous cell carcinoma (SCC) and SCC in situ (SCCIS) are reported in the genital region, in the digital skin is less well recognized, especially associated with HPV16. Digital SCC occur independently of the patient's immune status is more aggressive and can be difficult to treat. We reported 2 cases of HPV-associated SCCIS of the periungueal region in patient's immunocompromised.
Method: We reported two men of 55 and 52-years-old with verrucous lesion on the right hand, in the third and first fingers, respectively. The first, had chronic linfatic leukemia with a history of a condyloma on the penis, and the second patient with human immunodeficiency virus (VIH), a history of a SCCIS on the mandibular angle associated with HPV16. A biopsy specimen and HPV genotyping test were performed.
Results: Both patients, had SCCIS with HPV16. Tumours were treated by surgical excision and the first was treated with photodynamic therapy with no recurrence and the second patient, the lesion persist and he will receive radiotherapy.
Conclusion: High-risk mucosal HPV types, such as HPV16, have an apparent predilection for the nailbed. These tumours necessitate prompt surgical treatment and close follow-up as they tend to be locally aggressive.

E-PS-04-031
Malignant chondroid syringoma of scalp—a rare tumour
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Objective: Malignant chondroid syringoma (malignant mixed tumour) is an exceedingly rare cutaneous adnexal carcinoma with a significant risk for aggressive behaviour. They usually present as large asymmetrical, lobulated biphasic tumour with infiltrative margins and adjacent satellite tumour nodules. Unlike its benign counterpart, malignant form occurs predominantly in females and is observed on the extremities. Tumours greater than 3 cm in size have a greater likelihood of malignancy.
Method: A 60-year-old male patient presented with multipl large tumour nodules with the biggest dimension of 8 cm in the occipital and temporal region of the scalp. He has a history of tumour excision in the same region 2 years ago which was diagnosed as mixed tumour. Total tumour excision was performed. Macroscopic examination of the largest excision specimen showed 8 × 8 × 4 cm and others between 1 and 2.5 cm tumour nodules with focal gelatinous cut surfaces. Microscopically tumour composed of epithelial and mesenchymal components in a chondromyxoid stroma. Focal necrosis, infiltrative margins and mild/moderate atypia was observed.
Results: The final diagnosis was malignant chondroid syringoma.
Conclusion: In the evaluation of neoplastic growths of scalp chondroid syringoma should be considered in the differential diagnosis.

E-PS-04-032
Giant pilomatrixoma mimicking soft tissue sarcoma
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Objective: Pilomatrixoma is a benign cutaneous tumour of hair matrix origin and characterized by the presence of subcutaneous nodules of up to 3 cm in diameter. It is usually seen in children and more frequently located in the head and neck. We present the case of a 52 years-old-woman with a 17 cm mass depending on the inner face of her left arm, who presented with constitutional syndrome and iron-deficiency anemia. Because of the large size and clinical symptoms, sarcoma was the first clinical suspicion.
Method: Surgical resection was performed. Macroscopically, the tumour was pediculated with an expansive growth pattern and free surgical margins.
Results: Histopathologic study revealed nodules of basaloid cells, which mature centrally to produce ghost cells. The stroma also showed numerous multinucleated giant cells of foreign body type and bone metaplasia. Numerous mitosis and atypical features were also seen, which made us consider the differential diagnosis of pilomatrix carcinoma and the proliferative variant of pilomatrixoma.
Conclusion: The largest reported case was 24 cm pilomatrixoma presenting in the posterior thorax. Thus, our case is the second one and the largest located in the arm. Pilomatrixoma should be suspected in the differential diagnosis of giant adnexal tumours.

E-PS-04-033
Epidemiological and clinicopathologic characteristics of Kaposi's sarcoma: A retrospective analysis of 89 cases in Tunisian center
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Objective: We propose to study the Clinicopathologic characteristics of KS in our center.
Method: A retrospective analysis of 89 histologically confirmed cases of KS over a period of 14 years was undertaken. Immunohistochemical study was carried using CD31, CD34 and HHV8.
Results: The average age was 67,3. The classic form represented 84,3 % of all cases, followed by iatrogenic form (15,7 %). No cases of AIDS-related KS were recorded. Cutaneous involvement was observed in all cases. The most common location the distal lower extremity (88,8 %). Cutaneous lesions presented as papules/nodules in 43 cases (48,3 %), erythematous/angiomatous plaques in 14 cases (15,7 %) and a mixture of both lesions in 32 cases (36 %). In addition to skin involvement, mucosal KS was diagnosed in 9 cases while visceral spread was found in 2 patients. Cutaneous biopsy was performed in 78 cases, the histopathologic features varied so significantly with respect to the stage of the lesions. Surgical excision of the cutaneous lesions was performed in 12 cases and 5 patients received systemic chemotherapy.
Conclusion: Classic KS is the major form of KS in Tunisia, it is predominantly a male disease which exhibits some special characteristics, including disseminated skin disease at diagnosis, uncommon visceral or lymph node involvement.

E-PS-04-034
Neutrophilic panniculitis is an emerging side effect of BRAF inhibitors: A report of 2 cases
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Objective: Panniculitis is a rare emerging side effect of BRAF inhibitor(BRAFi) therapy used to treat patients with BRAF-mutated metastatic melanoma. Only 18 cases are documented in the literature.
Method: We present two additional cases and review the clinicopathological findings of the cases reported to date.
Results: Patient 1 was a 65-year-old female who presented with fever, rash, generalized arthralgia and painful nodules in the inferior and superior limbs

10 days after starting vemurafenib. A punch biopsy showed a lobular panniculitis with a mixed infiltrate with numerous neutrophils and foci of necrosis and apoptosis. A diagnosis of vemurafenib-associated neutrophilic panniculitis was rendered and vemurafenib dosage was reduced with complete resolution of the lesions. Patient 2 was a 35-year-old female who, after 6 weeks of treatment with vemurafenib, developed painful nodules in the the inferior limbs. A punch biopsy showed a lobular panniculitis with neutrophilic infiltration without vasculitis. A diagnosis of vemurafenib-associated neutrophilic panniculitis was rendered. She was started on steroids with total remission of the lesions.
Conclusion: BRAFi associated panniculitis can present under a range of histological presentations, documented in the literature and in our cases. As clinical course is generally benign, recognition of this side effect is important in order to prevent BRAFi discontinuation.

E-PS-04-035
Sebaceous carcinoma, a rare and aggressive cutaneous malignancy: A report of nine cases
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Objective: Sebaceous carcinoma (SC) is a rare aggressive skin cancer exhibiting diverse clinical presentations and histologic patterns, often mimicking other cutaneous malignancies. Several studies have reported SC in association with Muir-Torre syndrome (MTS), a disorder characterized by visceral malignancies and gene abnormalities.
Method: We present nine cases of SC(two cases on periocular and seven on extraocular regions) diagnosed in our department between 2008 and 2015. Also, 4284 cases of basal cell carcinoma(BCC) and 1092 cases of squamous cell carcinoma(SCC) were diagnosed in the same period of time.
Results: SC was more frequent in males and most commonly presented as a nodular ulcerated mass. Histopathologically, there were varying architectural patterns with irregular solid lobules of basaloid cells and variable sebocytic differentiation, areas of comedo-necrosis(four cases) and/or squamous differentiation(three cases); duct or cystic differentiation was seen too; one case was associated with SC "in situ" and pagetoid invasion of supraiacent epidermis. Infiltration of subcutaneous fat/skeletal muscle was evident in three cases. Six tumours were grade 2. All SCs presented at least focal positivity for EMA and adipophilin and intense p53 nuclear staining. None of them showed microsatellite instability.
Conclusion: In our experience, SC is a rare tumour with morphology similar to BCC and SCC; EMA and adipophilin facilitate appropriate diagnosis.

E-PS-04-036
Study of the association between the MCV polyomavirus and Merckel cell carcinoma: About 11 cases of a Tunisian series
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Objective: To study the anatomo- clinical characteristics of Merkel cell carcinoma and to determine the prevalence of the MCV virus in these carcinomas through the study of a series of 11 tunisian cases between 1990 and 2014.
Method: Clinical data have been collected from the medical records of patients and a rereading of slides has been made. The search for the MCV virus was carried out by PCR technique on tumourous tissue samples.
Results: The average age at the time of diagnosis was 73,5 years. The cervico-facial locations were the most frequent, 3 patients had ganglionic metastases and 1 patient presented ganglionic and hepatic metastases, 3 patients had developed tumour relapse after surgical resection. Two architectural types were noticed: the form of intermediate cells and the form of small cells. The virological status has been studied as well for the primary tumour as the ganglionic metastases. The prevalence of the MCV virus in our series was 80 %. A positive virological status detected in the primary tumour was also positive in the ganglionic metastases testifying to the stability of the infection by MCV virus and the strong association between it and the Merkel cell carcinoma.
Conclusion: The detection of MCV virus could represent an additional tool for the anatomo-pathological diagnosis of Merkel cell carcinoma.

E-PS-04-037
Lymphangioma-like Kaposi Sarcoma: A case report of 3 cases
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Objective: Kaposi sarcoma (KS) is a multifocal vascular neoplasia characterized by angioproliferative multifocal tumours, affecting mainly the skin. Lymphangioma-like Kaposi sarcoma (LLKS) variant is a rare morphologic expression, accounting for less than 5 % of all KS cases.
Method: The first patient was a 76-year-old woman with erythematous plaque on right foot (3–4 cm). The second, a 61-year-old woman with erythematous papules on legs, arms and nose (<1 cm). The third, a 48-year-old man with violaceous plaque (10 × 4cm) and numerous papules on left foot. Biopsies were performed, with subsequent studies through microscopy with HE staining.
Results: Histopathological examination of specimens revealed a proliferation of dilated anastomosing empty channels lined by flattened endothelial cells, dissecting the dermis and surrounding pre-existing blood vessels in some areas. Lymphocytes and plasma cells were present in the stroma adjacent to vascular channels. Typical areas of KS were not present. Immunohistochemical studies for HHV8 and D2-40 revealed positive staining.
Conclusion: LLKS variant of KS is very uncommon. Bulla-like lessions have been considered as a clinical hallmark. When findings of typical KS are not found, differential diagnosis with other vascular tumours may be difficult. Positive staining for HHV-8 can be useful to distinguish it from its mimics.

E-PS-04-038
Neurocristic hamartoma of the scalp
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Objective: Neurocristic hamartoma (NCH) is a rare lesion characterized by several lineages of differentiation, including melanocytic, nerve sheath and mesenchymal. So far, there are few (about 15) cases reported. Herein we describe a case of congenital NCH and review the literature.
Method: A 51 year-old man, without relevant previous clinical history, was referred to our hospital due to a large (18 cm dimension) cutaneous/subcutaneous congenital lesion localized in the occipital region. The lesion was partially removed (spindle shape specimen, measuring 7.2 × 3.6 × 3.0 cm).
Results: The epidermis was slightly brownish and lobulated. Histology revealed a complex lesion with interfolicular growth pattern, displaying nests with common melanocytic nevus and blue nevus-like features, neurofibroma and perineurioma-like components, characterized by immunohistochemistry. There were no signs of malignancy. Diagnosis: NCH.
Conclusion: NCH is a complex hamartomatous lesion. The diagnosis might be challenging and misleading if not recognised. Due to the variability of

NHC features it may raise several differential diagnoses, namely pigmented neurofibroma. Importantly, NCH has high propensity to melanoma transformation, but with better prognosis than classical melanomas.

E-PS-04-039

HPV detection and TP53 immunohistochemical expressionin non melanoma skin cancer

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Objective: High risk Human papillomavirus (HR HPV) infection in non melanoma skin cancer (NMSC) was reported in several studies but its role in the development of these tumours is not yet established. To assess the involvement of HPV in the carcinogenesis of NMSC we evaluated the expression of Tp53 according to HPV infection.
Method: 51 NMSC formalin fixed paraffin embedded tissues (21 squamous cell carcinoma, 13 keratoacanthoma and 17 basal cell carcinoma) were enrolled. HPV detection was performed by nested PCR (PGMY09/PGMY11/GP5+/GP6+) and reverse line blot hybridization. The immunohistochemical expression of Tp53 was investigated using P53 monoclonal antibody (Novocastra). Tp53 was considered as over expressed if more than 30 % of nuclei stained positive.
Results: HPV positive samples account for 50.9 % (26/51). HR HPV types were found in 80.1 % (21/26). Over expression of Tp53 was observed in 64 % of HPV negatives and it was significantly associated with the absence of HPV infection ($p = 0.08$). The over expression of Tp53 was not associated with the histological type of tumour. However, negative staining of Tp53 was found in 81 % of HR HPV types ($p = 0.064$).
Conclusion: This study shows an inverse correlation between HPV infection and Tp53 positive staining. This could be explained, as in cervical cancer, by the role of E6 in the degradation of p53. Hence mucosal HR HPV could be involved in skin cancer carcinogenesis.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-05 Endocrine Pathology

E-PS-05-002

WT-1 Immunreactivity in primary thyroid neoplasms

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Objective: Wilms tumour gene (WT1) is a tumour-suppressor gene located at chromosome 11p13 and antibodies against the product of this gene applicable to formalin-fixed paraffin-embedded tissue have become available. These antibodies may stain both the cytoplasm and the nucleus of cells but only the nuclear immunreactivity must be evaluated for WT1 gene.
Method: The expression levels of WT1 gene were examined in 60 primary thyroid neoplasms(30 papillary carcinomas, 30 follicular neoplasms) and 30 benign thyroid tissues (adenomatous hyperplasia) immunohistochemically.
Results: There wasn't any difference between three groups and no expression of this gene product was detected in all groups. Only cytoplasmic staining that we ignored in oncocytic cells was seen.
Conclusion: Nuclear reactivity of WT1 was shown in some kinds of tumours like Wilms tumour, mesothelioma,serous carcinomas of ovary and peritoneum, metanephric adenoma, as well as some types of leukemia. Papillary structures and psammoma bodies can be seen in papillary throid carcinoma as well as ovarian and peritoneal serous papillary carcinomas. Although, these two tumours resemble each other histopathologically, there was no expression of WT1 gene product in papillary throid carcinomas in our study. These findings showed that in the tumourigenesis of primary throid carcinomas WT-1gene has no role.

E-PS-05-003

Anaplastic thyroid carcinoma: A case report of a rare lesion with favourable evolution

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Objective: We report here a case of a 61 years old male diagnosed with an anaplastic thyroid carcinoma (ATC) associated with a prominent component of papillary thyroid carcinoma that underwent total thyroidectomy and evolved favorably.
Method: Macroscopic examination followed by histological and immunohistochemical analysis of the specimen was performed.
Results: Gross examination of the specimen showed a 5/4/3.2 cm left thyroid nodule with areas of necrosis without extra thyroidal extension. Tumour histological analysis revealed a predominant component of papillary carcinoma comprising different variants (follicular, solid and oncocytic) associated with a minor component showing spindle cell transformation, pleomorphic features and necrosis. The latter component was diagnosed as anaplastic dedifferentiation. The papillary component showed positivity for TTF-1 and thyroglobulin and CD56 different patterns of expression according to the variant. The anaplastic component showed negativity for all these markers and gain of vimentin expression. Twelve months after surgical resection the patient remained well without clinical and paraclinical evidence for cancer recurrence.
Conclusion: This is an unusual case of ATC in that it is combined with a papillary thyroid carcinoma with different morphological variants and which proved to display mild pathologic behavior and relatively long-term patient survival probably due to the presence of a prominent papillary component

E-PS-05-004

A rare case of pituitary sarcoidosis

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Objective: To demostrate a rare case of isolated pituitary sarcoidosis in a 26-year-old man.
Method: A 26-year-old patient complaining of a decrease in semen volume but without loss of libido sought advice from the urologist. Class III obesity, testicle shrinking, decreasing the blood level of pituitary hormones, adrenal insufficiency, hypothyroidism were found. MRI showed a sellar region tumour with infra-, supra- and parasellar extension. Clinical preoperative diagnosis was a craniopharyngioma. Transnasal transsphenoidal surgery was performed to remove the tumour. Histological samples were stained with haematoxylin-eosin, Masson's trichrome, CD3, CD38, CD68, HLA-DR, chromogranin A, synaptophisin.
Results: A histologic study of the pituitary gland showed granulomas similar in size and morphology. They consisted of multinucleated giant cells, epithelioid cells, lymphocytes, histiocytes and a peripheral rim of fibrosis. Immunohistochemical analysis confirmed rimmed granulomas. The central distribution of CD68+ cells and the peripheral distribution of CD3+ were detected. A chest CT scan revealed no evidence of thoracic pathology.
Conclusion: The differential diagnosis for sarcoidosis in the pituitary gland after the MRI results is quite complicated. Immunohistochemical analysis enables to detect the monomorphic granulomas and to distinguish sarcoidosis from other granulomatous processes.

E-PS-05-005

Primary and secondary hypophysitis: 5 cases

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Objective: Hypophysitis is a rare disease of pituitary gland. We report 5 cases of primary and secondary hypophysitis.
Method: Among 207 examined pituitary masses removed through a transnasal-transsphenoidal approach, we reveal 5 cases of hypophysitis. Dynamic contrast-enhanced MRI of the pituitary gland, biochemical testing of pituitary hormone blood levels, histological examination with haematoxylin-eosin and Masson's trichrome staining were performed in this cases. Semi-quantitative immunohistochemical assay was carried out using antibodies to all pituitary hormones, Ki-67, CD3, CD38, CD45, CD68, HLA-DR.
Results: Hypophysitis was diagnosed only morphologically in 2 women and 4 men at the age from 23 to 55 years. MRI showed an increase in the size of pituatuiry gland in 4 cases, 1 case was with cystic changes and 1 case was diagnosed as a craniopharyngioma. The morphological study identified the presence of an inflammatory infiltrate with fibrosis in all cases and with necrosis in one case. HLA-DR expression was observed in all cases. Secondary hypophysitis was diagnosed in 2 cases.
Conclusion: Hypophysitis remains challenging to diagnose, because its clinical and imaging features are not specific to distinguish from those of pituitary tumours. The IHC/morphology analysis is the method of choice.

E-PS-05-006
Loss of ATRX expression in two metachronous pancreatic neuroendocrine neoplasms
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Objective: ATRX is part of a chromatin remodeling complex that plays an important role in the repression of the Alternative Lengthening of the Telomeres pathway, preventing the continuous maintenance of the telomeres and the infinite proliferation of the cells. Inactivating mutations of ATRX characterize diffuse and anaplastic astrocytomas. We present a case of two metachronous pancreatic neuroendocrine neoplasms with loss of ATRX expression.
Method: A male patient presented with multiple liver metastasis, received three different therapeutic regimens within 5 years after which a new liver biopsy was performed.
Results: The first liver biopsy showed a G2 pancreatic neuroendocrine tumour which was Synaptophysin, Chromogranin, PDX-1 and Isl1 positive and CDX-2, PAX8, Progesterone negative. Insulin was detected in <5 % and the ki-67 index was 10 %. Five years later the new biopsy showed a G3 pancreatic neuroendocrine carcinoma which was focally and weakly TTF-1 positive and strongly CDX-2 positive while it was Isl1 and Insulin negative. ki-67 was 85 %. In both neoplasms ATRX was negative.
Conclusion: According to literature inactivating mutations of ATRX are common in pancreatic neuroendocrine tumours. Loss of ATRX protein is associated with hepatic metastasis and decreased overall survival, although the tumour cells are more sensitive to agents such as 5-fluoracil.

E-PS-05-007
The thyroid cancer: A descriptive study of 84 cases
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Objective: Actually with the current progress of the management of thyroid cold nodules and the improvement of pathological practices, there is a significant increase in the incidence of cancer
Method: This descriptive study allows to identify retrospectively the number of cases of thyroid cancer in the pathology department of the University Hospital of Constantine during the period 2012–2014. The addressed surgical specimens were fixed in 10 % formalin. A thorough macroscopic examination of the piece, samples according lesions were performed. Lymph node dissection is included in full. After processing and inclusion of sections with a thickness of 3 μm thickness were cut and stained in eosin Hemalun .A immunohistochemical study with different antibodies was performed according to the diagnostic orientation.
Results: In total, our series of 84 cases of thyroid cancer of all types collected during this period (2012–2014). The female thyroid cancer is evident in our series with a sex ratio female / male 3/1. The average age is 45 years for both sexes and the minimum age is 18 years. Of the 84 cases of thyroid cancer collected, 82 % are papillary carcinoma, 8 % are vesicular carcinomas, 5 % are poorly differentiated carcinomas. Anaplastic carcinoma and medullary carcinoma Each one represents 2.5 % of each of thyroid cancers. One case of Langerhans cell histiocytosis was objectified.
Conclusion: The thyroid cancer is among the few tumours represent only 01 % of cancers of the entire body. However, mastery of the decision tree we observe a significant increase in the incidence of cancer that occurs mainly at the expense of papillary microcarcinomas good prognosis.

E-PS-05-008
Primary pigmented nodular adrenocortical disease in carney complex with familial association
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Objective: Primary Pigmented Nodular Adrenocortical Disease (PPNAD) accounts for approximately 10 % of ACTH independent Cushing's syndrome, 50 % being sporadic and 50 % familial; associated with Carney complex. PPNAD is characterized by brown-black pigmented adrenocortical nodules. We present a rare case of PPNAD in Carney complex with strong familial association.
Method: 21-year old female presented with features of Cushing's syndrome (weight gain, moon face, abdominal striae, hirsuitism and proximal muscle weakness, hypertension & diabetes) of 2 years' duration, lentigenes on the lower lip and medial aspect of the conjunctiva, multiple hyperpigmented spots over lower lips and eye lids. Breast nodularity noted. Basal cortisol was raised and ACTH normal. An uncle & three first cousins also showed lentigenes and similar pigmentation. CT abdomen showed bilateral multinodular adrenal enlargement. Patient underwent bilateral adrenalectomy and surgical specimens subjected to histological examination.
Results: Both adrenals showed characteristic gross and microscopic features of PPNAD. The patient fulfilled diagnostic criteria of Carney complex. A strong paternal familial association observed.
Conclusion: Patients with histopathological diagnosis of PPNAD should be investigated for Carney complex and familial association. Molecular genetic testing for characteristic mutation of the PRKAR1A gene is conclusive. Bilateral adrenalectomy indicated as mortality is same as in Cushing's syndrome.

E-PS-05-009
Oncocytic adrenocortical carcinoma: Report of a case
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Objective: Oncocytic neoplasms of the adrenal glands are rare, usually nonfunctional and mostly benign. Herein, we report a case of an oncocytic carcinoma arising in the cortex of the right adrenal gland.
Results: In a female patient, 55-years-old suffering from multiple sclerosis a right nonfunctional adrenal gland mass was found incidentally 3 years ago. During the last year the mass increased rapidly in size and was surgically excised. In the Pathology laboratory we received the right adrenal gland measuring 7.8 × 6.5 × 5 cm and weighting 94.8 g. Upon sectioning a circumscribed, encapsulated mass measuring 5.5 cm in

greatest dimension and surrounded by a thin rim of normal-appearing adrenal gland, was noted. The mass was yellow-tan and exhibited a central radiating, stellate grey zone, of softer consistency. Microscopically, the neoplastic cells were arranged diffusely, in trabeculae or nests. The cells were large, polygonal with abundant granular and eosinophilic cytoplasm, with large hyperchromatic and pleomorphic nuclei. The mitoses were numerous, many of them atypical. Microscopic areas of necrosis were also noted. Upon immunohistochemical evaluation the neoplastic cells were positive for: vimentin, Melan A, synaptophysin and inhibin (focally) and were negative for: pan-cytokeratin, cytokeratins 7,8,14,18 and 20, EMA, chromogranin, CD3 and CD163. Peripherally, a thin rim of residual adrenal gland cortex was identified. Based on the existing criteria the diagnosis of oncocytic adrenocortical carcinoma was made.
Conclusion: Oncocytic adrenocortical carcinomas are quite rare neoplasms, with less than 20 cases reported in the literature. In most published cases, similar to our case, they are nonfunctional tumours, and complete surgical removal is the treatment of choice.

E-PS-05-010
Clinicopathological features in large parathyroid adenomas: A study from India
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Objective: Large parathyroid adenomas (LPTA) weighing >2 g show distinctive clinicopathological features compared to small adenomas. All consecutive parathyroid adenomas (PA) were evaluated for clinicopathological and immunohistochemical (IHC) features with an aim to study the behavioural difference between small and large PA.
Method: Clinical, biochemical and histological findings of 180 consecutive PAs in a 21 year period were reviewed. IHC was performed for parafibromin, APC, galectin-3 PGP9.5 and Ki67. All findings were compared between PAs of <2 and >2 g.
Results: Ninety eight (54.5 %) adenomas were >2 g. Larger PAs showed significantly higher association with bony deformities including cystic lesions ($p = 0.006$), proximal muscle weakness ($p = 0.009$), hypercalcemia ($p = 0.01$), hypercalcemic crisis ($p = 0.02$) and elevated alkaline phosphatase ($p < 0.001$). No significant difference was noted in parathormone levels amongst the two groups. There was no significant association between weight and histological features. High expression of galectin-3 ($p = 0.03$) and PGP9.5 ($p = 0.02$) was seen in larger PAs (>2 g). Parafibromin, APC and Ki67 did not show any significant difference between two groups.
Conclusion: More than half of parathyroid adenomas in Indians are larger than 2 g and qualify for LPTA. Despite having adverse clinical, biochemical and IHC features, they show benign histology.

E-PS-05-011
The mind map in pituitary/sellar pathology: A practical approach
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Objective: Most sellar region masses are pituitary adenomas; however, this location is affected by a large number of pathologic entities. The aim of this work is to provide a practical, non-electron-microscopically based approach, for the daily practice of diagnosing and subclassifying adenomatous and non-adenomatous lesions of pituitary specimens.
Method: Literature review and primary material from the Academic Medical Center in Lisbon (Santa Maria University Hospital).
Results: The initial examination requires routine haematoxylin-eosin, to establish whether the lesion is a primary adenohypophysial proliferation or one of the many other types of pathology that occur in this area. After formulating a differential diagnosis, with a single mind map that easily illustrates the range of lesions present in the sellar region, the general pathologist can generate a confident final diagnosis with a few special stains and immunohistochemical markers that are now available to accurately classify these tumours.
Conclusion: Adenomas and non-adenomatous masses can be easily diagnosed in a limited panel of stains and immunostains that can be used in daily practice at most centers. The complex and necessary subclassification of pituitary adenomas is now recognized to reflect specific clinical features and genetic alterations that predict targeted therapies for patients with pituitary disorders.

E-PS-05-012
Adrenal cortical neoplasms: A review of clinicopathological features of 21 cases from a single institute in light of Weiss criteria
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Objective: Weiss criteria (WeC) have been proposed to distinguish between benign and malignant adrenocortical neoplasms(ACN). However, definitive criteria for malignancy are distant metastasis and/or local invasion. Our aim is to review the distribution of WeC and the clinical outcome of cases where the differential diagnosis of benignVSmalignant ACN was at stake.
Method: We reviewed the slides and clinical files of 21 patients with ACN diagnosed at our institution (1998–2015) that showed a) ≥3WeC; b) <3WeC, but had concerning pathological features (weight ≥ 100 g and/or size ≥ 6.5 cm) which prompted a closer follow-up of patients.
Results: ACN with malignant behavior ($n = 13$) showed a median weight/size of 214 g/11.3 cm. Capsular invasion, nuclear grade III/IV and ≤25 % clear cells were the most frequently observed WeC on malignant neoplasms. Of the patients with ≥3WeC ($n = 17$), 13 (76 %) had a malignant behaviour (disease recurrence and/or metastases). Of the patients with ≥5WeC ($n = 11$), 7 (63 %) died of disease or its complications. All cases with <3WeC had a benign course, with patients showing no evidence of disease at present.
Conclusion: The differential diagnosis of ACN is challenging. Despite concerns about their subjectivity, WeC seem to be useful on predicting malignant behaviour especially in cases with high scores. Close follow-up of patients with borderline scores is important.

E-PS-05-013
Malignant succinate dehydrogenase subunit B-associated paraganglioma in a black African patient
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Objective: Most studies regarding susceptibility genes in paragangliomas are from Europe and the United States and there is currently no literature on the occurrence of specific genetic abnormalities in the black African population.
Method: A 23 year old black African male presented with an abdominal mass and uncontrolled hypertension. His father and a paternal uncle died from complications secondary to hypertension at less than 35 years of age. The cause of the hypertension had not been investigated.
Results: On examination a mass was found extending from the third part of the duodenum to the aorta bifurcation with multiple vertebral metastases. The 24 h urine normetanephrine level was 141 881 nmol/24 h. Histology confirmed a paraganglioma infiltrating the wall of the duodenum. The tumour cells showed loss of expression of SDHB and retention of SDHA expression and Sanger sequencing confirmed a mutation in the SDHB gene.
Conclusion: To the best of our knowledge, this is the first reported case of an African patient with an SDHB associated paraganglioma. Mutations in the SDHB gene are associated with extra-adrenal, abdominal and pelvic paragangliomas and are known to increase the risk of malignancy. Screening is therefore recommended in patients with metastatic disease.

E-PS-05-014

Significant predictive biomarkers expression throught immunohistochemistry on gastroenteropancreatic neuroendocrine tumours

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Objective: To establish the relationship between biomarkers expression (ATRX, HES1, mTOR, NOTCH1, PDGFR-β, VEGFR2 and MGMT) with predictive significance and the biological behavior of gastroenteropancreatic neuroendocrine tumours (GEP-NETs).
Method: A retrospective evaluation of the total samples diagnosed as GEP-NETs (period 2003–2016) was conducted, clinical and pathological characteristics were evaluated in all cases. Biomarkers expression was assessed trough immunohistochemistry using tissue microarrays
Results: 143 cases of GEP-NET mainly from ileum/jejunum (23,8 %), appendix (19.6 %), colon/cecum/rectum (16,8 %), pancreas (15,4 %) and stomach (14 %) were included. Average age was 55(11–83 years-old). Tumours were more frequent in males (61.5 %) and patients older than 18 years-old (93 %). Expression was positive in Hes1 (95.8 %), Notch 1 (91.6 %), ATRX (89.5 %), VEGFR2 (74.8 %), PDGFR-β (62.9 %), mTOR (39.9 %), and MGMT (23.8 %). VEGFR was more commonly expressed in jejunum/ileum (p: 0.00; OR: 0.24 IC95% 0.10-0.57), cecum/colon/sigmoid (p:0.02; OR: 5.84; IC95%:1.06-31.98) and in grade 2 GEP-NETs (p = 0, 01). MGMT lost expression more commonly in appendix (p: 0.00; OR: 0.13 IC95% 0.02-0.76). Finally, a significant loss of expression of MTOR in colon/sigmoid/cecum (p: 0.03; OR: 0.34 IC95% 0.12-0.95) was identified
Conclusion: Our results must conduct to new studies focused on strict follow up of specific alternative therapies (alkylating agents, oxaliplatin-based chemotherapy, growth factor and protein kinase inhibitors) and biomarkers expression to evaluate a possible improve in survival rates of this patients

E-PS-05-015

Lymphoepithelial cysts of the thyroid gland in association with papillary carcinoma: Two rare cases

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Objective: Lymphoepithelial cysts of the thyroid ("branchial cleft-like cyst") are very rare lesions which may arise from intrathyroidal remnants of branchial derivatives, frequently associated with Hashimoto or chronic lymphocytic thyroiditis. They may coexist with thyroid carcinoma, but are not related pathogenetically.
Method: We present two cases of a 66 respectively 41-year-old woman with a cyst located on the left lobe of thyroid gland and isthmus region, diagnosed in the Pathology Department "St.Spiridon" University Hospital with histopathological examination and immunohistochemically analysis.
Results: Each cyst was lined by a stratified squamous epithelium associated with an abundant lymphoid tissue with reactive germinal centers. Benign lymphoepithelial lesions can be mistaken with Warthin-like tumours because of the presence of oncocytic metaplasia. Immunohistochemically, squamous epithelium was positive for CK19 and CK5, but negative for HBME1 and CD56. Oncocytic metaplasia was positive for CK19, HBME1, CD56 and negative for CK5. In both cases the thyroid parenchyma shows Hashimoto's thyroiditis and multifocal conventional papillary thyroid carcinoma (0.1–1.5 cm).
Conclusion: Lymphoepithelial cysts of the thyroid are very rare, their association with carcinoma is occasional and the immunohistochemically analysis may be useful for differentiating from Warthin-like tumours.

E-PS-05-016

Retrosternal nodular amyloid goiter associated with papillary microcarcinoma

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Objective: Endocrine pathologies can cause wide scope of symptoms and objective changes, ranging from asymptomatic to life-threatening acute course. Although amyloid goiter is usually symptomless, in advanced stage the rapid thyroid enlargement can suggest an aggressive carcinoma, thymoma or lymphoma. Our objective is to report an advanced, life-threatening amyloid goiter associated with initial carcinogenesis.
Method: Patient's medical history, clinical and laboratory investigations, as well as the treatment and surgical pathology data were retrospectively reviewed.
Results: A 65-year-old woman underwent emergency hospitalisation because of dyspnoea and dysphagia. Blood tests were within laboratory reference ranges. Computed tomography showed a large retrosternal pathological mass that compressed trachea for 80 %, oesophagus, brachiocephalic veins. Total thyroidectomy was performed. Grossly, right lobe measured 11.5 × 10.5 × 6 cm, left—10 × 7 × 5 cm; both lobes were multinodular. By microscopy, the whole gland was composed of atrophic follicles surrounded by fat cells and eosinophilic homogenous deposits exhibiting positive reaction with Congo red and apple-green birefringence under polarized light. Papillary microcarcinoma measuring 0.4 cm was discovered in the right lobe. The postoperative period was uneventful.
Conclusion: Amyloid goiter can initially be clinically silent while causing life-threatening situations in advanced stage. Although follicles are atrophic, carcinogenesis can be induced as confirmed by the incidentally found papillary microcarcinoma in the present case.

E-PS-05-017

Paragangliomas: Report of 6 cases

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Objective: Paragangliomas are rare neuroendocrine tumours arising from the extra-adrenal autonomic paraganglia. They have been described at any site where autonomic ganglia were found. This report describes six cases of paraganglioma occurring in various locations.
Method: All patients were women with a mean age of 44 years-old. They were presenting in two cases with a carotid body tumour, in two cases with an abdominal mass associated in one case to spells of headache, palpitations and flushing, in one case with intra-peritoneal mass and the last one, the patient presented with catecholamine-secreting symptoms associated to paraganglioma.
Results: Histologic examination revealed in four cases an encapsulated benign neoplasm composed of characteristic clusters of epithelioid cells with eosinophilic cytoplasm arranged in a nested pattern and peripherally surrounded by some spindle-shaped cells. These features are typical of paraganglioma. In the other case, characteristic paraganglioma have been diagnosed in association to a benign nerve tumour composed of Schwann cells. In the last case, capsule and vascular invasion were noted.
Conclusion: Paragangliomas are rare tumours occurring in different sites with usually good prognosis. Pathologic features of malignant transformation should be attentively sought.

E-PS-05-018

Primary leiomyosarcoma of the adrenal gland: A case report

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Objective: Primary leimyosarcoma of the adrenal gland (PLA) is an extremely rare mesenchymal adrenal tumour with only 30 documented cases available in the literature. PLA is believed to originate from the smooth muscle walls of the adrenal vena branches. A case of PLA is described.
Method: A 69 years-old Caucasian female, presented with a 6 months history of pain in the right flank. Radiological investigation detected an heterogeneously mass with a maximum diameter of 8 cm, located in the right adrenal area. No other neoplastic mass was revealed. The patient underwent transperitoneal right adrenalectomy. Surgery detected widespread adrenal and vena cava invasion. Postoperative recover was uneventful. Local adjuvant rathiotherapy was planned.
Results: Histologically, a mesenchymal tumour of spindle shaped cells, in close vicinity to the adrenal parenchyma, was revealed. Tumour cells with moderate nuclear pleomorphism and occasional bizarre features had abundant intracytoplasmic glycogen. A mitotic activity of 7–8 mitoses /10hpf and areas of necrosis were demonstrated. Neoplasm was immunoreactive for SMA, vimentin, desmin, HHF35, h-caldesmon, an immunophenotype compatible with leimyosarcoma.
Conclusion: In view of the rarity of this tumour and the absence of any hormonal derangement or imaging characteristics, the diagnosis is based entirely on histological and immunohistochemical evaluation.

E-PS-05-020
Biphasic production of immunoglobulin from Epstein-Barr virus reactivated lymphocytes in Graves' disease patients and controls
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Objective: Graves' disease is an autoimmune hyperthyroidism caused by excessive thyrotropin receptor antibody (TRAb). Epstein-Barr virus (EBV) persists mainly in human B lymphocytes. We have reported that TRAb-predisposed EBV-infected cells (TRAb(+)EBV(+) cells) could produce TRAb in response to EBV-reactivation in both patients and controls. In this study, we compared the amount of total immunoglobulin (Ig)G and IgM produced during EBV-reactivation induction between patients and controls.
Method: We separated PBMCs of 9 Graves' disease patients and 9 controls, and cultured for 2 days. The cultured PBMCs were then transferred to 33 °C to reactivate persistent EBV. We collected culture medium and measured Ig concentration by ELISA at day 0, 5, 10, 12. At the same time, we confirmed AID-mRNA expression of culture cells.
Results: We observed biphasic production of IgG and IgM in day 0 and day 10, 12. The increase in day 0 may be influenced by pre-culture; thus, the rise in day 10, 12 would be production induced by EBV reactivation.
Conclusion: In our previous data, EBV-induced TRAb production in Graves' disease patients was higher than that of controls. However, in this study, total Ig secretion was not different between patients and controls, suggesting the polyclonal B cell activation.

E-PS-05-021
Effect of gender on estrogen and progesterone receptors expression in nasal polyps
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Objective: Nasal polyposis is one of the common and disturbing diseases in otolaryngology. Few researches were done about sex steroid receptors in nasal polyps till yet. In this study, the difference between estrogen and progesterone receptors (ERs & PR) expression in nasal polyps due to gender, has been investigated.
Method: In this cross-sectional study, 90 samples of nasal polyps were studied after polypectomy in Mostafa Khomeini Hospital- Tehran Iran, during 2007 to 2011. Information about sex and age of patients detected from their medical documents. Three slides were prepared from every paraffin embedded block by 3 μm cuts. One slide with Hematoxylin-eosin and 2 others by Immunohistochemistry were stained, and percentage of ERs and PR-positive cells determined in the epithelium using monoclonal antibody, via light microscopy.
Results: In this research, 36.6 % of samples belong to women and 63.3 % belong to men. There was no significant correlation between ERs & PR expression with age. A significant correlation was seen between ERs and sex ($p = 0.001$), while no significant association found between PR and sex.
Conclusion: As regards the incidence of ERs in females are significantly more than males; it can be used as an effective factor in pathogenesis for treatment of polyps.

E-PS-05-022
Association of pituicytoma and ACTH-dependent Cushing's disease: Report of a case
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Objective: To report on the association of ACTH-dependent Cushing's disease and pituicytoma.
Method: A 48-year-old woman was diagnosed with ACTH-dependent Cushing's disease based on symptoms and signs of hypercortisolism and laboratory tests. Magnetic resonance imaging revealed a small nodule in the right half of the pituitary gland around the pars intermedia. Catheterization of petrosal sinuses showing central gradient of ACTH secretion and hypoadrenalism resulting from the endoscopic transsphenoidal excision of pituitary nodule were consistent with pituitary adenoma.
Results: Histological examination with haematoxylin and eosin stain disclosed samples of normal adenohypophysis and a small spindle cell tumour. At immunohistochemistry, the latter was negative for pituitary hormones, cytokeratins, GFAP and chromogranin and positive for S100, vimentin and TTF—1. Staining for EMA was observed focally. Proliferation index evaluated with Ki67 immunohistochemistry was 1 %. Histological and Immunohistochemical findings were consistent with pituicytoma.
Conclusion: Association of ACTH-dependent Cushing's disease and pituicytoma represents a rare event. Only four cases were previously described in the English literature: in two male and in two female patients, one of whom was 7-year old child. The relationship between these diseases has not been explained; however it may likely depend upon their origin from a common progenitor cell.

E-PS-05-023
Ultrastructural characteristics of intracellular contacts in convenient sporadic cases of insulinoma
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Objective: Up to 95 % of insulinomas are benign neuroendocrine neoplasias without evidence neither of metastases nor recurrence. The absence of metastatic potential is determined by low proliferative index and intracellular contacts condition.
Method: The study based on the surgical pathology material obtained from 23 patients with sporadic pancreatic insulinoma (NET). 21 tumour ware grade 1 (pT1) and only 2 tumours—grade 2 (pT2) (WHO, 2010). Diagnosis of insulinoma was confirmed by IHC. All cases were undergone to EM (G1-21 cases and G2-2 cases) (JEOL JEM 100-CX).
Results: There were two types of B-cells: 1- with large clear nuclei; 2 - with dark nuclei. We noticed the dissolution of cell membranes on the majority of inter-cell borders longitude. The cells were connected by

means of desmosomes. After dissolving of the cellular membranes secretory granules were seen to migrate from one cell to another. There was no evidence of destructive any other cell structure. Dark cells had predominantly hormone-secreting function and between contacts dark cells more frequently demonstrated their membrane preservation. Dissolution of dark cell membrane caused the transfer of the granules in to clear cells. Neuroendocrine cells lacked the ability for invade intracellular matrix, so they excreted granules in the adjusted cells.
Conclusion: Electron microscopy revealed no evidence of malignancy in cases of cell membrane dissolution with desmosomes saving. That phenomena reflects high cell activity secreting the granules in the intracellular space a s well in the adjusted cells.

E-PS-05-024
Parathyroid carcinoma: Two cases report in Khon Kaen Hospital
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Objective: Parathyroid carcinoma is the rare malignant disease of endocrine tumour. The incidence is less than 1 % of all patients with primary hyperparathyroidism in Western countries.
Method: Two patients with a diagnosis of parathyroid carcinoma in Khon Kaen hospital were included for this review.
Results: The first case was a 24-year-old woman who had a midline neck mass for 4 months. Her blood calcium was 18.7 mg/dL. On examination, she has a firm midline neck mass is about 4 cm in diameter and movable. The total thyroidectomy was performed. The pathological diagnosis was parathyroid carcinoma. After that, she was loss follow up. The second case report was a 53 years old lady present to the hospital complaining fatigue and midline neck mass. The investigation revealed severe hypercalcemia and hyperparathyroidism. Surgical exploration revealed an enlarged left parathyroid mass, 2.5 cm. Histological findings and immunohistochemical report confirmed as parathyroid carcinoma.
Conclusion: Parathyroid carcinoma is a rare endocrine malignant tumour. Furthermore, the diagnostic criteria have always been a challenge for pathologists. It's very important to carefully evaluate this lesion on histological diagnosis and also require the clinical data for correlation. In complicated cases, the suggestion from expert endocrine pathologists is needed.

E-PS-05-025
C-cell hyperplasia in thyroids resected for medullary carcinomas and in other thyroid lesions
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Objective: Although C-cell hyperplasia (CCH) is frequently observed in thyroids of patients with hereditary and sporadic medullary carcinomas(MC), it has also been observed in other neoplastic and nonneoplastic conditions. The study aimed to clarify the type and frequency of CCH in different thyroid lesions.
Method: Thyroid tissue samples in distance >1 cm from nodule (18 cases of MC: 3 hereditary, 15 sporadic; 20 cases of papillary carcinomas; 20 cases of chronic lymphocytic thyroiditis) were analyzed. C-cells were identificated by immunohistochemical staining for calcitonin. The criterion of CCH was >50 cells per (x100) field.
Results: We revealed reactive CCH in 7(39 %) thyroids with MC, 2(10 %) with papillary carcinoma, 4(20 %) with thyroiditis. CCH was focal in 9(69 %), diffuse and nodular in 4(31 %): in 2 cases of MC, in 2 cases of thyroiditis. Neoplastic bilateral CCH in 3 cases of MC was found, and groups of C-cells estimated as intrathyroidal spread of MC in 4 cases. C-cells showed different sizes and form, mild to moderate nuclear pleomorphism, and cytoplasm parameters widely varied. In 5(38 %) cases of CCH fibrotic response to cells was noted.
Conclusion: Calcitonin-stained sections of thyroid tissue with MC helps to diagnose multifocal growth, early medullary microcarcinomas or intrathyroidal spread of MC.

E-PS-05-027
Bilateral medullary thyroid microcarcinomas associated with neoplastic C-cell hyperplasia and primary hiperparathiroidism, suggestive for a MEN2A syndrome
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Objective: This case presentation aims to highlight the utmost importance of providing the pathologist with patients' clinical data together with the resected specimen.
Method: A total thyroidectomy specimen and the right inferior parathyroid adenoma (PA) of a 31-year-old male was submitted to the pathology department of Tirgu-Mures county hospital, with the diagnosis of nodular goiter and PA.
Results: Macroscopically, two whitish nodules of 3 and 4 mm, simetrically situated in superior-part of right and left lobes were found. Microscopically, the nodules were well-defined and composed of nests of spindle or globular cells, with finely granular abundant cytoplasm, with spindle-cells arranged in swirls, separated by fine bands of fibrosis. Immunohitochemically, they expressed calcitonin and chromogranin but no thyroglobulin. Secondary foci of medularry thyroid microcarcinoma (MTMC) and neoplastic C-cell hyperplasia were noticed in both lobes. The PA had an usual microscopical-appearance. Suspicion of multiple endocrine neoplasia (MEN) was raised. Reviewing the medical history, we found that 6 years before, the patient had undergone bilateral adrenalectomy for bilateral pheocromocytoma and consecutively a MEN2A syndrome was genetically confirmed.
Conclusion: Given the small size of tumours, in the absence of correct clinical information, the pathological examination could miss the presence of MTMC, with impact on clinical management of the patient.

E-PS-05-028
Complex parathyroid tumours—importance of histopathological diagnosis in patient management.
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Objective: Parathyroid carcinoma is an extremely rare, and poorly understood endocrine malignancy, and causes an estimated 0.005 % of all human cancers and about 1 % of primary hyperparathyroidism. Preoperative diagnosis is challenging and definitive diagnosis can only be made with specialised histological techniques. Due to its low incidence, there is a lack of evidence-based treatment guidelines. The identification and management of these cases have been especially challenging to clinicians.
Method: Retrospective analysis of patients who underwent parathyroid surgery (primary and renal hyperparathyroidism) in a tertiary center between January 2011 and December 2015 for complex parathyroid tumours (atypical adenomas, hyperplasia and parathyroid carcinoma).
Results: 219 parathyroidectomies were carried out during this period, of which 11 (5 %) were complex parathyroid tumours, with a subdivision of 4 parathyroid carcinomas, 6 atypical adenomas and 1 atypical hyperplasia. Mean age was 49.9, F>M, 9 sporadic and 2 familial. Mean serum ca 3.2 mmol/l and mean PTH 75.8 pmol/l. 9 had Vit D deficiency. Frozen section was used in half of the cases. All parathyroid carcinoma cases had bilateral neck exploration.5 patients had ipsilateral thyroid lobectomy. 1 patient developed multiple neck and lung metastases with several repeat surgeries.

Conclusion: Diagnosis of complex parathyroid tumours is made by histology. High suspicion preoperatively in patients with marked elevated serum calcium and PTH could guide surgery extent. Patient with parathyroid carcinomas and atypical adenomas should be offered a long term follow-up for early detection of recurrences.

E-PS-05-029

Nesidioblastosis and pancreatic islet cell hyperplasia arising in a mediastinal mature teratoma

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Objective: Nesidioblastosis is a rare condition characterized by hyperplasia and hypertrophy of pancreatic islet cells and presence of islets in intimate association with ducts. Mediastinal teratoma with pancreatic tissue is also rare. Herein, we report a case of nesidioblastosis and pancreatic islet cell hyperplasia in a mediastinal mature teratoma in an adult.
Method: 32-year-old male presented with chest discomfort and revealed to have a large mass in his anterior mediastinum. The patient underwent an excision of the mass with a clinical diagnosis of mediastinal teratoma. Histologic examination including hematoxylin-eosin stain and immunohistochemical stains were performed.
Results: Histologically, the mass showed large areas of mature pancreatic tissue with various elements including intestine, squamous epithelium, skin appendages, respiratory epithelium, bone, cartilage, and fat which were supporting the diagnosis of a mature teratoma. In the area of pancreatic tissue, diffuse and non-mass forming hyperplasia of pancreatic islet cells was observed. Ductulo-insular complexes were also frequently noted. The hyperplastic cells were positive for neuroendocrine markers in immunohistochemical stains.
Conclusion: We report a very rare case of nesidioblastosis and pancreatic islet cell hyperplasia arising in a mediastinal teratoma. The patient has stayed healthy without any endocrine symptom during 10 months after surgery.

E-PS-05-030

Metastatic papillary thyroid carcinoma with squamous cell carcinoma differentiation in a cervical lymph node

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Objective: Papillary thyroid carcinoma (PTC) showing squamous cell carcinoma (SCC) differentiation is rare, and may appear in metastatic site rather than the primary site. We reviewed the clinical and histological features of this rare occurrence.
Method: The histological findings of a transformation of a metastatic PTC into SCC are described with a review of the related literature.
Results: A 84-year-old female, presented with a 4-year history of an enlarging right-sided neck mass. Cervical ultrasonography followed by computed tomography (CT) revealed a 6 cm cm solido-cystic mass, associated with two thyroid nodules. A fine needle aspiration of this mass suggested a SCC. Clinical examination, panendoscopy, CT scan and nasopharyngeal biopsy didn't reveal any possible primary site for this SCC. Histopathological examination of the total thyroidectomy specimen revealed a multifocal classic PTC with bilateral lymph node metastasis. The resected mass showed a biphasic tumour comprising area of PTC merging with moderately differentiated SCC. Four months later, she developed SCC recurrence in the neck's soft tissue. After surgery, the patient was referred for external beam radiotherapy.
Conclusion: Transformation of differentiated thyroid cancer into SCC is rare and was puzzling in our case. Such a transformation usually confers a poor prognosis.

E-PS-05-032

Macrofollicular variant of papillary thyroid carcinoma: A rare but "tricky" papillary carcinomas subtype

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Objective: We want describe a case of this extremely rare variant, focusing about the differential diagnosis.
Method: Having a "cold" nodule in Hystmus and goiter condition, a 52 years old patient was referred to surgery. Macroscopically a relatively well demarcated colloidal 3.8 cm nodule has been observed. Formalin fixed, paraffin embedded tissue samples of this thyroid colloidal nodule have been examined in the HE routine stain. To support the final diagnosis an Immunostain with HBME-1 was also performed.
Results: Microscopically the tumour, capsulated, was characterized by the large size of its follicles. They represented the great majority of the lesion. The thyreocytes showed larger nuclei, sometimes irregularly spaced, clear chromatin and "grooves". Some follicles were lined by cells with on slight enlarged nuclei with dark chromatin. Focally small, abortive papillae have been noted. To confirm the suspicion of a macrofollicular variant of papillary thyroid carcinoma (MFVPTC) the tumour cells exhibit a membrane-apical reaction for HBME-1.
Conclusion: It is important to identify this subtype because in the routine it can be easily underdiagnosed as hyperplastic nodule or follicular adenoma. To avoid a misdiagnosis careful search for cytological atypia is important: lymph node and distal metastasis are present respectively in 20 and 6 % of cases.

E-PS-05-033

Ectopic intrathyroidal thymoma: A case report

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Objective: To report an exceedingly rare case of ectopic intrathyroidal thymoma.
Method: Tumour samples were colored with HE and a large panel of antibodies were used.
Results: A 62-year-old tunisian woman presented with multinodular thyroid gland. The right lobe included an encapsulated, firm nodule of $7 \times 5 \times 3$ cm. In the other lobe were two nodules of 0,8 and 2,5 cm. Microscopic examination of the right lobe showed a highly cellular tumour with sclerotic bands forming incompletely demarcated nodules. The tumour was made of monotonous spindle cells within a lymphoid stroma. Immunohistochemically, cells was intensely positif for cytokeratin and Pax8 but not for TTF1, Thyroglobulin, calcitonin, CD5 and CD117. Ectopic normal thymic tissue was found at the periphery of the tumour. Residual thyroid tissue was absent. This immunohistochemical profile and the biphasic histologic pattern were considered characteristic of a type AB thymoma. The samllest left nodule matched with a non-encapsulated papillary microcarcinoma.
Conclusion: Intrathyroidal thymoma is rare especially in old adults. It seems to arise in ectopic intrathyroid thymus. Proper diagnosis requires appropriate histopathologic assessment and staining, which in turn requires an awareness of a clinical index of suspicion for this condition.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-06 Digestive Diseases Pathology — GI

E-PS-06-001

A rare case of primary gastric mantle cell lymphoma

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Objective: Gastrointestinal tract is the most common extranodal site involved by lymphoma, representing about 5–20 % of all cases. Histopathologically, roughly 90 % of the primary gastrointestinal lymphomas are of B cell lineage with very few T-cell lymphomas and Hodgkin lymphoma. However, primary gastrointestinal lymphoma is extremely rare, accounting for only 1–4 % of all gastrointestinal malignancies with DLBCL (Diffuse, large B-cell lymphoma) and MALT (Lymphomas of the mucosa-associated lymphoid tissue)being the most common entities, while mantle cell lymphoma (MCL) accounts for less than 1 %.
Method: We report the case of a 74-year-old male presenting with a 5-month history of abdominal pain associated with nausea and vomiting. Gross examination of the specimen revealed two gastric masses: a 10/8/2 cm smaller mass with a crater-like ulcerating area of 3/1/0.5 cm located in the fundus and a 14/12/3 cm larger mass located near the antrum. Invasion was found in 18 out of the 22 examined lymph nodes (from both greater and lesser curvature of the stomach).
Results: Standard staining was suggestive of a MALT lymphoma but immunohistochemical investigations established the final diagnosis of primary gastric mantle cell lymphoma (MCL)
Conclusion: Although primary gastrointestinal tract mantle cell lymphoma (MCL) is extremely rare and there is paucity of literature regarding natural history and outcome of this unusual entity, we emphasize the importance of immunohistochemical examination for establishing a correct diagnosis when assessing rare tumours of lymphoid lineage within unusual sites.

E-PS-06-002
Ectopic sebaceous glands in the esophagus

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Objective: Sebaceous glands in the esophagus are very rare and have been reported mostly in autopsy studies. Only a few cases have been reported in living persons and have been considered of no clinical significance. We report a unique case of sebaceous glands in the esophagus diagnosed by endoscopy and biopsy in a 50-year-old woman.
Method: The patient history of presented at another hospital with a dysphagia and appetite loss after treatment for fungal change. She came to the Third Central Hospital, Department of Endoscopy complaining of 2 months of unchanged symptoms.
Results: Endoscopy revealed multiple small yellowish mucosal nodules scattered throughout the esophagus. Biopsy revealed fragments of squamous esophageal mucosa showing sebaceous gland formation. These glands consisted of units of large polyhedral cells with clear vacuolated cytoplasm.
Conclusion: In this case, our patient had no history of GERD. Further studies are required to elucidate the causes and clinicopathological significance of such an unusual epithelial change.

E-PS-06-003
Poorly differentiated neuroendocrine carcinoma of colon: A case of 61-year-old female patient

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Objective: Here we present a case of a hepatic flexure colon tumour of 61-year-old woman with no history of lung tumour.
Method: Immunohistochemistry was applied and 50 genes were analyzed by next generation sequencing technology (NGS).
Results: An ulcerated, 5 cm-in-diameter tumour invaded the entire thickness of colon. The cancer contained medium to large size neoplastic cells with evident nucleoli with some focal features of adenocarcinoma that constituted less than 30 % too little to designate the tumour as mixed adenoneuroendocrine carcinoma (MANEC). It was diagnosed poorly differentiated neuroendocrine predominantly large cell carcinoma of colon ("unfortunate" (according to Odze & Goldblum) category G3: WHO 2010) (pT3 N0: 7th edition pTNM). CK1AE/AE3 staining was predominantly membranous with partial distribution in dot-like pattern in perinecrotic cancer fields to be reminiscent of small cell carcinoma of lung counterpart. Ki67 labeled over 90 % of cancer cells with partial positive nuclear staining for TTF1. To our surprise no lymph nodal metastases were revealed in H&E staining as well as lymph nodes didn't show keratin positive deposits of cancer cells in labeling with CK1AE/AE3. We detected nonsense mutations in four tumour suppressor genes (APC R1114X (molecular evidence that the cancer was a primary tumour of colon), TP53 R113X, RB1 E137X and FBWX7 R393X & S282X) and mutations in three receptor tyrosine kinases (RET A919V of high transforming activity, EGFR E114K and FLT3 L601I).
Conclusion: Gene profiling of this rare carcinoma confirmed its primary colon origin in differential diagnosis to be helpful in choice of postsurgical treatment therapy option.

E-PS-06-004
Strong positives correlation between COX-2 and FasL expression in colon mucosa of patients with colorectal cancer and inflammatory bowel disease

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Objective: Colorectal cancer (CRC) is observed in 5.5–13.5 % of patients with ulcerative colitis (UC) and in 0.4–0.8 % of patients with Crohn disease (CD). The aim of this study was to evaluate the relationship between COX-2 and FasL expression in colon mucosa of patients with CRC, UC and CD in order to assess its value for prognosis of CRC.
Method: Expression of COX-2 and FasL was analyzed immunohistochemically in the samples of colon mucosa taken from the affected areas of 10 CRC patients CRC, 4 UC patients, 6 CD patients with CD and from unaffected areas of 7 CRC patients.
Results: Average expression of FasL in both unaffected and affected areas of CRC patients was higher than in CD patients. Average expression of FasL in affected areas of CRC patients was higher than in UC patients and the same as in unaffected areas. Multiple linear regression analysis has shown that FasL expression together with the duration of anti-COX-2 treatment was among the strongest predictors of COX-2 expression.
Conclusion: The revealed strong relationship between COX-2 and FasL expression in CRC, CD and UC patients supports the possibility to use expression of FasL as a prognostic marker of efficacy of anti-COX-2 treatment and probability of tumourogenesis.

E-PS-06-005
Non-syndromic intestinal lipomas are probably not associated with mutations of PDGFRA

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Objective: To test the hypothesis that non-syndromic intestinal lipomas might represent a sporadic counterpart of lipomatous tumours occurring in PDGFRA-mutant syndrome.
Method: A series of 20 intestinal lipomas were obtained from 17 patients and mutational analysis of exons 12, 14 and 18 of the PDGFRA gene (accession number D50017) was performed using PCR and direct sequencing.
Results: M/F ratio was 8/9, age of the patients ranged from 45 to 84 years (average: 64.7). One patient presented with 3 lipomas, another one with 2

lipomas, 15 patients each had only 1 lipoma detected. DNA of 4 tumours was non-analyzable, all remaining 16 tumours were found to bear wild-type alleles of exons 12, 14 and 18 of PDGFRA gene.
Conclusion: PDGFRA-mutant syndrome is a genetically defined subtype of Familial GIST syndrome. Although PDGFRA-mutated GISTs, Vanek's tumours and fibrous tumours are known to occur also in non-syndromic sporadic setting, sporadic PDGFRA-mutated lipomas have not been recorded yet. Our first study didn't show PDGFRA mutations in any of the 16 analyzable tumours. Thus, PDGFRA mutations probably do not play an important role in the development of sporadic lipomas of the intestines.

E-PS-06-006
Utility of immunohistochemical detection of phosphorylated S6 in the diagnosis of Squamous Cell Carcinoma (SCC) of the esophagus in endoscopical biopsies: A preliminary study
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Objective: To evaluate the possible role of immunohistochemical detection of phoshorylated ribosomal protein S6 (PS6) in the differential diagnosis of esophageal squamous cell carcinoma and its benign mimics in small endoscopical biopsies.
Method: We collected a series of 30 specimens of esophageal squamous cell carcinoma (SCC), 5 specimens of esophageal granular cell tumours (GCT), and 6 specimens of esophageal squamous cell papillomas (SCP). The histological diagnosis was correlated with abnormal staining of PS6 (at least 5 contiguous basal cells in the superficial epithelium) and with abnormal staining of p53.
Results: 29 (96.7 %) cases of SCC showed pathological expression of PS6. All cases of SCC showed abnormal expression of p53. 2 (40 %) cases of GCT were PS6 positive, 3 (60 %) showed overexpression of p53, but only 1 tumour showed abnormal staining for both markers. 2 (33.3 %) cases of SCP were PS6 positive, 3 (50 %) showed at least focal overexpression of p53, 2 of these showing abnormal staining for both markers.
Conclusion: Although this first preliminary study of esophageal squamous cell lesions suffers from a small number of cases, the results seem to support the thesis that adding immunohistochemical investigation of PS6 may increase accuracy of differential diagnostics of squamous cell proliferations of the esophagus.

E-PS-06-007
WT1 and BCL2 expression in neurogen appendix: Relevance for histogenesis and diagnosis
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Objective: The objective of this study was to study the expression of WT1 in neurogen appendix and the relationships to Bcl2 protein. Neurogen appendix (NAP) is relatively frequently encountered in adults and is supposed to interfere with motility and fecal stagnation. The S100-protein is consistently expressed in such lesions. Recently, WT1 expression has been reported in peripheral nerves and neuromas.
Method: WT1 and Bcl2 expression was studied by immunohistochemistry in 18 NAP previously confirmed by S100 positivity. The expression was evaluated as negative, focal (<50 % stained cells) and diffuse (≥50 %). The Kendall rank correlation test was used for statistical analysis.
Results: The gender ratio was 11/7 (man/woman) and the age range 21–79 years. 15 NAP associated to acute appendicitis and 3 associated to subacute appendicitis. WT1 was expressed focally in 6 and diffusely in 11 NAP. WT1 expression correlated to increased age and male gender ($p = 0.06$/tau = 0.333 and, $p = 0.09$/tau = 0.299, respectively). Focal Bcl2 expression was seen in 5/11 WT1-positive NAP.
Conclusion: In conclusion, the results of our study suggest that WT1 was expressed in almost all cases of NAP, suggesting a potential use as neurogen marker. WT1-positive NAP were more frequently associated to acute than to subacute appendicitis. The co-expression of Bcl2 suggests a possible interference with programmed cell death/apoptosis/necroptosis.

E-PS-06-008
Autophagy-related protein LC3 in Egyptian colorectal cancer: Impact and possible relation to STAT3 and miRNA 101
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Objective: Colorectal cancer (CRC) is a common worldwide cancer. it is the fourth most common worldwide overall cause of cancer death. Autophagy has been highlighted as a promising molecular target in cancer. Detecting LC3 has become a reliable method for monitoring autophagy and autophagy-related processes, including autophagic cell death. Signal transducers and activators of transcription (STAT) proteins are latent cytoplasmic transcription factors. microRNAs (miRNAs) are small non-coding RNAs which post-transcriptionally regulate gene expression.
Method: Twenty five CRC and 25 normal mucosa specimens were obtained. Immunohistochemical assessment of LC3 expression and assessment of STAT3 and microRNA 101 expressions by real time—PCR were done.
Results: Revealed a statistically significant increase in LC3 ($p < 0.001$) and STAT3 expression in tumour samples (mean ± SD = 6.31 ± 1.96 folds) than normal mucosa ($p < 0.001$). Both of them were directly correlated together ($r = 0.833$, $p < 0.001$). MicroRNA 101 was inversely correlated to both LC3 and STAT3 ($p < 0.001$) and was significantly reduced in tumour samples (mean ± SD = 0.37 ± 0.16 folds) ($p < 0.001$) with a possible correlations to tumour grade ($p = 0.006$), pathological stage ($p = 0.009$) lymph node involvement ($p = 0.017$) and advanced clinical stage ($p = 0.011$).
Conclusion: LC3, STAT3 and miRNA 101 may be valuable as biomarkers that may predict the poor prognosis of a cancer colon patient and the critical role of STAT3 and miRNAs in autophagy would expand our knowledge of the molecular mechanisms of autophagy regulation.

E-PS-06-009
Eosinophilic gastroenteritis-institutional experience with pictorial review
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Objective: To study the varied clinical presentations of Eosinophilic gastroenteritis, a relatively rare inflammatory disease of unknown origin.
Method: We retrospectively reviewed nine cases of Eosinophilic gastroenteritis diagnosed in our institution over a period of 2 years with correlation to radiological, endoscopic and histological features. Representative images will be presented.
Results: Amongst the 9 cases, one presented with small bowel obstruction, one with diarrhoea, one with dyspepsia and six with abdominal pain. Eight cases were diagnosed on duodenal biopsies and once case on full thickness ileal biopsy. All the cases responded to steroids and no relapses were seen in any of the cases till date. CT scan was performed in six of the nine cases, four of which did not show any significant findings, one showed mild jejunal thickening and one showed features compatible sub-acute intestinal obstruction. Peripheral eosinophilia was noted only in two of the nine cases.
Conclusion: Eosinophilic gastroenteritis should be considered in the differential diagnosis of unexplained abdominal pain. Correlation with high peripheral eosinophilic counts is helpful though not necessary in all cases. Timely treatment with steroids is curative.

E-PS-06-010

Relationships of P38 to AKT pathway protein mTOR and cell proliferation in colorectal adenomas

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Objective: We aimed to study the relationships of P38 expression patterns in human CRAs to the AKT pathway protein mTOR and to the cell proliferation Ki67 protein.
Method: We have studied the immunohistochemical expression of P38 (clone 12F8-antibody detecting the phosphorylated/activated isoforms) in a series of colorectal adenomas (124) on tissue microarrays. The results were analyzed (Kendall rank correlation test, MedCalc) with regard to mTOR and Ki67 reported data.
Results: Nuclear P38 correlated to cytoplasmic or membrane mTOR ($p < 0.01/tau = 0.223$ et $p < 0.01/tau = 0.340$). An inverse relationship was observed to Ki67 ($p < 0.00/tau = -0.110$).
Conclusion: The results of this study showing a correlation between P38 and mTOR suggest a biological crosstalk/interference between the MAPK- and AKT-signaling-pathways in colorectal adenomagenesis at P38 level.

E-PS-06-014

Chronic active cholecystitis with xanthogranulomatous features and hyperplasia of Luschka ducts: Case report

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Objective: Xanthogranulomatous cholecystitis, an uncommon form of chronic cholecystitis, is considered to have an uncertain pathogenesis. It has been proposed that this condition appears due to rupture of Rokitansky-Aschoff sinuses, with extravasation of bile or ulceration of gallbladder mucosa. Both of these conditions can easily be mistaken for malignancy, both clinically and histopathologically. Therefore, the presence of both lesions makes for a challenging diagnosis and it requires additional testing to exclude other conditions.
Method: We report the case of a 40-year old woman who was clinically diagnosed with a pancreatic tumour and a cholecystectomy was performed.
Results: We received one paraffin block requiring a consult. Microscopically, the gallbladder wall showed numerous round lipid-laden macrophages and other types of inflammatory cells (neutrophils, eosinophils, lymphocytes). Adjacent to the liver bed, less than 1 mm in diameter, small ducts were found surrounded by a collar of connective tissue. Differential diagnosis considered a malignant process, so immunohistochemistry assays were performed and they showed an intense positive reaction for CK7, S100, SMA, a low Ki67 index and a negative reaction for MUC1.
Conclusion: The purpose of this report is to outline the great difficulty that comes from differentiating benign from malignant processes and the importance of additional testing when confronted with a rare diagnosis.

E-PS-06-015

Mucinous adenocarcinoma of the gallbladder

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Objective: Mucinous Adenocarcinoma of the Gallbladder(MAGB) is a very rare neoplasm of the gallbladder(GB),constituting 2.5 %. Cholelithiasis is well-established predisposing factor for the development of GB carcinoma.It is characterized by extracellular mucin comprising 50 % of the tumour volume. Tumours with less than 50 % stromal mucin were considered as adenocarcinoma with focal mucinous differentiation. When the mucinous component exceeds 90 %, the tumour is classified as pure mucinous/colloid carcinoma. We present a case of primary carcinoma of the GB as an unexpected histopathological finding in an elective cholecystectomy specimen.
Method: A 67-year-old female underwent simple cholecystectomy because of cholelithiasis in our surgical clinic. There was a nodular mass measuring $4 \times 4 \times 2.5$ cm in the corpus. The cut surface of the mass was tan to yellow, shiny, solid and firm.
Results: Suprisingly,sections from the mass revealed a tumour composed of tumour cells floating in the pools of extracellular mucin,a signet-ringlike cells can be seen in clusters or lying individually within the mucin. The tumour was seen to infiltrate into the muscle layer. Displasia, intestinal metaplasia and calcification were also found. A diagnosis of incidental MAGB was made.
Conclusion: MAGB exhibit important clinicopathologic differences from conventional GB carcinomas. Therefore a routine histopathological examination of all cholecystectomy specimens is a necessity. Histological type,grade and stage of the disease are the predictors of prognosis.

E-PS-06-016

Braf expressions profile in serrated adenomas vs hyperplastic polyps, tubular adenoma and aberrant crypt foci

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Objective: Colon carcinoma, as one of the most common cancers, has been investigated for genetic alterations. Besides wellknown adenoma-carcinoma sequence, it is recently found that BRAF mutation has an important role particularly in early stages of adenocarcinomas with serrated features. To the best of our knowledge, there isn't any study concerning BRAF mutational status of serrated polyps in Turkish population. In this study, we aimed to investigate the immunohistochemical expression profile of BRAF in colon polyps.
Method: 49 sessile serrated and traditional adenomas, 10 hyperplastic polyps, 10 tubular adenomas, 10 aberrant crypt foci and 10 cases of normal controls were immunohistochemically evaluated for the presence of BRAF mutation with VE1 antibody. Results were statistically compared.
Results: There was positive staining with VE1 antibody in 55.1 % of serrated adenoma cases, although 80 % of control groups and 70 % of aberran crypt foci were negative. Despite the hyperplastic polyps are regarded as members of the serrated polyp family, 90 % of these lesions showed no antibody expression.
Conclusion: Our study results, in concordance with the recent literature suggest that serrated adenomas have BRAF mutation which may contribute in their malignant behavior.

E-PS-06-017

CD47 expression in gastric cancer using immunohistochemistry and mRNA in situ hybridization

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Objective: CD47 is a transmembrane receptor in the immunoglobulin superfamily. It interacts with signal-regulatory protein alpha (SIRPα) on the membrane of macrophage and neutrophils. There are some researches that CD47-SIRPα pathway worked as antiphagocytic "don't eat me" signal, and when the tumour expressed CD47 higher level, it could get ability to escape the innate immune system. The aim of this study is evaluation of CD47 expression in gastric cancer using immunohistochemistry (IHC) and mRNA in situ hybridization (mRNA ISH).
Method: This study performed analysis of CD47 RNA expression status with RNAscope in a cohort of 55 surgically resected

primary gastric cancers, using tissue microarray. RNAscope results were reported by manufacturer's scoring system. Protein expression was evaluated using commercial CD47 antibodies.
Results: The proportion of cases with strong membranous expression in CD47 IHC was 1.8 % (1 out of 55). The proportion of cases with high cytoplasmic expression in CD47 IHC was 63.6 % (35 out of 55). Cytoplasm CD47 positive cases have tendency of poorly differentiated histology, lower lymph node metastasis, lower invasion, higher lymphoid stroma, lower tumour stage, microsatellite instable and better prognosis.
Conclusion: We suggest that CD47 protein has some roles in gastric carcinogenesis and cancer progression.

E-PS-06-018
Serrated lesions: Clinical, morphological and genetic studies
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Objective: To study clinical-morphological and genetic features of serrated lesions.
Method: We have evaluated 70 serrated polyps from 58 patients. Histological sections were steined with hematoxylin and eosin and PAS-reaction with alcian blue. After determining the histological type of polyps (sessile serrated adenoma (SSA), traditional serrated adenoma (TSA) and hyperplastic polyps) we selected 36 polyps equal each type for genetic research. Determination of KRAS and BRAF gene mutations was performed by real-time PCR, analytical panel includes a mutation in exon 2,3,4 KRAS and gene mutation BRAF p. V600E. Runs data were processed using software the CFX Manager v 2.1.
Results: Serrated lesions were found most frequently in the ascending (25,7 %) part and sigma (20 %) of the colon; sexual differences are not determined. Genetic research has revealed that 50 % of SSA present only BRAF mutation. In 58 % of cases TSA identified mutation KRAS. BRAF mutation was identified in 42 % of HP, KRAS mutation was found in 17 % of HP, and without mutations was 42 % HP.
Conclusion: Serrated lesions occur equally in the right and left halves of the colon in both women and men. Gene mutation has been identified at 61 % of the serrated lesions; 25 % had KRAS and 36 % BRAF.

E-PS-06-019
Carcinosarcoma of the stomach: A case study
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Objective: Histogenesis and progression of carcinosarcoma are still unknown. We report a case of carcinosarcoma of the stomach, with attention to its clonality, distribution of immunophenotypes and relationship between original and metastatic lesions.
Method: [Case report] A 72-year-old woman with a history of appetite loss, anemia and weight loss, was admitted to our hospital. The patient underwent an esophagogastro- duodenoscopy that revealed a red-colored huge mass (13 × 13 × 6 cm) with erosion in the antral region of the stomach, and a distal gastrectomy sequentially. The metastatic tumour was detected in one regional lymph node.
Results: Histologcal findings: The largest cross section was examined. The tumour, composed of 5 % carcinomatous and 95 % sarcomatous elements, were diffusely positive for p53 with a point mutation of TP53. The carcinomatous elements consisted mainly of well to moderately differentiated adenocarcinoma that was focally positive for HER2/neu and CD10, and partly of squamous cell carcinoma that was positive for p40 and/or p63. The sarcomatous elements, consisted mainly of spindle-shaped cells and partly of large cells with eosinophilic cytoplasm, were largely positive for CD10 and partly positive for cytokeratin(AE1/AE3), desmin and myogenin. Regarding lymph node metastasis, the tumour also consisted of carcinomatous and sarcomatous elements, diffusely positive for p53 and CD10.
Conclusion: Diffusely positive finding of p53 with a point mutation of TP53 indicates that this tumour is monoclonal, and CD10 expression may be related to lymph node metastasis in this case. Focal overexpression of HER2/neu suggests that HER2 alteration is a late event during progression of this tumour.

E-PS-06-020
Early cancer of the stomach: Clinical-morphological and genetic features
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Objective: To study clinical-morphological and genetic features of early cancer of the stomach (ECS).
Method: ECS was diagnosed in 21 patients in the period from 2014 to 2016, of which 10 patients was conducted genetic research. Determination of KRAS and BRAF gene mutations was performed by real-time PCR (PCR PB). The study perfomed a set of reagent «KRAS/BRAF Mutation Analysis Kit» (EntroGen) on the C1000 Touch thermocycler with an optical module CFX96 (Bio-Rad Laboratories). The data were processed using the CFX Manager software v 2.1.
Results: Of the studied cases ECS was appeared in 66 % of women and 34 % men. Most of all were high-grade adenocarcinoma—81 %, 19 %—low-grade adenocarcinoma and Signet ring cell carcinoma. In 90 % of all cases the tumour does not grow into the submucosa (pT1a by TNM) and there were no cancerous emboli in the vessels. In 80 % of all cases ECS existed on the background of colonic metaplasia, in 86 % of all cases had dysplasia of varying severity. Genetic research revealed that 10 % of ECS detected KRAS p.G13D mutation (male, high-grade adenocarcinoma, pT1a). 100 % ECS was not detected BRAF mutations.
Conclusion: Thus, ECS prevailed frequency in women (66 %), and histological type—high-grade adenocarcinoma (81 %) without germination stomach submucosa (90 %). In most cases, ECS occurred colonic metaplasia (80 %) and dysplasia (86 %). In 10 % of cases detected KRAS mutation, 100 % ECS was not detected BRAF mutations.

E-PS-06-022
Serrated-like lesions and colorectal adenocarcinoma in patients with Inflammatory Bowel Disease IBD): Report of two cases with emphasis on morphology and mismatch repair status
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Objective: Report of two cases of colorectal adenocarcinoma (CRC) arising in a background of inflammatory bowel disease (IBD) both associated with well-differentiated morphology and serrated-like lesions in surrounding mucosa is presented.

Method: Patient 1 (female, 44 years old) with ulcerative colitis for 15 years and was admitted for elective surgery for DALM lesions and colon ascendens stenosis. Patient 2 (female, 29 years old) presented with ileus and was diagnosed with IBD with concurrent stenosis of lienal flexure.
Results: Patient 1: Resection specimen showed signs of ulcerative colitis with partial mucosal remission. Infiltration of colon ascendens with well differentiated adenocarcinoma was seen up to subserosal adipose tissue. Surrounding and distant mucosa showed several inflammatory pseudopolypous as well as serrated lesions. Patient 2: Resection specimen showed signs of Crohns disease, reported stenosis was due to well differentiated colorectal adenocarcinoma with partial mucinous differentiation infiltrating bowel wall to subserosa. Several foci of mucosal hyperplasia with serrated morphology was seen. There was no loss in immunohistochemical expression of mismatch repair proteins (MLH1, MSH2, MSH6, PMS2) and BRAF V600E staining was negative in both cases.
Conclusion: Patients with IBD has increased risk of CRC with precursor adenomatous DALM lesions. We are reporting two carcinomas showing bland and well differentiated morphology and serrated lesions. These two cases are pointing to an importance of reporting serrated lesions in IBD patients regarding their possible association to CRC via serrated pathway.

E-PS-06-023
Phlebosclerosis of submucosal veins leading to ischemic necrosis of the large bowel: The first reported European case of so-called phlebosclerotic colitis with unusual features
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Objective: Phlebosclerotic colitis is a fibrous degeneration ultimately leading to threadlike calcifications along colonic and mesenteric vessels and colonic wall thickening. Resulting mucosal ulceration causes expected symptoms of ischemic colitis: fever, abdominal pain, severe constipation, bowel obstruction, vomiting, diarrhea. Presentation of a 63 year old Caucasian woman: 1997 cervical carcinoma with radiation proctitis. No known intestinal disease. 2015 emergency hospitalization (rupture of an aneurysm of the pericallosal artery, ventricular hemorrhage). Four weeks into hospitalization, colon resection was performed due to rectal perforation and peritonitis.
Method: CT scan, MRI, pathologic evaluation including immunohistochemistry.
Results: No calcification was found by CT/ MRI. Gross Pathology of the resected colonic frame revealed confluent mucosal damage, and beginning transmural necroses reaching from the ascending colon to the rectum with perforation. Microscopy showed extensive and circumferential calcifications of the walls of medium sized, submucosal veins, not involving arteries or veins in the subserosal fat. No signs of viral, bacterial or fungal infection.
Conclusion: This represents an unusual differential diagnosis of an ischemic colitis. Diagnosis was hampered by the unconsciousness due to the aneurysmal bleed. Colonic vascular calcifications suggest a so-called phlebosclerotic colitis, while histology shows unique features different from cases reported so far from Asia and Canada.

E-PS-06-025
Lithiasis in septate gallbladder: Relationship to body mass index and gallbladder length
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Objective: We aimed to report the characteristics of lithiasis in septate gallbladder (SGB) occurring in adults. Septate gallbladder is a rare congenital abnormality defined by the presence of intercommunicating locules that may impact on bile streaming and stagnation.
Method: A total of 62 surgically resected SGBs were analyzed for the main clinical and morphological features of the resected specimens. Relationships were analyzed by using the Kendall rank correlation test (Medcalc).
Results: and, was supracentimetric (>1 cm) in 18 (34 %) cases. The gallbladder length varied between 3.5 and 12.7 cm. A body mass index (BMI) >25 was observed in 10 cases (8 cases: BMI >30). The presence of supracentimetric lithiasis correlated an increased gallbladder length and to BMI > 30 ($p = 0.02$/tau = 0.214 and $p = 0.03$/tau = 0.201, respectively).
Conclusion: The results of our study suggest that supracentimetric lithiasis occurred in one third of the SGBs. The biological background of the correlation between an increased gallbladder length or obesity and supracentimetric lithiasis remains to be further studied.

E-PS-06-026
Clear cell adenocarcinoma of the colon: A case report and review of the literature
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Objective: Primary clear cell adenocarcinoma is rare in the colorectum, with fewer than 20 cases reported in the literature. We present a case of clear cell adenocarcinoma of the colon in a 59 year old man.
Method: Colonoscopy revealed a 30 mm pedunculated polyp in the descending colon, and a polypectomy was performed.
Results: Microscopic examination of the polyp revealed a moderately to poorly differentiated adenocarcinoma with prominent clear cell change, which was invading the submucosa to Haggett's level 3. The tumour was positive for CDX2, focally positive for CK20 and negative for CK7. Alcian blue, PAS and PASD were negative. Two months later the patient underwent a sigmoid colectomy. A second polyp was found to be a tubulovillous adenoma with areas of clear cell change. There was no residual adenocarcinoma.
Conclusion: Clear cell adenocarcinoma in the colon is usually a metastatic deposit from other organs. Most of the reported cases of primary colonic clear cell adenocarcinoma have occurred in men, in the left side of the colon. Nearly all formed part of a larger conventional adenoma. The prognosis of these tumours is currently unclear, and further studies will be required in order to improve our understanding of this condition.

E-PS-06-027
Signet ring cell carcinoma of the ampulla of Vater
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Objective: To illustrate an uncommon variant a gastrointestinal cancer affecting duodenal ampulla with little known experience as only 20 previous cases are reported in international literature. Diagnosis criteria and

therapeutic approach can be useful to understand the nature and prognosis of these tumours.
Method: Pancreaticoduodenectomy specimen (Whipple procedure) was studied from a 47-year-old female with a previous clinical report of abdominal pain, distension. A computed tomography scan and magnetic resonance imaging of the abdomen showed an ill defined mass afecting pancreatic head and duodenal ampulla
Results: Microscopic examination showed showed a neoplastic proliferation composed by sheets of signet ring cells without any glandular differentiation and with wide extension in duodenal mucosa and some extracellular mucin lakes. There was Infiltrative growth in the entire thickness of the bowel wall and pancreatic acini in a 2,5 cm global area. No metastases in regional lymph node were found.
Conclusion: Signet ring cell carcinoma of the ampulla of Vater is a tumour with not well known origin and heterotopic gastric tissue has been postulated as the source of signet ring cells. Prognosis in cases described is closely related with stage and complete surgical resections. After a 6 month follow-up our patient remains free of disease.

E-PS-06-030
Clinicopathological significance of RacGAP1 on gastric gastrointestinal stromal tumours
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Objective: Investigation of the biomarkers that affect the pathogenesis and/or prognosis of gastrointestinal stromal tumours (GISTs) are being carried out seriously. RacGAP1 (Rac guanosine triphosphatase-activating protein 1) is a protein that has crutial roles in cytokinesis, cell growth regulation, cell transformation and metastasis. It has recently been reported to participate in progression of various tumours, such as breast carcinoma. The aim of the study was to evaluate the clinicopathological significance of RacGAP1 on gastric GISTs for the first time in the literature.
Method: RacGAP1 expression in 62 cases of gastric GISTs were analyzed immunohistochemically and correlated with the clinicopathological features [age, gender, risk group, mitotic count in 50 high power fields, tumour size, growth pattern, cellularity, nuclear pleomorphism, ulceration, hemorrhage, necrosis, tumour cell type], and Ki-67 labeling index, statistically.
Results: RacGAP1 expression showed direct correlation with Ki-67 labeling index (p: 0.014), mitotic count (p: 0.036), high-risk groups according to both Fletcher's and Miettinen&Lasota's criteria (p: 0.032, p:0.022, respectively), epithelioid cell type (p: 0.038), and higher cellularity (p: 0.008).
Conclusion: We suggest that overexpression of RacGAP1 is an indicator of adverse prognosis for gastric GISTs, and RacGAP1 might be used as an alternative marker instead of Ki-67 as a proliferation marker.

E-PS-06-032
Circumferential margin involvement after total mesorectal excision for rectal cancer: Are patients all equals?
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Objective: To assess the prognostic influence of the exact value of the circumferential margin (CM) when it's ≤1 mm after total mesorectal excision (TME) for cancer.
Method: From 2005 and 2013, among 321 patients, 49 (15 %) presenting R1 resection. CM was assessed in μm using Aperio digital pathology slides scanner®. Four groups were defined: Gr 1: CM = 0 mm (n = 21); Gr. 2: 0 < CM ≤ 0.4 mm (n = 13), Gr. 3: 0.4 < CM ≤ 1 mm (n = 15), Gr. 4: CM > 1 mm (n = 272).
Results: After a mean follow-up of 42 months, 2-year disease-free survival (DFS) was significantly lower in Gr.1 vs Gr.4 (33 vs 75 %, p < 0.01) and Gr.2 vs Gr.4 (38 vs 75 %, p = 0.01); no difference was noted between Gr.3 and 4 (58 vs 75 %, p = 0.07). In multivariate Cox analysis, a CM ≤0.4 mm was identified as an independent factor impairing DFS (p = 0.03) whereas CM > 0.4 mm was not (p = 0.53). Similarly, locoregional DFS was significantly lower in Gr.1 and 2 vs Gr.3 (66 vs 85 %, p = 0.01), and in Gr.1 and 2 vs Gr.4 (66 vs 97 %, p < 0.01).
Conclusion: Our study suggests that only a CM ≤ 0.4 mm worsened oncologic outcome and probably justify adjuvant chemotherapy. Oncologic results seem similar between patients with 0.4 < CM ≤ 1 mm and patients with R0 resection.

E-PS-06-033
Metastasis of neoplasm with Hepatoid features in a young patient, diagnostic challenge in small biopsy
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Objective: Neoplasm with hepatoid features is a special type of cancer characterized by morphological features similar to hepatocellular carcinoma; It has been found in different organs such as the stomach, lung, pancreas,esophagus, papilla of vater, gallbladder, colon/rectum, kidney, urinary bladder, uterus, ovaries and peritoneum. Gastric Hepatoid AdenoCarcinoma (GHAC) have an incidence of 0,38–1 % among all gastric cancers. The diagnosis is based on recognition of characteristic histologic features.
Method: A 54-year-old male patient with a history of squamous cell carcinoma in piriform sinus. Which presents DVT, inflammatory arthropathy 2 months of evolution, back pain radiated to lower limbs that prevents ambulation and unresponsive to analgesic treatment. It presents osteolytic lesion in left hip which is biopsied. The microscopic examination showed atypical poligonal neoplastic cells with abundant eosinophilic cytoplasm, prominent nuclei and high mitotic activity.
Results: Immunohistochemical staining revealed positive for: CK7, CK8, CK19, CDX2, MUC2, MUC 5AC, Hepatocyte. And histochemical +: PAS, PAS-D. And negativity for: CK20, AFP, TTF1, S-100, CD 117, CD10, PSA. The diagnosis was compatible with GHAC. The patient died four days after diagnosis.
Conclusion: - GHAC usually occurs in older people, although occasional early cases have been detected. -Clinically, a characteristic of these neoplasms is the extensive vascular infiltration, reflected in the high incidence of metastases (liver, lymph node). - GHAC is characterized by aggressive behavior and extremely poor prognosis compared with conventional gastric adenocarcinoma. -The majority of patients demonstrate an elevated serum AFP level, however 46 % of GHAC tissues were negatively stained with AFP. -Immunohistochemistry may help the differential diagnosis of primary hepatocellular carcinoma.

E-PS-06-035
Granulomatous inflammatory lesions of the terminal ileum and colon: Histological approach of three cases
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Objective: The etiology of granulomas in the GI tract is heterogeneous, making the differential diagnosis challenging.
Method: We analized the cases of three young patients, a female and two males, who underwent ileocolic resection, with granulomas on the H&E slides.
Results: In all the cases we identified areas of mucosa that were severely inflamed, ulcerated, covered by granulation tissue and exudate. In two

cases the remaining mucosa had preserved architecture and granulomatous lesions with central necrosis. From these two cases, one had family history of tuberculosis that correlated with the confluent pattern of granulomas with central, amorphous, eosinophilic necrosis, favoring the diagnosis of intestinal tuberculosis, despite the negative Ziehl-Neelsen reaction. The other case with necrotizing granulomas presented suppurative intramural inflammation, also involving the lymph nodes, without chronic abnormalities. The most reliable diagnosis was infectious enterocolitis. Ziehl-Neelsen reaction was negative, while serology was positive for Salmonella typhimurium and Salmonella enteridis. Whereas, in the third case we observed architectural crypt distorsion, basal plasmacytosis and pyloric gland metaplasia. The inflammation was transmural, forming granulomas and nodular lymphoid hyperplasia. Muscularis mucosae and muscularis propria were hypertrophic, causing 'muscularization of submucosa'. Histological features favored the diagnosis of Crohn disease.
Conclusion: When confronting with intestinal granulomatous inflammatory lesions it is very important to corelate the pathologic features with clinical history and endoscopic appearence.

E-PS-06-036
MDM2 as a prognostic marker for GIST: A retrospective study of 43 cases
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Objective: Gastrointestinal stromal tumours (GIST) are the most common primary mesenchymal tumours of the gastrointestinal tract. Our objective was to correlate MDM2 immunohistochemical overexpression to clinicopathological features of GIST.
Method: It was a retrospective study of 43 cases of GIST (2009–2012). The diagnosis was based on CD117 immunohistochemical expression. MDM2 immunohistochemical staining was performed on archival paraffin-embedded and formol-fixed specimens. The risk assessement was based on mitotic and tumour size according to AFIP criteria.
Results: The mean age was 55.11 ans. The stomach was the most affected site (51.2 %). Twenty five cases (61 %) had high risk tumours. The overall MDM2 expression was found in 68.4 % cases; high risk tumours stained mostly for MDM2 (78,6 %). Matastasis occured in 36 % of cases, with statistical correlation to MDM2 overexpression ($p = 0{,}001$), as much as the local agressiveness ($p = 0{,}01$). MDM2 was positive in 76.9 % among tumours >5 cm; positive in 64.3 % when mitosis >5/50HPF.
Conclusion: MDM2 was mostly overexpressed in high grade GIST tumours, and was correlated to metastasis occurrence. Further studies are needed to confirm MDM2 as a marker of poor prognosis.

E-PS-06-037
Mucosal Schwann cell hamartoma of the Colon: Case report
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Objective: Mesenchmal colorectal polyps are uncommon lesions, particularly those of neurogenic origin. Mucosal Schwann cell hamartoma, newly proposed disease entity is a rare mesenchymal polyp that presents in intestine.
Method: A 54 year old woman with lower abdominal pain and tenderness presented to gastroenterology clinic. She had no family history of familial adenomatous polyposis, multiple endocrine neoplasia type II or Cowden syndrome. Colonoscopy revealed a 2 mm polyp in descending colon and removed by forceps biopsy. There were no remarkable findings in terminal ileum and the other segments of colonic mucosa.
Results: Histopathologically, H-E stained sections showed a polypoid fragment of colonic mucosa and mildly palisaded diffuse spindle cell proliferation with oval and elongated nuclei within the lamina propria. The lesion was poorly circumscribed and colonic crypt architecture was separated and distorted by the spindle cell proliferation and muscularis mucosa was not involved. The surface epithelium was intact without erosion or ulceration and there was no evidence of any dysplasia. The lesion had a benign cytologic appearance, no nuclear atypia, pleomorphism or mitosis. At immunohistochemistry all proliferated cells stained strongly with S100 protein and no immunoreactivity for smooth muscle actin, CD34 and CD117.
Conclusion: It should be in mind in differential diagnosis of mesenchymal polypoid lesions in the colon.

E-PS-06-038
Mixed Adenoneuroendocrine Carcinoma (MANEC): The Gazi experience
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Objective: The purpose of the study was to bring together the Mixed Adenoneuroendocrine Carcinoma (MANEC) entities between the years of 2014–2015 in our institution to revisualize there morphologic aspects.
Method: The cases were retrieved from the electronic database and were picked up from the institutions slide archives. H&E slides were the elementary objects but the immunohistochemistry slides were examined as well by the authors.
Results: The female / male ratio was 1,5:1. The patients were between the ages of 58 and 82. All of our examples were from different localizations which are stomach, choledoch duct, gallbladder, ascending colon and perianal region. The biggest tumour bulk was 8 cm in diameter at the ascending colon with metastatic lymph nodes. The patients distant organ metastasis situation was enabled to identify because the lack of clinical information.
Conclusion: MANEC's are rare tumours but they are poorly differentiated malignant neoplasms. From our five patients the longest lived for 8 months only and all had high pT grades. The five tumours all had high grade neuroendocrine components although most of the epithelial components were low grade. The metastasis of the lymph nodes were also neuroendocrine carcinomas.

E-PS-06-039
Regression grading in neoadjuvant treated pancreatic cancer: An interobserver study
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Objective: Several regression grading (RG) systems have been proposed for neoadjuvant chemoradiation (NCRT) treated pancreatic ductal carcinoma (PDAC). This study aims to examine the utility, reproducibility and concordance of three most frequently utilised grading systems.
Method: Four gastrointestinal pathologists used the College of American Pathologists' (CAP), Evans, MD Anderson Cancer Centre (MDA) RG systems to grade 14 selected cases of NCRT treated PDAC. A post-scoring discussion was conducted and statistical analyses were performed.
Results: The results showed little concordance across the three systems. The Kendall coefficient of concordance (KCC) agreement scores were: CAP: 2-poor, 2-fair; Evans- 1-fair, 1-moderate, 2- good; MDA- 1-poor, 2- moderate, 1-good. Using fibrosis in RG for the CAP system was a source of discrepancy. In the Evans system, quantifying tumour viability using artificial percentage cut-offs (ie. 9 vs 10 %,etc.) was fraught with difficulty. Although the MDA system generated greatest concordance, it is felt this was due to "oversimplification" surrounding arbitrary thresholds (</> than 5 % of tumour).

Conclusion: It was felt that these systems lacked precision and clarity for accurate RG. However, presently the clinical utility and impact of histologic RG in patient management is questionable. There is a need to re-evaluate RG in the pancreas and establish a reproducible, clinically relevant grading system.

E-PS-06-041

An asymptomatic small polypoid esophageal malignancy consisting of carcinomatous and sarcomatous elements: Possible early-stage lesion of esophageal carcinosarcoma

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Objective: We report a case of possible "early stage" esophageal carcinosarcoma.
Method: A healthy asymptomatic male in his 40's visited our hospital for a medical checkup, and a gastroendoscopy revealed a small polyp at the esophagocardiac junction. Since endoscopic biopsy revealed growth of pleomorphic mesenchymal cells, we chose the esophagofundectomy for the method of treatment.
Results: Pathology of the resected specimen revealed a pedunculated polyp (size: 6-mm), the top of which was covered with atypical squamous epithelium and underneath were the dissociative pleomorphic spindle cells. Immunohistochemically, only the epithelial element was positive for AE1/AE3 and p40, whilst the spindle cells were positive for vimentin and negative for AE1/AE3 and p40. Both elements showed frequent labeling with p53 and Ki-67. HMB45 was negative in both elements. The malignant cell growth was restricted in a small area of the upper half of the polyp. The postoperative course has been uneventful as of the 12-month follow-up.
Conclusion: The lesion in our case, despite its smaller size compared to those of esophageal carcinosarcoma reported so far, already comprised of carcinomatous and sarcomatous elements as evidenced by their immunephenotype. It is suggested that the two way differentiation occurs at quite an early stage.

E-PS-06-043

Gastrointestinal Stromal Tumour (GIST) of an obliterated vermiform appendix: A case report

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Objective: We report an interesting case of GIST involving an appendix with fibrous obliteration of the lumen. Gastrointestinal stromal tumours (GISTs) of the appendix are a rare entity. Some studies have reported that the fibrous obliteration of the appendix can mimic an acute appendicitis.
Method: An 43-year-old male presented to the emergency department complaining of lower abdominal pain for several days. He underwent laparoscopic appendectomy for acute appendicitis. For histopathological evaluation we used hematoxylin and eosin (H-E) staining. Five immunohistochemical staining antibodies were performed (vimentin, CD117, S100, CD34 and Ki67).
Results: Macroscopic examination revealed an obliterated lumen of appendix and an irregular and asymmetrical thickening of the appendiceal wall. Histological examination show the lack of normal appendiceal mucosa and the lumen was displaced by a fibrous proliferation. In the subserosal layer we found a small nodule that consists densely packed cellular structure formed by spindle-shaped cells. These cells were positive for vimentin, CD117 (c-kit), CD34 and S100. The Ki-67 proliferation index of the tumour was 3 %.
Conclusion: The tumour was diagnosed as very low risk GIST of vermiform appendix. Appendiceal GISTs can be associated with appendicitis symptoms.

E-PS-06-044

The expression of mesothelin associated with tumour aggressiveness in gastric adenocarcinoma

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Objective: In Korea, gastric cancer remains the most common cancer in men. The pleural metastasis with gastric cancer patients was associated with poor survival. Due to diversity of morphologic features, the immunohistochemical stains are performed to assist in the differential diagnosis. The objective of this study is to evaluate the expression of mesothelial markers and discuss their clinicopathological significance associated with patient's outcome.
Method: A total of 117 patients who had histologically confirmed gastric adenocarcinoma and who underwent radical resection in Inje University Ilsan Hospital between 2005 and 2011. For the tissue microarray, two cores with a diameter of 0.3 mm were extracted from the representative tumour area. The staining of calretinin, WT1, mesothelin, and D2-40 were evaluated.
Results: Mesothelin positively stained 52 cases. All 117 cases did not react for calretinin, WT-1, and D2-40. The mesothelin expression was be relative to increased degree of pT stage ($p = 0.006$), AGC ($p = 0.001$), lymph node metastasis ($p = 0.020$), distant metastasis ($p = 0.0001$), and presence of lymphovascular ($p = 0.039$) and perineural invasion ($p = 0.018$).
Conclusion: The expression of mesothelin expression was associated with factors of poor prognosis. Based on the findings of this study, a panel composed of WT-1 or D2-40 or calretinin makes it possible to distinguish gastric adenocarcinoma from mesothelioma.

E-PS-06-045

Secondary neoplasms in young patients with colorectal cancer

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Objective: Present a series of cases of young patients with colorectal cancer that present a new onset malignancy not related to the primary tumour and describe its MLH1,MSH2, and BRAF mutations.
Method: Data was collected retrospectively from the electronic database between years 2004–2014. Selection criteria were: colorectal carcinoma, <50 years and new onset malignancy not related to the primary tumour following the recommendations of the modified Bethesda guidelines. Immunohistochemistry staining was made for MLH1, MSH2, PMS2 and MSH6 using automatized equipment. BRAFV600 mutation analysis was made using a real-time PCR.
Results: Initially 334 cases were retrieved, but only 18 were adequate for analysis. Mean age was 40.39 ± 7.28 years. The most common histopathological staging of their colorectal cancer was IIIB (38.8 %). New onset malignancies were located most frequently in colon (50 %) followed by endometrium, stomach, ovary, skin, adrenal gland, and pancreas. MLH1 was the most common molecular alteration (61.1 %) and all cases were negative to BRAFV600E mutation, which strongly suggest a Lynch syndrome.
Conclusion: This is the first series of cases realized in the northern part of Mexico, which includes second neoplasms associated with Lynch syndrome. The absence of BRAF mutation in all cases opens a possibility for new studies to clarify the role of other molecular alterations in the pathogenesis of early-onset colorectal cancer. Understanding of these processes may lead to new treatments targeting specific molecular pathways.

E-PS-06-046

Amyloidosis of the colon associated with multiple myeloma: A case report

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Objective: Amyloidosis of the colon is a rare disease presenting with non-specific symptoms, but can lead to life-threatening conditions. The purpose of the abstract is to describe the diagnostic and therapeutic behavior in a case of amyloidosis associated with multiple myeloma.
Method: We present a patient with abundant hematochezia, anemia, polypoid lesions in the colon, diagnosed by fibro colonoscopy. Total colectomy was performed. The histological result shows amyloidosis and polyposis of the colon. Bone marrow puncture confirmed myeloma in the same patient.
Results: Total colectomy was performed urgently due to massive hematochezia. Gastrointestinal passage is recovered through ileo-recto anastomosis with Stapler. The histological result shows AL amyloidosis with polyposis, associated with multiple myeloma. The therapy with melphalan and prednisolone was started following the NCCN guideline for treatment of amyloidosis. The patient was followed up for 1 year and is alive up to the moment.
Conclusion: Surgical procedure should be contemplated only in an emergency setting (bleeding or perforation), as it is in our case because of the risk of decompensation of organs affected by amyloidosis. If a patient with hematochezia unresponsive to conservative treatment and polyposis, amyloidosis of colon should be considered. Knowledge of the disease provides timely standardized treatment.

E-PS-06-047

Pathology review of surgically removed colon cancer in Lebanon: A 7-year single institution experience

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Objective: To analyze the pathological characteristics of surgically removed colon cancer in Lebanon.
Method: All 187 patients with colon cancer surgery at Hôtel-Dieu de France University Hospital between 2005 and 2012 were included.
Results: The mean age was 66.0 years and the Male/Female sex ratio was 1.3. Fourteen patients (7.5 %) had two tumours within the resection; the more aggressive tumour was studied. Overall, 101 patients (54.0 %) had a right colon tumour, 12 (6.4 %) a transverse colon tumour and 74 (39.6 %) a left colon tumour. The mean size of tumours per location ranged from 4.8 to 5.0 cm. Most tumours were predominantly conventional adenocarcinomas (88.2 %), followed by mucinous adenocarcinomas (9.1 %), signet-ring cell carcinomas (1.6 %) and neuroendocrine carcinomas (1.1 %). Most cases of mucinous adenocarcinomas (64.7 %) and neuroendocrine carcinomas (100 %) were located in the right colon. Vascular, lymphatic or perineural invasion was found most frequently in neuroendocrine carcinomas (100 %) and signet-ring cell carcinomas (66.7 %), compared to conventional adenocarcinomas (31.5 %) and mucinous adenocarcinomas (17.6 %). Finally, most cases were stage II (39.6 %), followed by stage III (30.5 %), stage IV (21.9 %) and stage I (8.0 %).
Conclusion: We can now confirm for the first time the similarity in the pathological characteristics of surgically removed colon cancer in Lebanon and other countries.

E-PS-06-049

Clinicopathologic impact of acellular and cellular mucin pools in rectum cancer

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Objective: Colorectal cancer is the third most common cancer in Turkey and in the world. Although surgery is curative for stage I, II and III A diseases, neoadjuvant chemoradiotherapy has emerged as a standard care of locally advanced diseases. Pathologic response is considered a treatment effect. The objective of this study is to evaluate the clinicopathologic impact of mucin pools for the rectum cancer.
Method: Totally 91 cases of rectal cancer were underwent surgery followed by neoadjuvant chemoradiotherapy between 2010 and 2015. Eighty of 91 cases were re-evaluated by histopathologically for mucin pools.
Results: The complete pathological response rate was 4,3 % (4 of 91). At a median follow up period of 43 months, 23 (25,2 %) had died of disease, 3 (3,2 %) had recurrence, 3 (3,2 %) had metastasis. Mucin pools were present in 28 specimens (30 %); 3 were acellular (3,2 %). Most often recurrent and metastatic diseases had subserosal mucin pools.
Conclusion: This study suggested that deeply invasive mucin pools had poor outcome. The pathologic assessment is important to detect response of therapy. Especially specimen sampling and sections of tissue may cause to miss single tumour cells in the mucin pools.

E-PS-06-050

Intra-abdominal heterotopic ossification following previous partial colectomy

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Objective: Intra-abdominal heterotopic ossification (IHO) is an uncommon, reactive condition where areas of metaplastic bone are seen in mesentery or peritoneum. In most cases it follows abdominal trauma. Mechanism of bone formation in soft tissue is not clear.
Method: We present a case of 53 year old man with IHO diagnosed 5 years after partial colectomy, performed because of sigmoid carcinoma. The patient was admitted to the hospital with acute symptoms of bowel obstruction. During the operation part of small intestine was excised and sent for the histological examination.
Results: Hematoxylin and eosin stained slides revealed the presence of multiple areas of heterotopic bone, granulation tissue with multinucleated giant cells and clusters of macrophages in mesentery. The diagnosis of IHO as a cause of bowel obstruction was rendered.
Conclusion: Intra-abdominal heterotopic ossification is a very rare condition considered as a reactive process. In most cases IHO follows abdominal trauma. It may be asymptomatic or may lead to bowel obstruction. Surgical intervention is performed only in symptomatic cases. IHO ossification shows the tendency for recurrence but has no malignant potential. Prognosis for the patient is usually good, in rare cases morbidity is connected with bowel obstruction.

E-PS-06-051

Mastocytic colitis: A case report and literature review

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Objective: Mastocytic colitis is a new entity, characterized by increased mucosal mast cells (more than 20 per high- power field) in the colon. There is no correlation with any type of mastocytosis. Some studies suggest that increased mast cells are present in patients with irritable bowel syndrome and diarrhea. The aim of our study was to determine the clinical, histological and immunohistochemical features of mastocytic colitis.
Method: We present a case of mastocytic colitis, in a 72 years old male who had a 4-year history of chronic watery diarrhea.
Results: A colonoscopy revealed grossly normal findings. Microscopically of random biopsies of the sigmoid colon showed non specific mild inflammatory edema in the lamina propria. A CD117 immunohistochemical stain was revealed more than 20

mast cells per high-power field. A finding consistent with the diagnosis of mastocytic colitis.
Conclusion: The presence of mast cells was either missed due to lack of ability to see mast cells on biopsies, it may be useful to perform a CD 117 immunostain in patients with unexplained chronic diarrhea with normal colonic mucosa. Counting mast cells in gastrointestinal mucosal biopsies is becoming an increasingly common practice.

E-PS-06-052
Desmoid tumours: Clinical, histological, immunohistochemical and evolution on a series of 20 cases
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Objective: To determine the clinical and pathological features of desmoid tumours (DT) and discuss the diagnostic difficulties and the importance of the immunohistochemistry in the management of these tumours.
Method: Retrospective study of the histologically proven cases of DT, diagnosed between 1990 and 2015 in the Pathology Department of Military Hospital.
Results: A total of 20 patients with histologically proven DT were included. The majority of patients were female (85 %) and the mean age at the time of diagnosis was 32. The average tumour size was 7.32 cm. Two groups were distinguished: The first represented 60 % of cases found mainly in women and localized to the abdominal wall, although well limited in radiological imaging, with a tendency to frequent recurrence. The second group represented 40 % of cases, intra-abdominal or at the expense of members. They were poorly limited in imaging with recurrence even after complete resection. Tumour cells expressed Vimentin intensely in all cases. CD34, C-kit and Ki67 were negative in all cases. Hormone receptors were positive in one case.
Conclusion: In addition to the purely diagnostic interest, immunohistochemistry is important in the choice of treatment and prognosis of DT.

E-PS-06-053
Bismuth Tripotassium Dicitrate (BTD) histologic pigmentation of the gastric mucosa: Unusual histologic finding and differential diagnosis
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Objective: Pigmentation of the gastric mucosa is a rare endoscopic and histologic finding and can be induced by different deposits: iron, calcium, barium sulphate, charcoal, melanin, lipofuscin and other.
Method: We present the case of a 34-year-old female patient with ulcer-like dyspeptic syndrome and underwent BTD and proton pump inhibitors treatment. Because of persistent symptoms, gastroscopy with biopsies was performed three days later and BTD was discontinued. One month later, gastroscopy showed a normal mucosa.
Results: The first gastroscopy revealed an extensive and diffuse inflammatory mucosa, with a friable and "solid plaque"-like aspect, raising the suspicion of a gastric lymphoma. The biopsies taken from the corpus and fundic region of the stomach showed a diffuse mild chronic gastritis, active, erosive, non-atrophic, negative for Helicobacter pylori, with mild hyalinosis of the lamina propria and the presence of diffuse amorphous black-brown pigment deposits located on the mucosal surface, within the exudate, within the foveolae and under the superficial regenerative epithelium. Perls stain was negative, excluding iron deposits. The second biopsies showed a normal mucosa, with no pigmentation.
Conclusion: This case highlights the need for the differential diagnosis and shows the importance of communication between the gastroenterologist and pathologist. Bismuth is known to induce oral pigmentation (black tongue, a blue-black line along gingival margin and even mucosal esophageal necrosis when associated with salicylates).

E-PS-06-055
Heterotopic pancreas of the gallbladder: A case report
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Objective: The gallbladder is an unusual location for heterotopic pancreas (HP) which is defined as the presence of pancreatic tissue without any anatomic or vascular continuity with the main body of the pancreas.HP has been noted in the stomach (24–38 %), duodenum (9–36 %), jejunum (0.5–27 %), ileum (3–6 %) and Meckel's diverticulum (2–6.5 %), but has been rarely seen in the gallbladder.
Method: We report a case of a 55-year-old female, complaining of biliary colic. The patient was hospitalized and a laparoscopic cholecystectomy was performed for acute cholecystitis. On macroscopic examination, the gallbladder measured 10 cm in length and 3.5 cm in circumference, with a wall thickness from 0.3–0.5 cm.On cutting open, the mucosa was velvety flattened and a single yellow stone measuring 0.7 cm in diameter was found in the lumen of the gallbladder. In the neck region in the pericholecystic fat a firm, round, yellow nodule, measuring 1,2 cm in diameter was found. The tissue specimens were formalin fixed, paraffin embedded and stained with H&E.
Results: On microscopic examination the nodule showed a well-circumscribed ectopic pancreatic tissue composed of lobules of exocrine pancreatic acini, ducts without any connection to the gallblader lumen and no islet cells. The remaining sections had features of chronic cholecystitis with acute exacerbation.
Conclusion: In our case the heterotopic pancreas has been classified as type 2 by von Heinrich classification.

E-PS-06-056
An unusual tumour with an unusual presentation
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Objective: We aim to report a case of a desmoplastic small round cell tumour from the pelvic region that was thought to be a colorectal tumour.
Method: A 41-year-old man came to the emergency room with rectal bleeding and abdominal cramping. During colonoscopy a rectal mass was found and biopsied. A CT scan showed multiple heterogeneous masses in the pelvic region, hepatic metastasis and abdominal and retroperitoneal adenopathies.
Results: Rectal biopsy showed an infiltrating neoplasia composed of nests and trabeculae of small round cells, round nuclei with dispersed chromatin and inconspicuous nucleoli. Immunohistochemically, the cells were positive for cytokeratins 8/18 and 7, EMA, desmin (dot pattern), CD57, vimentin and NSE (moderate intensity) and negative for chromogranin A, synapthophysin, CD56, S100 protein, CDX-2 and PSA. There was cytoplasmatic glycogen. It was diagnosed as desmoplastic small round cell tumour.
Conclusion: Desmoplastic small round cell tumour is a rare and highly aggressive tumour of undetermined histogenesis that caused the death of our patient 3 weeks after the diagnosis. In this specific case the diagnosis was challenging since it was histologically similar to a neuroendocrine tumour.

E-PS-06-057
Schwannoma of the gallbladder: Case report
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Objective: Gallbladder schwannomas are extremely rare and usually discovered incidentally. We report on the case of a gallbladder

schwannoma in 73 year old male patient with recurrent episodes of upper abdominal pain and jaundice.
Method: The ultrasonography and CT scan revealed gallstones and thickening of the gallbladder wall. The patient underwent ERCP with gastric biopsy due to a suspicious lesion on the posterior wall. Under the diagnosis of early gastric cancer and cholecystolithiasis, gastrectomy and cholecystectomy were performed. On gross examination the gallbladder measured 4 x 3 cm with thickening of parts of the wall up to 0,7 cm. The mucosa was velvety, flattened, with six solid yellow stones present in the lumen. Formalin fixed, paraffin embedded tissue samples of the thickened parts were stained with HE and immunohistochemically with monoclonal antibodies against S-100, CD-56, CD-57, Ki 67 and CK19.
Results: Microscopic examination revealed a tumour mainly consisted of spindle shaped cells (Antoni A), admixed with extremely rare Antoni B cells. Neither atypical cells, nor signs of malignancy were found. Immunohistochemically the cells were positive for S-100, CD-56 with Ki67 < 2 %.
Conclusion: Gallbladder is unusual and extremely rare localization for schwannomas, therefore immunohistochemistry is a necessary tool for definite diagnosis.

E-PS-06-058
Surgical pathology and MMR protein expression in colorectal carcinomas
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Objective: The aim was to determine the histological characteristics and frequency of microsatellite instability in colorectal cancers in Abuja, Nigeria with a view to suggesting possible aetiological factors.
Method: Histopathological and immunohistochemical review of 175 paraffin tissue blocks with colorectal carcinoma over a 10 year period.
Results: Colon cancer was 3 % of all tumours reviewed with (M: F ratio-1.08:1). Mean age was 50.8 years (range 21–94 years), mode was 40 and 69 years (69.8 %). Also 21.6 % patients were below 40 years. Most (43.6 %) were well differentiated carcinomas with the poorer grade tumours occurring in the younger age groups. Of the 140/175samples tested for microsatellite instability (MSI) status, 45 patients (32.1 %) were high frequency MSI (MSI-H). A right sided location and poor differentiation correlated with MSI-H tumours (p values of 0.013 and <0.001 respectively). The strongest associations were found between MSI-H status and residual adenomatous tissue, worse tumour grade, more Crohn-like feature and more advanced pathological staging with p values <0.001 each.
Conclusion: High frequency MSI (MSI-H) colorectal carcinomas were frequent in the study. The disease occurred earlier. Premalignant (adenomatous) lesions were few possibly accounting for the low rate. These point to the CIMP pathway in their tumourigenesis.

E-PS-06-059
Atypical presentation and location of two gastrointestinal stromal tumours: Prognostic implications
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Objective: Gastrointestinal stromal tumours (GISTs) are mesenchymal neoplasms occurring mainly in the gastrointestinal tract. Tumour size, mitotic rate and location are the main prognostic features. We present two unusual cases, one presenting as a gastric cyst, and the other localized in the head of the pancreas.
Method: Case1: 69-year-old female was admitted with upper abdominal pain and a palpable epigastric lump. Ultrasonography and CT revealed a cystic mass with 58 × 58 × 61 mm. She underwent atypical gastrectomy. Case2: 67-year-old female presented with upper abdominal pain. CT revealed a pancreatic mass with 50 × 38 mm and was submitted to cephalic duodenopancreatectomy.
Results: Case1: Macroscopic examination revealed a well circumscribed, cystic lesion with 7 cm, with an irregular inner surface. Histology revealed an epithelioid neoplasm with 2mitosis/15 mm2. Case2: Grossly, revealed an intrapancreatic, well circumscribed, whitish, solid tumour with 55 × 40 × 35 mm. Histology revealed a predominant fusiform neoplasm with 2mitosis/15 mm2. Both cases were positive for DOG-1 and CD34.
Conclusion: Literature suggests that in cystic GISTs, tumour size is not a true indicator of aggressiveness. The larger the cystic component, the lower the objectivity in determining tumour size. Extra-GISTs, especially pancreatic origin, are very rare thus its biological behavior is unknown. More cases and long-term follow-up studies are needed to predict the outcome of unusual GISTs.

E-PS-06-060
Extranodal extension of nodal metastases is a poor prognostic indicator in the upper gastro-intestinal malignancies
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Objective: The extranodal extension (ENE) of nodal metastases, i.e. the extension of neoplastic cells through the nodal capsule into the perinodal soft tissue, is a histological feature that has recently been considered an important prognostic factor in various types of tumour. It has yet to be taken into account by the TNM staging system for upper gastro-intestinal cancer, however.
Method: To provide a complete evaluation of the prognostic role of ENE in such neoplasms, a systematic review and a meta-analysis were conducted. Comparing patients with ENE (ENE+) vs. intra-nodal extension (ENE-), we summarized the data using risk ratios (RR) for the number of deaths/recurrences, and hazard ratios (HR) with 95 % confidence intervals (CI), adjusted for potential confounders, for the time-dependent risk related to ENE positivity.
Results: The presence of ENE was associated with a significantly higher risk of all-cause mortality (relative risk and hazard ratio both statistically significant), cancer-specific mortality (relative risk and hazard ratio both statistically significant), and disease recurrence (relative risk and hazard ratio both statistically significant).
Conclusion: For upper gastro-intestinal cancers, our results indicate that ENE should be considered for prognostic purposes from the gross sampling to the pathology report, and also by future oncologic staging systems.

E-PS-06-061
Correlation between pathologic tumour regression grade in the primary tumour and liver metastases with neoadyuvant chemotherapy in Stage IV colorectal cancer
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Objective: To asses the pathologic tumour response (PTR) in patients with colorectal carcinoma (CRC) with synchronous liver metastases treated with an inverse strategy of chemotherapy first followed by surgery resection and correlates both with chemotherapeutic agents.
Method: Forty-two patients were included. Chemotherapeutic agents were classified into: Cytostatic agents (CA), combination with monoclonal antibody against the epithelial growth factor (anti-EGFR) or with vascular endothelial growth factor (VEGF). PTR was assessed using a four grade score based on residual tumour cells.

Results: Twelve patients showed PTR more than 50 % in both liver and intestine. Liver PTR was greater with the association of CA+VEGF (median 95 %) followed by CA+anti-EGFR and CA. In the primary was greater with CA anti-EGFR (median 55 %), followed by CA and CA+VGEF. No response or poor tumour response was significantly more frequent in primary tumours than metastases. Liver chemotherapy with CA causes more fibrosis as a form or regression (median 65 %) than other associations and CA+VEGF more necrosis.
Conclusion: PTR is greater in liver metastases than in primary tumours and increases when CA is associated with anti-EGFR. In primary tumours all chemotherapeutic agents produce fibrosis as the main form of regression and in the liver by CA.

E-PS-06-064
Survive on with cajal cells: A retrospective clinicopathologic analysis of 87 gastrointestinal stromal tumours
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Objective: Gastrointestinal stromal tumours (GISTs) are distinctive tumours that show differentiation characteristics of the interstitial cells of Cajal, the gut pacemaker cells. GISTs represent 85 % of all mesenchymal neoplasms that affect the gastrointestinal tract. The aim of this study is to report a case series of 87 GISTs in a single centre and to discuss the diagnostic issues and follow-up results.
Method: A retrospective search of unit's archive to collect all cases diagnosed for GISTs between January 2003 to April 2016. The localization, histopathological findings, size, Ki-67 proliferation rates of the tumours, clinical and surgical features, recurrences if any, follow up, and survival of the patients were evaluated.
Results: Eighty seven cases of GIST were identified. 44 tumours were located in the stomach, 25 tumours in small bowel, 1 tumour in sigmoid colon, and 1 tumour in rectum. 16 cases involved extra-gastrointestinal locations. The mean age at diagnosis was 63,7 (range 27–93), while the male to female ratio was 0,74 (37 males/50 females). Patients presented with a variety of symptoms.
Conclusion: The prognosis of these tumours is unpredictable and the prognosis depends on localization, tumour size and mitoses. Benign tumours have excellent prognosis after surgery, while malignant tumours therapy resistant. Reviewing the variables and relation with the prognostic factors were evaluated according to current literature.

E-PS-06-066
Primary extra-gastrointestinal stromal tumour of the retroperitoneum: A rare, challenging entity
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Objective: Although extremely rare, neoplasms with overlapping histological and immunohistochemical features to gastrointestinal stromal tumours (GISTs) may occur outside the gastrointestinal tract (extra GISTs - EGISTs).
Method: A 64-year-old female was admitted to the hospital for myalgia and diffuse abdominal back pain present for several months. The abdominal CT scan revealed a sparsely delimitated, heterogenous, solid, tumour mass in the right paravetebral region. Consecutively, surgery was indicated.
Results: Macroscopical examination revealed a nodular, encapsulated, yellow-whitish, elastic tumour, measuring 7 × 6 × 5 cm. On light microscopy, the tumour was infiltrating the surrounding connective capsula, extending into the adjacent skeletal muscles. The tumour was composed of large, pleomorphic spindle cells, arranged in a storifom or fascicular pattern, with a high mitotic index (40mitoses/50HPF). Immunohistochemistry showed positivity for CD117, CD34, Vimentin, and negativity for S100, SMA, CD99. Morphological and immunohistochemical features leaded to a diagnosis of EGIST (intermediate risk form).
Conclusion: We herein report a rare, challenging case of primary EGISTs of the retroperitoneum. This diagnosis should be considered when imaging studies reveal an abdominal, retroperitoneal mass, without connection to the gastrointestinal tract. The pathogenesis, prognosis and optimal treatment of these tumours are not yet fully elucidated. In absence of these data, an accurate follow-up is recommended.

E-PS-06-067
Primary mesenterial leiomyosarcoma presenting as metastatic cancer of unknown primary location
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Objective: Solid primary mesenterial tumours are characterised by low incidence (1:200,000-1:350,000) and predominance of lipomas. Our objective is to present a rare tumour—primary mesenterial leiomyosarcoma.
Method: Medical documentation, pathology/immunohistochemistry (IHC) slides and radiologic investigations were reviewed in the context of up-to-date scientific literature.
Results: A 47-year-old woman complained of mild right upper abdominal pain. The computed tomography disclosed multiple liver metastases from cancer of unknown primary location. Liver biopsy showed loose bundles of spindled cells exhibiting nuclear polymorphism and atypical mitoses. High-grade sarcoma was evident, suggesting differential diagnosis of gastrointestinal stromal tumour or malignant peripheral nerve sheath tumour, among others. On exploratory laparoscopy, a neoplasm (5.5 × 5 × 4.3 cm) was found in mesentery below lig. Treitzi next to a.mesenterica superior. The mass was excised simultaneously with liver metastasis. Microscopically, tumour was composed of disarrayed spindle cell bundles in hypocellular myxoid stroma with hyalinosis. There were 21 mitoses/10 high-power fields. IHC was positive for actin and desmin, but negative for cytokeratin AE1/AE3, CD34, CD117. The proliferation fraction (Ki-67) was 72.0 %. No other masses were found elsewhere, including stomach, intestines or uterus. Thus, high-grade mesenteric leiomyosarcoma with hepatic metastases was diagnosed.
Conclusion: Here we show a well-documented primary mesenterial leiomyosarcoma: highly unusual cause of metastatic liver lesion.

E-PS-06-068
Gastritis Cystica Profunda mimetizing gastric GIST
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Objective: Gastritis cystica profunda is a rare polypoid lesion characterized by the presence of dilated cystic glands in the submucosa and even muscularis propria, usually presenting at gastroenterostomy stomal sites. We report this entity in a patient without history of previous surgeries.
Method: A 67 year old woman who underwent an atypical gastric resection due to a clinical diagnosis of gastric GIST.
Results: Macroscopically, a polypoid lesion with a nodular surface and a central ulcer was observed, with multiple cysts and solid areas on cross-section. Histologically, the gastric mucosa showed focal lesions of chronic atrophic gastritis with activity, hemorrhage and ulceration, whereas the submucosa and muscularis propria displayed an abundant cystically dilated pyloric-type and foveolar-type glandular proliferation, without mitoses or atypia; surrounding the glands there was a thin layer of lamina propria and fibromuscular hyperplasia. The diagnosis of Gastritis cystica profunda was made.
Conclusion: Gastritis cystica profunda must be differentiated from gastric well-differentiated adenocarcinoma and pancreatic heterotopia. Since

pancreatic ducts were not observed, there was no desmoplasia and the glands had a benign morphology, without atypia, these entities were excluded. Even though it is a benign lesion it can be associated with dysplasia and stump carcinoma, thus follow-up is advised.

E-PS-06-069

Hereditary Diffuse Gastric Cancer (HDGC): Case report of 3 related CDH1 mutation carriers and review of the literature

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Objective: HDGC is a form of gastric cancer familial aggregation, characteristically with increase lifetime risk of developing diffuse gastric cancer (DGC) and lobular breast cancer (LBC). Germline mutations in the CDH1 gene is detected in 30 % a 40 % of cases (WHO). Our aim is to study the clinico-pathological features of HGDC with the help of 3 CDH1 mutation carriers that met the clinical criteria of HGDC as well as review of the literature and recommended guidelines.
Method: Gastric biopsies (Cambridge Protocol) and one surgical specimen, from 3 CDH1 mutation carriers, were examined thoroughly and put in perspective with clinical context and previous studies.
Results: No lesions were found in endoscopy/macroscopic examination. However, histology showed tiny intramucosal foci of DGC in 1/25 and 3/38 fragments from the biopsies of each patient and in a few slides from the gastrectomy. The absence of atrophic gastritis or intestinal metaplasia was noted.
Conclusion: Our results emphasize recommendation of extensive sampling and careful evaluation of the lesions by a pathologist with experience in this pathology. HGDC patients are advised endoscopic surveillance and/or prophylactic total gastrectomy. These options are highly individualised.

E-PS-06-070

Two synchronous adenocarcinoma of large intestine, both colliding with ovarian serous carcinoma

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Objective: Synchronous or collision tumours of colon are rare, but two synchronous adenocarcinoma, both colliding with an ovarian carcinoma, are exceedingly rare.
Method: A 67-year-old woman with 4-month history of constipation and weight loss was diagnosed with rectal cancer infiltrating the uterus, with peritoneal carcinomatosis. Rectosigmoidectomy with total hysterectomy and bilateral salpingo-oophorectomy were performed and the specimen was submitted to the department of pathology.
Results: Gross examination of the intestine revealed two cancers, separated by a distance of 11 cm, apparently both infiltrating the peritoneal surface. Ovaries were enlarged, white nodular and firm. There were numerous white firm nodules on the peritoneal surface, of 0,5–3 cm in size, and the omentum was transformed into a white, solid mass. Microscopically, both colon tumours were well differentiated adenocarcinoma invading subserosal tissue. Tumours in ovaries, as well as all the nodules on the peritoneum and omentum, were diagnosed as serous ovarian carcinoma, confirmed by immunohistochemistry. Both colon adenocarcinomas were colliding with metastases from the ovarian serous carcinoma, which infiltrated from the surface of peritoneum into the muscularis propria, without admixture at their interface (confirmed with CK7 and CK20 stainings). All the lymph nodes metastases were of serous carcinoma.
Conclusion: Even our patient had two colon adenocarcinomas, the most aggressive was the ovarian serous carcinoma.

E-PS-06-071

Incidental histopathological findings in class III obese patients that underwent sleeve gastrectomy

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Objective: Individuals with a body mass index (BMI) ≥40 kg/m2 are defined as class III obese. Laparoscopic sleeve gastrectomy (LSG) is a commonly used surgical method for weight loss in these patients.
Method: Histopathological findings in LSG specimens of 129 consecutive class III obese patients were re-evaluated.
Results: Ninety-four patients (73 %) were female. Mean age was 37,43 (range 17–65 years). Their BMI differed between 40 and 62 kg/m2. The vast majority of the cases had chronic gastritis (97 %), with active inflammation in nearly one third (29 %). Helicobacter Pylori (HP) associated gastritis with nodular lymphoid hyperplasia (NLH) was seen in 63,5 %. Notably, NLH without evidence of HP was detected in almost one quarter (n = 31; 24 %). Twenty-three percent had mucosal changes due to proton pump inhibitors. None had gastric dysplasia, however regenerative mucosal changes were seen in 30 %. Intestinal metaplasia and atrophy were rarely detected (6 %). Prior endoscopy was performed in only 4 patients (3,1 %). No significant association was found between BMI and presence and/or severity of gastritis.
Conclusion: A wide spectrum of histopathological findings has been reported in LSGs, as gastritis being the most common finding. We also found a higher prevalence of HP, compared to previous reports, suggesting that HP eradication may be necessary in majority of patients undergoing LSG.

E-PS-06-072

DEK Expression in gastric carcinoma

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Objective: Gastric carcinoma is a common cancer type and serious cause of death. In this study, we have investigated in clinical prognostic effect of DEK expression in gastric cancer and the correlation between survival and expression rate.
Method: A total of 34 cases of gastric cancer patients who underwent surgery in our hospital, between 2010 and 2015 were selected for this study. Immunhistochemistry for DEK was performed on paraffin embedded tumour tissues. A nuclear staining in tumour cells was considered to be positive for DEK. The percentage of cells expressing DEK scored as <25 %, 25–50 %, >50 %. Staining intensity was recorded as weak or moderate/strong. High level DEK expression was defined as a moderate/strong staining in at least 25 % of tumour cells. Low level DEK expression was defined as positive nuclear staining with weak intensity.
Results: The patients age varies between 7 and 77, male female ratio was approximately 2.14 of the cases were tubular adenocarcinoma, 20 of the cases were poorly cohesive carcinoma according to WHO 2010 classification. 23 of the cases were identified as high level, 11 of the cases showed low level DEK expression. Half of the low level stained cases lived more than 24 months, on the other hand 22 of the 24 cases which was categorized as high level staining lived far less than 24 months. This findings was statistically significant.
Conclusion: Increased expression of human DEK proto-oncogen has been associated with numerous malignancies. High level DEK expression is though to be associated with poor prognosis, and low survival rate. Further research is needed to determinate prognostic value of this proto-oncogene expression in gastric carcinoma.

E-PS-06-073

Adenocarcinoma of the anal canal: Report of two cases

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Objective: Adenocarcinoma (ADC) of the anal canal is a rare disease comprising only 5 % of all anorectal neoplasias and 1.5 % of all gastrointestinal tumours. We report 2 new cases of this rare neoplasm with long proctologic medical history but with two different outcomes.
Method: We identified in our database two cases of ADC of the anal canal diagnosed in 2 women.
Results: The first patient was a 71 year old woman followed for more than 10 years for hemorrhoids and anal prolapsed treated medically. After, physical examination found a 3 cm bulging mass 1 cm from the anal verge. The biopsies concluded to a moderately differentiated adenocarcinoma expressing CK7 and CK20. The second patient was a 62 year old female patient, with a long medical history of anal fistula treated many times with surgery but no anatomopathology exam were made. A bulging mass of the anal canal was discovered in physical examination measuring 4 cm with 3 anal fistula. The patient had neoadjuvant chemoradiation followed by surgery. The anatomopathology concluded to a mucinous adenocarcinoma of the anal glands CK7- and CK20+. The follow up of the patient showed no sign of recurrence.
Conclusion: The pathogeny is still unknown. Symptomatology has no specificity and the diagnosis is often late, in an advanced stage of the sickness. Recurrent or non recurrent fistula-in-ano requires multiple biopsies for pathology analysis in order to screen a related cancer. Tumour dimension, lymph node involvement, histologic grade and treatment modality are independent prognosis factors for survival. Early suspicion is crucial to avoid delayed diagnosis and treatment.

E-PS-06-074

Intestinal endometriosis mimicking stenosing Crohn's disease: A case report

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Objective: Endometriosis is a rather frequent condition of fertile women, and often cause of sterility and chronic pelvic pain. Endometriosis is gonadal or extragonadal, the last, seldom occurs in the intestinal wall. Intestinal foci cause diarrhea or constipation through impaired peristalsis and obstruction.
Method: Our patient is a 44 years old woman with a few months alteration of constipation and diarrhea. She was admitted for subocclusive syndrome, mild inflammatory syndrome with normal fecal calprotectin, mild anemia and hypoalbuminemia. Colonoscopy describes an incomplete stenosis in lower sigmoid, suggestive of Crohn's disease, while abdominal tomography reveales a diffuse thickening of the sigmoid wall. Laparotomy found an intramural tumour adherent to the left ureter.
Results: Intramural colonic endometriosis infiltrating subserosa, muscularis propria and submucosa with areas of hemorrhage was diagnosed extemporaneously, and confirmed on paraffin embedded tissue with immunohistochemistry and special stains. Postoperative evolution was favorable.
Conclusion: Endometriosis may evolve aggressively, extending in muscularis propria along the nerve plexi, and in lymph nodes. It can have a pseudo-acute presentation with intestinal obstruction or severe diarrhea and may be confused with inflammatory bowel disease or intestinal tumours.

E-PS-06-075

Histopathologic changes seen in cases of sleeve gastrectomy in a Turkish population

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Objective: Sleeve gastrectomy (SG) is a bariatric surgical procedure used in morbid obesity. In this study, histopathologic changes in the SG specimens of obese Turkish patients have been characterized.
Method: 50 SG cases re-evaluated using H&E, PAS-Alcian Blue and Modified Giemsa staining. For cases with gastritis, Sydney classification was used. Location and distribution of lymphoid aggregates/follicles in the gastric mucosa noted.
Results: Average age was 38 year with a female to male ratio of 6:1. BMI ranged from 40 to 65 kg/m^2. 37 cases (68 %) had chronic active gastritis, 11 cases (22 %) had chronic inactive gastritis and 4 cases (4 %) had normal histology. Presence of H. pylori was detected in 34 cases (68 %). In almost all cases (98 %), lymphoid aggregates/follicles were present. Lymphoid tissue extended from muscularis mucosae to the lumen, filling the entire mucosa, in 27 cases (54 %). Intestinal metaplasia, cystic dilatation of mucosal glands due to PPI usage, and hyperplastic polyps were other changes. No statistically relevant relationship was found between histopathologic changes and patient parameters.
Conclusion: Histopathologic changes seen in Turkish SG cases have not been previously studied. Compared to other SG studies in the literature, there was a higher rate of chronic gastritis and H. pylori in our cases.

E-PS-06-076

Variations in diagnosis of gastric epithelial neoplasia in endoscopic biopsies: Interobserver study from Istanbul Gastrointestinal pathology Working Group (IGIP)

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Objective: The aim of this study is to evaluate the concordance in diagnosis of gastric epithelial neoplasia among pathologists with different levels of experience.
Method: The study included gastric biopsies from 32 cases from different Institutes (Medical Faculties and Training and research hospitals) in Istanbul. They were diagnosed with spectrum from normal to invasive carcinoma. All biopsies were renanalysed according to Vienna Classification blindly by 29 pathologists who were working different Institutes with different experience level in GIS. Intraclass Correlation Coefficient and kappa analyses were applied for agreement among observers.
Results: Distribution of the initial diagnosis of the biopsises: Negative for Displasia :2; Indefinite for neoplasia: 4; Low grade displasia: 5; High grade displasia: 11; invasive neoplasia: 10. Overall agreement was high (96,5 %; p:0.000). Pathologists were two grouped as more than 15 year and less than 15 year of experience. Agreement was relatively lower in less experienced group. Lowest agrement was in cases with ¨ Indefinite for displasia¨. The concordance was high in invasive carcinoma cases in both pathologist group.
Conclusion: In diagnosis of gastric epithelial neoplasias, the interobserver agreement is depended on the experience of pathologist especially on Gastrointestinal system pathology. Diagnosis of Indefinite for displasia is still problem even in experienced pathologists.

E-PS-06-078

Protein regenerating liver-3 (PRL-3) up regulated the expression of MMP-2 and down regulated the expression of E-cadherin in colorectal carcinoma

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Objective: Colorectal cancer is the third most common malignant neoplasm worldwide. PRL-3 (phosphatase of regenerating liver-3/PTP4A3) was reported play a role in the progression of colorectal cancer. However, how the mechanisms of PRL-3 induce progression and metastatic ability, interact with others molecule such as MMP2 and E-Cadherin, remain largely unknown. To clarify the molecular proteins that involved in colorectal cancer development and progression, we investigate the expression of PRL-3, MMP2 and E-Cadherin in colorectal cancer and correlate the expression with the clinicopathologic parameters.
Method: Expression of PRL-3, MMP2 and E-Cadherin in 76 colorectal cancer specimens were examined by immunohistochemistry.
Results: Among colorectal cancer specimens examined, there were 30 (39.5 %) well differentiated, 36 (47.4 %) moderately differentiated and 10 (13.2 %) poorly differentiated CRC. There were a significant correlation between histological grading and PRL-3 ($p = 0.044$), MMP2 ($p = 0.040$) and E-cadherin expression ($p = 0.039$), respectively. The expression of PRL-3 was significantly correlated with the expression of MMP2 ($p < 0.001$) and the expression of E-cadherin in colorectal cancer ($p = 0.003$). The result showed that more frequent expression of PRL-3, the higher expression of MMP2 and the lower expression of E-cadherin in colorectal cancer.
Conclusion: These study strongly suggest that PRL-3 may play a role to up regulated expression of PRL-3 and down regulate the expression of E-cadherin in the development and progression of colorectal cancer. PRL-3 and MMP2 might be a novel molecular marker for aggressive colorectal cancer.

E-PS-06-079

Small cell neuroendocrine carcinoma involving the right colon: Case report

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Objective: Small cell neuroendocrine carcinoma (SC-NEC) is a rare type of colon neoplasm with an incidence of only 0,6 %. It is associated with a poor prognosis and usualy with distant metastasis at the time of diagnosis
Method: In this report we present the case of a 41 year-old man who underwent an abdominal computed tomography and a gastrointestinal endoscopy in our institution which revealed a large tumour located in the right colon. A right hemicolectomy was performed and a large 6 cm tumour was identified in the cecum.
Results: Histologically the tumour was composed with small to medium neoplastic cells arranged into irregular sheets consisted with small cell NEC. Immunohistochemistry exam was performed using eight biomarkers and a positive reaction was identifed for Synapthophisin, NSE, CD56, CDX2 and AE1/AE3. A negative imunostain was noted for Chromogranin A, TTF1 and CEA. Also it was observed a high Ki67 index prooving the high malignancy of this tumour. The most frequent molecular abnormalities identified are those involving MEN1, p53 and CDKN2/Rb genes.
Conclusion: Small cell NEC is a rare diagnose in which histologic, immunophenotype and molecular features can help in understanding the biological behaviour of this type of neoplasm

E-PS-06-080

Unusual association of colonic carcinoma and tuberculosis: Evidence from autopsy

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Objective: Coexistence of colonic carcinoma with tuberculosis is an extremely rare condition. Here we describe the case showing association of colonic adenocarcinoma with colonic tuberculosis in the course of generalized tuberculosis.
Method: An 83-year-old female was subjected to autopsy at Institute of Pathology, University of Belgrade - Faculty of Medicine, with a clinical diagnosis of severe sideropenic anemia.
Results: External examination revealed pronounced cachexia and pale skin. Numerous small whitish nodules were spread within the lungs, pleura and liver. Microscopic analysis confirmed that they corresponded to generalized tuberculosis. Examination of the colon showed an ulcerated nodular mass ($6 \times 5 \times 3$ cm) in the caecum. Histopathological evaluation demonstrated well-differentiated adenocarcinoma of the caecum where carcinomatous tissue was intermingled with tuberculous granulomas containing caseous necrosis, epitheloid cells and Langhans giant cells. No sarcoid-like granulomas and reactive lymphoid follicles, characteristic for Crohn disease, were seen in any segment of the colon. In liver, the tuberculous granulomas were associated with colonic metastases.
Conclusion: Clinically undiagnosed adenocarcinoma of the caecum was closely associated with tuberculosis of the same site in the course of clinically unrecognized generalized tuberculosis. It is essential to record such cases in order to clarify the potential causal relationship between the carcinoma and tuberculosis.

E-PS-06-081

p53 polymorphism in gastric cancer patients of Karachi, Pakistan

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Objective: To study p53 mutation status in gastric patients of Karachi, Pakistan.
Method: Total 77 formalin fixed Paraffin embedded (FFPE) tissues were collected from gastric cancer patients. Followed by DNA extraction. Extraction of DNA was confirmed by amplifying a fragment of internal β-globin gene. Exon 5, 6 and 7 were amplified by primer specific PCR. Furthermore single stranded conformational polymorphism was performed on 12 % polyacrylamide gel electrophoresis. Mobility shift was observed by Silver staining the Gels.
Results: PCR-SSCP analysis of p53 exons 5–7 revealed by band mobility shift indicative of mutation in 39 (50.6 %) from 77 FFPE of gastric cancer patient samples. Fourteen mutations were found in exon 5, six in exon 7 and nine mutations in exon 7. One sample sequence mutated in both exons 5 and 6. One sample sequence mutated in both exons 6 and 7. Three samples have mutated sequence in both exons 5 and 7. To confirm the presence of mutation, 29 cases in which aberrantly migrating bands were observed by SSCP were sequenced.
Conclusion: Results outcome support the statement that cancer progression might be facilitate by mutation in various exon of p53 tumour suppressor gene.

E-PS-06-082

Abdominal cocoon syndrome: An unusual pathologic finding

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Objective: Sclerosing encapsulating peritonitis(SEP)/Abdominal cocoon syndrome is a rare condition that is generally identified in young females

from tropical/subtropical regions. It may cause acute or sub-acute intestinal obstruction and it's usually diagnosed during surgery.
Method: We describe a 58-year-old male patient presenting with small bowel obstruction without relevant surgical or medical history. CT of the abdomen revealed collapsed loops of small bowel. Laparotomy was performed, with a resection of jejunum-ileum of 45 cm.
Results: Grossly, the surgical specimen revealed membranous adhesions enclosing the intestinal loops in a concertina-like fashion, giving a cauliflower-like appearance (figure 1). Histological examination revealed formation of thin sheets of dense fibrocollagenous tissue and focal fat necrosis with xanthomatous histiocytes (figure 2). No other type of inflammatory reaction was observed. The intestinal wall didn't show any pathology.
Conclusion: Abdominal cocoon syndrome is a rare pathology and is difficult to diagnose. Several mechanisms in secondary forms include chronic peritoneal dialysis and less frequently prior abdominal surgery, several infections, beta-blocker treatment or chemotherapy. However, in some cases as in ours, the etiology remains obscure. A high index of clinical suspicion and recognition of a radiological findings should be considered in order to ensure proper management.

E-PS-06-083
Extremely rare case of synchronous gastric and colonic metastases occurring 9 years after an uterine leiomyosarcoma
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Objective: Uterine leiomyosarcoma (ULMS) is a rare tumour, representing 1–2 % of uterine malignancies. It is highly aggressive, has poor prognosis, a 5-year survival rate of 40 % and high metastatic rate, especially in lungs.
Method: A 58-year-old woman who had undergone hysterectomy, bilateral adnexectomy and radiochemotherapy for ULMS 9 years ago presented with gastrointestinal bleeding. Gastroscopy showed two tumoural masses, while colonoscopy identified two pedunculated polyps on the descending colon. CT revealed abdominal and pelvic lymphadenopathy. Total gastrectomy and polypectomy were performed.
Results: Histologically, both sites revealed proliferations of spindle cells with whorled pattern, nuclear atypia, 5 to 8 mitotic figures/10HPF and additional necrosis in the gastric tumours. Immunohistochemistry was negative for CD117, DOG1, S100, CD34 and positive for SMA, ER, PR. 20 % of nuclei stained positive for Ki67. Considering the patient's history and the immunohistochemical profile, we diagnosed the lesions as gastric and colonic metastases of ULMS.
Conclusion: Regardless of the primary tumour, colonic metastases are exceptionally rare. The peculiarity of the case stands in both an extended disease-free survival and the gastrointestinal involvement. The gross appearance is similar to other types of polyps. As the experience is limited, multidisciplinary approach and long-term follow-up in managing such patients may be the best available option.

E-PS-06-084
Further morphological characterization of tumour deposits in colorectal carcinomas
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Objective: We aimed to further define the characteristic features of tumour deposits (TD) with perpendicular sections.
Method: Thirty paraffin blocks representing 47 TD of 15 colorectal carcinomas were selected. A median of 4(2–10) perpendicular sections of 2–3 mm-thickness were made and embedded on their cut surface. Sections were evaluated for the clues of lymph node (LN) structures (presence of capsule, capsular sinus or lymphoid tissue).
Results: Of 47 TD, 18(38 %) had a round shape with a thick capsule-like fibrosis, 10(21 %) were encapsulated with irregular infiltration, and 19(40 %) had irregular borders without a capsule. We highly suspected of lymph node in 6/18 tumour deposits with round shape and thick capsule-like fibrosis due to the presence of minimal lymphoid tissue. After examination of additional perpendicular sections, a more organized lymphoid tissue (4), subcapsular sinus (1) and involvement of efferent lymphatics and subcapsular sinus (1) led a call for LN in 6 cases. In the rest 41 cases, additional perpendicular sections were unable to reveal any feature suggestive of LN, except one case. Overall, 7/47(15 %) TD were reclassified as metastatic LN.
Conclusion: In the majority of the cases, a more detailed examination of TD with perpendicular sections was unable to uncover any relevant feature suggestive of a metastatic LN.

E-PS-06-086
A strange benign lesion of the Esophagus: Benign bizarre stromal cell polyp
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Objective: To report a challenging case of an esophageal polyp.
Method: Slides were colored with hematoxylin and eosin. Immunohistochemistry using a large panel of antibodies was performed.
Results: A previously operated 63-year old patient for colonic adenocarcinoma presented with an esophageal polyp. On histological examination, esophageal mucosa was ulcerated with many atypical, large, discohesive cells in the lamina propria (Panel a). Nuclei were pleomorphic, sometimes multiple, with prominent eosinophilic nucleoli (Panel b, arrow). They were intermingled with many granulocytes and plump vessels, in a backround of granulation tissue. Immunohistochemical study showed only positivity with vimentin (Panel c). All the other markers were negative (pan-cytokeratin, CK7, CK20, EMA, S-100, CLA, HMB45, CD31, FactXIII a, AML, CD-1a, CMV). Ki67 showed a low proliferative index. The diagnosis made was that of a benign bizarre stromal cell polyp of the esophagus. The patient is free of disease 6 months later.
Conclusion: History of colonic adenocarcinoma made the diagnosis of this stromal bizarre polyp difficult and the main differential diagnosis was metastases, ruled out with immunohistochemistry.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-07 Gynaecological Pathology

E-PS-07-001
Role of her2neu (c-erb-2) expression in premalignant and malignant lesions of uterine cervix
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Objective: To evaluate the role and significance of Her 2neu as biomarker in premalignant and malignant lesions of uterine cervix, and to correlate its expression with stage and grade of cervical cancer.
Method: This 3 year study included all the cases diagnosed as premalignant, carcinoma-in-situ, and invasive carcinoma on cervical biopsies. Immunohistochemical (IHC) staining for Her 2neu was done using Biogenex, Clone CB11 antibody, and results were scored according to Wolff etal 2007. Her 2neu IHC scores were correlated with the clinicopathological parameters namely grade, stage and histological type of the lesions. Statistical analysis was done using SPSS software (v.16.0).
Results: Higher Her 2neu score correlated positively with the grade and stage of premalignant and malignant cervical lesions. Higher score was seen in malignant cases with positive lymph node status. Although

adenocarcinoma showed a higher score than squamous cell carcinoma, the difference was not statistically significant.
Conclusion: Her 2neu expression evaluation may provide additional and independent prognostic information in the clinical course of cervical cancer; and it could be a potential therapeutic target in cervical cancer treatment.

E-PS-07-002
Endometrial carcinoma and its precursor lesions: One-year experience in one center
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Objective: Endometrial carcinoma is the 4th most common malignancy of the female reproductive system in Romania which is currently recording an increasing trend worldwide as well as in our country. Endometrial intraepithelial neoplasia (EIN) or atypical hyperplasia is the immediate precursor lesion in endometrial carcinoma which can be detected in endometrial biopsies performed due to abnormal vaginal bleeding.
Method: This is a retrospective analysis performed in the Department of Pathology of the University Emergency Hospital Bucharest, Romania over a period of 1 year (January 2015–January 2016) which involved a total of 264 cases of female patients with endometrial carcinoma and hyperplastic precursor lesions. We investigated 183 cases of non-atypical hyperplasia, 26 cases of atypical hyperplasia (EIN), 46 cases of endometrioid carcinoma, 5 cases of clear cell carcinoma, 3 cases of serous carcinoma and 1 case of mucinous carcinoma.
Results: The most notable finding was that 23 % of the women preoperatively diagnosed with EIN on an endometrial biopsy were postoperatively discovered with endometrial carcinoma upon hysterectomy sampling.
Conclusion: Although EIN has a high likelihood of progression to carcinoma, we consider these findings to be simultaneous occurrences of endometrial carcinoma due to the short time interval between diagnosis and treatment.

E-PS-07-003
Bilateral congenital multicystic renal dysplasia associated with polydactyly
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Objective: Congenital malformations are the most important causes of fetal death and they can be defined as structural or functional anomalies that occur during intrauterine life. In the last year, in Emergency University Hospital, Bucharest, were performed 7 fetus autopsies with the clinical diagnosis of Polycystic Renal Disease. 4 of them, including this case, had Congenital Multicystic Renal Dysplasia.
Method: We performed the autopsy of a 22 week old male fetus from an uninvestigated pregnancy. The autopsy report highlighted multiple malformations. We collected representative tissular fragments for histological examination, which have been processed by the classical stain H&E.
Results: During the autopsy, the following were noted: ELBW-700 g fetus, postaxial polydactily of all limbs, club feet and distended abdominal wall by the presence of bilateral renal enlargement: kidneys with multiple cortical and medular cystic spaces, without pelvocaliceal occlusion, bladder abnormalities and urethral athresia. Histologically, the kidneys showed noncommunicating, irregular cysts of varying sizes in the renal and cortical region and dysplastic ducts lined by a columnar epithelium surrounded by fusiform cells. There were also few normal tubules and dystropic ones.
Conclusion: This is our hospital's first case of congenital renal dysplasia that associates polydactyly and club feet, without having other urogenital malformation and liver pathological features.

E-PS-07-005
Role of frozen section to provide an accurate intraoperative diagnosis for suspicious ovarian masses in postmenopausal women
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Objective: This study aims to evaluate the accuracy of intraoperative frozen section (FS) in the diagnosis of ovarian neoplasms in postmenopausal women.
Method: The study was conducted in Oncology Center, Mansoura University from March 2008 to December 2014. A retrospective analysis was done for intraoperative FS for suspected ovarian neoplasms. The FS and permanent paraffin section (PS) results were compared and the overall accuracy, sensitivity, specificity, positive and negative predictive values were determined.
Results: The study included 105 patients and the overall accuracy of FS in determining malignancy was 81.7 %. The sensitivity for malignant tumours was 75.32 % with specificity of 100 %. For benign tumours, the sensitivity and specificity were 100 and 93 %, respectively. Borderline tumours had the lowest sensitivity of 100 % with specificity of 95.19 %.
Conclusion: The present study concurs that frozen section is an accurate test for diagnosis of benign and malignant tumours in postmenopausal women thus determining the extent of surgery done for them. On the other hand, accuracy rates for borderline tumours are low.

E-PS-07-006
Metastatic endocervical adenocarcinoma in a mature cystic teratoma: A case of tumour-to-tumour metastasis
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Objective: Tumour-to-tumour metastasis (TTM) is a rare phenomenon corresponding to metastasis in a histologically distinct tumour. Adenocarcinoma represents 5–15 % of invasive cervical carcinomas and ovarian metastasis are not unusual. Mature cystic teratomas (MCT) account for 60 % of benign ovarian tumours and somatic malignant transformation is uncommon (1–2 %). There are no previous reports of MCT involved in TTM events.
Method: We report a case of tumour-to-tumour metastasis of an endocervical adenocarcinoma to an ovarian mature cystic teratoma.
Results: A 51-year-old patient presented with a cervical lesion histologically diagnosed as a poorly differentiated, HPV18+, adenocarcinoma. Staging showed a IIA2 (FIGO 2009) cervical carcinoma associated with a left ovarian multicystic tumour suggestive of teratoma with a radiological suspicious area. A bilateral salpingo-oophorectomy was performed. A left MCT with $11 \times 4 \times 3$ cm was confirmed and a solid area with 2 cm of adenocarcinoma, morphologically similar to the cervical adenocarcinoma, was found. A similar immunoprofile (p16+, CEA+, vimentin-, ER-) in both adenocarcinomas was documented. HPV18DNA+ in both confirmed the diagnosis of metastatic endocervical adenocarcinoma in a mature cystic teratoma.
Conclusion: Similar morphology, immunohistochemistry and HPVDNA in both malignant component of MCT and endocervical adenocarcinoma confirmed a TTM and excluded a more common, although rare, MCT malignant transformation in a perimenopausal patient.

E-PS-07-008

Immunohistochemical pecularities of recurrent ovarian endometriosis

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Objective: To investigate the immunohistochemical pecularities of recurrent ovarian endometriosis.
Method: The study included 52 patients with recurrent ovarian endometriosis and 36 patients without recurrence, who undergone laparoscopy with stripping technique using «Karl Storz» equipment with histological investigation. Immunohistochemistry was performed using immunohistostainer Bond-max (Leica, Germany) with the use of monoclonal antibodies: to estrogen (ER) and progesterone (PR) receptors, Ki-67, bcl- 2, p53, b-katenin.
Results: The expression of ERβ was 33 % in recurrent endometriosis, in non-recurrent samples—30 % ($p < 0,05$). The expression of PR was significantly higher in Group II (30 vs 55 %, $p = 0,045$). Analysis of bcl-2 expression showed that its level was higher in group I—59 % ($p = 0,039$). The expression of p53 was 4 times less than in group of recurrence (4 vs 19 %, $p = 0,048$). There was a statistically significant increase in the expression of Ki-67 and b-catenin (respectively, 25 vs 12 %, $p = 0,042$ and 51 vs 38 %, $p = 0,039$).
Conclusion: Immunohistochemical assessment revealed significant differences in the expression rates of proliferation, apoptosis and intercellullar adhesion indicators in recurrent ovarian endometriosis, which will subsequently allow to work out a personalized approach to the management of patients.

E-PS-07-009

Atypical endometriosis: A clinicopathological study of 6 cases

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Objective: Endometriosis is a common condition found in women undergoing laparotomy. However, atypical endometriosis is rare. It is characterized histologically by endometriotic glands with cytologic and/or architectural atypia.
Method: The incidence of ovarian atypical endometriosis (AEM) in a consecutive series of cases during the period 2013 to 2016 was studied The diagnosis of atypical endometriosis was based on the presence of large hyperchromatic or pale nuclei with moderate to marked pleomorphism; increased nuclear to cytoplasmic ratio; and cellular crowding, stratification, or tufting. Three or more of these criteria must be present.
Results: 6 cases of atypical endometriosis were found in a series of 175 typical endometriosis (3,5 %), 5 were in the ovary and 1 in the fallopian tube.Of the ovary AEMs, 3 were associated with a borderline or malignant tumour, 1 was associated with teratoma.
Conclusion: The ovary is the most common site for development of malignancy in endometriosis; however, little is known about the incidence of ovarian atypical endometriosis and its association with ovarian malignant epithelial tumours The process of damage, repair, and scarring over a long period may play a role in the development of endometriosis into AEM and eventually into tumour formation.

E-PS-07-010

Pattern-recognition receptors of innate immunity of placenta villi and myometrium in the pathogenesis of severe preeclampsia

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Objective: To investigate expression anti-viral receptors of innate immunity NOD1, TLR9 in the structural elements of placenta and myometrium samples in patients with severe preeclampsia.
Method: The immunohistological study was performed on the 15 serial paraffin slices of placenta and myometrium: 9 samples collected from women with severe preeclampsia (PE), 6 samples—with normal pregnancy (NP), using NOD1 primary monoclonal antibodies (1:100; Termo scientific), TLR9 (1:500; Genetex). The intensity of immunohistochemical reaction was estimated by means of Nikon Eclipse microscope imaging software (NIS-Elements).
Results: The immunohistochemical study indicated NOD1 and TLR9 cytoplasmic staining in amnion, major and minor subset of decidual cells, syncytiotrophoblast, syncytial knots, cells of stroma, endothelium of vessels of placental villi. NOD1 demonstrated more intensive staining in syncytiotrophoblast and endothelium of stem and intermediate placental villi in women with NP, than with PE ($p < 0,05$)($0,46 \pm 0,052$, $0,40 \pm 0,043$ and $0,45 \pm 0,24$; $0,36 \pm 0,038$, respectively). We observed irregular with marked fluctuations TLR9 expression staining in syncytiotrophoblast and endothelium of placental villi in preeclamptic women than in NP. In PE NOD1 and TLR9 demonstrated irregular expression of markers with significant variations in neighboring cells in myometrium.
Conclusion: Disturbance of innate immunity receptors expression (NOD1, TLR9) both in placenta and myometrium associated in severe PE.

E-PS-07-011

Cytopathological results of cervical cancer screening in Tunisian population

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Objective: To study distribution of cervical lesions diagnosed by pap smear in Tunisian population in which cervical cancer incidence is known to be low.
Method: A retrospective study with analysis of results in pap smears with epithelial cell abnormalities.
Results: Out of 44,057 pap smears, 247 cases (0,6 %) demonstrated epithelial abnormalities. Patients' age ranged from 22 to 77 years (mean age = 48). Reporting of the slides was done according to the 2014 Bethesda system and results were as follows: Atypical squamous cells of undetermined significance (ASC-US) was seen in 37 (15 %), atypical squamous cells that cannot exclude HSIL (ASC-H) in 13 (5 %), low grade squamous intraepithelial lesion (LSIL) in 43 (18 %), high grade squamous intraepithelial lesion (HSIL) in 37 (15 %), squamous cell carcinoma in 68 (28 %), Atypical glandular cells (AGC) in 33 (13 %) and adenocarcinoma in 16 (6 %) cases.
Conclusion: In our study, less than 1 % of all pap smears contained epithelial cell abnormalities. This could be explained by the low incidence of cervical cancer in our country. It has been shown that about two thirds of cervical cytology were for malignant and premalignant lesions and one third for undetermined lesions.

E-PS-07-012

Immunohistochemical features of endometrial carcinoma in Egyptian population: A pilot study

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Objective: We investigated the expression of ER, PR, Her2/neu, Ki67 in 38 cases of endometrial carcinomas (EC) from Egyptian patients to evaluate the correlation with histopathologic features, in an attempt to sub classify endometrial carcinoma based on molecular parameters.

Method: Immunohistochemical (IHC) study of ER, PR, Her2/neu and Ki67 was performed on hysterectomy specimen of 38 patients diagnosed with EC between January 2004 and December 2007.
Results: ER was detected in 45 % of cases and significantly associated with old age, absence of necrosis and absence of associated hyperplasia (P = 0.022, 0.012 and 0.034, respectively). PR positivity was determined in 58 % of cases and was significantly associated with old age, infiltrative pattern of invasion and cervical invasion (P = 0.031, 0.037 and 0.026 respectively). Her2/neu was expressed in 5 % of cases. Low expression of Ki67 was encountered in 37 % of cases while 63 % exhibited high Ki67 labelling index. PR and ER expressions in endometrial carcinoma cases were significantly correlated (P = 0.005). On the other hand, neither PR nor ER expression was significantly associated with Her2/neu or Ki67 expression in endometrial carcinoma.
Conclusion: Immunohistochemical markers should be thoroughly investigated and considered as reliable parameters in the selection of hormonal or targeted therapy for endometrial carcinoma.

E-PS-07-013
A clinicopathological study of ovarian high-grade serous carcinomas
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Objective: Carcinogenic pathways in ovarian high-grade serous carcinomas are a problem of debate in gynecological pathology. We intended a contributive study to the panel of information for this malignant tumour.
Method: We performed a 5-year retrospective study of 85 ovarian high-grade serous carcinomas registered at Victor Babes National Institute of Pathology. We analyzed patients' age, clinical history, histopathological features and immunohistochemistry expression for WT1, p53, ER, PR, Ki67, VIM, CK7, CK20, CEA, VIM, CA125.
Results: The mean age of patients was 58 years old. 4 patients had bilateral tumours and 6 presented with extrapelvic peritoneal extension. Positivity for WT1 was focal in 6 cases of 77 (8 %) and diffuse for the rest; p53 wild pattern expression was noticed in 12 of 27cases (44 %); PR was positive in 30 of 51 cases (59 %); Ki67 > 60 % was observed in 24 of 60 cases (40 %); VIM was positive in 7 of 21 cases (33 %). We had one case of CK7 negative and two cases of CEA focally positive.
Conclusion: We found higher percentages of p53 expression of wild pattern type (not associated with TP53 mutation) and PR positivity than other data in the literature. Our study emphasizes the high variability of this type of malignancy and that further studies are still necessary in understanding its biology and molecular mechanisms.

E-PS-07-014
Bilateral high-grade serous carcinoma of the fallopian tube: Case report
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Objective: We report the case of a 47 year-old woman with bilateral tubal high-grade serous carcinoma forming large intraluminal masses associated with serous intraepithelial lesions which is a rare finding in pathology practice.
Method: The patient previously diagnosed with HSIL, presented with normocytic anemia and abnormal vaginal bleeding and discharge and underwent total hysterectomy with bilateral adnexectomy. Both fallopian tubes were dilated at their fimbriated end (maximum 7 cm in diameter) and were intraoperatively mistaken for hematosalpinx. Histopathological examination and immunohistochemistry tests were performed.
Results: Histopathological examination revealed bilateral intraluminal masses with parietal invasion and serous tubal intraepithelial lesions consistent with primary bilateral tubal high-grade serous carcinoma with extension to the ovaries (pT2a), intramural uterine leiomyoma, HSIL of the uterine cervix. Immunohistochemistry results of the tumour specimen: WT1 positive, p53 moderate nuclear expression in 40 % tumour cell nuclei, ER positive 20 %, PR negative, AR negative, CD44 patchy positive and predominant in cells at the subepithelial invasion front, Ki67 proliferation index of 50 %.
Conclusion: Diagnosis of primary high-grade serous carcinoma of the fallopian tube can be challenging especially when ovarian involvement is present. Thus, careful examination in search of evident invasion from intraluminal mass and associated tubal intraepithelial neoplasia or carcinoma is necessary for making the correct statement.

E-PS-07-015
Impact of light/dark cycle alteration on circadian antioxidant pattern in female Wistar rat ovary
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Objective: Effects of photoperiodism alteration on reproductive cycle have become widely reecognized, involving a distinct oxidative damage. Oxidative stress, based on the excessive production of reactive oxygen species, alters the ovulation and the ovarian integrity. Our study defines the relationship between the extent of the oxidative stress and its impact on ovarian histomorphology in rats as a result of light/ dark cycle alteration.
Method: Female Wistar rats aged 7 weeks were randomly divided in two groups, a control group kept under conditions of controlled temperature (22–24 °C) and a 12:24 light/dark cycle and an experimental group, maintained on a continuous light exposure during the whole experiment. Appropriate markers were chosen in order to analyse the extent of the oxidative stress(SOD, CAT, MDA); histopathological examination and immunohistochemistry study of monoclonal anti-8 Hydroxiguanosine antibody(8-OHdG) were realized to determine the ovarian oxidative impact.
Results: We identified a high ovarian 8-OHdG immunoexpression level, together with significant increased follicular atresia, alteration of follicular development stages, apoptotic and degenerative processes, inhibitory action on thecal cells and affected oocyte quality.
Conclusion: Light/dark cycle alteration is responsible for oxidative alteration in the rat ovary.

E-PS-07-017
Can PAX8 distinguish the metastasis of ovarian papillary serous carcinoma of other cell lines in ascitic fuild?
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Objective: Ovarian cancer is often diagnosed at stage of peritoneal seeding. Accurate diagnosis of peritoneal extension has paramount prognostic implication. Irritation of the peritoneum may lead to the presence of reactive mesothelial cells and make the diagnosis more difficult with metastatic ovarian cancer. PAX8 was found to be frequently expressed in primary epithelial ovarian carcinoma and increased the overall detection rate of metastatic ovarian carcinoma. The purpose of this study was to compare the immunostaining of PAX8 in malignant peritoneal effusion containing cells considered as coming from serous carcinoma of the ovary and the original tumour.
Method: Retrospective anti-Pax8 immunostaining of 27 specimens (16 tissue blocks, 9 cell blocks and 5 cytocentrifugation slides, destained and immunostained) was performed.
Results: . Detections rate of Pax8 was 100 % (16/16) of paraffin embedded serous carcinoma of the ovary, while detection rate in cell blocks and cytocentrifuge was 86 % (9/11).

Conclusion: We conclude that Pax8 is a useful, sensitive and specific marker of ovarian serous carcinoma but the rate of negative PAX8 questions its use in the differential diagnosis of malignant ascites. Cell blocks and/or supplementary cytocentrifuges slides should be systematically prepared in all cases of peritoneal effusion.

E-PS-07-018

Malignant inflammatory myofibroblastic tumour of the uterus: A case with unusual features and fatal outcome

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Objective: To describe a case of uterine inflammatory myofibroblastic tumour (IMT) with unusual histological features, aggressive clinical course and fatal outcome.
Method: A 61 year old woman presented with a 10 cm uterine mass and extensive extrauterine disease. The uterine tumour had a multinodular appearance with areas of necrosis. The tumour exhibited varied morphology with cellular areas of spindle cell proliferation in a myxoid stroma as well as sheets of highly pleomorphic epithelioid cells with vesicular nuclei, large nucleoli and abundant amphophilic to eosinophilic cytoplasm mimicking anaplastic large cell lymphoma. Tumour cell necrosis and frequent mitoses including, atypical mitotic figures were found. The tumour showed strong ALK expression by immunohistochemistry. Fluorescence in situ hybridization for ALK gene rearrangement was positive in the tumour. The patient died of disease within 3 months of presentation.
Conclusion: IMT of the female genital tract are rare and diagnostically challenging. These tumours are frequently under recognized and should be considered in the differential diagnosis of mesenchymal tumours of the female genital tract. It is critical to recognize these tumours especially the aggressive forms given the recent development of a novel ALK-targeted therapy, which may have a role in managing aggressive cases.

E-PS-07-019

Female adnexal tumour of wolffian probable origin two cases report and review of the literature

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Objective: fatwo is a rare usually benign tumour of presumptive wollfian origin that is characterized by a variety of epitheloide patterns simulating other pelvic tumours. it occurs mainly in the broad ligament. this tumour deserves to be well known because of its rarity that prompts to the confusion with other frequents tumours of a poor outcome.
Method: we report cases of two patients aged 51 and 45 yo who presented with a painful pelvic swelling. ultrasound study shows adnexal masses that located respectively on the right broad ligament and in the left ovary.
Results: the average size of tumours is 7 cm, they are firm with a solid and cystic appearance in the cut surface containing clear to hemorrhage fluid the tumour is well circumscribed and shows an admixture of different histological patterns of variably shaped bland cells that are positive for pan ck, ck7, ck19, vimentin, calretinine.
Conclusion: fatwos are rare benign tumours with a potential malignant behavior in some cases. it should be differentiated from other possibilities diagnosis with careful pathological and immunohistochemical examination. no standard therapeutic protocol and the role of adjuvant therapies is questionable after the surgery after which a carful fellow up of patients for long period is necessary.

E-PS-07-020

Bilateral dysgerminomas arising in gonadoblastomas in a 46XY karyotype phenotypic female

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Objective: To describe the incidental discovery of bilateral gonadal malignancy in a young female presenting with amenorrhea and to review the literature on these malignancies.
Method: An 18 year old female was being investigated for primary amenorrhea. Hormone analysis revealed high levels of leuteinizing hormone and follicle-stimulating hormone and low levels of oestradiol and progesterone. Ultrasound assessment showed bilateral atrophic ovaries. Menarch was induced with norethisterone but menstruation was irregular and ceased shortly after treatment withdrawal. Genetic analysis revealed a 46XY karyotype and hence, prophylactic bilateral salpingoöphorectomy was performed. Both ovaries had a speckled calcified cut surface and soft white nodules were visualised bilaterally. Histology showed an infiltrative dysgerminoma arising in a background calcified gonadoblastoma in both ovaries. The ovarian parenchyma was heavily calcified and no primordial follicle formation could be defined.
Results: The patient is well and is undergoing treatment with bleomycin-etoposide-cisplatin chemotherapy.
Conclusion: Bilateral dysgerminomas arising in gonadoblastomas are exceedingly rare malignancies and occur almost exclusively in cases of ovarian dysgensis, particularly in the presence of the gonadoblastoma locus-harbouring Y-chromosome. They carry an excellent prognosis if caught early and prophylactic oöphorectomy is suggested in such cases.

E-PS-07-022

Ovarian Sertoli-Leydig cell tumour with elevated AFP: A case report and review of literature

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Objective: Ovarian Sertoli-Leydig cell tumours are rare and usually are unilateral with a median age of less than 30 years at presentation. Functionally; they are classified into three groups based on hormonal secretions; Androgen, estrogen and no endocrine activity. Alpha fetoprotein is associated with germ cell neoplasms particularly yolk sac tumour.
Method: Here we present a case of a 27 year old female with huge left ovarian mass and mildly elevated Alpha Fetoprotein (AFP), diagnosed as intermediate to poorly differentiated Sertoli-Leydig cell tumour with minor germ cell component. AFP staining was negative in most of the tumour except in small glands in a single focus (2 × 1 mm) which was also positive for glypican-3 and SALL-4, thus representing a small focus of yolk sac tumour, the source of AFP.
Results: Review of literature revealed only 30 cases associated with elevated AFP. We suggest that cases of Sertoli-Leydig cell tumours with elevated AFP must be examined thoroughly with multiple levels for small foci of yolk sac tumour, which may be the source of AFP elevation.
Conclusion: We suggest that cases of Sertoli-Leydig cell tumours with elevated AFP must be examined thoroughly with multiple levels for small foci of yolk sac tumour, which may be the source of AFP elevation.

E-PS-07-023

Expression of Glut-1 in endometrial lesions: Analysis of 336 cases

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Objective: Glucose transporter-1 (Glut-1) is a membrane glycoprotein responsible for the regulation of glucose uptake. Increased expression of Glut-1 seems to be an important not only as a cell

adaptation mechanism against hypoxia, but also as a general feature of several malignant tumours.
Method: Immunohistochemical expression of Glut-1 was assessed in 336 endometrial lesions. Results were assessed semi-quantitatively by H-score method.
Results: We detected expression of Glut-1 in 174/183 endometrioid carcinomas, 29/29 serous carcinomas, 17/17 clear cell carcinomas, 11/16 hyperplastic polyps with atypias, 9/24 hyperplastic polyps without atypias, 13/16 hyperplasias with atypias, 5/11 hyperplasias without atypias, 15/15 secretory and 4/25 non secretory endometrium. Glut-1 expression was detected in various extents in all tumour types, with more common expression in poorly differentiated tumours.
Conclusion: Our study confirms high expression of Glut-1 not only in endometrioid carcinomas, but also in other carcinomas of endometrium. From the diagnostic point of view, Glut-1 expression can be used as a surrogate marker in differential diagnosis between hyperplasia with and without atypia. However, the specificity is relatively low.
Acknowledgement: This work was supported by Ministry of Health, Czech Republic (Project RVO 64165), by Charles University in Prague (Project PRVOUK-P27/LF1/1), and by OPPK (Research Laboratory of Tumour Diseases, CZ.2.16/3.1.00/24509).

E-PS-07-024
Androgen-secreting stromal luteoma of the ovary: Case report
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Objective: We present a case of androgen-secreting stromal luteoma of the ovary in a patient of 41 years old with clinical manifestations of virilization.
Results: 41 year old woman presenting 6 month of progressive virilization and amonorreha and high serum levels of testosterone. A left oophorectomy was performed making the diagnosis of a 1.8 cm Stromal Luteoma. After surgery the testosterone serum level decreased and virilization manifestations gradually disappear.
Conclusion: Steroid cell tumours account for 0.1 % of all ovarian neoplasms and 20 % of them correspond to benign stromal luteoma. An important feature of this tumour is its hormonal secretion and only 12 % are associated with androgenic manifestations. The microscopic examination of these tumours must include an exhaustive study to discard the presence of crystals of Reinke. It is important to not make an equivocal diagnosis of steroid cell tumour not otherwise specified which can have a malignant behavior and a worst prognosis, with presence of extraovarian disease in the momento of diagnosis in some cases. Histologically these lesions should be differentiated from pregnancy luteoma, clear cell carcinoma, hepatoid carcinoma, luteinized thecoma, and metastatic renal cell carcinoma and melanoma.

E-PS-07-025
Beta-catenin expression and effect on long-term survival in advanced epithelial ovarian cancer
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Objective: Classical factors as histomorphology, grade, International Federation of Gynecology and Obstetrics stage (FIGO stage) and residual tumour size have prognostic value in advanced epithelial ovarian carcinomas (AEOC). AEOCs have poor overall survival (OS), and early recurrence rate. Despite poor prognosis and advanced stage at time of diagnosis in particular cases long-term survival (LTS) was observed. We have studied how classical prognostic factors and molecular factors as β-catenin, E-cadherin, MiB-1, p53 predict long-term survival.
Method: The expression of β-catenin, E-cadherin, MiB-1, p53 proteins was determined immunohistochemically, with Tissue Microarray (TMA) technic. The effect of protein expressions and classical factors on overall survival was evaluated with Kaplan-Meier estimation and Cox proportional-hazards model.
Results: Residual tumour size as classical marker was observed as adverse independent prognostic factor for OS supporting previous observations ($p = 0.003$). Nuclear expression of β-catenin was observed as an independent favourable predictor for LTS ($p = 0.025$). Additionally strong correlation was found between nuclear β-catenin expression and sensitivity or re-induction of platinum therapy.
Conclusion: Nuclear β-catenin expression has significant correlation with LTS and has important role in platinum sensitivity. Moreover is supports the possibility of platinum re-induction in AEOC.

E-PS-07-026
IHC study in cervical cancer: Biomarkers VEGF and HIF-1
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Objective: Cervical cancer is one of the most common malignancies. Variables studied more often are: the stage (FIGO), nodal status and histology of the primary tumour. There are currently more interest in biomarkers able to predict the evolution of these tumours. Expressions of VEGF and HIF-1 are observed.
Method: Sample taken 115 women aged 22–89 years with cervical carcinoma in advanced stages (IIA IB2- VAT) being 51 % FIGO stage IIB. The immunohistochemical expression of VEGF and HIF-1α parameters could be performed in 111 patients assessing their cytoplasmic expression (VEGF) and nuclear (HIF-1α), classifying them as negative (less than 10 % positive cells), weak expression (<25 %), moderate (26-50 %) and diffuse (>50 %).
Results: VEGF expression was positive in 90.4 % with a slight predominance of diffuse expression (33 %). However HIF-1 was positive in 45 % and mostly with weak expression.
Conclusion: VEGF and HIF-1 are biomarkers related to angiogenesis and neovascularization and there are targeted therapies against them. Routine antibodies performed in tissues pretreatment provides pathways for response, survival and prognosis of patients with expression of these markers.

E-PS-07-027
Florid diffuse peritoneal decidual reaction (Deciduosis) mimicking carcinomatosis in a primigravida patient
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Objective: Decidual cell groups outside the endometrium are named ectopic decidua or deciduosis, this condition can be seen rarely on the peritoneum during laparotomy for a cesarean section for pregnancy. Deciduosis is a benign transient condition, most commonly localized in the ovary, cervix and uterine serosa while the peritoneal localization is rare. It generally has no clinical symptoms; it therefore requires no therapeutic intervention.
Method: A 30-year-old woman G1P0 asymptomatic underwent cesarean section at 39 weeks gestation. The laparotomy revealed greyish-yellow soft nodules on the parietal peritoneum. On histologic examination, the lesion was composed of large polygonal decidualized cells with abundant eosinophilic focally vacualated cytoplasm. The nuclei were regular with fine chromatin and inconspicuous nucleoli.
Results: Decidual cells showed immunoreactivity for vimentin, D-240 and progesterone receptor; CK EA1/EA3 (+ mesothelial cells). And negativity for: Calretinin, CK 5/6, S-100, HMB-45, EMA and CEA.
Conclusion: -Pregnancy-related peritoneal deciduosis develops as a result of metaplasia of subserosal stromal cells with the effect of the

progesterone hormone during pregnancy and it regresses within the 4–6 weeks duration after pregnancy with decidual involution. - Immunohistochemistry may help the differential diagnosis of peritoneal deciduosis where problems are experienced differentiating the case from malignant mesothelioma, metastatic carcinoma or melanoma.

E-PS-07-028

Cellular pseudosarcomatous fibroepithelial stromal polyp of the vulvovaginal region associated to invasive Squamous Cell Carcinoma (SCC)

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Objective: To describe a case of vulvovaginal cellular pseudosarcomatous fibroepithelial stromal polyp (CPFSP) associated to invasive squamous cell carcinoma in a post-menopausal woman.
Method: A 83-year-old woman presented with a 6 cm vulvovaginal polypoid mass that underwent biopsy, followed shortly by an "explosive" recurrence. A left vulvectomy was performed. To date neither recurrences nor metastasis have been detected.
Results: Histology revealed a polypoid ulcerated heterogeneous neoplasm. The stromal component consisted of a patternless, densely cellular, mitotically active proliferation of fusiform or stellated cells with markedly pleomorphic, hyperchromatic nuclei in a myxoid or variabily collagenized matrix with necrotic foci. Immunohistochemically these cells were positive for vimentin, actin and CD10 and negative for cytokeratins, EMA, CEA, estrogen and progesterone receptors, desmin, S100, CD34, CD31 and p16. Overexpression of p53 was observed. The epithelial component consisted of an infiltrating, moderately-differentiated, keratinising squamous cell carcinoma with in situ component.
Conclusion: Although concomitant hyperplastic-dysplastic changes of the epithelial surface have been described in CPFSP, to our knowledge an association with invasive carcinoma, that can lead to misdiagnosis of carcinosarcoma, has not been reported. A hypotetical relationship with overexpression of p53, not previously evaluated in these neoplasms, is considered.

E-PS-07-029

Chemotherapy-induced endometrial pathology: Mimicry of malignancy and viral endometritis

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Objective: Chemotherapy is a common type of preoperative neoadjuvant treatment and postoperative adjuvant or palliative therapy for many different types of malignancy. Certain chemotherapeutic agents can induce bizarre epithelial atypia that mimics malignancy. Unfamiliarity with these changes could potentially cause confusion with a neoplastic or infectious process. The endometrium is one of the few sites where chemotherapy-induced epithelial atypia has not been appreciated.
Method: We identified four patients with marked cytologic atypia of the endometrial glandular epithelium from the surgical pathology files of the Severance Hospital. The medical records of these patients were reviewed. All patients underwent hysteroscopic examination with endometrial curettage for investigation of vaginal bleeding. They had previously undergone chemotherapy for uterine cervical cancer (n = 1), rectal cancer (n = 2) and myelodysplastic syndrome (n = 1). The chemotherapy regimens included alkylating agents (busulfan, cyclophosphamide, ifosfamide, cisplatin and oxaliplatin), pyrimidine antagonists (capecitabine, decitabine and 5-fluorouracil), taxane (paclitaxel) and topoisomerase inhibitors (irinotecan and etoposide).
Results: Histopathologically, the atypical epithelial changes included marked nuclear enlargement and pleomorphism, degenerative-looking chromatin pattern, microvacuolation of abundant cytoplasm and preservation of nuclear/cytoplasmic ratio.
Conclusion: This study demonstrated that certain chemotherapeutic agents may cause bizarre, reactive atypia of the endometrial glandular epithelium. These changes should not be interpreted as neoplastic or infectious in nature. An awareness of prior exposure to cytotoxic agents, and a familiarity with the nature and distribution of these bizarre alterations is essential to avoiding misinterpretation of the morphologic features and preventing unnecessary treatment.

E-PS-07-030

Psammocarcinoma in peritoneal washing: A case report

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Objective: Psammocarcinoma is a rare form of serous carcinoma that can arise from the ovaries or peritoneum. It is characterized by massive psammoma body formation, invasion to surrounding structures and low grade cytologic features.
Method: We report a case of a 60- year- old hysterectomized woman who presented with ascites and raised CA-125 level. On microscopic examination, the cytologic findings in ThinPrep and cell-block of peritoneal washing were three-dimensional papillary columnar cell groups with low grade cytologic atypia and psammoma bodies. Immunohistochemically, the neoplastic cells were positive for WT-1, Estrogene, Ca-125, MOC-31, TAG-72, negative for Calretinin, D2-40, CDX2, TTF-1. After that, the paraffin blocks of the patient which was diagnosed as endosalpingiosis is re-evaluated in our pathology department.
Results: Histological examination of paraffin block revealed tumour with numerous psammoma bodies with occasional small epithelial clusters between psammoma bodies on the surface of both bilateral ovaries and fallopian tubes. Neoplastic epithelial cells showed mild-moderate cytological atypia.
Conclusion: Psammomatous calcification is associated with benign and malignant pathology in different organ system including the gynaecological tract. The condition should be considered in the differential diagnosis. Clinical behavior is similar to borderline serous tumours with a favorable prognosis.

E-PS-07-031

Comparison of Human Papillomavirus (HPV) detection in urine and cervical samples using high-risk HPV DNA testing in Northern Thailand

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Objective: To compare the detection of human papillomavirus (HPV) using high-risk HPV DNA testing in paired urine and cervical samples from women in Northern Thailand.
Method: Paired urine and cervical samples were collected during the follow-up of women who had a previous positive HPV test. HPV testing was performed using Cobas 4800 HPV test.
Results: Paired urine and cervical samples were obtained from 168 women. The rate of invalid testing was higher in urine samples than in cervical samples (26.8 versus 0.6 %, $p < 0.001$). Among 123 paired samples with valid test results, 24 were HPV-positive in both samples, 11 in cervical samples only, and 6 in urine samples only. Using HPV detection in cervical samples as a reference, the sensitivity of urine HPV testing was 68.9 %, specificity; 93.2 %, positive predictive value; 80.0 %, and negative predictive value; 88.1 %. In 24 HPV-positive paired samples, 22 (91.7 %) had concordant genotyping results provided by Cobas test.

Conclusion: HPV DNA testing in urine samples has a rather low sensitivity compared with that of cervical samples in this study. Standardization of specimen collection and processing techniques or application of a more sensitive test may improve HPV detection in urine samples.

E-PS-07-032

Epithelioid trophoblastic tumour arising in the endometrioid cyst of the fallopian tube: A case report

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Objective: Epithelioid trophoblastic tumour (ETT) is a very rare tumour with a differentiation toward chorionic-type intermediate trophoblastic cells. The tumour originates mostly in the uterine corpus, lower uterine segment or cervix. Only about 20 cases arising in the extrauterine location have been reported so far.
Method: We report a case of a 31-year-old female with ETT arising in endometrioid cyst of the fallopian tube.
Results: A 31-year-old female underwent unilateral salpingectomy during a laparoscopic surgery for a suspicion of tubal endometriosis. Grossly, the fallopian tube was dilated with a cystic lesion in the wall. Histologically, the cystic formation consists of typical structures of endometrioid cyst with multiple foci of trophoblastic cells, which re-epithelialized the inner surface of the cyst.
Conclusion: Hereby we described the first case of ETT arising in endometrioid cyst, which was moreover located in the fallopian tube. We should be aware of the possibility of unusual primary locations of this rare tumour. The differential diagnosis includes the other trophoblastic tumours and lesions, epithelioid smooth muscle tumour and squamous cell carcinoma.
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E-PS-07-033

Mitotically active cellular fibroma of the ovary: A case report

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Objective: A fibroma is a benign stromal tumour composed of spindled to ovoid fibroblastic cells producing collagen. About 10 % of fibromas are densely cellular but exhibit no more than mild aytpia. These are referred to as cellular fibromas. In 2014 World Health Organization(WHO) histological classification, mitotic activity of >4 per 10HPF in an ovarian cellular fibromatous neoplasm in the absence of moderate to severe atypia is defined as mitotically active cellular fibroma(MACF).
Method: A 42-year-old women presented with adnexial mass. Unilateral salpingo-oophorectomy was performed, with a 11 × 9.5 × 8 cm mass being disclosed from the right ovary. Macroscopically, the tumour was firm, fibrous, well delimited, yellow-white without gross necrosis. Histologically, it was composed of a densely cellular proliferation of fibrolastic-like cells with bland nuclear features and arranged in a fascicular pattern. There was no significant atypia or necrosis. Mitotic index was 7/10HPFs. The spindle cells were positive for SMA while the kaldesmon was negative. Ki67 proliferative index of tumour was determined as 2 %.
Results: MACFs are in general associated with favorable outcome, but they may recur especially with rupture, adherence, or difficult dissection. Thus, long-term clinical follow-up is recommended.
Conclusion: MACF is a recent histopathologic entity and should be distinguished from ovarian fibrosarcoma.

E-PS-07-034

Primary Ewing sarcoma/peripheral primitive neuroectodermal tumour of the vulva: A case report

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Objective: Ewing sarcoma/primitive neuroectodermal tumours(ES/PNET) are high-grade malignant neoplasms that typically arise within the skeletal system. Primary extraskeletal ES/PNETs are uncommon and have been reported in various sites, the most frequent being the chest wall, lower extremities, and the paravertebral region. Few cases of primary vulvar of ES/PNET have been published before.
Method: A 27-year-old patient presented with 3 cm solid mass located on her right labium minus. The pathological evaluation revealed a malignant neoplasm with nodular growth pattern in a fibrous background. The cells had uniform round nuclei, coarse chromatin, inconspicuous nucleoli, and eosinophilic or clear scanty cytoplasm. The brisk mitotic activity and necrosis were observed. PAS staining showed cytoplasmic positivity in neoplastic cells. In the immunohistochemical analysis, the cells exhibited diffuse-positive membrane staining with CD99, vimentin, NSE, Bcl-2 while the HMB45, CK20, CK7, EMA, S100, TTF-1, LCA, TdT, desmin and myogenin were negative. We could not applied Fli-1. There was no tumour in other regions by whole-body scan. The patient did not receive any treatment.
Results: She is still alive with stable disease after 1 year of follow up.
Conclusion: Based on the literature, it appears that extraskeletalES/PNET arising in superficial sites such as the vulva have better prognosis.

E-PS-07-035

An audit of pathological and radiological correlation of myometrial invasion and histological features associated with lymph node metastasis in endometrial cancers

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Objective: An important prognostic factor for endometrial cancer is the degree of myometrial invasion. In the absence of deep myometrial invasion, lymph node metastasis is very low.
Method: The study included all cases of total hysterectomy with pelvic lymph node dissection performed between 01/01/10 and 31/12/2013 at Royal Surrey County Hospital. Histology data regarding the histological type, grade, depth of myometrial invasion, presence/ absence of lymphovascular invasion and lymph node metastasis, and stage of disease was obtained from Winpath database. Correlation was made with depth of invasion and lymphadenopathy documented in the radiology reports where available.
Results: Of the 98 cases analysed, 7(7.1 %) showed lymph node metastasis. Six out of seven (86 %) of the lymph node positive cases were grade 3 carcinomas involving outer half of the myometrium with lymphovascular invasion. Of the 47 cases (48 %) available for radiological correlation, 27 (57 %) showed concordance with regards to FIGO stage.
Conclusion: Lower grade endometrial cancers and those with no or less than 50 % myometrial invasions are unlikely to have lymph node metastasis. However, the best predictor of this pre-operatively is accurate staging of endometrial cancers on imaging. Further detailed evaluation is necessary to improve pathological-radiological concordance.

E-PS-07-036

Uterine arteriovenous malformation arising in a uterine stromomyoma

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Objective: While the true incidence remains undetermined, arteriovenous malformation (AVM) in the uterus is a rare entity that is potentially life-threatening from massive hemorrhage. Uterine AVM can be either congenital or acquired with the latter being more frequent and often preceded by uterine trauma including artificial abortions via dilatation and curettage, surgeries, cesarean delivery, trophoblastic diseases, endometrial and cervical carcinomas and infections. Patients with acquired AVM usually present with menorrhagia or menometrorrhagia following a miscarriage or recurrent pregnancy loss. Stromomyoma, also known as endometrial stromal tumour with smooth muscle cell differentiation, is another rare entity of the uterus. Uterine AVM associated with benign mesenchymal tumour is very rarely reported.
Conclusion: We report a 45-year old woman who was initially diagnosed with a 10 cm leiomyoma. She presented to the clinic for menorrhagia for 4 years. Dysmenorrhea accompanied the profuse menorrhagia. She had a parity of 2-0-2-2 with 2 natural abortions. Transvaginal ultrasound showed a 10 cm mass at the anterior wall of the uterus, and magnetic resonance imaging (MRI) showed the same mass with strong heterogeneous enhancement protruding from myometrium into uterine cavity suspicious of a submucosal leiomyoma Postoperative pathologic examination revealed AVM arising in a stromomyoma.

E-PS-07-037
Mullerian adenosarcoma: An uncommon case and review of the literature
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Objective: To describe an uncommon neoplasm of the uterine cavity, a Mullerian adenosarcoma with sarcomatous overgrowth and presence of heterologous elements. Review of the literature.
Method: A 31 year-old female consulted because of vaginal bleeding. Physical examination revealed blood clots and tissue fragments protruding from the external os, which were sent to pathological analysis. After the initial diagnosis the patient underwent hysterectomy with bilateral salpingo-oophorectomy.
Results: Gross examination showed a polypoid neoplasm with 2,4 × 1,2 cm, located in the uterine corpus. Microscopically, the tumour was biphasic with a benign epithelial component scattered among a malignant stromal component. The later showed typical periglandular cuffing and focal formation of polypoid fronds that projected into glands. The stromal component showed sarcomatous overgrowth with high grade features and presence of heterologous elements (rhabdomyoblasts).
Conclusion: This is an interesting case of Mullerian adenosarcoma, with unusual features. The most relevant adverse prognostic factors are deep myometrial invasion, sarcomatous overgrowth, malignant heterologous elements, high grade sarcomatous component and high mitotic index. Pathologists should be aware of this fact when reporting such tumours.

E-PS-07-038
Ectopic paratubal adrenal tissue associated with endometrial cancer: A series of 3 cases
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Objective: Heterotopic adrenal cortex is a rare entity usually discovered in male infants, around the kidney, retroperitoneum, spermatic cord or in the para-testicular area. There is little information about adults with ectopic adrenal glans in the scientific literature. Incidence in females is noticeably lower and occasionally identified in hysterectomy specimens.
Method: We report a series of 3 cases of postmenopausal females ages 66, 67 and 76 years, histopathologically diagnosed with endometrial cancer. All women presented with abnormal vaginal bleeding and underwent endometrial biopsy followed by radical hysterectomy with bilateral salpingo-oophorectomy and regional lymph node excision.
Results: A though histopathological analysis of the three hysterectomy specimens established the diagnoses of well and moderately differentiated endometrial endometrioid carcinoma, stages pT1bN0M0 and pT2N0M0 respectively, as well as carcinosarcoma of the uterine corpus, stage pT1cN0M0. Sections from the fallopian tubes of all three women revealed well encapsulated ectopic adrenal cortical rests of various sizes, located in the paratubal region.
Conclusion: We report this series of cases due to the rarity of ectopic adrenal tissue in females, its interesting presentation in association with unrelated gynaecological pathology, as well as its potential complications and possibility for malignant transformation.

E-PS-07-039
Distinctive features of the expression of aromatase cytochrome P-450 in ectopic endometrium during active and inactive adenomyosis
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Objective: To determine the features of the aromatase cytochrome P-450 (ACP-450) expression in ectopic endometrium during active and inactive adenomyosis.
Method: Biopsy material of 33 women with active (n = 22; average age 48,8 ± 1,02 years) and inactive adenomyosis (n = 15, average age 49,3 ± 0,85 years). IHC studies were conducted with the use of antibodies to ACP-450 (Abcam, 1: 200). Number of positive cells was counted in 5 fields of view at 400x magnification using Aperio ImageScope program. The program «Statistica 10.0» (U-test by Manny Whitman) was used for statistical processing of the results.
Results: The ACP-450 expression was revealed in the cytoplasm of epithelial glands of ectopic endometrium, cytogenetic stroma, in vascular endothelium, in the cytoplasm of myocytes. The expression level of ACP-450 is higher in active foci than inactive foci of adenomyosis ($p < 0,05$: positivity $p = 0.000$). During ROC-analysis excellent quality of the model was confirmed: the area under the ROC-curve was 0.9. The cut-off point between the groups—0.372, specificity of the method—80 %, sensitivity—75 %.
Conclusion: High level of the ACP-450 expression in active foci of adenomyosis ensures their growth through local hyperestrogenimia.

E-PS-07-040
The role of p16 immunohistochemistry in the diagnosis of pre-invasive cervical lesions and its applications in a low resource setting
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Objective: Cervical cancer is caused by the sexually transmitted Human Papilloma virus (HPV) which is the most common viral infection of the reproductive tract. Long standing infection with specific types of HPV (especially types 16 and 18) may lead to pre-invasive lesions. Recently, attention has been focused on p16 and Ki67 as biomarkers with potential utility in the identification pre-invasive cervical lesions.
Method: We assessed the application of p16 in the detection of pre-invasive cervical lesions on cervical samples seen in our department in 2012 and 2013.
Results: The age range of the subjects was from 24 to 76 years with a mean age of 42 years. The initial diagnosis were as follows: chronic nonspecific cervicitis:38.5 %, CIN1: 23.1 %, CIN2: 7.7 %, CIN3: 11.5 %, CIS: 7.7 %, moderate dysplasia: 3.8 % and normal cervix: 7.7 %. After p16 staining, 76.9 % were interpreted as negative for p16, atrophy 3.8 %, CIN1 7.7 %, CIN2 7.7 % and CIN3 3.8 %.

Conclusion: We conclude that p16 is of great importance especially in differentiating between reactive/chronically inflamed cervix and CIN and also in differentiating between the various stages of CIN. We propose that with the limited resources available, p16 staining should be done after peer review of cervical biopsies that are suspicious on H&E.

E-PS-07-041

Malignant mixed mullerian tumour: An aggressive ovarian tumour

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Objective: Malignant mixed mullerian tumours are a rare histologic subtype of ovarian cancer composed of an admixture of both malignant epithelial and mesenchymal elements. Its infrequency and aggressiveness make this subtype interesting to know.
Method: We report a case of a 59 year old woman, who presented with abdominal pain. The CT scan showed a solidocystic latero-uterine mass extended to the sigmoid. Histology combined to immunochemistry showed an admixture of malignant epithelial and stromal elements. The malignant epithelial element was a high grade endometroid carcinoma. The stromal component was a chondrosarcoma.
Results: Malignant mixed mullerian tumour is a rare histologic subtype diagnosed in 1–4 % of all ovarian cancer survivors. It is an aggressive tumour occurring in postmenopausal, often diagnosed in advanced stages. The clinical presentation is similar to ovarian epithelial tumours. On imaging, it is not possible to differentiate it from other ovarian neoplasms; therefore the diagnosis is essentially based on histopathologic findings. In addition to conventional histology, immunohistochemistry is an essential low cost ancillary technique in highlighting biphasic nature and areas of heterologous differentiation which may have a prognostic impact.
Conclusion: This case illustrates a rare tumour that should be distinguished from other forms of ovarian carcinomas because of its ominous prognosis.

E-PS-07-042

A lot of high grade serous carcinoma, a little bit of everything else: Findings from a series of 84 imaging-guided biopsies of mentum

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Objective: Imaging-guided omental biopsy(IGOB) is commonly used to diagnose advanced stage malignancy. Data on diagnostic findings in IGOB are scant and our impression is that primary site and subtype information is non-specific. As the specific diagnosis of extrauterine high grade serous carcinoma(HGSC) has therapeutic, prognostic and genetic implications, we particularly wished to establish the frequency of HGSC and thus potentially guide appropriate immunohistochemistry(IHC).
Method: 84 consecutive reports (In-house = 60, referral = 24) of malignant female IGOB (March 2013-December 2015) were retrieved and relevant data (clinical,IHC,diagnosis) collated.
Results: The pre-test probability(PTP) of HGSC in female IGOB was high with a final HGSC diagnosis in 57 cases(68 %), rising to 77 % in patients with no prior histologic diagnosis of malignancy. Historic or non-specific terminologies were common including; papillary serous carcinoma(18 %), ovarian adenocarcinoma(12 %). The remainder of diagnoses comprised a miscellany of primary sites, with gastrointestinal adenocarcinoma comprising 5 cases.
Conclusion: The majority of malignancies in female IGOB were HGSC with the frequency of this diagnosis being over 10-fold that of any other malignancy. Awareness of this finding may assist the general pathologist to avoid non-specific diagnoses and deploy a more targeted IHC panel ab initio (such as WT1, P53, PAX-8, P16) in the setting of a malignant IGOB.

E-PS-07-043

Primary extrauterine endometrial stromal sarcoma: Case report

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Objective: Extrauterine endometrial stromal sarcoma, also known as endometrioid stromal sarcoma, represents a rare occurrence, with less than 100 cases reported. This neoplasm is frequently associated with endometriosis and may involve the ovaries, fallopian tube, vagina, bowel wall, pelvic cavity, abdominal cavity and retroperitoneum.
Method: We present the case of a 65 years old woman with a large pelvic tumour, 113/72/60 mm and secondary grade IV ureterohydronephrosis. Fourteen years before the patient underwent hysterectomy for cervical squamous cell carcinoma followed by radiotherapy and the pelvic lesion was clinically considered tumour recurrence.
Results: Microscopic examination of the pelvic mass revealed a hypercellular diffuse and vague-fascicular proliferation of mildly atypical spindle cells with stromal arterioles, stromal hyalinization areas and cystic spaces. The tumour presented hypocellular areas towards the periphery. The tumour cells were positive for vimentin, CD10, WT1, CD56, synaptophisin, CD99 and desmin and negative for cytokeratins. A final diagnosis of high grade extrauterine endometrial stromal sarcoma was rendered.
Conclusion: The diagnosis of an extrauterine endometrial stromal sarcoma is challenging, requiring clinical-pathological correlations and exclusion of a primary uterine lesion, of other more frequent types of sarcoma and exclusion of sarcomatoid carcinoma.

E-PS-07-044

Pure large cell neuroendocrine carcinoma of the ovary: A case report

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Objective: We report a case of pure large cell neuroendocrine carcinoma of the ovary in 32-years old woman. Her past medical history includes juvenile granulosa cell tumour of the left ovary, she presented with a pelvic mass measuring 10 cm in diameter.
Method: the patient underwent an exploratory laparotomy for resection of the right palpable adnexal mass.
Results: Histologically, the tumour is composed of islands, nests and cords separated by a thin stroma. The cells are medium to large in size with hyperchromatic and nucleoli with numerous mitoses. Immunohistochemicaly, the tumour cells are positive for EMA, synaptophysin, chromogranin A and CD56, and negative for inhibin and calretinin.
Conclusion: Large cell neuroendocrine carcinoma (LCNEC) of the ovary is a rare and aggressive tumour, frequently associated with ovarian surface epithelial tumours. The prognosis of LCNECs is generally very poor even when the diagnosis is made at an early stage. Only 9 cases of pure large cells neuroendocrine carcinoma have been reported in the literature.

E-PS-07-045

A case of giant ovarian endometrioid adenofibroma of borderline malignancy

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Objective: Report clinicopathologic features of a rare case of giant ovarian endometrioid adenofibroma of borderline malignancy. Emphasize diagnostic criteria and difficulties of atypical proliferative ovarian endometrioid tumours.
Method: A 60-year-old woman presented with a voluminous left pelvic mass of 1 year duration. Computed tomodensitometry confirmed the presence of a solid and cystic pelvic mass, measuring 34 × 25 × 15cm.

On laparotomy, the mass was found to be of ovarian origin. A left salpingo-oophorectomy was performed.
Results: On gross examination, the ovary measured 38 × 38 × 20 cm and had a firm smooth surface. On cut section, it was solid and cystic. Microscopic examination of the tumour showed an adenofibromatous pattern. The epithelial component was made of mildly crowded glands that had focal moderate cytologic atypia and epithelial stratification. The stromal component was fibrotic, without cytonuclear atypia. On immunohistochemistry (IHC), the epithelial component was positive with CK7 and EMA. The tumour cells did not stain with CD10 and α-inhibin. A diagnosis of a borderline endometrioid tumour developed on an adenofibroma was retained.
Conclusion: Ovarian endometrioid adenofibroma of borderline malignancy is a rare tumour that often requires proper sampling and IHC for the correct diagnosis. Pathologists should be aware of this entity such as not to misdiagnose it as a malignant tumour.

E-PS-07-046
Ovarian fibroma associated to peritoneal tuberculosis mimicking advanced ovarian cancer: A case report
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Objective: To present the case of a patient who had an ovarian fibroma associated to peritoneal tuberculosis that was clinically misdiagnosed as an advanced ovarian cancer. To discuss means of differentiating peritoneal tuberculosis from advanced ovarian cancer in light of literature data.
Method: A 65-year-old woman presented with progressive abdominal distension. Abdominopelvic MRI showed an ovarian heterogeneous mass suspicious for malignancy. The patient underwent exploratory laparotomy, a 10 cm ovarian tumour was found, with peritoneal seedings that were misdiagnosed as carcinomatosis. A bilateral salpingo-oophorectomy was performed.
Results: On gross examination, the right ovary measured 10,5 × 8 × 5 cm, had a firm consistency, a whitish cut surface with myxoid change. There was miliary seedings scattered over the surfaces of the two ovaries and fallopian tubes. Histologic examination showed a spindle cell proliferation on the right ovary, morphologically consistent with an ovarian fibroma. This was associated to extensive granulomatous inflammation with epithelioid cells and typical multinucleated giant cells of Langhans type,involving bilateral adnexa. The diagnosis of an ovarian fibroma associated to peritoneal tuberculosis was made.
Conclusion: The treatment of peritoneal tuberculosis is based on medical therapy, it is therefore important to take tuberculosis into account when treating women with massive ascites and adnexal tumours in order to avoid unnecessary extensive surgery. We suggest exploratory laparotomy and intraoperative frozen pathology for the diagnosis of pelvic tuberculosis.

E-PS-07-049
A rare type of endometrial carcinoma: Glassy cell carcinoma
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Objective: Glassy cell carcinoma (GCC) was first described in the uterine cervix. Although uterine cervix is the most frequent site for this tumour, less than 1 % of cervical tumours are GCCs. Also, it has been described in endometrium, fallopian tubes, vagina, and colon. The incidence of GCC is extremely rare, only 14 cases have been reported in the English literature.
Method: A 63-year-old woman, referred to gynecology clinic due to postmenopausal vaginal bleeding. After the diagnostic curettage, surgical staging has been performed. Macroscopic examination of the endometrial cavity showed no prominent residual mass, except for focal irregular areas. Right ovarian cut surface showed nodular solid area that was suspicious for metastasis. Only one right pelvic lymph node was invaded by tumour. Other organs were unremarkable.
Results: Microscopic examination of endometrial curettage, focal tumour limited to the endometrium, ovary, and lymph node revealed solid irregular nests of large pleomorphic cells with moderate to abundant finely granular cytoplasm. Tumour cells nests were separated by fibrovascular septa with dense inflammatory background composed predominantly of plasma cells with an admixture of neutrophils, eosinophils and lymphocytes.
Conclusion: Although cervical GCC has poor prognosis, the prognosis of its endometrial counterpart is unknown. But it seems to have an aggressive behavior.

E-PS-07-050
Incidental lymphangioleiomyomatosis in staging pelvic lymphadenectomy
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Objective: Lymphangioleiomyomatosis is a rare progressive disease that tends to affect young women of child-bearing age and is characterized by cystic destruction of the lung due to the proliferation of smooth muscle cells. Extrapulmonary lymphangioleiomyomatosis may or may not be associated with pulmonary lymphangioleiomyomatosis and/or tuberous sclerosis complex. Here we present a case of lymph node lymphangioleiomyomatosis detected incidentally during surgical staging of ovary carcinoma, not associated with pulmonary lymphangioleiomyomatosis or tuberous sclerosis.
Method: A 51 year-old woman diagnosed with endometrioid carcinoma of the ovary underwent an elective pelvic and paraaortic lymph node dissection.
Results: As an incidental histological finding, some lymph nodes revealed a proliferation of myoid-appearing spindle cells arranged in intersecting fascicles disposed around irregular vascular spaces lined by flattened endothelial cells. No cellular atypia or mitotic activity was observed. Inmunohistochemistry revealed that cells showed expression for smooth muscle actin, desmin, focally for HMB-45, MITF, estrogen receptors and the D2-40 staining highlighted the endothelial cells revealing lymphatic vascular nature.
Conclusion: Clinically occult lymphangioleiomyomatosis can be detected during surgical staging of pelvic cancer and is not commonly associated with pulmonary lymphangioleiomyomatosis or tuberous sclerosis complex, although these patients should still be formally evaluated for both of these diseases.

E-PS-07-051
Hyperreactio luteinalis: An often mistaken diagnosis
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Objective: Hyperreactio luteinalis is a rare condition in which there is massive cystic enlargement of the ovaries mimicking malignancy during pregnancy. When confronted with this condition, the fear of missing a cancer diagnosis often leads the physician to react with unnecessary surgical intervention, potentially resulting in impaired future fertility. The purpose of this study is to emphasize the importance of recognizing the clinicopathological features of this tumour.
Method: We report two cases with hyperreactio luteinalis. Clinical data and microscopic slides were reviewed.
Results: They were two women aged 33 years old. The first patient presented at 39 weeks of gestation in labour and underwent

a caesarean section. In a systematic exploration of the annexes, bilateral, enlarged cystic ovaries were seen. The cysts were thin-walled and without vegetations. Ovarian biopsy was performed showing cysts with regular luteinized cells within the wall and no histological evidence of malignancy, consisting with a diagnosis of hyperreactio luteinalis. In the second case, a left ovary cyst was fortuitously discovered during the first quarter ultrasound. Conservative treatment was done in the two cases.
Conclusion: Management of hyperreactio luteinalis must be conservative and continued education of health care professionals who may encounter this entity is vital.

E-PS-07-054
Endometrial stromal nodule of vagina: An extremely rare case
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Objective: A 27-year-old nulliparous patient consulted for vulvo-vajinal pain, bleeding and dysuria. On physical examination a soft bleeding mass filling the distal posterior vaginal wall was detected. Computerized tomography results showed a heterogenous mass of 15 × 13 × 10 cm which contain necrotic and cystic foci that is indistinguishable from the isthmus and cervix uteri. The patient underwent total abdominal hysterectomy and partial vaginectomy.
Method: On gross examination, the mass composed of solid, necrotic and cystic areas. Microscopically the vaginal epithelium lined the external circumference of the nodule which composed of endometrial stromal cells. Mitotic activity was low and neither stromal nor lymphovascular invasion were detected.
Results: İmmunohistochemistry showed diffuse CD10 positivity by tumour cells. Desmin and caldesmon were negative.
Conclusion: ESTs are usually uterin and myometrial lesions which can be intramural, subserozal and submucosal. Vagina is a very rare location for ESTs. Diagnosis can be quite difficult especially in curettage speciments.

E-PS-07-055
Morphologic assessment of different endometrial components reactivity in an experimental endometriosis
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Objective: Experimental models of endometriosis successfully reproduce human pathology, offering basic support in deciphering the particular dynamics of its components. This study focused on the surgical induction of endometriosis in rats by autotransplantation of uterine fragment in the abdominal wall, followed by a morphologic evaluation of changes that occur in responsiveness of vascular, glandular and stromal components of endometrial implant.
Method: Endometriosis was surgically induced in Wistar female rats by suturing distal uterine horn autoimplants to the abdominal wall. After 60 days, the implants were prelevated together with fragments of normal uterine horn, paraffin embedding, H&E staining and examined under Nikon Eclipse 50i light microscope, for the description of the endometrial status.
Results: Inflammatory areas were absent and the glandular proliferative processes were abundant, with no specific sensitivity endometrial variations. Angiogenic processes were detected together with some stromal proliferation.
Conclusion: There were no significant differences between the autotransplanted and control endometrium, supporting the use of such experimental models in approaching the unsolved aspects of endometriosis.

E-PS-07-056
Immunohistochemical expression of estrogene, progesterone receptors, CerbB2 and BRCA1 in ovarian carcinoma and their prognostic value
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Objective: Ovarian cancer is the most sixth common cancer in women. In gynecologic cancers, it is the second most cancer after endometrial cancer and the most lethal cancer. FIGO stage, residue tumour after surgery, patient's age, histological type, grade, capsule rupture, peritoneal washing status are the prognostic factors. The aim of this study is to investigate estrogene, receptor(ER) progesterone receptor(PR), CerbB2, p53 and BRCA1 expressions and determine its prognostic value in ovarian cancer.
Method: The study population was comprised 85 patients with epithelial ovarian cancer who are diagnosed between 2002 and 2012. Immunohistochemical expression of ER, PR, CerbB2, P53 and BRCA1 and their relationship with clinicopathological parameters were evaluated.
Results: In serous carcinomas (SC), there were significant correlations between ER expression with metastasis to fallopian tube, PR expression with patient's age, p53 expression with progression free survey (PFS) and cytoplasmic expression of BRCA1 with overall survey (OS) and PFS. There were significant differences with ER, PR and p53 expressions between type 1 and 2 tumours. In our study, PR and p53 were prognostic factors in SC.
Conclusion: Large studies that contain more cases in each histological group are needed to determine the prognostic value of these five immunohistochemical markers.

E-PS-07-057
Tumour-to-tumour metastasis: Unexpected diagnosis to an expecting woman
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Objective: Krukenberg tumour is a rare form of metastatic gastric signet-ring cell carcinoma. Thecomas rarely occur during pregnancy and represent approximately 1 % of all ovarian tumours. The phenomenon of tumour-to-tumour metastasis has been described in roughly 100 cases and, to the best of our knowledge, thecoma have never been reported as receiving tumour. We present a unique case of gastric signet-ring cell carcinoma metastatic to a luteinized thecoma in a pregnant woman.
Method: During a routine ultrasound to a 28 year-old pregnant woman, on the 13th gestational week, an ovarian tumour was incidentally discovered; oophorectomy was performed.
Results: Grossly, the ovary was 14 × 10.7 × 5 cm and 462.1 g, with a white, lobulated cut surface, cystic and fasciculate areas. Histologically, the bulk of the tumour was composed of uniform cells, with pale cytoplasm and round to oval nuclei, without atypia; infiltrating signet-ring cells were detected, exhibiting a characteristic immunostaining pattern of gastro-intestinal origin. A Krukenberg tumour on a luteinized thecoma was diagnosed; gastric biopsy confirmed the diagnosis of poorly cohesive carcinoma of signet-ring cell type.
Conclusion: Tumour-to-tumour metastasis is a rare event; nevertheless, we should bear it in mind as it can explain the presence of an unusual cytological pattern in a specific tumour.

E-PS-07-059
Correlation of visual inspection with cytological and histopathological findings in cervical neoplasia
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Objective: To evaluate the diagnostic value of Papanicolaou (PAP) smear and visual inspection with acetic acid (VIA) as methods of cervical cancer screening.
Method: The study population consisted of women with histologically confirmed cervical intraepithelial neoplasia or invasive carcinoma who had undergone prior PAP smear.
Results: During the study period 160 patients underwent both PAP smear and cervical biopsy. Of these patients, 49 had a histological diagnosis of cervical intraepithelial neoplasia or invasive carcinoma. The histopathological and cytological diagnoses were compared. VIA status was available for 31 of the 49 cases. The sensitivity of PAP smear was 61 %, specificity 97 %, positive predictive value (PPV) 91 %, negative predictive value (NPV) 85 % and diagnostic accuracy 86 % in detection of cervical neoplasia. VIA had a sensitivity of 74 %, specificity 48 %, PPV 64 %, NPV 60 % and diagnostic accuracy of 63 %. Combining the two procedures increased sensitivity by 26 %, NPV by 11 % and diagnostic accuracy by 2 %.
Conclusion: PAP smear has a higher specificity, PPV, NPV and diagnostic accuracy but lower sensitivity than VIA. VIA by itself is not an effective screening method. A combination of PAP smear and VIA can ensure adequate screening of cervical neoplasia.

E-PS-07-061
Neoplasms arising in endometriosis. Frequency and comparison of ovarian and extraovarian types
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Objective: Evaluation of the frequency and types of neoplasms associated with endometriosis in and outside the ovary from a 15 year review of a medium size Hospital Pathology Department.
Method: 768 histological diagnosis of endometriosis were identified in the files of the Department of Pathology of Parc Tauli University Hospital, between 1999 and 2015. Data collected included the location of endometriosis, the presence of an associated neoplasia, the histological type and their anatomical relation. Sampson and Scott criteria were applied.
Results: 523 (68%) of endometriotic foci were located in ovaries, 160 (21%) were extraovarian and 85 (11%) affected ovary and extraovarian sites. 27 tumours were recorded: 12 endometrioid (EC), 7 clear cell (CCC) carcinomas, 2 adenosarcomas (AS), one with sarcomatous overgrowth, 1 endometrioid stromal sarcoma (ESS), 2 seromucinous borderline (BDRL), 2 clear cell BDRL and 1 serous BDRL tumours; representing 3,5% of endometriosis. CCC cell and EC were the malignancies most commonly seen in ovaries containing endometriosis (17/21), while all AS and ESS were seen in conjunction with extraovarian endometriosis (3/6 extraovarian neoplasms).
Conclusion: Several types of neoplasms can exhibit an association with endometriosis, stronger in CCC and EC, with a selected anatomical distribution.

E-PS-07-062
Mature cystic teratomas: A clinicopathologic evaluation of 225 cases
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Objective: To study the clinicopathologic behavior of mature cystic teratomas (MCT).
Method: We conducted a retrospective study on a series of cases of MCT from April 2011-March 2016. Patient data were obtained and histology reviewed at Department of Pathology, Patan hospital, Lalitpur, Nepal.
Results: MCT comprised 225 (56.1 %) out of total 399 cases of ovarian neoplasms. Bilaterality was noted in 9.8 % of the patients. The age range of patients was 8–74 years and majority (82, 36.4 %) were in age group of 21–30 years. The size of tumours ranged from 3.5 to 20 cm. Ischemic modifications, presumably due to torsion, were noted in 10.2 % of cases, mostly in tumours larger than 10 cm. None of the tumours of less than 5 cm presented with signs of torsion. Malignant transformation was present in 7 (3.1 %) cases and was seen especially in older patients and in larger tumours. Squamous cell carcinoma was the most common malignant tumour (5 cases). One case was a mixed germ cell tumour with components of MCT and yolk sac tumour.
Conclusion: MCT is the most common germ cell tumour in patients of reproductive age group. Complications such as torsion and malignant transformation occur mostly in larger tumours.

E-PS-07-065
Pathological evaluation in autologous ovarian tissue transplantation for fertility preservation in cancer patients
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Objective: As ovarian tissue cryopreservation (OTCP) has proved to be a successful method for fertility preservation, the need for pathological evaluation of ovarian tissue in cancer patients prior to autologous transplantation has emerged. Our objective was to establish a structured methodology for histopathological evaluation prior to autologous ovarian transplantation in cancer patients.
Method: A single team was responsible for a collaborative work between the Pathology Department, the Fertility Preservation Center, IVF unit, Obstetrics and Gynecology Division and the Cancer Research Center at the Sheba Medical Center. Herein we describe our experience in pathological assessment of ovarian tissue performed on samples from patients with varied background malignancies as part of fertility preservation procedure by OTCP and autologous transplantation.
Results: We have established guidelines for the evaluation of ovarian tissue prior to autologous transplantation that rely on histomorphological evaluation assisted by immunohistochemistry and fluorescence in-situ hybridization (FISH). In isolated cases tumour-specific molecular markers were sought using PCR.
Conclusion: A tight collaboration between the pathologist and the fertility preservation unit is vital for the accurate assessment of ovaries prior to their transplantation. Adherence to the established guidelines may reduce the risks for the patients and increase the success rate of the procedure.

E-PS-07-066
Leiomyoadenomatoid tumour of the uterus report of a rare entity and review of the literature
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Objective: Leiomyoadenomatoid tumour of the uterus is a variant of adenomatoid tumour which is extremely rare and may be difficult to recognize on microscopic examination. We reviewed the histopathological features of this rare entity and we discuss its differential diagnosis.
Method: The morphologic and immunohistochemical findings of a leiomyoadenomatoid tumour located in the uterine wall are reported with a review of the related literature.
Results: A 37-year-old woman presented with vaginal bleeding during the past 6 months. Pelvic ultrasonography revealed three masses in the myometrium. Laparoscopy transvaginal masses removal was performed under the clinical impression of uterine leiomyomas. Histological examination followed by immunohistochemistry straightened the diagnosis of leiomyoma in 1 mass and confirmed the presence of a biphasic proliferation: an adenomatoid component, which was immunoreactive with calretinin, intermingled with interlacing fascicles of neoplastic muscle

cells. The diagnosis of leiomyoadenomatoid tumour along with two leiomyomas was made. The outcome was favorable without any complications at the 4 months follow up evaluation.
Conclusion: Here in we report the tenth case of leiomyoadenomatoid tumour of the uterus. Ignorance of this rare entity may lead to false diagnoses, such as a malignant epithelial or mesothelial neoplasm, resulting in a more aggressive therapy.

E-PS-07-068
Sex cord tumour with annular tubules: About 4 cases with a literature review of 166 cases
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Objective: We studied, through a systematic review of the literature, the clinical, radiological, and pathological particularities of Sex cord tumour with annular tubules (SCTAT).
Method: Our work has focused on four cases of SCTAT collected at our department with a systematic review of the literature.
Results: The average age was 30 years, ranging from 4 to 76 years. It was associated with Peuz-Jeghers syndrome (PJS) in 1/3 of cases. The age of our patients ranged from 10 to 32 years. One of our patients had a concomitant diagnosis of PJS. The tumour was unilateral in all cases, and was revealed by precocious puberty in one case. Gross findings, showed a solid tumour, with yellow cut surface. The size ranged from 0,5 to 28 cm. The morphological features were characteristic but intermediate between granulosa and sertoli cells. Immunohistochemistry showed that tumour cells expressed inhibin and claretinin. The treatment was surgical, often conservative. The diagnosis of malignancy wasn't focused on histological features, but on tumour extension, clinical course, and presence of metastases.
Conclusion: SCTAT is a rare tumour, usually benign. Its diagnosis is based on histological examination. Malignant potential is noted in sporadic forms. Treatment is most often conservative, based on oophorectomy.

E-PS-07-069
A preliminary study evaluating the survival of patients with locally advanced cervical cancer
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Objective: The objective of this study was to evaluated the survival in locally advanced cervical cancer (LACC) with metastatic lymph nodes. To which we considered the size of nodules and their location.
Method: From 2006 to 2016, 36 patients with stages IIA-IVA cervical cancer had metastatic adenopathies and were underwent pretherapeutic laparoscopic staging procedure including abdomino-pelvic exploration and pelvic-paraaortic lymphadenectomy. These patients were treated with chemoradiotherapy.
Results: The median age was 51.83 years old. Most lesions were squamous (n = 26) having a better prognosis than the ones with adenocarcinoma. Clinical stage was evenly distributed. The pathology results revealed that 12(33.3 %) patients had metastatic paraaortic(PA) lymph nodes and all of them measured were >5 mm. The 24 remaining patients were found to have metastatic pelvic nodes ($6 \leq 5$ and $18 > 5$ mm). Event-free survival rates in patients without PA involvement and with PA metastasis were 85,38 %(SE9,68 %) and 46,64 %(SE15,64 %); $P < 0,05$. With a median follow-up of 23 months (average39.36), 13(36.1 %) patients had recurrent disease and died.
Conclusion: Pretherapeutic laparoscopic assessment of patients with LACC offers valuable information for individualized treatment planning. Moreover the survival of patients with PA nodal involvement greater than 5 mm remained poor. More studies are needed including patients with laparoscopic staging surgery without metastatic nodes for future results.

E-PS-07-070
A uterine collision tumour or mixed Mullerian tumour
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Objective: Most uterine carcinosarcoma are monoclonal with the carcinomatous component being the driving force. However, it is also apparent that a small proportion of these neoplasms are true collision tumours, consisting of independent unrelated carcinomas and sarcomas.
Method: We presented a case of a 75 year's old woman who came in our institution with vaginal bleeding. An endometrial curettage was performed.
Results: On microscopic examination correlated with immunohistochemistry a diagnosis of high grade stromal sarcoma was made. On CT we found a voluminous uterine tumour with both neoplastic ovary and lymph node metastasis on pelvicaorta. Total hysterectomy and bilateral adnexectomy was performed. On gross examination we observed a well delineated mass, white, with the following dimensions of 10/10/9 cm; bilateral ovarian mass, white-grey, firm consistency with necrotic areas. On microscopic examination we revealed a high-grade uterine stromal sarcoma and bilateral ovarian high-grade serous carcinoma with lymph node carcinomatous metastases.
Conclusion: A small proportion of uterine carcinosarcomas are true collision tumours and this is important because the prognosis can sometimes be better than in a similar stage carcinosarcoma. Further investigations are required.

E-PS-07-071
Expression of beta-catenin in Müllerian adenosarcoma of the Uterine Cervix
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Objective: Müllerian adenosarcoma is an uncommon neoplasm of female genital tract composed of a malignant stromal component and a relatively benign glandular element, producing an architecture resembling mammary phyllodes tumour. The pathogenesis of this rare neoplasm however has not yet been well clarified. The purpose of this study is to determine whether dysregulation of Wnt-β-catenin signaling pathway, which plays a critical role in the oncogenesis of mammary phyllodes tumour, has also contribution in the development of this gynecologic neoplasia.
Method: Immunohistochemical analysis of stromal β-catenin expression was performed on five Müllerian adenosarcomas of the cervix and three endocervical polyps. The expression was further divided into the membranous, cytoplasmic, or nuclear activity and was graded as a total score 0 to 5 (membranous (negative: 0, positive: 1)), cytoplasmic (negative: 0, focal: 1, diffuse: 2)) and nuclear (negative: 0, <5 % of cells: 1, >5 % of cells: 2)).
Results: All cases of adenosarcoma revealed diffuse membranous and cytoplasimic staining and focal nuclear reactivity of β-catenin in the stroma (score 4), comparing to the weaker staining in the endocervical polyps (score 2).
Conclusion: The Wnt-β-catenin pathway may be associated with the proliferation of stromal cells in the Müllerian adenosarcomas of the uterine cervix.

E-PS-07-072
Myoepithelial carcinoma of the breast: A rare neoplasm
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Objective: We aim to discuss the histological criteria of breast myoepithelioma (MM) and to emphasize diagnostic difficulties.
Method: We describe a rare case of breast malignant myoepithelioma in a 45-year-old woman.
Results: The patient was admitted because of a huge, rapidly enlarging tumour in the left breast. She had a history of tumourectomy for an adenomyoepithelioma of the same breast. A mastectomy with axillary lymph node dissection was performed. Grossly, the resected breast showed a huge white solid tumour measuring 17 cm in its greatest diameter, which took up almost all of the breast tissue. Histologically, the tumour was composed of spindle shaped, pleomorphic and atypical cells. There were many mitotic figures and several areas of necrosis. Invasion into the skin and adipose tissue was recognized. Immunohistochemically, the tumour cells were diffusely and strongly positive for vimentin. P63 was positive indicating a myoepithelial cell lineage of tumour cells. Pancytokeratine and EMA were focally expressed. The tumour was negative was triple negative. Ki 67 was higher than 99 %. The lesion was diagnosed as a malignant myoepithelioma.
Conclusion: Myoepithelial carcinomas are extremely rare lesions of the breast. Their diagnosis is difficult but crucial as it determines the overall treatment and prognosis.

E-PS-07-073
Cervical cancer incidence, demographic and pathological characteristics in Bosnia and Herzegovina
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Objective: Cervical cancer represents a significant cause of morbidity and mortality in less developed countries, and is closely associated with HPV infection. Data about cervical cancer status in Bosnia-Herzegovina (BH) are scarce and inconsistent. We report the epidemiology, clinical and pathological characteristics of cervical cancer in a representative population of BH.
Method: Medical records from year 2014 were searched for cervical cancer cases. Demographic and pathological characteristics were recorded. Epidemiological data were approximated based on the accurate population number covered by our institution.
Results: There were 64 new cases in 2014, per 438,000 population (crude incidence rate 14.6/100,000). The average age was 58.4 years (range, 27–74). The most affected group were women age <40 years (40 %), age 51–60 (31 %), and 41–50 (20 %). The most frequent histotype was squamous cell carcinoma (91 %), followed by adenocarcinoma (5.5 %), and adenosquamous carcinoma (3.5 %). Most of the tumours were grade 1 (49 %) and grade 2 (40 %). Tumours were at stage pT1 (83 %), pT2 (14 %), and pT4 (3 %).
Conclusion: Cervical cancer incidence in BH is higher than incidence reported in Southern-Europe (8.5/100,000), and is closer to Central-Eastern Europe (16.3/100,000). Lack of screening program and public health strategy is the main reason for higher HPV prevalence in this population.

E-PS-07-074
Adenomatoid tumours of female genital system: Not always incidental: Report of 11 cases
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Objective: Adenomatoid tumours (AT) are uncommon benign mesothelial tumours with a predilection for the genital tract.
Method: We retrospectively analysed adenomatoid tumours of female genital system diagnosed in our hospital, from January 2010 to December 2015.
Results: There were 11 cases of AT; 7 were uterine and 4 were tuboovarian in origin. The median age of the 7 patients with uterine ATs was 46 years. The 6 of uterine adenomatoid tumours were incidental findings in resection specimens. One case was preoperatively diagnosed as a cystic pelvic mass. Uterine ATs had a median size of 5.7 cm (range, 1.3-23 cm). Six tumours presented grossly as circumscribed but non-encapsulated firm nodular masses. The case with a diameter of 23 cm showed a cystic cutsurface. The ages of patients with tubal AT were 51 and 59. Tumours were 0.2 and 1 cm in diameter and both were incidental. There were two ovarian cases; one case was 0.3 cm in diameter and incidental. The other ovarian AT measured 6 cm in diameter and had a preoperative diagnosis of ovarian cystic tumour. The cut surface was predominantly cystic.
Conclusion: Adenomatoid tumours are mostly incidental lesions but, large sized cystic variants may lead to differential diagnostic considerations of various benign and malignant diseases.

E-PS-07-076
Human leukocyte antigen-G expression in ovarian carcinoma
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Objective: HLA-G is a nonclassical histocompatibility class I molecule with a restricted tissue distribution. Its expression is induced in some pathological conditions including cancer. The objective of this study was to evaluate the expression of HLA-G in ovarian carcinoma tissues and to study its association to clinical characteristics.
Method: We used 54 blocks of ovarian carcinoma tissue from patients diagnosed within the Salah Azaiz Institute in Tunisia. Immunohistochemical study was performed using the monoclonal antibody anti-HLA-G. Five groups of expression marked HLA expression semi-quantitatively.
Results: Ovarian cancer was diagnosed in four stages in our groups. HLA-G expression was positive in 68.5 % of cases. This positivity was assessed in 70 % of patients with stage I, 66.7 % of stage II patients, in 53.3 % of patients with stage III and in 81.8 % of patients with stage IV. These differences are not statistically significant ($p > 0.05$). The expression was intense and diffuse 7.4 % (4+ score). However, the level of HLA-G expression was significantly higher in I and IV stages in comparison with the other stages ($p < 0.0001$).
Conclusion: HLA-G was expressed in approximately half of ovarian carcinoma patients. Our results suggest no significant differences in HLA-G expression between different stages. Interestingly, we demonstrate an increased significant level of HLA-G expression in stages I and IV.

E-PS-07-077
Thyroid transcription factor-1 (TTF-1) expression in ovarian carcinoma
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Objective: Thyroid transcription factor-1 (TTF-1) is widely used in the diagnosis of lung and thyroid carcinoma, but thyroid transcription factor 1 immunoreactivity is seen in other malignancies. Our study evaluated the distribution of TTF-1 expression in ovarian tumours and correlation with clinical parameters.
Method: Forty ovarian carcinoma (6 low grade, 34 high grade) were retrieved and were stained with TTF-1. The hematoxylin-eosin, and anti-TTF-1 antibody stained sections were reviewed, and the presence and distribution of TTF-1 nuclear positivity was recorded.
Results: The mean age was 54.57 years. The majority of cases had advanced stage disease (67.5 %) 32 of samples were collected before chemotherapy started. TTF-1 expression was present in 12 of 40 (30 %) of cases. 1 % (1/6 cases) of patient in low-grade ovarian carcinoma and 32.35 % (11/34 cases) of patient in high-grade ovarian carcinoma have positive TTF-1

expression. This differences are almost significant ($p = 0.0565$). The difference of TTF-1 expression and stage chemotherapy and metastasis are not statistically significant ($p > 0.05$) and did not correlate.
Conclusion: In our study was no apparent correlation between clinicopathologic characteristics and TTF-1 positivity. However, high grade can be correlated. TTF-1 immunostaining has the potential to misguide a pathologist in ovarian carcinoma.

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E-PS-08 Haematopathology

E-PS-08-001
Histopathological profile of lymphoma in Yogyakarta, Indonesia
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Objective: Lymphoma is the second most common lymphoid malignancy after leukemia. The incidence of lymphoma is varied among sexes, age groups, and sites. In Indonesia, data regarding the incidence of lymphoma and its description are still inadequate. Thus, this study was performed to evaluate the incidence of lymphoma and its description based on age groups, sexes, sites, clinical diagnosis, and histopathological type in Indonesia.
Method: This research is a descriptive analytic study of histopathological profile of lymphoma in Yogyakarta from 2010 to 2014, using a cross-sectional design. The data was based on secondary data from several hospitals and laboratories in Yogyakarta, Indonesia.
Results: The result showed an increased incidence of lymphoma in Yogyakarta in 2010–2014 ($p = 0.039$). Lymphoma is more common at an age of 45–64 years ($p = 0.004$). Males are dominant compare with females with ratio 1.6:1 and Diffuse Large B-Cells Lymphoma (DLBCL) is the most common histopathological type (44.4 %). Sex, age, and clinical diagnostics have a statistically significant correlation with the histopathological type of lymphoma ($p < 0.001$).
Conclusion: In conclusion, lymphoma mostly occur in older people and male, DLBCL is the most frequent type, and there are statistical correlations between gender, age, and clinical diagnostics with the histopathological type of lymphoma.

E-PS-08-002
Hematological and immunophenotypic profile of acute myeloid leukemia: An experience from a developing country
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Objective: To study Morphological, Cytochemical and Immunophenotypic profile in Acute myeloid Leukemia cases.
Method: 95 cases of AML were evaluated in a period of 1 year. Peripheral blood samples and bone marrow aspirates were studied for morphology, cytochemistry and immunophenotypic profile of blast cells using FACS Calibur, cytogenetics data was collected.
Results: Patients aged 7 months to 80 years. Most common subtype was AML M2 followed by M1, M3, M0, M6, M4, M7, M5. Complete concordance was seen between morphological and Immunophenotypic diagnosis while 76.19 % between cytochemical and Immunophenotypic diagnosis. CD33 was expressed in 93.98 %, CD13 in 85.54 %. AML M0, M1, M2 cases were positive for CD34, CD13, CD33, CD117, MPO, HLADR.
 APML showed strong MPO, CD13 and CD33 positivity while CD34 and HLADR negativity. CD14 and CD11b positivity was seen in AML M4. Aberrant markers most commonly expressed were CD19 followed by CD7 and CD2. Therefore, extended panel as per WHO is advised to rule out mixed phenotypic acute leukemia. t(15;17) was most commonly seen in APML and t(8;21) in AML with maturation
Conclusion: AML accounted for 46 % of all leukemia cases. Most common subtype was AML M2. MPO, CD 13 and 33 were the most useful diagnostic markers.

E-PS-08-003
Primary cutaneous gamma-delta T-cell lymphoma with complete response after chemotherapy
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Objective: To report a first case of PCGD-TCL from Thailand with tumour cell immunophenotype of CD4+ and CD56- and complete remission after CHOP chemotherapy.
Results: Primary cutaneous gamma-delta T-cell lymphoma (PCGD-TCL) is a rare disease with mature activated gamma delta cytotoxic phenotype. Clinical presentations vary from patch/plaque to ulcer and commonly seen at extremities. The tumour cells are usually medium to large cell size with immunophenotype of CD3+, betaF1+, TCR-gamma+ or -delta+, cytotoxic protein+, CD56+, CD5-, CD4- and CD8-. PCGD-TCL is usually resistant to multi-agent chemotherapy and has aggressive clinical course with median survival 15 months. A 19-year-old Thai male with no known underlying disease presented with multiple flesh color, velvety surface nodules at face and scalp, which had progressed in 3 months. Skin biopsy demonstrated epidermotropism with superficial dermal infiltration by small to medium size atypical lymphoid cells and immunophenotype of CD3+, TCR-gamma/delta+, TIA-1+, CD4+, betaF1-, CD5-, CD8-, CD56-, CD34- and EBER-. Investigations (nasal endoscopy, bone marrow biopsy, CT brain-chest-whole abdomen) were negative for systemic involvement, indicating stage IE. After treatment with 8 cycles of CHOP chemotherapy regimen (cyclophosphamide 750 mg/sq.m., doxorubicin 50 mg/sq.m., vincristine 1.4 mg/sq.m., prednisolone 60 mg/sq.m.), the patient achieved complete remission without relapse for 30 months.

E-PS-08-006
Comparative study between fine needle aspiration cytology and histology of the lymph nodes
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Objective: The aim of this work is to evaluate the reliability and diagnostic accuracy of fine needle aspiration cytology (FNAC) of cervical lymph nodes (CLN) with an emphasis on discordant cases between the cytology and the histopathology.
Method: We analyzed a series of 42 cases of FNAC of CLN and we correlated the result of the biopsy when performed.
Results: Patient age ranged between 5 months and 14 years old. Cytological diagnosis were found to be benign in 17 cases (40,5 %), malignant in 24 cases (57,2 %) and 1 case of hypocellular cytology (2,4 %). 20 cases were explored by biopsy. The overall diagnostic sensitivity, specificity value of FNAC of cervical lymph nodes were 90,1 % and 66,7 % respectively. The overall diagnostic accuracy was 80 % (16/20), while the overall discordance rate was 20 % (4/20). The diagnostic accuracy of reactive lymphoid hyperplasia, chronic granulomatous lymphadenitis, metastatic carcinoma, Hodgkin lymphoma, non Hodgkin lymphoma and suspect lesion was 80 %, 100 %, 50 %, 100 %, 100 % and 60 % respectively. We recorded 3 false positive (viral infections) and one false negative cases (lymphoma).

Conclusion: FNA cytology can distinguished reactive lymphoid hyperplasia from malignant lymphoma in 80 % of cases. To increase the fiability of FNAC, biopsy is advisable in cases with apparent clinical discrepancy.

E-PS-08-011

Monoclonal gammopathy of undetermined significance: Utility of anti-CD56 immunophenotypic study as a prognostic factor

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Objective: Monoclonal gammopathy of undetermined significance (MGUS) is a common plasma cell dyscrasia, comprising the most indolent form of monoclonal gammopathy. However, approximately 25 % of MGUS cases ultimately progress to plasma cell myeloma (PCM) or related diseases. It is difficult to predict which subset of patients will transform. Based on the fact that the majority of PCMs aberrantly express CD56, in this study we examined its immunophenotypic expression as a prognostic factor in MGUS.
Method: A retrospective, descriptive analysis of 42 patients with MGUS, diagnosed between 01/01/2000 and 31/12/2010 was performed, using the expression of the monoclonal antibody anti-CD56 over bone marrow specimens, and analysing 5 years follow-up.
Results: Three of the 42 MGUS cases (7.14 %), 2 of 10 (20 %) with CD56 immunoreactivity and 1 of 32 (3.12 %) CD56 immunonegative, showed progression of disease (a progression rate in MGUS with CD56 expression 6.4 times higher).
Conclusion: The ability to identify MGUS patients with potential of progression of disease, can offer to this group of patients early treatment options without increasing the morbidity of what is otherwise a relatively indolent entity. A higher relative proportion of CD56+ plasma cells in MGUS may be associated with a higher potential for disease progression.

E-PS-08-012

Erdheim Chester Disease is a new entity among the histiocytic disorderes: Clinicopathological and molecular features via case presentations

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Objective: Erdheim Chester disease is a rare neoplastic histiocytic disorder of adults characterised by the accumulation of foamy macrophages with CD68+, CD1a-, S100-(+), langerin- immunophenotype. Clinical features and organ manifestations are diverse, but skeletal manifestation almost always occur. Current classification of the histiocytic disorders considers it as a member of the Langerhans-related (L) group. Somatic mutations of the MAP Kinase pathway have been described, and may play essential role at the pathogenesis of the disease.
Method: Three Erdheim-Chester Disease cases have been diagnosed at our Department between 2013 and 2015. Bone biopsy were performed each cases and lead to diagnosis. Immunohistochemistry panel CD68, S100, CD1a, Langerin have been used, Sanger sequencing have been performed for mutation analysis of BRAF, MAP2K1, NRAS and KRAS genes each case.
Results: Two of the cases had BRAFV600E point mutation, the third case harboured another mutation at the MAP Kinase pathway.
Conclusion: A few years ago the diagnosis of Erdheim-Chester disease was challenging because of the varying clinical manifestations and lack of special markers, but clinicopathologycal features and molecular methods together may make the diagnose easier and more precise.

E-PS-08-014

Langerhans cell histiocytosis with follicular lymfoma in a lymph node: Case report

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Objective: Langerhans Cell Histiocytosis is a type of proliferation of CD1a and S100 positive Langerhans cells.
Method: Lymphomas, some other malignancies, viral infections, cigarette smoking can cause this stiuation.
Results: A 56 years old woman presented with left inguinal lymphadenopathy. Lymph node excision was performed. Microscopically, focal Langerhans cells presented in the lymph node also involved by follicular lymphoma.
Conclusion: The presence of langerhans cell proliferations with malignant lymphoma is rare. Today the presence of these cells does not change the treatment. We present the case because of its rarity.

E-PS-08-015

Concurrent diagnosis of two leukemia types: B-chronic lymphocytic and acute myelogenous

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Objective: AML can be found after treatment for CLL and is regarded as secondary or therapy-related. However, there are exceptionally rare reports of AML cases concerning patients with untreated CLL or cases with a simultaneous diagnosis of AML and CLL. This case refers to the second category.
Method: A 79-year-old male patient presented to the hematological clinic, without any specific symptoms, for the investigation of macrocytic anaemia, an external laboratory finding. A bone marrow biopsy was performed and examined morphologically and immunohistochemically.
Results: A mainly nodular and partly interstitial 20 % infiltration by small size neoplastic lymphoid cells with ovoid nuclei and inconspicuous nucleoli was observed, with the following immunophenotype: CD20+, CD45RA+, CD79a+, PAX5+, BCL2+, CD5+, CD23+, CD45RO-, CD3-, CD10-, CD38-, CD43-, DBA44-, CCND1-, k-, λ-. Staining with CD34 showed >20 % positive blast cells of myeloid origin. All three marrow cell lineages were dysplastic.
Conclusion: The concurrent presence/diagnosis of B-CLL and AML is exceptionally rare, seems to be coincidental and regards two independent clonal neoplastic processes, as shown by cytogenetic and molecular analyses. While arising from two different cellular lines, a common pathogenetic mechanism is rather unlikely. The phenomenon is attributed to a chance coexistence of two uncommon hematologic neoplasms.

E-PS-08-016

Metachronous B and T cell post-transplant lymphoproliferative disorders (PTLD): One case with literature review

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Objective: Co-existence of T and B cell PTLD are extremely rare but the presence of monoclonal T cell populations in patients with B cell PTLD has been described without features of T cell malignancy.
Method: We present one case of metachronous B and T cell PTLD with literature review.
Results: 43 years old male transplanted of heart 8 years ago developed generalized lymphadenopathy with a polymorphic PTLD diagnosis, EBV associated and IgH rearrangement. The patient was classified in IVB stage and initially treated with rituximab with no clinical response. The patient starts R-CHOP until partial remission. Two years later of the diagnosis presents a nodular skin lesion with diagnosis of T cell PTLD (CD2+, CD3+, CD8+, CD5-, CD4-) with anaplastic morphology, EBV

associated and a TCR monoclonal population with no IgH rearrangement in the cutaneous lesion.
Conclusion: We present a metachronous B and T cell PTLD. Co-existence of T and B cell PTLD are extremely rare with only six cases reported. T/NK cell PTLD are infrequent and EBV is usually negative. Most of primary cutaneous PTLD are of T-cell origin (mostly mycosis fungoides) in the largest series published.

E-PS-08-018
Heparin-tryptase complex in mast cells
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Objective: Mast cells play a central role in numerous diseases. When activated, mast cells degranulate and release granule-derived mediators including tryptase and heparin. Much knowledge has been gathered about tryptase activation by heparin, but little is still known about the state of heparin-tryptase complexes. To address this issue, we examined in situ heparin-tryptase complexes of mast cells in human tissues.
Method: We performed double fluorescent labeling of heparin and tryptase in mast cells. Heparin was visualized using a fluorescent dye berberine. Tryptase was detected using immunohistochemical technique.
Results: Double labeling of tryptase and heparin allowed us to differentiate mast cells of three distinct physiological states: (a) mast cells containing only tryptase, (b) mast cells containing only heparin, and (c) mast cells containing both tryptase and heparin in their secretory granules. Furthermore, we compared the efficiency of counting mast cells stained for heparin and tryptase with other methods used for mast cell detection.
Conclusion: Tryptase immunolabeling permits to identify significantly much more mast cells than other staining methods and therefore can be recommended as a routine stain for counting mast cells in diagnostic labs. Double staining of heparin and tryptase can also be used for characterization of mast-cell sub-populations depending on tissue localization.

E-PS-08-020
Bone marrow cryptococcal infection revealing human immunodeficiency virus (HIV) infection: A case report
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Objective: Disseminated cryptococcal infection is an uncommon initial manifestation with acquired immunodeficiency syndrome.
Method: We report a rare case of a 50-year-old male without medical history, who was referred to our hospital for evaluation of pancytopenia. He presented with fever and bilateral cervical and axillary lymphadenopathy. On examination, there was mild splenomegaly. Complete blood count reading showed mild anemia, leucopenia with severe neutropenia and thrombocytopenia. Bone marrow aspiration and biopsy were done to evaluate pancytopaenia.
Results: The bone marrow aspiration showed no hemoparasites or immature cells. Bone marrow biopsy showed small aggregates of histiocytes, foamy cells, showing a diffuse hyperplasia, and the presence of refractile yeast like organisms suggestive of cryptococcal species. Alcian PAS stain showed thick capsule positive for acid mucopolysaccharide. No granulomatous response was seen. A diagnosis of cryptococcosis of bone marrow was made. A HIV infection was suspected and the elisa test result and westernblot confirmed the diagnosis.
Conclusion: Bone marrow examination plays a critical role in diagnosing opportunistic fungal infection like cryptococcosis as a cause of pancytopenia and leads us to suspect and confirm HIV infection in this case.

E-PS-08-021
Biclonal plasma cell myeloma in a patient with rheumatoid arthritis
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Objective: Sporadic reports have documented concomitant plasma cell myeloma (PCM) in patients with rheumatoid arthritis. Most PCMs result in a monoclonal gammopathy with IgG monoclonal protein (M-protein) and only rare in biclonal gammopathy with the production of two heavy and /or light chains.
Method: An 80-year-old male with rheumatoid arthritis presented with IgG M-protein (37 g/L) and a bone marrow biopsy was performed.
Results: Bone marrow was infiltrated with 30 % of medium sized atypical plasma cells with lambda light chain restriction and 10 % of larger multinucleated plasma cells with kappa light chain restriction. All plasma cells were positive for CD138 and CD117 but negative for CD20 and CD56. Lambda to kappa ratio was 5 to 1. Lambda positive plasma cells were also positive for Bcl-2 and Cyclin-D1, while kappa positive plasma cells were negative for both. Bone marrow biopsy revealed two morphologically and immunohistochemically distinct plasma cell populations, one expressing lambda and the other expressing kappa light chains, while serum protein electrophoresis identified only one IgG M-protein and no light chain restriction.
Conclusion: Biclonal PCMs producing two different types of immunoglobulins are rare. Bone marrow biopsy is essential to make the correct diagnosis as serum protein electrophoresis may miss cases with biclonality.

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E-PS-09 Head and Neck Pathology

E-PS-09-001
Pseudoangiosarcomatous Carcinoma (PAC) of the head and neck regions
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Objective: Acantholytic squamous cell carcinoma (ASCC) is seen rarely in the head and neck, and pseudoangiosarcomatous carcinoma (PAC) is one of extreme subtype of this tumour, which is exceeding rare in the head and neck regions. We report 2 cases of PAC.
Method: We selected PAC cases from pathology file of Shizuoka Cancer Center, Shizuoka, Japan, during 2002–2015, and examined them, clinicopathologically and immunohistochemically.
Results: We could extract 2 cases (0.07 %) of PAC. Case1 was 79 year-old Japanese female, who suffered from rapid swelling of the right buccal region. The tumour resection was performed. Local recurrence and multiple lung metastases occurred 2 months after operation, and she died. Case 2 is 63 year-old Japanese male, who suffered from the pain of the right mandible. The bulky tumour of the oral floor replaced the tongue and invaded to mandible. X-P showed multiple metastases to the left lymph nodes and bone. He died. Histologically, both tumours showed vascular channel-like structures by atypical cells, and some areas consisted of proliferation of spindle cells or hobnail cells. Immunohsitochemically, the tumour cells were positive for cytokeratins, p40 and vimentin, whereas they showed loss.
Conclusion: PAC is exceeding rare and it is an extreme phenotype of ASCC, like "angiosarcoma". Since EMT occurs, the cell-cell adhesion was lost, and then "pseudo-vascular structure" was formed. PAC indicates worse prognosis than conventional squamous cell carcinoma.

E-PS-09-002
Extragonadal primary yolk sac tumour of temporal bone
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Objective: Yolk sac tumour also known as endodermal sinus tumour (EST) are malignant germ cell tumours seen in children less than 3 years of age, involving the testis. It is rarely found primarily in extragonadal sites with no involvement of the gonads. Only four cases of temporal bone primary yolk sac tumour have been reported in the literature.
Method: Case report: We describe a rare case of extragonadal primary yolk sac tumour of the temporal bone in a 2.5 years old child presenting with a left sided postauricular mass and facial nerve palsy.
Results: Biopsy showed reticular areas formed by a loose meshwork lined by flat and cuboidal cells with pleomorphic nuclei, prominent nucleoli, frequent mitotic figures and vacuolated cytoplasm, with a perivascular organoid arrangement of tumour cells (Schiller-Duval bodies). Immunohistochemistry was strongly positive for AFP with focal expression of pancytokeratin and vimentin, consistent with yolk sac tumour. Patient was treated with chemotherapy including cisplatin, etoposide, and bleomycin.
Conclusion: EST of temporal bone are rare tumours and high degree of suspicion is required to diagnose them. Biopsy of such tumours must be examined by an expert histopathologist to arrive at a diagnosis along with serum alpha protein level to confirm.

E-PS-09-003
Lymphoepithelial carcinoma of the parotid gland: A rare entity
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Objective: Lymphoepithelioma-like carcinoma (LELC) of the salivary gland is a rare tumour accounting for 0.4 % of all malignant salivary gland tumours. We herein present a rare case of LELC of the parotid gland.
Method: A 61 year-old man was diagnosed with a mass in the left parotid gland with no other symptoms or past medical history. Ultrasound revealed hypoechoic, inhomogeneous mass of the parotid gland. Patient underwent surgical removal of the mass by a superficial parotidectomy.
Results: Initial frozen sections analysis rendered a diagnosis of malignancy. A complete neck dissection was performed. Histopathologic examination of the specimens revealed a parotid gland with solid carcinomatous sheets, trabeculae and isolated small groups of malignant epithelial cells intermingled with lymphoid stroma. The satellite lymph node showed no infiltration. Immunohistochemical analysis showed neoplastic cells with positive staining for pancytokeratin and epithelial membrane antigen and focal expression of LMP1. Lymphoid cells were positive for both CD20 and CD3 markers. On the basis of these findings, a diagnosis of stage II, undifferentiated LELC of the parotid gland was made.
Conclusion: LELC of the salivary gland is a rare entity with a better prognosis than other poorly differentiated tumours; surgical excision with post-operative radiotherapy is the treatment of choice.

E-PS-09-004
A rare case of Carcinosarcoma ex Pleomorphic Adenoma of the Parotid Gland with no history of long-standing or recurrent Pleomorphic Adenoma
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Objective: The aim of this report is to describe a rare case of Carcinosarcoma Ex Pleomorphic Adenoma involving the left parotid gland with no history of a long standing Pleomorphic Adenoma, or a Recurrent Pleomorphic Adenoma, and to describe its morphology and important immunohistochemistry findings.
Method: The histopathologic findings of the left parotid gland are correlated with the clinical history and ancillary procedures, and surgical pathology staging, including assessment of the draining lymph nodes. Immunohistochemistry studies, assessment of proliferative capacity, and possible treatment target is also done. The tumour is also compared with other reported cases with such diagnosis.
Results: Carcinosarcoma Ex Pleomorphic Adenoma contains features of the two tumours under Malignant Mixed Tumours, which are Carcinosarcoma and Carcinoma Ex Pleomorphic Adenoma. Immunohistochemistry studies were done to document the epithelial and mesenchymal areas for both malignant and benign sections from the tumour. Immunohistochemistry studies were done to classify the epithelial component, consisting of Adenocarcinoma, Not Otherwise Specified, and sarcoma component consisting primarily of Myxoid Chondrosarcoma.
Conclusion: Approximately ten cases of Carcinosarcoma Ex Pleomorphic Adenoma have been documented in scientific publication. The case contributes to the fund of knowledge for diagnosis and improvement of quality of care.

E-PS-09-005
Atypical carcinoid of the larynx: A typical immunohistochemical diagnosis
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Objective: Also known as malignant carcinoid, the atypical laryngeal carcinoma is the most frequent neuroendocrine laryngeal neoplasia. This tumour typically presents as a grey polipoid supraglottic mass, with compressive effects and lymph node metastasis, in male patients, with a median age of 61-years-old.
Method: We present the case of a 60-year old male who noticed a neck mass and complained about dysphagia and hoarseness. The patient underwent laryngectomy.
Results: We received the 8,5/4,5/5 cm laryngectomy specimen, that contained a 5/4,5/2,5 cm, brownish-grey, polipoid, supraglotic tumour. Histopathological examination revealed an epithelial proliferation, with eosinophilic cells, pleomorphic vesicular nuclei, arranged in trabecules, with mucinous areas, oncocytoid cellular transformation, areas of necrosis and haemorrhage and a mitotic rate of 3/10 HPF. Immunohistochemically, the tumour cells were positive for CK7, CK34Beta12, CEA, TTF1, Ki67, Chromogranin A and Synaptophysin, confirming the diagnosis of atypical carcinoid of the larynx.
Conclusion: Although it has heterogeneous clinical and histopathological aspects, the atypical carcinoid of the larynx may present itself in a typical form, usually confirmed by specific immunohistochemical stains.

E-PS-09-006
Inulin induced oral tissue remodeling in rats with type 2 diabetes mellitus
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Objective: There is limited evidence on the effects of prebiotics on morphology of rats oral tissues under II type experimental diabetes mellitus conditions.
Method: Diabetes was induced in 42 Wistar rats with the intramuscular injection of the protamine sulfate. Long-term administration of protamine sulfate caused persistent hyperglycemia, reduced glucose tolerance and high insulin resistance. Animals were divided into experimental (1st) and group of comparison (2nd). 1st group of animals was treated with the prebiotic inulin supplementation. Oral tissues and salivary glands samples were examined morphologically, then with the help of computer morphometry.
Results: Metabolism disorder due to alloxan-induced hyperglycemia resulted in pathomorphological changes in rat's mucous membrane of

cheek, tongue and in minor salivary glands. Inulin treated animals presented with the activation of compensatory-adaptive processes, mucous membranes of cheek and tongue repair, as well as the restoration of the structure of salivary glands. Administration of inulin resulted in a significant decrease of keratinization disorder. Vascular pathology, perivascular edema, macrophage and lymphoid infiltrates had a smaller volume fraction compared with 2nd group. Inulin mediated reduction of a glycemia's level and had the significant antioxidant effect. The beneficial effect on the homeostasis of the oral cavity was also found due to stimulation of bifidum bacteria and lactobacilli growth.
Conclusion: Inulin supplementation may improve morphological repair of rats' oral tissues with experimental type 2 diabetes. The prebiotic had proven useful to prevent mucosal inflammatory disorders. Enhanced structural adaptation stimulated the microbiocenosis optimization in the oral cavity.

E-PS-09-007
Low-grade sinonasal sarcoma with neural and myogenic differentiation: A diagnostic challenge
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Objective: Low-grade sinonasal sarcoma with neural and myogenic features (LGSSNM) is a recently described distinct spindle cell sarcoma of the sinonasal region characterized by concomitant neural and myogenic differentiation. We reviewed the clinical and histological features of this rare sarcoma.
Method: We present a case of this new entity, diagnosed in the department of pathology at Habib Bourguiba University Hospital.
Results: A 52-year-old female, presented with congestion and periorbital pressure which caused blurred vision. Computed tomography (CT) revealed a right sinonasal mass, filling the ethmoid cavity and extended to skull base, periorbitary fat and nasal mucosa. Pathologic examination showed morphologic features similar to those reported for LGSSNM : Moderate to high cellular spindle cell proliferation. The cells had elongated nuclei with coarse chromatin. Some of the cells had nuclear pleomorphisme. The tumour was positive for S100 protein and AML and negative for desmin, CD34, and pankeratin. Ki-67 was assessed at less than 1 % of the spindle cells. A post operative CT scan revealed gross residual tumour, so that the patient received radiotherapy. After 7 months, the patient is disease-free with no signs of recurrence or metastasis.
Conclusion: LGSSNM is a recently defined entity that provides a challenge to the managing clinician due to its novelty and to the interpreting pathologist due to its homology with other lesions.

E-PS-09-008
Seromucinous hamartoma of the sinonasal tract: A diagnostic challenge
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Objective: The sinonasal tract is a complex anatomic site, home to a wide variety of lesions. Although inflammatory polyps and papillomas are the most common diagnoses, occasional cases are more difficult, and separating reactive or benign from malignancy can be challenging. We report the case of a seromucinous hamartoma (SH) in a 53-year-old woman.
Method: Microscopically, the lesion consisted of a mixed population of small and large glands lined by cuboidal to flattened cells within a hypocellular variable stroma. The glands did not show infiltrative growth or confluent, back to back architecture. The constituent cells were cytologically bland without mitosis and stained positive for CK7, CK19 and HMWK while CK20 was negative. Although P63 staining within the serous glands was negative, S100 showed patchy, weak positivity.
Results: The main differential diagnosis for SH is low-grade sinonasal adenocarcinoma, non-intestinal type (LGSNAC), with which they are cytologically and immunohistochemically identical. However, the latter typically has complex growth patterns including micropapillary architecture and glands which are back-to-back or fused.
Conclusion: SH is a rare benign lesion of the sinonasal tract. The lack of myoepithelial/basal cells is an important diagnostic feature and could be a diagnostic pitfall leading to an erroneous diagnosis of malignancy.

E-PS-09-009
Peripheral ossifying fibroma: Case report
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Objective: POF is a reactive gingival overgrowth occuring frequently in the anterior maxilla in teenages and young adults. POF predominatly affects women. It is beliewed to arise from the periodental ligament and comprises of 9 % of all gingival overgrowths. Trauma or irritation have been implicated in the etiology of POF. Due to its clinical and histopathological similarities, some POFs are believed to develop initially as a pyogenic granuloma that undergoes fibrous maturation and subsequent calcification.
Method: We present a 13-years-old male patient who has a swelling in the front of upper palate that had gradually increased in size during previous 3 months. Intraoral examination revealed a solitary, pedunculated mass. Intraoral periapical radiograph showed no significant bony changes. An excisional biopsy was done.
Results: Histopathologic examination showed fibrocellular connective tissue interspersed with plump fibroblasts in between the collagen bundles, surfaced by stratified squamous epithelium. Stroma also revealed foci of calcification which resembled bone like ossifications. POF was diagnosed. Healing was uneventful and patient is followed up for 3 months without any recurrence.
Conclusion: Identification of any reactive lesions (pyogenic granuloma, peripheral giant cell carcinoma, peripheral odontogenic fibroma..) requires the formulation of differential diagnosis to enable proper patient evaluation and management.

E-PS-09-010
Pure oncocytic carcinoma of the of minor salivary gland: Case report and review of the literature
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Objective: Pure oncocytic carcinoma arising from a minor salivary gland is an extremely rare neoplasm with only a few cases reported in literature.
Method: We present a case of 56 years old man with enlarged left cervical adenopathies. Fine needle aspiration was done and the smears showed an abundant epithelial cells with well-defined cell borders, round to oval, central to eccentrically located moderately pleomorphic nuclei with fine chromatin, prominent nucleoli and abundant eosinophilic granular cytoplasm. CT scan showed pathological cervical adenopaties without evidence of primary lesion. Oral cavity examination showed a swelling in oral mucosa localized around the superior left molars. Biopsy was performed. Microscopic examination showed solid sheets, nests, islands and cords of oncocytic cells with severe atypia and numerous figures of mitosis. Immunohistochemical studies were positive for CK 7 and antimitochondrial antibody.
Results: The diagnosis of oncocytic carcinoma was made and it was based on clinical, radiological and morphological findings. Surgical excision of the lesion was not performed duo to advanced stage.
Conclusion: However oncocytic carcinoma of the minor salivary gland is a very rare tumour, it has to be suspected if morphology and inmmunohistoquimical studies suggest that and antimitochondrial antibody has always to be performed.

E-PS-09-012

Endolymphatic sac tumour: A rare tumour with bland morphology and aggressive behaviour

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Objective: Endolymphatic sac tumour, also known as aggressive papillary tumour or low grade adenocarcinoma, is a rare neoplasm of the inner ear. It may occur sporadically or in the setting of Von Hippel-Lindau. It is characterized by an aggressive clinical behavior. We hereby report two cases diagnosed in 3 years.
Method: Case 1: A 57-year-old male patient with a 35 mm right jugular foramen tumour invading the surrounding bone. Case 2: A 34-year-old male patient with Von Hippel-Lindau syndrome and a 27 mm left jugular foramen tumour showing bone erosion on imaging.
Results: Microscopic examination showed, in both cases, a tumour composed of papillary formations and tubular structures. The lining was single-layered, cuboidal with very mild atypia. Mitoses were scarce in the 1st case and inconspicuous in the 2nd. Immunostaining showed that the tumour cells expressed CK7, EMA, and focally GFAP. The proliferation index (Ki67) was low.
Conclusion: Endolymphatic sac tumour is a rare tumour of the inner ear, characterized by aggressive clinical and radiological features and bland architectural and cytological microscopic morphology. Recognition of this entity is important to prevent misdiagnosis especially on frozen section.

E-PS-09-013

Laryngeal cancer: A retrospective study on 5 years. A review study of 150 cases

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Objective: Laryngeal cancer accounts for 5 % of male cancers and 25 % of cancers of the upper aerodigestive tract. The highest incidence is found in Europe. he aim of this work is to have a rough idea of its impact in our population.
Method: Our study focused on 150 samples collected at the pathological anatomy department of the University Hospital of Constantine extended over a 5 year period from January 2010 to December 2014. The fixer used is Formalin 10 %. Close examination of the surgical specimen after inking allows to take samples buoyant compared to surgical excision margins. The samples are cut into thin sections of 4 μm thickness and plated onto glass slides and then colored with hematoxylin eosin. Immunohistochemical examinations are made at the request case by case.
Results: Among the 150 laryngeal tumours diagnosed, 148 cases of squamous cell carcinoma, fibrosarcoma and malignant non-Hodgkin lymphoma. The gender distribution has shown a male predominance a sex ratio of 1M / 0,08W. The age of our patients varies between 37 and 87 years with an average age of 63,40 years. The age group most affecteted is between 60 and 69 years. The mature well-differentiated squamous cell carcinoma is the most frequent histological type represented by 112 cases.
Conclusion: Cancers of the larynx are linked to a vast majority predominantly male which is consistent with the literature smoking and partly alcoholism. The mature well-differentiated squamous cell carcinoma is the most frequent type. Early diagnosis at the time of dysphonia allows conservative treatment.

E-PS-09-014

Full-field optical coherence tomography for fast diagnostic of head and neck cancer

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Objective: The purpose of our study was to evaluate the clinical value of Full-Field Optical Coherence Tomography (FFOCT) imaging in the management of patients with Head and Neck cancers, by making a reliable histological diagnosis on FFOCT images produced from surgical specimens. FFOCT produces "optical biopsy" images quite similar to that obtained with classical histological procedures, but without any tissue preparation and in a few minutes.
Method: We performed images of healthy and cancerous samples from surgical specimens of oral cavity, pharynx and larynx. All images were interpreted in a random way by two pathologists. The FFOCT based diagnostic was compared with the histological slides, in order to constitute an image atlas.
Results: FFOCT images provided a quick assessment of microscopic tissue architecture and could be easily used by both pathologists. The correlative study is in progress and preliminary results are reported here.
Conclusion: FFOCT is a fast, non-invasive imaging tool that can be inserted into the pathology lab workflow to provide a quick microscopic assessment of tissue. With a similar system with a rigid endoscopic probe, in vivo and in situ imaging could be performed and thus guide the surgeon in real time during endoscopy or surgery.

E-PS-09-017

Droplet digital PCR and qRT-PCR to detect circulating miR-21 in laryngeal Squamous Cell Carcinoma (SCC) and premalignant laryngeal lesions

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Objective: To investigate a sensitive marker that contributes to progression from normal tissue to premalignant laryngeal lesions (PLLs) and from PLLs to laryngeal squamous cell carcinoma (LSCC).
Method: In 116 PLLs and LSCC patients and 19 without dysplasia matched sets of tissue and plasma samples from Beijing Tongren Hospital, miR-21 was analysed by droplet digital PCR and quantitative real-time polymerase chain reaction based on paraffin-embedded tumour tissue and plasma.
Results: Compared with controls, miR-21 levels in tissue and plasma were significantly higher for both PLL and LSCC groups (for both groups vs controls: $P < 0.0001$ for tissue; $P < 0.05$ for plasma). Areas under receiver-operating curves (AUC) for tissue miR-21 were PLL group vs controls: 0.9026 and LSCC group vs controls: 0.8681. For plasma miR-21, AUCs were PLL group vs controls: 0.7355 and LSCC group vs control: 0.6723.
Conclusion: The present study indicates that miR-21 is involved in progression from normal to PLLs and from PLLs to LSCC. Furthermore, normalized PCR results for miR-21 might be used to discriminate between normal and ordinary hyperplasia before the emergence of dysplasia and premalignant lesions with malignant potential.

E-PS-09-018

Intramucosal lipoblastoma-like tumour of the lip

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Objective: "Liopoblastoma-like tumour" defines an adipocytic tumour which histopathologically resembles a lipoblastoma, but presents with clinical features militated the diagnosis of lipoblastoma. Lipoblastoma-like tumour of the lip is exceptionally rare entity which has been reported

as 2 cases with intradermal location, previously. We present a distinctive adipocytic mesenchmal tumour with intramucosal location in adult woman.
Method: A 60 -year-old woman was presented with an asymptomatic 3 cm diameter slightly elevated nodular lesion on the lower lip mucosa that had occurred for 6 months. The clinical examination was unremarkable. Total excision was performed.
Results: Histopathologically, lesion was lobulated and composed of variable proportions of mature adipocytes, bland univacuolated and multivacuolated lipoblasts that extends to the submucosa. There was neither mitotic figure nor necrosis. The tumour involved the surgical margins. The cells showed no staining with mucicarmine, PAS and dPAS. There was negative staining for pan-cytokeratin, smooth muscle actin, PLAG 1 and positive expression for vimentin and S-100. The 9 months of fallow- up revealed no recurrence.
Conclusion: To our knowledge, the present case is the first report of the lipoblastoma-like tumour with intramucosal location of the lip.

E-PS-09-019
Salivary gland tumours in a Monterrey-Mexico, University Hospital: A retrospective study of 237 cases
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Objective: To present a retrospective study of 32 years of the experience of our institution with respect salivary gland tumours.
Method: A retrospective and descriptive study was desgined. Demographic and histopathologic variables were analyzed. Data was retrieved from the department patient's database and hospital clinical records.
Results: Over a 32-year period, a total of 237 major and minor salivary gland tumours were identified. Benign tumours represented 120 (50.6 %) and malignant tumours 117 (49.3 %). The mean age of diagnosis for benign lesions was 40 years and for malignant lesions was 47 years. The most common site affected was the parotid gland for both groups. The most frequent benign tumour was pleomorphic adenoma in 90 (75.0 %) cases, Warthin's tumour in 16 (13.3 %) cases, followed by myoepithelioma and oncocytic tumours in 3 (2.5 %) cases. The most frequent malignant neoplasia identified were mucoepidermoid carcinoma in 29 (24.7 %) cases, adenoid cystic carcinoma in 15 (12.8 %) cases and lymphoma in 13 (11.1 %) cases. Only 9 (3.79 %) cases corresponded to the pediatric population (less than 15 year-old).
Conclusion: Pleomorphic adenoma and mucoepidermoid carcinoma were the most frequent benign and malignant tumours respectively. The data presented is similar to reports in other centers.

E-PS-09-020
Extracranial meningioma presenting as a left parietal soft tissue tumour
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Objective: A minority of meningiomas can occur in extracranial locations, the head and neck region being most frequently involved.
Method: We report a case of extracranial meningioma in a 71 year old female, presenting as tumefaction in the left parietal region. Ultrasound examination revealed a tumour developing under the epicranial aponeurosis, with an underlying area of bone lysiss. The tumour's vascular pedicle originated from the intracranial space. There was no history of trauma. Total tumour removal followed by cranial reconstruction was performed in the Department of Oral and Maxillofacial Surgery.
Results: Macroscopic examination showed a 5/5/2 cm whitish nodule, with elastic consistency, infiltrating the underlying skull fragment in an area of 2/1.5 cm. No tumour was visible on the inner part of dura mater. Light microscopic examination revealed an encapsulated lesion composed of spindle cells arranged in whirls. They infiltrated the entire thickness of the bone, but were limited to the outer layer of the dura. Immunohistochemical staining was positive for vimentin and EMA and negative for SMA, S100, CD34 and PR.
Conclusion: The identification of the intracranial blood supply could explain this tumours main extracranial mass as arachnoid cells can be found in the sheaths of vessels that emerge through the skull foramina.

E-PS-09-021
Tracheal hamartoma: An uncommon tumour
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Objective: Primary tracheal tumours are rare in adults and usually malignant. Only 10 % of them are benign. Hamartomata are tumour-like malformations in which occurs only abnormal mixing of the normal components of the organ. They frequently localized in lung parenchyma and rarely only in trachea. We report a case of a 69-year-old man with a 4-year history of progressive breathlessness. MRI revealed a well-circumscribed dilobe, polypoid mass in the upper third of the tracheal lumen. The lesion was obliterating the tracheal lumen by 40 % and bronchoscopy was performed.
Method: We received a grayish, solid, elastic tumour measuring $2 \times 1 \times 0.6$ cm.
Results: Microscopically we observed the mucosa with respiratory and focal squamous epithelium and in submucosa a well-defined tumour with plenty, slightly abnormal vessels with size variety in a myxoid fibrous tissue. There were also adult fat tissue, groups of mucous secreting glands, cartilage and chronic inflammatory cells. There was no cytological atypia and a diagnosis of tracheal hamartoma was made.
Conclusion: Benign tumours of trachea grow slowly and they don't have the potential to become malignant. However, based on its localization, they can even cause death due to airway obstruction. For this reason, early diagnosis is crucial.

E-PS-09-022
A current histomorphological spectrum of salivary gland lesions in Pakistan: Seven years experience (2009–2015)
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Objective: To describe Pathology based spectrum of salivary gland lesions in Pakistani population.
Method: A 7 years observational study conducted at the Department of Histopathology, Dow diagnostic, reference and research laboratory (DDRRL), Dow University of Health Sciences, Karachi, Pakistan. All salivary gland lesions received at the laboratory during 2009–2015 were included in the study.
Results: A total of 473 samples were investigated. Of these, a total of 124 (26.2 %) were non-neoplastic and 349(73.7 %) were neoplastic lesions. Out of 124 non-neoplastic lesions, chronic sialadenitis, 55 cases (44.3 %) was the most common lesion followed by extravasation mucoceles, 42 cases (33.8 %). Submandibular gland was the most common effected site. For mucoceles, lower lip was the most common site. Of the 349 neoplastic lesions, a total of 267 (76.5 %) were benign while 82 cases (23.4 %) were malignant. Pleomorphic adenoma was the commonest salivary glands benign neoplastic lesions, 236 (88.3 %). Parotid glands were involved in majority of

pleomorphic adenoma cases, 167 (70.7 %) out of 236 cases. Of the 82 malignant tumours, Adenoid cystic carcinoma 31 cases (37.8 %) was the most common salivary gland malignant neoplastic lesion followed by mucoepidermoid carcinoma 27 cases (32.9 %). Submandibular gland was the most common site in adenoid cystic carcinoma while parotid gland involved in majority of mucoepidermoid carcinoma.
Conclusion: Chronic sialadenitis was the most common non-neoplastic lesion, pleomorphic adenoma was the most common benign lesion and adenoid cystic carcinoma (followed by mucoepidermoid carcinoma) was the most common malignant lesion.

E-PS-09-024
High grade chondroblastic osteosarcoma: A case report
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Objective: Osteosarcomas are the most common tumours of the bone, a heterogenous group of primary malignant neoplasms affecting bones or mesenchymal tissues that ahve histopathologic evidence of osteoid production. We present a rare case of high grade chondroblastic osteosarcoma of the maxillary bone.
Method: A 28-year-old, woman in fourth month of pregnacy was admitted to Surgery Department, for the evaluation of the newly diagnosed and rapidly growing mass of the upper jaw. Clinical examination revealed a significant swelling of the left cheek. Intraoral examination revealed a mass that was palpatory hard in consistence and was bleeding focaly. MRI examination showed a poorly defined tumour with indistinct margin. Patient underwent surgery. Frozen section revealed a malignant chondroid tumour suspected on chondrosarcoma. Macroscopically, tumour was fragmented, grayish in colour, hard in consistence.
Results: Histology showed malignant neoplasm of mesenchymal origin which was consist of malignant appearing cartilage with peripheral spindling and osteoid production. High grade tomor component showed high mitotic rate. Immunochistochemically tumour cells showed S100, Vimentin, and focally Podoplanin positivity. The diagnosis was consistent with chondorblastic osteosarcoma, high grade.
Conclusion: Postoperative course has been regular without unexpected adverse events. Osteosarcoma is a highly malignant bone tumour and it is a relatively a rare disease in the head and neck region. It occurs infrequently in the jaws where they have a better prognosis.

E-PS-09-025
Adenoid cystic carcinoma of the external ear canal
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Objective: Adenoid cystic carcinoma of the external auditory ear canal are extremely rare. They can clinically mimic granulation tissue and mistaken for inflammation.
Method: A 46-year old male presented with progressive right ear blockage, associated with excessive ear digging. There was evidence of bleeding and on examination appeared like granulation tissue. A provisional diagnosis of right traumatic ear canal polyps was made. Excised specimen consisted of multiple bits of greyish brown tissue, measuring 10 mm in aggregate diameter. Entire specimen was submitted for analysis. Sections were stained with routine H&E and later with a panel of IHC markers, comprising pan keratin AE1/AE3, S-100, p63 and CD117.
Results: Histology exhibited both cribriform and tubular pattern of adenoid cystic carcinoma component. IHC studies further confirmed the nature of the lesion. The epithelial cells were strongly positive for AE1/AE3 and the myoepithelial cells showed patchy expression for S-100. p63 highlighted the prominent myoepithelial cells. CD117 showed strong positivity for the tumour element.
Conclusion: Adenoid cystic carcinoma should be considered in the differential diagnoses of all external auditory malignant lesions by both pathologists and surgeons alike. Apart from conventional squamous cell carcinoma and ulcerating melanoma, adenoid cystic carcinoma can present as traumatic appearing pseudo polyps.

E-PS-09-026
Four cases of mandibular calcifying cystic odontogenic tumour
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Objective: Calcifying odontogenic cyst or Gorlin cyst, was first described by Gorlin et al. in 1962. The World Health Organization classified it as calcifying cystic odontogenic tumour in 2005. It's a benign, uncommon neoplasm, represents less than 2 % of all odontogenic tumours. Calcifying cystic odontogenic tumour has a unique structure: a solid lesion with a cystic formation that's why it has a variable clinical behaviour; cystic, neoplastic or infiltrating malignant behavior. Malign transformation to ghost cell odontogenic carcinoma is very rare. It can be extraosseous or intraosseous. Histologically calcifying cystic odontogenic tumour consists of ameloblastoma -like strands, islands of odontogenic epithelium and ghost cells in a mature connective tissue stroma. Odontoma may accompany this lesion, also the lesion may be multilobulated.
Conclusion: This review consisting of four cases of calcifying cystic odontogenic tumour. All of them were from male patients, the age ranging from 50 to 70 years old. The clinical location of one lesion was mandibulary anterior and the other cases were in mandibulary posterior area. Only one lesion showed multilobular radiographic features.

E-PS-09-027
Microcystic acinic cell carcinoma of the submandibular gland: A diagnostic challenge
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Objective: Defining the histologic features of microcystic acinic cell carcinoma of the salivary glands (MACC) and discussing its main differential diagnoses.
Results: A 60-old-year woman with no medical history presented with painful right submandibular swelling lasting for many years. On cervical ultrasound it corresponded to a hypoechoic lymph nodes. FNA cytology concluded to a salivary gland tumour that couldn't be typed. Frozen section examination concluded to a malignat salivary tomor. Further microscopic examination of the paraffin embedded tissue showed a tumour composed of sheets and microcysts. Tumour cells had a clear or eosinophilic cytoplasm. There were areas of mucosecretion. P 63 staining was negative. We concluded to a MACC.
Conclusion: MACC has many overlapping features with mucoepidermoid carcinoma of salivary gland. P63 immunohistochemical staining can be useful in the differential diagnosis.

E-PS-09-029
Hyalinizing clear cell adenocarcinoma of the gingiva
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Objective: Hyalinizing clear cell adenocarcinoma (HCAC) of the salivary glands is a rare and low-grade malignant tumour which lacks features of other specific tumours that have predominant clear cell population. We present a hyalinizing clear cell adenocarcinoma of salivary gland in an unusual localization.

Method: A 45 year old man was presented with an ulcerated maxillary gingival mass with the duration of 3 months. The clinical examination was unremarkable. Total excision was performed.
Results: Histopathologically, lesion was characterized by nests of glycogen-rich monomorphic clear cells within a hyaline stroma. Tumour cells were positive with pan-cytokeratin, cytokeratin-7 and revealed low proliferative index for Ki-67.
Conclusion: Since, HCCC has a better prognosis and the adequate treatment is wide excision, it should to be differentiated from other clear cells carcinomas. No further therapy was given to the patient. Ten months after the surgery, the patient is symptom free without local recurrence and on regular follow up.

E-PS-09-030
Fibrolipoma of the palatine tonsil
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Objective: Benign tumours of the palatine tonsil are estimated to 25 % of all neoplasms of the tonsil. Among these benign tumours most of them are squamous papillomas or lymphangiomas. Histologically, the normal tonsillar framework is usually devoid of adipocytes. That may explain the fact that adipocytic tumours are rare in this tissue. We present a rare case of a fibrolipoma of the palatine tonsil.
Method: A 25 years old man presented with a foreign body sensation in the throat. Clinical examination revealed a polypoid smooth yellowish mass arising from the right tonsil. The patient underwent a bilateral tonsillectomy and the resected specimen was addressed for a pathological examination. Macroscopic analysis found a lobular yellowish mass measuring $1.5 \times 1 \times 0.7$ cm arising from the right tonsil.
Results: Microscopy showed tonsillar tissue with a polypoid lesion composed of mature adipose tissue surrounded with strands of fibrous tissue. The mass was covered of non-keratinised stratified squamous epithelium.
Conclusion: Fibrolipoma is a benign, slow-growing neoplasm composed of an abnormal collection of mature adipose cells with prominent bundles of mature fibrous tissue traversing fatty lobules. They usually occur in subcutaneous tissues but rarely in the aerodigestive tract especially palatine tonsil.

E-PS-09-031
A case of diffuse large B-cell lymphoma misdiagnosed as an odontogenic infection: A clinicopathological report
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Objective: To report an unusual case of diffuse large B-cell lymphoma (DLBCL) misdiagnosed as an odontogenic infection.
Method: Using a retrospective study design, we analysed the patient file and pathological data.
Results: A healthy 44-year-old Caucasian man presented with multiple dental caries and swelling of the left mandible for a month. There was neither any discomfort nor B-symptoms except lymphocytosis. An initial diagnosis with the first histopathological confirmation was buccal cellulitis. However, the patient had no response to antibiotic and surgical treatments. The second histopathological findings demonstrate diffuse, monotonous proliferation of large, round cells. The immunohistochemical analysis revealed positivity to CD20, BCL-2, CD10, negativity to cyclin-D1, TdT and CD3 and no chromosomal change of BCL-2 and BCL-6 genes. Ki-67 reactivity was 90 %. The diagnosis of DLBCL-Stage IE was made. An MRI demonstrated a 3.8×3.1-cm mass involving peri- and paramandibular and parapharyngeal spaces with osteolytic area of the mandible. The patient was opted to 6 cycles of CHOP-R-14.
Conclusion: Oral lymphomas are very rare, especially those present as a swelling in patients with poor oral hygiene. Maxillofacial/head and neck surgeons should be aware of this uncommon condition. We also review the clinicopathological aspects of the oral DLBCL.

E-PS-09-032
A report of an exceptional case of acinar cell carcinoma of the parotid gland
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Objective: Describe the pathological characteristics of acinar cell carcinoma of the parotid gland.
Method: We report the case of a 64-year-old female patient who presented with a parotid mass whose characteristics were clinically and radiologically suspected. The patient had an enlarged lumpectomy. We proceeded to a frozen section, then the tumour was embedded in formalin 10 %. Afterwards, we performed parafin sections and colored them with hematoxilin eosine.
Results: Frozen section concluded to a benign lesion. However, the definitive examination showed a malignant epithelial proliferation often organized in full spans. Tumour cells line glandular lights or wider cavities. They are large and have round or polyhedral shape with granular cytoplasm. The nuclei are round and concentric. Cytoplasmic granules are PAS positive. The diagnosis of acinar cell carcinoma of the parotid gland was retained.
Conclusion: The acinar cell carcinoma is a rare malignant tumour of the parotid gland. Histologically, the tumour is characterized by serous acinar cells. It has a recurrence rate of 35 % with a risk of metastases of 16 %.

E-PS-09-033
Carcinoma ex pleomorphic adenoma of the parotid gland: A case report
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Objective: Describe the pathological characteristics of the carcinoma ex pleomorphic adenoma of the parotid gland.
Method: We report the case of a 55-year-old woman who presented with a huge swelling of the parotid region evolving for a year. Physical examinaton and MRI were in favor of malignancy. The patient underwent a lumpectomy and lymph node dissection. The samples were embedded in formalin 10 %, then we performed parafin sections and colored them with hematoxilin eosine.
Results: By microscopic examination, there was an invasive tumour consisting of malignant epithelial proliferation and benign myoepithelial proliferation within a fibromyxoid stroma. Malignant epithelial proliferation was composed of large round cells with abundant cytoplasm. They exhibit large nuclei that are often vesicular, with nucleoli and sometimes mitotic. The tumour cells form clusters sometimes centered by horny globes. These clusters are surrounded by regular myoepithelial cells. Lymph node dissection was negative and the resection limits were unscathed. The diagnosis of carcinoma was retained.
Conclusion: Carcinoma ex pleomorphic adenoma is a type of malignant mixed tumour of the parotid gland. It results from the malignant transformation of a preexisting pleomorphic adenoma. Its prognosis is dominated by the capsular invasion and histological grade.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-10 History of Pathology

E-PS-10-001
History of pathology
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Objective: Regarding my extreme enthusiasm in pathology, I decided to arrange a search to obtain the most important and beautiful events which helped to improve this fascinating type of science.
Method: Sites, books and articles related to pathology were searched and interesting parts were selected. Then they were arranged by time order and suitable photos attached.
Results: The results of this study were more than interesting to me, especially in the fields of frozen section, cytopathology and molecular pathology.
Conclusion: We can learn from our ancestors how to think, to do research and how to try so much to reach advances in our careers.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-11 Infectious Diseases Pathology

E-PS-11-002
Trichinella Spiralis: Two cases associated with neoplasia
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Objective: Finding of Trichinella spiralis in two patients with neoplasia rise an alert in Argentina to adopt preventive measures, since prevalence is unknown due to lack of mandatory obligatory communication.
Method: Patient I: 61 years old female with laryngeal squamous cell carcinoma. Patient II: 54 years old female with invasive ductal carcinoma. Quadrantectomy and breast reconstruction with muscle flap was performed. Due to intercurrent infections the flap was removed and submitted to pathological study.
Results: Patient I: Laryngeal squamous cell carcinoma diagnosis was confirmed. Trichinella Spiralis larvae in pre laryngeal muscle was detected as a casual finding. The patient died 15 months after the trichinellosis diagnosis without parasitic treatment. There were no parasitism family history. Patient II: Trichinella Spiralis larvae was detected in the myocutaneous flap. Anti-parasitic treatment was contraindicated by the oncologist and the patient is asymptomatic after 2 years evolution. Breast cancer is in progression.
Conclusion: Pork consumption non submitted to official surveillance should be avoided and penalized. It is necessary to remark the importance of mandatory communication of illegal slaughter to eradicate the disease.

E-PS-11-003
A case of human pulmonary dirofilariasis clinically mimicking lung carcinoma
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Objective: Dirofilaria, is a nematode parasite that is spread through mosquito bites. The definite host is the dog. Rarely humans may be infected but since they are not a suitable environment for the nematode, the worm first inhabits cutaneous tissues, then migrates to the right heart ventricle where it eventually dies. Fragments of the worm may reach the pulmonary arteries and lodge in a small calibre vessel to cause infarction or embolism that can be clinically silent or associated with chest pain, fever and haemoptysis.
Method: A 58-year-old woman presented with chest pain. Imaging studies revealed a solitary nodule at the inferior lobe of the left lung that was surgically removed.
Results: Upon gross examination the nodule appeared well circumscribed. Microscopically the central necrotic area was enclosed by a zone of granulomatous inflammation within a dense fibrous capsule. Masson trichrome, Elastica and Reticulin revealed the vessel wall as well as the prominent muscular lateral cords and the bilateral internal cuticular ridges of the worm which assumed a characteristic "bat wing" appearance
Conclusion: Dirofilaria is a parasite that rarely affects humans and may clinically resemble a malignancy. A definitive diagnosis of dirofilaria species can be achieved by tissue biopsy for histopathology and molecular testing.

E-PS-11-004
Sarcina ventriculi: A case report of a rarely seen organism and discussion of its significance
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Objective: Sarcina ventriculi is a gram positive giant cocci that was discovered by J. Goodsir in 1842 and described in his paper published in the Edinburgh Medical Surgery Journal. Further reports have since been made in medical and veterinary literature. Sarcina is most commonly found in the stomach and is often associated with gastric outflow obstruction. Its appearance is distinctive and identification can be made on routine H&E staining. We present a case in which the presence of Sarcina was noted in a gastric biopsy, review the current literature, and discuss the significance of this organism.
Method: We present a case of a 48 year-old gentleman who presented with vomiting. A CT scan showed gastric thickening and an upper gastrointestinal endoscopy was performed. This revealed erythematous gastric mucosa and food residue. Biopsies were taken and histology showed a granulomatous gastritis. In addition, Sarcina-like organisms were seen. Special stains for micro-organisms (Ziehl Neelsen and PASD) were negative.
Results: Review of the literature shows that it remains unclear if Sarcina is pathogenic or simply more likely to be identified in cases of gastroparesis or gastric outflow obstruction. In a series of five patients where Sarcina was identified in gastric biopsies, the presence of a concurrent gastric ulcer may put the patient at increased risk of complications such as emphysematous gastritis or perforation.
Conclusion: The literature suggests that the presence of Sarcina organisms should prompt further investigation for functional causes of gastric outlet obstruction and delayed gastric emptying, such as occult malignancy. Other authors recommend treatment with antibiotics and anti-ulcer therapy in such cases.

E-PS-11-006
Cytokine storm in a fatal case of acute infectious mononucleosis
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Objective: Report of a rare case of fatal Acute Infectious Mononucleosis (AIM).
Method: Summary of clinical history, histopathology, pre- and postmortem laboratory tests.

Results: Clinical History: A 19 year-old female presented with throat pain and fever. A Monospot test was positive. She deteriorated progressively in 3 days with increasing throat pain, worsening fever and dyspnea. She was hospitalized and on the second day of admission was found in cardiorespiratory arrest. She was resuscitated successfully. Chest X-rays revealed possible ARDS. She coded three more times in a period of 6 h and died. Histopathology: Cervical acute lymphadenitis, necrotizing tonsillitis, Diffuse Alveolar Damage (DAD) and acute interstitial pneumonitis, acute splenitis and superficial splenic tear, acute hepatitis and severe hemophagocytic lymphohistiocytosis (HLH). Post-mortem laboratory tests: Elevated EBV Ab VCA IgG and IgM. Real-time PCR: 4.65 × 10^6 EBV copies/ml. Ferritin: >10,000 ng/ml (ref: 18–464 ng/ml). Pre- and Post-mortem cytokine serum levels (Human Cytokine 27-plex): The following showed marked elevation between pre- and postmortem serum samples: IL-1 beta; IL-6, IL-8, IL-12, IL-15, G-CSF, GM-CSF, IFN-gamma, CXCL10, CCL2, and TNF-alpha.
Conclusion: AIM is a very common infectious disease worldwide that affects children and adolescents. In very rare cases, the disease is fatal due to splenic rupture, encephalitis, DIC and severe HLH. In this case we were able to demonstrate diffuse alveolar damage and severe HLH which ultimately led to the patient's demise. Viral load was extremely high and the cytokine pattern was that of a "cytokine storm" leading to increased microvascular permeability, DAD, and HLH.

E-PS-11-007
Unusual course of tuberculosis in immunosupressed patient
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Objective: Morphological diagnostics of tuberculosis in immunosupressed patients may be extremely difficult due to unusual histopathological picture and appearance of acid resistant rods.
Method: Autopsy data of a patient X, 80 yearss old, suffering from chronic lymphocytic leukemia Rfi stage 0/BinetA with isolated deletion of 13q is presented in comparison of clinical, bacteriological, PCR data made during life time with morphological changes, including Ziehl-Nielsen staining.
Results: For 4 years she was suffering from chronic leukemia, within last 6 months was suspected tuberculosis. According recent clinical and X-Ray data patient had infiltrative tuberculosis with formation of the cavities with detection of M. tuberculosis in culture and PCR. On autopsy were seen only fungal lesions of trachea, bronchi mucous membranes and suspicious foci in lung tissue. During the routine histopathology were detected numerous fungal filaments probably Aspergillus) and foci with sclerosis. In Ziehl-Nielsen staining typical acid resistant rods were found practically in all fields of view. We considered as the most expressive the localization of the rods just upon fungus.
Conclusion: 1) In immunosuppressive patient typical macro- and histological picture of tuberculosis may be absent. 2) Mycobacteria tuberculosis can be localized on the surface of fungi.

E-PS-11-008
Parasitic infection presenting as an unusual soft tissue tumour in a 2 year old child
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Objective: In pediatric patients a malignancy is often the primary consideration when presented with a soft tissue tumour accompanied by weight loss. While sarcomas are common in this age group, non-neoplastic or infectious causes should also be considered. Our aim is to cause awareness that parasitic infections can present as aggressive soft tissue tumours.
Method: We present a case of a 2 year old female with weight loss and a gradually enlarging mass initially involving the vulva and extending to the abdomen, thigh, retroperitoneum, urinary bladder and ureter. The admitting impression was Rhabdomyosarcoma versus Lymphovascular Malformation. Histopathology specimen, complete work-up for malignancy, special stains and serum serology were done.
Results: Skeletal survey, bone marrow biopsy, serum alphafetoprotein and Beta-Human Chorionic Gonadotrophin were negative. Incision biopsy showed non-caseating granulomatous inflammation with giant cell formation and fibrosis. Gram stain, blood culture, tissue Acid Fast Bacilli, Galactomannan and Nitroblue Tetrazolium test were all negative. Serum enzyme immunoassay (EIA) for Strongyloides and Toxocara canis were positive.
Conclusion: Visceral larval infection can manifest as aggressive soft tissue tumours and should be included in the differential diagnosis. Serum EIA is useful to detect the causative agent when histology does not reveal the pathogen due to tissue reaction and degenerative changes.

E-PS-11-009
Disseminated strongyloidiasis: A challenging diagnosis
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Objective: Strongyloidiasis is an infectious disease caused by Strongyloides stercoralis. Disseminated form is associated with severe immunosuppression. It usually mimics severe sepsis and is challenging regarding diagnosis and treatment. Diagnosis depends on clinical suspicion and demonstration of the larvae on fluid or tissue. Cutaneous evolvement is rare.
Method: A 53-year-old men, HTLV-1 positive, presented with severe sepsis and neutrophilic leukocytosis without eosinophilia. Clinical suspicion was made because of a previous history of strongyloidiasis, vomiting, abdominal pain, hiporexia and maculous, brownish serpiginous abdominal skin lesions.
Results: Histology revealed Strongyloides stercoralis in faeces parasitological exam. Larvae were seen among collagen fibers in skin biopsy, together with scant perivascular lymphoid cells and extravased erythrocytes. Larvae were also seen in duodenal biopsies and broncoalveolar and gastric smears.
Conclusion: The diagnosis of disseminated strongyloidiasis is based on the finding of larvae in different parts of the body, particularly faeces, gastric and tracheal secretions, bronchial, skin, lung and jejunal biopsies. Strongyloidiasis may cause life threatening infection. Regarding our patient, clinical improvement occurred after 21 days of subcutaneous Ivermectin and the last parasitological exam was negative.

E-PS-11-010
Necrotizing fasciitis associated with injection drug use with fatal outcome: Report of two autopsy cases
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Objective: Necrotizing fasciitis (NF) is rare progressive infectious disease of fascia, subcutaneous fat and muscles, that may be fatal for intravenous drug abusers. We report two autopsy cases of NF in intravenous drug abusers.
Method: 36-year-old man was found dead in his house and the other 23-year-old man died in the hospital. Autopsies of both corps with histopathological examination were performed at the Institute of Pathology and Forensic Medicine, Military Medical Academy, Belgrade.
Results: Edematous and gagrenous skin with injection signs in left inguinal region of older and right tight of younger man were externally examined. Both men had purulent inflammation of subcutaneous fat, fascia and muscle. Older man had gross myocarditis and younger had pneumonia

signs. Histopahologically both men had moderate mixed, predominantly neutrophilic, inflammation in subcutaneous fat, fascia and around myocytes, with scant lymphocytes and plasmacytes and moderate necrosis. The same type of inflammation and fibrosis were found in myocard of older, and in lungs, kidneys end periportal liver spaces in younger man.
Conclusion: Necrotizing fasciitis usually occurs in middle age men, intravenous drug abusers and may cause death by spreading the infection to surrounding tissues and organs leading to sepsis.

E-PS-11-011
Spinal echinococcosis: A case report
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Objective: Spinal echinococcosis is a rare condition. Due to the lack of clinical suspicion of spine lesions in case of parasitic diseases, doctors face serious difficulties in diagnosing this condition before surgery.
Method: The 30-year old patient was operated at the orthopaedics department of the National Centre for Tuberculosis Control with a clinical diagnosis of active stage of tuberculous spondylitis (L1-2-3 vertebrae) with destruction of vertebral bodies. The condition of the patient was complicated by abscess. The patient complained of increasing back pain during the movement (and pain medication decreased the pain), fatigue and weight loss (5 kg during 5-month period), and he noted a deterioration of his condition within the last 4 months. The patient received treatment with anti-TB drugs, which did not have any effect but aggravated his physical condition. The patient received a routine examination, including CT, that allowed to identify destruction of multiple vertebral bodies (L1-2-3) and paravertebral abscess.
Results: The patient had right-sided lumbotomy, a surgery to drain paravertebral abscess, necroectomy of vertebral bodies (L1-2-3). During the surgery, multiple cysts containing fluid and bone fragments were removed. Histological examination revealed bone grafts with signs of destruction and cystic structures with inner germinal layer.
Conclusion: Our case demonstrates the problem in the diagnosis of spinal echinococcosis in clinical practice. Despite significant post-surgery improvement in the condition of the patient (absence of pain, the patient is able to walk independently), the presence of cystic structures with inner germinal layer creates a high probability of further contamination.

E-PS-11-012
Anorectal tuberculosis: A report of a challenging case
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Objective: The rarity of anorectal tuberculosis can lead to misdiagnosis of Crohn's disease or foreign body granuloma by unexperienced pathologist. In order to raise awareness of tuberculosis, we present a challenging case from high-incidence population (38.0/100 000).
Method: Medical documentation and pathology slides were reviewed in the context of up-to-date medical literature.
Results: A 44-year-old male complained about anal pain and bloody discharge for preceding 6 months. Haemorrhoids and chronic anal fissure were suspected clinically and excised. By pathology, foreign body granulomas were reported. A year later, patient experienced clinically recurrent anorectal symptoms; perirectal inflammation and bilateral inguinal lymphadenopathy by computed tomography; leukocytosis and high level of C-reactive protein. Despite antibacterial/antimycotic treatment, symptoms relapsed again 4 months later. Reevaluation of previous tissue material disclosed caseating granulomas with multinucleated giant and epitheloid cells surrounded by lymphocytes and fibrous tissue. Thus, anorectal tuberculosis was diagnosed. The following evaluation revealed pulmonary tuberculosis, history of human immunodeficiency virus (HIV) infection for 15 years and presence of multidrug-resistant Mycobacterium tuberculosis in sputum and anorectal tissue.
Conclusion: Tuberculosis can affect anorectal soft tissues mimicking haemorroids. The historic paradigm of careful search for caseous necrosis in granulomas still can disclose clinically challenging extrapulmonary tuberculosis, especially in high-incidence regions and HIV-infected patients.

E-PS-11-013
Endoscopic ultrasound-guided fine needle aspiration biopsy diagnosis of disseminated histoplasmosis in retroviral positive patient
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Objective: Endoscopic Ultrasound-Guided Fine Needle Aspiration Biopsy is a challenging field in cytology, carried out in specialized centres, and needs careful examination on limited material to make an accurate diagnosis. It is commonly practiced to diagnose both malignant and granulomatous lesions, rarely for suspected infective aetiology.
Method: A 23-year-old retroviral positive male presented with diarrhoea and abdominal pain. CT scan revealed multiple, enlarged intraabdominal lymph nodes. A provisional diagnosis of lymphoma was made and EUS-FNA biopsy was carried out. A grayish brown fragment of 1 mm was received and processed in microwave tissue processor.
Results: Histology showed mostly fibrinous material, with one localized fragment of lymphoid tissue exhibiting closely packed, diffusely distributed, yeast-like organisms measuring 2 to 4 μm in size. Similar yeast like organisms were seen in the surrounding fibrinous element, distributed in a loose fashion. The organisms were strongly positive for PAS special stain. Features of disseminated histoplasmosis involving abdominal lymph nodes were confirmed.
Conclusion: The diagnosis of histoplasmosis or other opportunistic infections on EUS-FNA biopsy material can be very challenging, but rewarding at the same time. Clinical correlation with histology findings is a necessity on all challenging cases of EUS-FNA.

E-PS-11-014
Ovarian actinomycosis and amebiasis mimicking a suspicious malignant mass
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Objective: Amebiasis is seen worldwide and is more prevalent in tropical regions. Incidence of amebiasis in Tunisia is 6 cases per year. The most frequent extraintestinal manifestation of amebiasis is liver abscess.
Method: We report a case of a 47-year-old woman who presented with a 6-month-history of pelvic pain and heaviness.
Results: Examination revealed a latero-uterine mass. Imagery based on ultrasound examination and CT scan found an ovarian suspicious malignant mass with ascites. Patient had hysterectomy with bilateral salpingo-oophorectomy, appendicectomy and omentectomy. Gross examination showed an ovary replaced by a 8x6cm mass of grayish-white nodular tissue. Histologic evaluation showed an intense inflammatory infiltrate, mainly composed of neutrophils, lymphocytes and histiocytes. Actinomycotic granules were seen as basophilic filaments radially arranged, In addition, we discovered numerous amebas among the inflammatory infiltrate and necrosis. Theses findings were consisting with an ovarian actinomycosis and amebiasis. The patient received specific antibiotherapy with a good clinical evolution.
Conclusion: Although ovarian actinomycosis is commonly seen, ovarian amebiasis has never been reported in literature.

E-PS-11-015

Gastric actinomycosis: A rare pitfall of local tumour recurrence

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Objective: Actinomycosis is a chronic suppurative granulomatous inflammation caused by anaerobic, Gram-positive bacteria of Actinomyces species. In abdominopelvic actinomycosis,primary gastric actinomycosis have rarely been reported. Factors that precipitate intra-abdominal actinomycosis include surgery, inflammation, and visceral perforation. There is no specific radiological or endoscopic appearance and the image findings usually include an infiltrative lesion with diffuse gastric wall thickening, highly suggestive of a neoplastic disease.
Method: Case report with literature review.
Results: A 70 years-old man with a tubular adenocarcinoma of antrum (pT2N0M0), submitted to a subtotal gastrectomy with sequent gastrojejunostomy. On the third year of follow-up he presented with diffuse abdominal pain and abdominal distention, with no history of fever or other symptoms. CT-scan and endoscopy were performed and findings were consistent with recurrence. Even though no tumour was documented by biopsies the patient was submitted to a resection of the anastomosis and residual stomach. The histologic examination revealed a transmural inflammatory process associated with the presence of suture material and of Grocott's, and Gram positive morphologically consistent with Actinomyces.
Conclusion: Although extremely rare, gastric actinomycosis should be considered in the differential diagnosis of gastric wall thickening and tumour-like or infiltrative lesions, particularly in patients with history of previous gastric surgery.

E-PS-11-016

Kaposi sarcoma in an HIV-negative patient with thymoma and myasthenia gravis

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Objective: Kaposi's sarcoma (KS) is a vascular proliferative disorder, occurs in HHV8 infected patients as is influenced by immune status. Usually limited to skin it may involve mucosae, visceral organs and lymph nodes. Myasthenia gravis (MG) is an autoimmune disorder affecting neuromuscular transmission. It is associated with thymoma in 15 % of the cases, and for those the neoplasm should be removed. The treatment can also include radiotherapy and/or pharmacological options, including immunosuppressive drugs.
Method: Case report with literature review.
Results: A 50 years old male patient with MG and thymoma submitted to thymectomy and treated with immunosuppressive therapy. During follow-up, after surgery, an expansive maxillary sinus was diagnosed and undertaken by endoscopic surgery. At that time, the histologic report concluded for a "kaposiform hemangioendothelioma". Five years after, his MG relapsed and more immunosuppressive therapy was prescribed. A few months after, newly pigmentation skin lesions appeared and were biopsied. The pathologic findings were consistent with KS. The previous maxillary tumour was then reviewed and the evidence of positivity for HHV8 turned it to a Kaposi sarcoma.
Conclusion: KS is a rare disease, but incidence varies according to individual factors such as immune status of the patient. A potential correlation between KS and MG can be considered.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-12 IT in Pathology

E-PS-12-001

Testing smart phone microscope adapter to use capturing pathologic image

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Objective: In era of smart phone, we send e-mail for second opinion, and discussed with each other in chatting smart phone application such as Line messenger, Google Hangouts or Kakaotalk. But scanning glass slide was time-consuming and hard work, whatever if you could use brand-new slide scanner from Leica's Aperio digital pathology. Capturing image from Olympus microscope with camera was used in daily practice for conference and hospital-to-hospital discussion, but it is expensive and there are a few microscopes with Olympus camera in one hospital. Microscope adapter for smart phone could be fascinating alternative method to get pathology photo. There are some adaptors in market, but they have some disadvantages for using daily practice by pathologists.
Method: Two commercial adaptors were tested to capture pathology image by smart phone for presentation and interdepartment consultation. Microscopes from Olympus, Nikon and Leica were also used.
Results: The quality of microscopic photo was suitable for use in presentation using any smart phone adaptors.
Conclusion: Microscope adapter for smart phone works well for capturing useful pathologic image.

E-PS-12-003

A survey of online pathology information users

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Objective: Determine sought after practice-related pathology information.
Method: We surveyed online pathology information users via an open access pathology website and recruited via informal appeals, Facebook and Twitter.
Results: Twenty-seven surveys were completed, relatively few in relation to the unique visitors numbers of the web site during the survey period (~4000). The most sought after elements (1–2 of 5 point scale) were images (80 %), microscopic descriptions (76 %), information on immunohistochemical stains (68 %), reporting/sign out language (68 %), and image annotations (60 %). Less sought after information included special stains (52 %), additional references (40 %), cancer staging (36 %) and grossing (32 %). Respondents frequently (1–2 of 5 point scale) sought information from colleagues (75 %), offline textbooks (60 %), search engines (56 %), open databases (e.g. PubMed, Google Scholar) (52 %), review journal papers (33 %), open access sources-other than the hosting web site (44 %), login services (36 %) and Wikipedia (20 %).
Conclusion: Images and microscopic descriptions are likely the most sought after elements online. The interest in sign out terminology may represent a desire to simplify and standardize reporting. Users of pathology information online still rely heavily on offline resources. A comparison of these findings to previously collected website usage information may result in further insights.

E-PS-12-004

Diagnostic biopsies for cancer in Africa: A system's approach to transforming care

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Objective: A primary goal of any health care system should be to attain universal access for all patients within a catchment area. In the cancer care model, this requires that any physician encountering a patient they suspect of having a malignancy have access to a system that ensures rapid, accurate, and reliable pathology for primary diagnosis of cancer. Sub Saharan Africa faces immense challenges in providing adequate coverage and each region, country, and district with unique obstacles to overcome when meeting the health needs of the population.
Method: The American Society of Clinical Pathology (ASCP), in partnership with the White House Office of Science Technology Policy and the Clinton Global Initiative, recently launched a 26.5 million dollar multi-year initiative which begins with assessment of potential countries with the greatest need–including collaboration and capacity program building with local officials and staff–to deploy full service pathology infrastructure for eligible countries to strategically to meet their population needs.
Results: Working in parallel and together, Steering Committees for Diagnostics and Technology, Care and Treatment, In-Country Medical Education, Bioethics, and Monitoring & Evaluation have focused on each potential country to optimize success. The maximal intervention includes deployment of automated histopathology systems and integrated whole slide imaging systems linked through a customized laboratory information system to a dedicated team of pathologists from the United States.
Conclusion: This long-term project will roll out to 10 or more countries in Africa as well as Haiti. An overview of the project will be presented as well as experiences data from countries launched to date.

E-PS-12-005
Immunohistochemistry and special stains automated instrument interfaces
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Objective: To implement an interface between the anatomic pathology LIS and automated immunohistochemistry and special stain instruments.
Method: We partnered with our vendors, Sunquest Information Systems and Dako, to implement a bi-directional HL7 interface between our AP-LIS, (Sunquest CoPath) and our automated immunohistochemistry (IHC) and special staining platforms, eliminating dual order entry and associated errors while improving workflow efficiency and capacity.
Results: System implementation resulted in direct time savings of 575.7 Hrs/YR for IHC staining automation and 118.2 Hrs/YR for special stains increasing capacity and efficiency in histology. Transposition, slide relabeling and run time errors were eliminated improving patient safety and diagnostic accuracy.
Conclusion: The impact this project was the simplification of the workflow and run setup process, as orders were seamlessly transferred electronically between the AP-LIS and the IHC and special stain autostainer instruments. The implementation of unique ID technology and the HL7 interface has greatly reduced patient mis-identification. By eliminating slide relabeling from the process, we have further automated the workflow, which has resulted in the savings of hundreds of hours of labor. The histology lab is now able to better allocate resources, while at the same time, increasing efficiency and capacity.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-13 Digestive Diseases Pathology — Liver and Pancreas

E-PS-13-001
Lipid histiocytosis of the gallbladder neck lymph node and obesity
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Objective: The objectives of this study were to report the features of lipid histiocytosis of the gallbladder neck lymph node. Such lesions are rarely reported nowadays.
Method: Two cases diagnosed with gallbladder neck lymph node lipid histiocytosis were analysed for clinical, morphological and immunohistochemical features.
Results: The two obese patients presented with gallbladder lithiasis detected on CT-scan. The treatment consisted in coelioscopic cholecystectomy. Microscopy revealed subacute/chronic lithiasic cholecystitis and foci of vacuolated cells in the gallbladder neck lymph node. These cells were positive for CD68, CD31, S100-protein, adipophilin and TIP47; negative for cytokeratin and Alcian blue.
Conclusion: In conclusion, we report lymph node lipid histiocytosis diagnosed microscopically after cholecystectomy. While such lesions may remain unidentified on imaging procedures, the microscopic analysis may require special stains and immunohistochemistries for ruling out adenocarcinoma metastasis.

E-PS-13-002
It's not so bad: Focal nodular hyperplasia of the liver in a 2 year-old male
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Objective: Focal nodular hyperplasia (FNH) represents 0.02 % of primary hepatic neoplasms in children. Here we present a case of an FNH from a 2 year-old male, review its epidemiology, pathophysiology, definitive histologic features, treatment and prognosis. Ultimately, we aim to raise awareness of a rare benign lesions in an age group where a primary liver mass usually represents a malignant tumour.
Method: Herein we describe the case of a 2 year-old male who presented with a year-long history of an abdominal mass, atypical radiologic findings and normal alphafeto protein levels.
Results: The tumour was thought to be a hepatoblastoma and was excised. Histopathological examination demonstrated focal nodular hyperplasia. The patient was discharged well after surgery.
Conclusion: Recognition of benign primary liver lesions in the pediatric age group where malignant tumours are more frequently seen is essential because prognosis and treatment greatly differs.

E-PS-13-004
Acrometastasis as the initial presentation of hepatocellular carcinoma
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Objective: Acrometastasis occur infrequently, accounting for approximately 0.1 % of all metastatic osseous involvement. Its presentation mimics infectious or inflammatory disease. Primary manifestation of HCC as acrometastasis is extremely rare.
Method: Case report: A 59 years old alcoholic male was admitted with sudden onset profuse bleeding from an ulcer involving middle and proximal phalanx of left middle finger. According to the patient this was a chronic wound following a road traffic accident. Patient underwent amputation of this finger for the clinical diagnosis of chronic osteomylitis. Macroscopy showed a continuous lesion from skin to bone with evidence of bone destruction. Microscopy together with immunohistochemistry (HepPar 1 antibody) confirmed a deposit of a HCC with skin and bone infiltration. Follow up radiological investigations revealed two foci of hepatocellular carcinoma with background cirrhosis.
Results: Discussion: HCC show a haematogenous spread usually via pulmonary circulation and vertebral circulation. Hence the mechanism of spread into bones other than the bones of the axial skeleton, bypassing the lung is not explained. Amputation, radiation, excision, and systemic

therapy are available treatment options. Radiotherapy is an effective and non-invasive treatment that improves patient's quality of life.
Conclusion: The presence of acrometastasis in patients with cancer helps staging the disease and usually indicates a very poor prognosis.

E-PS-13-005
Necrotizing acute pancreatitis following trans-arterial chemoembolization of liver metastasis from rectal cancer using irinotecan beads: An autopsy case
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Objective: To present a case of necrotizing acute pancreatitis (NAP) that resulted in patient's death after being submitted to trans-arterial chemoembolization (TACE) of liver metastasis (LM) from rectal cancer (RC), followed by a review of the Revised Atlanta Classification of acute pancreatitis.
Method: A 72 year-old man with RC submitted to surgery and chemotherapy was diagnosed with a LM deemed unresectable and underwent TACE. The patient died less than 48 h after the procedure and the autopsy was performed.
Results: External examination showed Cullen's sign on the abdominal wall. Internal examination revealed extensive cystosteatonecrosis. The pancreas and peripancreatic tissues exhibited hemorrhagic necrosis and the liver showed a 4 × 3 cm nodule. On histological examination we observed numerous vessels occluded by reddish microspheres (Irinotecan beads) on multiple sites, including pancreas, liver, biliary tract, soft tissue and retroperitoneal lymph nodes. The terminal accident was a sterile NAP (of both pancreatic and peripancreatic tissues) of embolic cause and the fundamental disease was a LM which was partially necrotic.
Conclusion: NAP is a described complication of TACE and presumably occurs due to regurgitation of embolic material, which can occur only after the procedure. NAP should be kept in mind even when TACE is thought to have been safely performed.

E-PS-13-006
Spontaneous regression of colorectal liver metastases
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Objective: Spontaneous regression of cancer consists in the complete disappearance or partial shrinkage of a malignant neoplasm without appropriate treatment. It is an extremely rare event, apparently more common for renal cell carcinoma, non-Hodgkin lymphoma and leukaemia, neuroblastoma and melanoma.
Method: A 51 years old woman underwent left colectomy for treatment of an adenocarcinoma (staged pT3N1M0), followed by adjuvant chemotherapy (twelve FOLFIRI cycles). Six years later two hepatic nodes, suggestive of metastases, were diagnosed by abdominal CT and MRI exams. Before the number and resectability of the hepatic lesions, the patient underwent a right hepatectomy.
Results: No complications occurred in the postoperative period, and the patient was discharged on 7th post-operative day. The pathological examination revealed two metastatic nodules, completely necrotic, with no viable tumour. The patient was submitted to adjuvant chemotherapy (FOLFIRI) and is currently in her 10th post-operative month, free of disease.
Conclusion: The authors report an exceedingly rare case of spontaneous regression of colorectal liver metastases. There are only 21 cases of spontaneous regression of colorectal cancer accounted for in the literature from 1900 up to 2005, nine of which relate to remission of liver metastases. The physiopathological mechanisms behind spontaneous regression are yet to be fully understood.

E-PS-13-008
Pathologic characteristics of resected hepatocellular carcinomas
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Objective: Hepatocellular carcinoma is the most common primary malignancy of the liver. The relation between the factors affecting the etiopathogenesis (viral hepatitis, alcohol, metabolic disorders, etc.) of hepatocellular carcinoma and microscopic pattern of tumour, differentiation, lymphovascular invasion, and prognostic parameters was investigated in this study.
Method: Eighty two cases that underwent resection for hepatocellular carcinoma between 2005 and 2010 were evaluated retrospectively.
Results: Average age of the cases was 53.47. Of the cases, 89 % (n = 73) were male and 11 % (n = 9) were female. The mean tumour diameter was 4.5 cm. Viral infection was the most important cause of hepatocellular carcinoma at a rate of 85 %, including viral hepatitis B, C, D and HIV. While in 91.5 % of the cases (n = 75) cirrhosis was observed in addition to tumour, %37.5 (n = 24) were established to have dysplastic nodules. Large portal vein or hepatic vein invasion was present in 23.1 % (n = 19) of the cases.
Conclusion: Viral etiology for hepatocellular carcinoma (predominantly Hepatitis B and Hepatitis C virus) is still the most significant risk factor in our region.

E-PS-13-009
Evaluation of muc expressions along with histopathologic prognostic parameters and their association with survival in pancreatic ductal adenocarcinomas
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Objective: Pancreatic ductal adenocarcinomas(PDAC) are difficult to diagnose, and do not have any specific immunohistochemical staining pattern . MUC expressions in PDAC can provide prominent clues to predict the prognosis. Evaluation of the relationship between MUC expressions, and survival in our cases is aimed in this study.
Method: 54 PDACs resected between 2012 and 16 were stained with CK7, CK20, MUC1, MUC2, MUC5AC, MUC6, and CDX2; and examined by 4 blind researchers under a multi-headed microscope. Diffusion and density of staining was scored as 0–3 using a certain scoring system. Histopathologic prognostic parameters were obtained from pathology reports. Survival informations retrieved from "National Death Information System". Datas were evaluated by "Spss Statistics Programme".
Results: F/M ratio was 2/3; and mean age was 65. 43 % was alive, while 53 % was dead. Mean survival was 16 months. MUC1 staining was correlated with lymph node metastasis (p = 0,009). MUC5 density was correlated with lymphatic invasion (p = 0,01). Widespread of MUC6 was correlated with grade (p = 0,008), and survival (P = 0,047).
Conclusion: MUC1, MUC5 and MUC6 stains might be useful to predict the risk of lymph node metastasis, grade, and survival of PDACs.

E-PS-13-010
The use of special stains in liver biopsy interpretation: Implications for the tropics
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Objective: This study aims to re-evaluate a set of liver biopsies which has been diagnosed solely on H&E stains by performing a standard set of special stains on them.
Method: The formalin fixed paraffin embedded (FFPE) blocks of liver biopsies reported in two histopathology laboratories between 2008 and 2013 were retrieved. These were stained with H&E and the following standard special stains for liver tissue histology—Perl's Prussian Blue, Reticulin, Sirius Red, Shikata Orcein and PAS with Diastase. The stained slides were re analysed.
Results: 74 liver biopsy paraffin blocks were received in the laboratories. 53 (71.6 %) were suitable for analysis out of which 51 (68.9 %) had their clinical details retrievable. In 29 cases (56.9 %), Perl's stain was positive for iron pigment within the hepatocytes with 17 (58.6 %) of these being Grade 1; 7 (24.1 %) Grade 2 and 5 (17.2 %) Grade 3. Shikata orcein revealed hepatitis B viral surface antigen in 15(29.4 %) of the cases while copper-associated protein was demonstrable in 6 (11.8 %) of the cases. The discovery of stainable iron implies some degree of disturbance of iron metabolism and a Grade 3 stainable iron requires investigation for genetic haemochromatosis. The demonstration of copper-associated proteins suggests biliary disease in a non-cirrhotic liver which also requires further investigation.
Conclusion: This study highlights the deficiencies of reporting liver biopsies with H&E stain alone which does not help to fully investigate and manage the patient.

E-PS-13-011
Neuroendocrine tumour and sarcoidosis
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Objective: The incidence of solid tumours is greater in patients with sarcoidosis. Joint presentation of the two diseases is an unusual finding.
Method: A 26-year-old male smoker with a history of systemic sarcoidosis who presented with right lateral lymph-node enlargement and weight loss of 15 kg over 6 months. CT scan of chest and abdomen revealed bilateral laterocervical lymph-node enlargement, multiple swollen thoracic lymph nodes, and bilateral poorly-defined pulmonary nodules, the largest of which measured 1.5 mm. the spleen was enlarged. And A 30 mm hypodense lesion was visible in liver segment VI, subsequently confirmed with PET/TC. Abdominal MRI scan showed a possibly-neoplastic hepatic nodule measuring 4 × 3.5 cm in segment VI.
Results: Examination of liver biopsy specimens revealed a population of neuroendocrine cells displaying positive immunostaining for CKEA1/EA3, chromogranin and CD56+, and negative staining for TTF1; 1–2 % of proliferating cell were Ki67+, and occurred in conjunction with CD68+ multinucleated giant cells. Histochemical staining to rule out the presence of mycobacteria yielded negative results. The lesion was diagnosed as a liver metastasis from an unknown primary neuroendocrine tumour, within the context of systemic sarcoidosis. The patient was given one subcutaneous injection of 120 mg Lanreotide Autogel every 28 days, as a result of which chromogranin levels and liver function returned to normal.
Conclusion: Sarcoidosis predisposes patients to certain types of tumours or whether it is the tumours that cause a sarcoid reaction remains a matter of debate.

E-PS-13-012
Supplemental use of Keratin 7 and 19 immunohistochemical staining in liver biopsy diagnosis
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Objective: Keratin 7 and 19 (K7, K19) immunohistochemical staining (IHS) was employed in past studies to highlight ductular reactions (DR), "untethered" hepatocytes, and early loss of canals of Hering (CoH) in primary biliary cholangitis (PBC). This study aims to determine utility of K7 and K19 as adjunctive diagnostic methods in diverse chronic liver diseases.
Method: 79 archival liver biopsy specimens (LBx) of biliary, non-biliary, and overlap cases were reviewed. Activity grading and staging was done on H&E and trichrome slides. CoH per portal tract (C/P ratio) on K19, extent of DR, amount and distribution of K7+ hepatocytes were assessed quantitatively and semiquantitatively as appropriate. Biliary and non-biliary groups, early and late stages of disease were statistically compared.
Results: C/P ratio is lower in biliary than non-biliary diseases ($P < 0.0001$) and diminished in PBC and overlap cases compared to PSC ($P < 0.0001$). More untethered K7+ hepatocytes are seen in early biliary than non-biliary diseases ($p < 0.0052$) significantly increasing in later stages ($p < 0.0011$). DR differs ($p = 0.00002$) between non-biliary and biliary diseases especially in PBC.
Conclusion: Early stage LBx K7+ untethered hepatocytes favor chronic cholestatic over hepatitic liver disease. Markedly diminished CoH strongly supports PBC. K7 and K19 is useful in assessment of LBx when characteristic histologic findings are absent.

E-PS-13-013
A pancreatic serous cystic neoplasm coexisting with high-grade pancreatic intraepithelial neoplasia mimicking an intraepithelial papillary mucinous neoplasm: A case report
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Objective: Serous cystic neoplasms (SCNs) of the pancreas are rare exocrine pancreatic neoplasms, most of which are benign and do not communicate with the pancreatic duct. Pancreatic intraepithelial neoplasia (PanIN) is considered to be a precursor of ductal adenocarcinoma which is microscopically recognised in pancreatic ducts.
Method: A 67-year-old Japanese woman presented with a 10-mm, multilocular, cystic lesion at the pancreatic body. Magnetic resonance pancreatography (MRP) showed stenosis of the main pancreatic duct at the pancreatic body and the dilatation of the distal side of the main pancreatic duct. Furthermore, communication between the cystic lesion and the main pancreatic duct was suspected by MRP. Distal pancreatectomy was performed under the preoperative diagnosis of an intraepithelial papillary mucinous neoplasm (IPMN).
Results: Histologically, the cystic lesion was lined with non-atypical cuboidal or flat epithelium with clear cytoplasm, and thus was diagnosed as an SCN. PanIN-2 or -3 lesions with stromal fibrosis were observed at the main and branch pancreatic ducts. Histological examination revealed no communication between the SCN and pancreatic ducts.
Conclusion: An SCN coexisting with another pancreatic neoplasm is rare. When dilatation of the main or branch pancreatic ducts coexists with an SCN, as in this case, it clinically mimics IPMN.

E-PS-13-014
Hepacam2 expression in hepatocellular carcinoma
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Objective: Hepatocellular carcinoma (HCC) is the most common type of malignant tumour in the liver. Cell adhesions are important regulators of

cell growth and motility and they are usually altered in cancer. The role of the hepatocyte cell adhesion molecule 2 (HEPACAM2), a member of the immunoglobulin family of adhesion genes, has not been analyzed so far in cancer. In the present study we studied protein expression levels of HEPACAM2 in HCC.
Method: Twenty HCCs with available tissue were recruited from Pathology Department between 2008 and 2016. Clinical information was also obtained. A tissue microarray was performed with representative tumour regions and normal liver. Immunohistochemical techniques were applied to study protein expression levels of HEPCAM2 (Sigma Aldrich).
Results: HEPACAM2 was weakly expressed in normal liver (nuclear staining). Most of HCCs showed a positive expression with three different staining patterns: nuclear, cytoplasmic and mixed. Statistical analysis showed a significant association between grade of differentiation and staining pattern. A significant correlation was noted between survival time, grade of differentiation and presence of metastasis. Staining patterns were also significantly correlated with presence of metastasis.
Conclusion: Our study has revealed three different staining patterns of HEPCAM2 expression in HCCs with clinical relevance.

E-PS-13-015
Primary non-hodgkin lymphoma of the liver revealed by a cholangitis
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Objective: Primary non-hodgkin lymphoma of the liver is an extremely rare entity. Fewer than 100 cases have been reported in the literature. Classically, it affects middle-aged males with non specific clinical expression and moderate biological perturbations. The purpose of this study was to analyze the clinicopathological features of this tumour and to discuss differential diagnoses.
Method: A case with primary non-hodgkin lymphoma of the liver was diagnosed in our department. Clinical data and microscopic slides were retrospectively reviewed.
Results: Our study was about a 94-year-old woman who presented with right upper-quadrant pain, jaundice and fever. Laboratory tests showed cholestasis and cytolysis. A cholecystectomy was performed as well as a hepatic surgical biopsy motivated by biological findings. Histological examination revealed chronic cholecystitis without acute lesions that could explain the symptoms of cholangitis. Immunohistological examination of the liver concluded to follicular B-cell non-hodgkin lymphoma, grade 1. There was no evidence of involvement of the lymph nodes or any other organ. These findings established the diagnosis of primary hepatic lymphoma.
Conclusion: The diagnosis of primary hepatic lymphoma is important because the disease is treatable and with new therapeutic drugs, such as rituximab, overall survival has improved for these patients.

E-PS-13-017
Classic and fibrolamellar hepatocarcinoma: A rare mixed condition
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Objective: A 49 years old male came to our hospital with a five days history of epigastric pain. Abdominal ultrasounds showed a solid hepatic lesion located in segments V-VI. CT and MRI scans revealed a 9,5 x 11,3 x 8,7 cm solid, irregular-shaped and heterogeneous mass. Radiologic diagnosis suggested a cellular hepatocarcinoma (HCC) in a noncirrhotic liver.
Method: A liver biopsy was performed obtaining two longitudinal cylinders of 0.4 and 0.7 cm. Hematoxiline&Eosine and special stains were done.
Results: Microscopically, an hepatocytic cellular proliferation growing inside a solid and trabecular pattern was noticed. Besides, a collagenous band was also pointed out. Furthermore, abundant atypical mitosis and endothelization phenomenon were also seen. Reticuline network was absent. Most of malignant cells overexpressed Hepacam2 and Glypican-3 and were negative for citokeratin 7. However, fibrollamelar carcinoma (FLC) part was negative for Glypican 3 and positive for citokeratine 7. Proliferation index Ki67 was about 30-35 %.
Conclusion: We present hereby the diagnosis of classical HCC coexistent with FLC in a patient with no predisposing factors. The prognosis is significantly worse. So far, there are only five cases described in scientific literature.

E-PS-13-018
Solitary squamoid cyst of the liver
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Objective: Primary epithelial/biliary (EB) liver cysts comprise benign/borderline [Solitary Bile Duct Cyst (SBDC), Ciliated Hepatic Foregut Cyst (CHFC), Biliary Cystadenoma (BCA), Biliary intraepithelial/Intraductal Papillary Neoplasm (BilIN/IPN), Mucinous Cystic Neoplasm (MCN)] and malignant tumours [Biliary Cystadenocarcinoma (BCAC), and Cholangiocarcinoma (CC)]. We report a benign EB liver cyst with squamoid features.
Method: A 57-year-old-male with renal transplantation disclosed (routine abdominal sonography) a solitary liver (segment VI/VII) subcapsular/unilocular cyst, 2 cm largest-dimension. Complete surgical excision was performed. Cystic fluid biochemistry—Carcinoembryonic Antigen (CEA): 13311.4 ng/ml.
Results: Macroscopy: well circumscribed/unilocular cyst, containing greenish fluid, thin fibrotic wall and smooth inner surface. Microscopy (whole specimen): variable epithelial lining (single-layer of cuboidal/flat, transitional-like, and predominant stratified/squamous) cells without atypia, expressing CEA, Epithelial Membrane Antigen, Cytokeratins 7 and 19, p63 and GATA3; few PAS-positive/diastase-resistant intraepithelial hyaline-globules; no evidence of mucinous/ciliated lining cells nor ovarian-type stroma. Post-surgery assessment without other liver lesions.
Conclusion: Our case shows distinct features compared to usual biliary liver cysts (SBDC, CHFC, BCA, BilIN/IPN, MCN, BCAC or CC). Notably, it shares features similar to benign Squamoid Cyst of Pancreatic Ducts (SCPD); interestingly, like SCPD, cystic fluid has high CEA content. So far, this is the first reported EB Solitary Squamoid Cyst of liver.

E-PS-13-019
Clinicopathological features and prognosis of pancreatic neuroendocrine neoplasms
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Objective: Pancreatic neuroendocrine tumours (NETs) are well differentiated by definition and exhibit an "organoid" histological pattern. Meanwhile, pancreatic neuroendocrine carcinomas (NECs) are poorly differentiated by definition; the tumours comprise small or intermediate to large cells. The histological pattern differs between NET and NEC. According to the World Health Organization 2010 classification, NETs are classified as NET G1 or NET G2. However, the Ki-67 index in NETs is >20 %, but this, is not indicated in the classification. This study compared, the clinicopathological findings and prognosis of NET (i.e.,NET G1, NET G2, and NET G3) and NEC.

Method: Fifty patients with pancreatic neuroendocrine neoplasm, who underwent surgical resection were enrolled. NET was classified as NET G1, G2, and G3 if the Ki-67 index was ≤2 %, 3–20 %, and >20 %, respectively.
Results: There were 30, 13, 6, and 1 patients with NET G1, NET G2, NET G3, and NEC, respectively; the median tumour size was 22, 53, 56, and 30 mm; the metastasis rate was 0.3, 62, 100, and 100 %; the 5-year survival rate was 100, 100, 80, and 0 %; Ki-67 index was 0.3–2.2 %, 3–14 %, 24–38 %, and 95 %; and the somatostatin reseptor (SSTR2a) positive rate was 83, 69, 50, and 0 %, respectively.
Conclusion: NET G3 exhibited pathological features and prognosis similar to those of NET G2. NET G3 has good prognosis compared to NEC. Moreover, NET G3 has possibility with effective somatostatin analogs therapy.

E-PS-13-020
2 in 1: Solid pseudopapillary tumour and insulinoma in MEN 1 patient—a case report
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Objective: Multiple endocrine neoplasia type 1 (MEN 1) is a rare autosomal dominant inherited endocrine disease characterized by pancreatic, parathyroid, and anterior pituitary tumours. Pancreatic islet tumours occur less frequently, among them insulinomas are the most prevalent. Solid pseudopapillary neoplasm (SPN) is another extremely rare tumour of the pancreas that frequently occurs in young females and is mostly benign.
Method: We report a MEN 1 case of a 16-year-old male patient with insulinoma and solid pseudopapillary tumour. The patient presented with seizures and hypoglycemia. Further laboratory results and imaging techniques revealed hyperinsulinemic hypoglycemia, parathyroid adenoma, and pancreatic mass. Distal pancreatectomy has been performed.
Results: In the gross evaluation of the pancreatectomy specimen, one 1.4 cm mass in the tail and one 1.1 cm mass close to the resection margin have been detected. The one in the tail was confirmed as "insulinoma" while surprisingly the other mass demonstrated "solid pseudopapillary tumour" based on the histological and immunohistochemical features.
Conclusion: We describe this rare case with clinical, morphological and immunohistochemical findings.

E-PS-13-021
IgG4-related sclerosing cholangitis: A misleading case
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Objective: IgG4-related disease is a fibro-inflammatory entity characterized by the presence of tumour-like lesions on variable locations, with a dense lymphoplasmacytic infiltrate rich in IgG4 plasma cells, storiform-type fibrosis, obliterative phlebitis and, usually, an abnormally high serum IgG4 concentration. We present a case of an IgG4-related sclerosing cholangitis mimicking cholangiocarcinoma.
Method: A 72 year-old male had a clinical history of a biliary tract obstruction. Cytology of the biliar tract was inconclusive. Imaging studies were strongly consistent with malignancy; a cephalic duodenopancreatectomy was performed.
Results: Macroscopically, a diffuse thickening of biliary ducts was prominent, involving the intra and extra-hepatic portions and also the pancreatic duct, with focal stenosis. Histologically there was a dense lymphoplasmacytic infiltrate of the biliary and pancreatic ducts, with a IgG4+/IgG+ plasmocyte ratio >40 %; there was also an abundant eosinophilic infiltrate and fibrosis, occasionally with a storiform pattern; no neoplastic tissue was observed.
Conclusion: Sclerosing cholangitis and autoimmune pancreatitis are a common form of presentation of IgG4-related disease and clinically can mimic malignant neoplasms. The combination of clinical and pathological criteria should bring the diagnosis to light, allowing an early start of medical treatment.

E-PS-13-022
Solid pseudopapillary pancreatic tumour metastasizing to Liver in a 16-year-old girl
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Objective: Demonstrating the epidemiologic, histologic, immunohistochemical and prognostic features of solid pseudopapillary tumour of the pancreas (SPTP) and discussing its main differential diagnoses.
Results: A 16-year-old girl complained of abdominal pain lasting for 6 months accompanied by weight loss, asthenia and anorexia. Physical examination identified an epigastric and right hypochondrial tenderness without a palpable mass. Abdominal CT and MRI showed a large pancreatic mass arising from the pancreatic body and tail measuring 10 cm and associated with two liver nodules, suggesting a pancreatoblastoma with hepatic metastases. A CT guided biopsy was performed. On histology, the tumour had a pseudopapillary architecture with fibrovascular stalks and small, uniform tumour cells with round nuclei. Tumour cells stained positively for CD 10, synaptophysin and Beta-catenin. We concluded to a SPTP that was confirmed after distal pancreatectomy with metastasectomy. The patient received post operative chemotherapy.
Conclusion: SPTP are uncommon low malignant tumours that are rare in children. Metastatic disease unusual and only occurs in around 10 15 % of patients. Histologic differential diagnoses are pancreatoblastoma and neuroendocrine tumour. Immunohistochemistry is essential. Long term follow up is necessary since local recurrence or distant metastases occur in 10 15 % of patients. The value of chemotherapy remains unknown.

E-PS-13-023
Carcinosarcoma of the gallbladder with chondrosarcomatous differentiation and hyaline eosinophilic globules
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Objective: Carcinosarcoma of the gallbladder is a rare aggressive neoplasm, accounting for 0.2 % of all gallbladder malignant neoplasms, and is composed of intermingled carcinomatous and sarcomatous components. The later can be heterologous, with osteosarcomatous or chondrosarcomatous elements present. We report a female patient who had advanced stage of this tumour, featuring chondrosarcomatous component with associated eosinophilic hyaline globules within the spindly component of the tumour.
Method: Case Report: A 52-year old woman presented with abdominal pain and vomiting. Computed tomography revealed a huge exophytic gallbladder mass, invading or displacing the surrounding structures. The patient underwent radical cholecystectomy, transverse colectomy, distal gastrectomy, liver bed resection and omentectomy.
Results: Gross Pathology: The resected gallbladder measured 13 cm and it contained a large exophytic friable tumour that measured 11 cm in length by 6 cm in diameter. Fleshy hemorrhagic tumour nodules were seen extending to the liver, omentum and wall of stomach and colon. Microscopic Findings: The tumour was biphasic featuring both solid malignant epithelial nest and spindly sarcomatous component with several islands of malignant cartilage, Several spindly cells show intracytoplasmic hyaline globules that was PAS positive.
Conclusion: This is a rare case of carcinosarcoma of the gallbladder. We found 15 similar cases with chondrosarcomatous

elements. However, this is the first case, to our knowledge, described with eosinophilic hyaline globules.

E-PS-13-024

Primary hepatic solitary fibrous tumour: Two case reports and review of literature

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Objective: Describe two rare cases of primary hepatic solitary fibrous tumour (SFT) and update the clinical, pathological and immunohistochemical features of this misdiagnosed entity.
Method: Here we report two cases of liver SFT and review all the cases described to date.
Results: The first case of a 61-year-old man who presented with an accidental finding of a large mass in the left liver and the second case of a 79-year-old man who presented with and 13 cm mass in the liver and multiple pulmonary lesions. Parcial hepatectomy was performed and revealed an SFT confirmed by histopathology and immunohistochemical findings.
Conclusion: Primary hepatic STF is a rare mesenchymal neoplasm. Originated in the submesothelial tissue of the liver, this entity is frequently misdiagnosed because of its rarity and unfamiliar characteristics. Despite of its, SFT of the liver should be included in the differential diagnosis of hepatic mesenchymal tumours. A consensus on the essential and definite diagnostic criteria for primary hepatic solitary fibrous tumour must be reached in a timely manner.

E-PS-13-025

Hepatic sclerosing hemangioma: Clinicopathologic study of five cases

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Objective: Sclerosing hemangiomas (SH) are unusual mesenchymal tumours of the liver. Due to their rarity and atypical imaging the differential diagnosis of SH with malignant hepatic lesions is often challenging.
Method: Case notes, histological and immunohistochemical slides of five cases of SH reported in the last 15 years in our hospital were reviewed.
Results: The average patient age was 74.6 years (67–82), two men and three women. In two cases the lesions were ressected as possible malignant hepatic tumours, two as suspected metastases and one as an incidental finding. The lesions, ranging from 3 to 55 mm were well-demarcated, firm, white nodules with, in the larger lesions, irregular contours. Microscopically, compressed thin walled vessels with flat endothelial lining without cytologic atypia were seen in a hypocellular densely hyalinised and sclerotic stroma. Immunoreactivity for CD 31 and CD 34 were seen in the lining cells and type IV collagen in the vessel wall.
Conclusion: SH are rare, benign hepatic lesions, often submitted for histopathological examination as suspected malignant tumours.

E-PS-13-026

Signet ring cell carcinoma of the ampulla of vater

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Objective: Most tumours of the ampulla of Vater are well-differentiated adenocarcinomas. Signet ring cell carcinoma (SRCC) at this site is uncommon, and only 30 resected cases have been previously reported in the English literature.
Method: We report the case of a 49-year-old man who presented an icterus evolving since 2 months. Endoscopic retrograde cholangiopancreatography (ERCP) showed a swollen papilla of vater, with a reddish, erosive mucosa.
Results: Histological examination of biopsy samples from the ampulla of vater showed signet ring cell carcinoma (SRCC). The patient underwent radical pancreatoduodenectomy. Pathological examination showed that the SRCC had infiltrated into the duodenal muscularis propria and pancreatic parenchyma, and lymph node metastases were identified. Based on the immunohistochemical staining patterns of the positive results for CD19, CD7 and CD20.
Conclusion: The origin of SRCCs remains controversial. Since they are predominantly found in gastric cancers, one theory is that these tumours originate from heterotopic gastric mucosa. Confirmation of the histological origin of SRCC by immunohistochemical staining may inform the appropriate treatment strategy.

E-PS-13-027

Hepatic encephalopathy due to delayed liver metastasis of uveal melanoma

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Objective: After cutaneous melanoma, uveal melanoma is the second most common type of primary melanoma. Herein, we present a patient with liver metastasis of an uveal melanoma.
Method: A 65 years old male presented to the hospital due to abdominal pain in the right upper quadrant of 15 days' duration. The patient had an uveal melanoma 9 years ago and had received local radiotherapy. On clinical examination, the patient appeared icteric with palpable liver. The CT revealed multiple lesions in the liver, the largest being 18 cm. Unfortunately, the patient died due to hepatic encephalopathy and multiple organ dysfunction syndrome without any chemotherapy, due to the high bilirubin levels.
Results: The biopsy revealed extensive infiltration of liver by a malignant tumour with solid growth pattern, spindle cells, prominent nucleoli, necrosis, pigment and multiple melanophages. Immunohistochemistry was positive for Melan-A, HMB45, S-100 protein and MITF-1, compatible with metastasis from uveal melanoma.
Conclusion: 40 to 50 % of patients develop systemic metastases and the liver is involved in 95 % of patients. While the median time to systemic tumour recurrence in a review was 3 years and 4 months, our case with such a late recurrence shows that close monitoring of the patients for many years is mandatory.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-14 Molecular Pathology

E-PS-14-001

NGS analysis on tumour and cfDNA for personalized genotype-directed therapy in NSCLC patients: Are the clinical benefits always there?

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Objective: We report two patients with metastatic lung adenocarcinoma (MLA) who underwent extensive NGS testing on both tumour and liquid biopsies.
Results: 49 years old male diagnosed in March 2014 with MLA. Immunohistochemistry (IHC) analysis was ALK negative/MET positive. Pyrosequencing analysis revealed an EGFR mutation at exon 21–p.L858R. Patient was treated with erlotinib until October 2014 due to

progression. A new biopsy was performed, p.L858R EGFR mutation remains. MET was not amplified by FISH. New biopsy was performed in February 2015. An NGS analysis (Oncomine panel; >1800 mutations in 22 cancer-associated genes) on Ion PGM sequencer (ThermoFisher) on all tumour biopsies and cfDNA showed concordant variants such as EGFR-p.L858R and TP53-p.I195T. No druggable pathways were found. Thirty-six years old male diagnosed in March 2014 with MLA. IHC analysis showed ALK/MET positive and ROS1 negative. FISH analysis found an ALK rearrangement. Patient was treated with crizotinib, new biopsy was performed after progression. ALK positivity persisted by IHC, FISH and RT-qPCR analysis. Same NGS modalities were performed on tumour biopsies and cfDNA. No hotspot mutations were found on 22 genes including ALK.
Conclusion: NGS is a promising technique; however it might have limited implications in daily clinical practice for some patients.

E-PS-14-002
The clinical relevance of testing for non-V600E BRAF mutations in melanoma—a single center experience
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Objective: The most common mutation in melanoma that is applicable for targeted therapy is the point mutation BRAFV600E on the exon 15 of the BRAF gene.
Method: We performed a retrospective analysis of 145 metastatic melanoma samples that were tested with next generation sequencing covering the codons 581 to 620 of the BRAF gene (on exon 15) and the exons 2,3 and 4 of the NRAS gene.
Results: 49 (33.8 %) samples were positive for a mutation in the BRAF gene and 24 (16.6 %) positive for a mutation in the NRAS gene. Of 49 BRAF-mutated samples 36 (73.5 %) were positive for BRAFV600E, 10 (20.5 %) BRAFV600K, one (2 %) BRAFN581S, one (2 %) BRAFK601E and one (2 %) harbored a BRAFK601N/E586K double mutation.
Conclusion: BRAF inhibitors are crucial in the treatment of BRAFV600E mutated melanoma. As the European medicines agency approved BRAF inhibitors for all mutations in BRAFV600, the testing of mutations in BRAFV600 is obligatory. Further, there are case reports and in-vitro data on mutations in exon 15 other than BRAFV600 that are sensitive to targeted therapy. Testing of these other mutations may provide further therapeutic options for patients and should thus be included in routine melanoma mutation analysis panels.

E-PS-14-004
Pulmonary adenocarcinoma with EGFR exon 19 duplication and TKi two years survival: A case report
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Objective: Bronchial-Pulmonary Adenocarcinomas induced the development of EGFR targeted therapies, including monoclonal antibodies and tyrosine kinase inhibitors, after molecular characterization. EGFR mutations are more frequently observed in patients with adenocarcinomas, female, non-smokers, East-Asian and predict response to TK Inhibitors (TKis).
Method: A 66 years old woman presented two PET positive nodules in right lung different lobes in 2014. Then a right upper lobe surgical biopsy demonstrated an adenocarcinoma (acinar and solid patterns) and formalin-fixed paraffin-embedded tissue was analyzed for EGFR mutations by dideoxy sequencing (exons 19 and 21) and the exon 19 was also studied by fragment analysis.
Results: EGFR exon 19 showed a duplication of the following amino acids: lysine, isoleucine, proline, valine, alanine and isoleucine; c.2214_2231dupTAAAATTCCCGTCGCTAT;p.Lys739_Ile744dupLysIleProValAlaIle. The mutated allele had more 18 bp than wild type allele and this region corresponds to the tyrosine kinase domain; exon 21 was wild type.
Conclusion: EGFR mutations are frequent, reflecting implication in lung adenocarcinomas pathogenesis and to prescribe personalized therapies. This case is similar to the rare case found by Kosaka T, Yatabe Y, Endoh H, et al. (2004) but biological significance and clinical outcome has not been referred yet. For now the patient is following Erlotinib with representative clinical outcome (RECIST).

E-PS-14-005
Screening pre-neoplastic lesions and lung cancer with next-generation sequencing becomes cost-effective
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Objective: NGS in Pathology routine cannot be understood as an expensive methodology, to understand tumoural behavior, and is useful when diagnosis/therapy genes are enrolled.
Method: Following three different histological types of lung cancer (micro-dissected: pre-neoplasic lesion and solid, acinar, and clear cell patterns separately sequenced) FFPE submitted to the Ion Torrent PGM for the 22 gene Oncomine panel analyzed from 10 ng of extracted DNA using 316 chips and 314 chips were analyzed, then data analysis was performed with the Ion Torrent Variant Caller Plugin (hg19) and Ion Report for prediction of the significance of the variants was produced.
Results: All pre-neoplasic lesions showed KRAS hotspot mutations (COSM522 and COSM516), presence of PIK3CA (COSM249908) and TP53 (COSM10995 and COSM45044) found in two pre-neoplasic lesions. Tumours had similar hotspot pattern, with the same variants: KRAS (COSM522 and COSM516); TP53 (COSM10995; COSM43746 and COSM45044); and PIK3CA (COSM249908). Without significant differences between studied patterns, somatic variations were also found in FGFR2, DDR2, ERBB4, EGFR and MET genes.
Conclusion: When compared with Sanger procedures, NGS brought easier interpretation of various sets of genes, related with carcinogenesis and allowing personalized therapy and/or previewing resistance to the treatment. The aim of NGS will be cost-effective lower procedures.

E-PS-14-007
Renewable RNA FFPE reference standards for the diagnostics of chromosomal re-arrangements resulting in mRNA fusions
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Objective: Fluorescence in-situ hybridisation (FISH) and Immunohistochemistry (IHC) have been the historical gold-standard diagnostic approaches for the detection of chromosomal translocations. However, these methods are technically demanding and the interpretation of the results is challenging, even to expert operators. In contrast, RNA workflows such as RT-PCR and targeted RNA-seq are being increasingly used in diagnostics to detect the cancer fusion transcripts because of their accuracy, precision and simpler interpretation. These highly sensitive

diagnostic workflows require the availability of high quality and consistent control material.
Method: To this end, using Horizon's proprietary genetic manipulation and manufacturing technologies, we have engineered highly characterised and renewable patient-analogue control material in the form of FFPE sections.
Results: Our single cell diluted clones and controlled manufacturing procedures ensure precise and reproducible expression levels of the most commonly found mRNA fusion biomarkers allowing kit manufacturers to develop their assays and diagnostic end-users to monitor their pre-analytical (RNA extraction) and analytical workflows (end-point RT-PCR, RT-dPCR and targeted RNA-seq). This allows continuous monitoring of the performance of RNA-based diagnostic assays giving increased confidence in results and better patient's outcomes.
Conclusion: Horizon will discuss the making, the applications, the performance and the future development of RNA FFPE Reference standards.

E-PS-14-008
KRAS and NRAS mutations in colorectal cancer: A study according to updated guidelines
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Objective: Activating mutations in the KRAS gene are found in 30-40 % of colorectal malignancies and are associated with poor response to anti-EGFR therapies. Until recently, the guidelines recommended testing for mutations in KRAS exon 2 (codons 12 and 13), the most common mutations in patients with metastatic colorectal cancer (CRCm) whose tumours harbor RAS mutations. The updated guidelines recommend that before treatment with anti-EGFR antibody therapy, patients with CRCm should be tested for mutations in both KRAS and NRAS exon 2 (codons 12 and 13), exon 3 (codons 59 and 61) and exon 4 (codons 117 and 146). The effect of this extended mutational analysis on the percentage of patients that is more likely to benefit from an anti-EGFR therapy is studied.
Method: 51 cases of CRCm were tested for detection of mutations in KRAS and NRAS exons 2, 3 and 4 using RealTime PCR (Entrogene).
Results: Mutations in KRAS gene were detected in 21 cases (41 %). 18 mutations were located in exon 2 (35 %), while 3 mutations were observed in exon 3 and 4 (6 %). In addition, 3 mutations were detected in NRAS gene (6 %).
Conclusion: The updated guidelines lead to the detection of 12 % of additional patients who are unlikely to respond to anti-EGFR therapy.

E-PS-14-009
Detection and genotyping of human papillomaviruses in invasive cervical cancers in Tunisia
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Objective: Determine the types of HPV isolated in invasive cancers in Tunisian patients in order to guide the introduction of the prophylactic vaccine in Tunisia.
Method: We worked on 76 cases of invasive cervical cancer. For detection, we used primers MY09 / MY11 and GP5 + / GP6 +. Genotyping was performed by the technique of Reverse Line Blot.
Results: All the samples were infected with at least one type of HPV. HPV 16 and 18 were the most frequent types, with a percentage of 94,8 %, the highest frequency was that of HPV 16 (86,8 %).
Conclusion: These results support the introduction of prophylactic vaccines to prevent infection with HPV 16 and HPV 18.

E-PS-14-010
Periostin expressions in ovarian carcinoma
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Objective: Our study aimed to analyze Periostin (PN) in ovarian cancer (OC), and to correlate its expression with clinico-morphological parameters.
Method: The study group consisted of 102 cases of OC histopathologically diagnosed as serous (67 cases), endometrioid (13 cases), clear cells (4 cases), mucinous (13 cases), and other subtypes (5 case); 37 cases were classified as stage I, 10 as stage II, and 55 as stage III; 22 cases were assessed as G1, 31 cases as G2, 46 cases as G3, and 3 cases as undifferentiated. Tissue fragments were immunohistochemically processed using anti-PN antibody.
Results: PN expression was positive in 10 cases and negative in 92 cases. The positive cases included 6 serous OC, 2 endometrioid OC, 1 clear cells and mucinous OC, respectively; 3 cases were stage I, and 7 cases stage II; tumour grade was G1 (3 cases), G2 (4 cases) and G3 (3 cases). No significant differences were noted between PN and histological subtypes, stage and grade.
Conclusion: PN expression in all tumour subtypes reflects a various distribution, unrelatedly to phenotype. Lack of statistical correlation could be explained by PN ability of architectural restructuring of extracellular matrix, with direct repercussion on invasion and metastasis.

E-PS-14-011
The frequency of NRAS and KRAS gene mutations in Turkish patients with metastatic colorectal carcinoma
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Objective: Colorectal cancer (CR) causes majority of mortality in the world. The cetuximab or panitumumab is an effective single agent or chemotherapy for metastatic CR treatment. Molecular markers of colorectal cancer, including KRAS, NRAS and BRAF gene mutations and the microsattellite instability status are evaluated for the development of personalized treatment. In colorectal ancer, frequency of KRAS and NRAS gene mutations are 30–42 % and 2.2–5 %, respectively. In this study, we aimed detection of the frequency of NRAS (codon 12, 13,and 61) gene and KRAS (codon 12, 13, and 61) gene mutations in Turkish population with metastatic colorectal carcinoma.
Method: We investigated KRAS gene (codon 12, 13, and 61) and NRAS gene (codon 12, 13, and 61) mutations by using pyrosequencing method in 60 patients with metastatic colorectal carcinoma. The Therascreen® KRAS Pyro® Kit (QIAGEN) and the Therascreen® NRAS Pyro® Kit (QIAGEN) were used.
Results: The KRAS and NRAS gene mutations were not detected in 37/60 (61.6 %) patients. The KRAS gene mutations were detected in 21/60 (35 %) patients, which were G12D mutation in 13/21 patients, G12V mutation in 3/21 patients, G12C mutation in 2/21 patients and Q61L mutation in 1/21 patient. The NRAS gene mutations were detected in 3/60 (5 %) patients, which were G12D mutation in 1/3 patient, Q61K mutation in 1/3 patient and Q61R mutation in 1/3 patient.
Conclusion: Our results demonstrated that the frequency of NRAS and KRAS gene mutations in Turkish patients with metastatic colorectal cancer is consistent with the literature.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-15 Nephropathology

E-PS-15-001
Utility of glomerular C4d immunostaining in renal biopsies in patients with immunoglobulin A nephropathy: A clinicopathological study
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Objective: IgA nephropathy (IgAN) accounts for about 20 % of biopsies performed for glomerular disease in Poland. Activation of complement plays a key role in the pathogenesis of IgAN. Recent data revealed the ability of polymeric IgA to activate the lectin pathway. Mesangial deposition of C4d is considered to be a consequence of lectin pathway activation. The aim of the study was to compare the clinical presentation, laboratory data, and histological lesions in renal biopsy in IgAN patients with positive and negative staining for mesangial C4d.
Method: Material consists of kidney biopsies obtained from 43 adult patients who underwent a renal biopsy between 2010 and 2015, and were diagnosed in Department of Nephropathology, Medical University of Lodz. Demographic, clinical, and laboratory data at the time of presentation were collected. The renal biopsy specimens were routinely processed by light microscopy and immunofluorescence. C4d in glomeruli was analyzed by immunofluorescence staining. Histological lesions were classified using Oxford pathologic classification criteria. Statistical analysis were performed to assess the differences in clinical presentation, laboratory data and the renal damage between C4d (+) and C4d (−) groups of IgAN.
Results: Of 43 patients with IgAN, 11 were classified as C4d positive, and 32 as C4d negative. Hypertension, severe proteinuria, high level of serum creatinine, low eGFR at the time of presentation, as well as tubular atrophy/interstitial fibrosis >50 %, and endocapillary proliferation were significantly more frequent in C4d (+) group than in C4d (−) group.
Conclusion: C4d positive mesangial staining in IgAN is associated with more severe clinical course of the disease and more severe renal damage.

E-PS-15-002
Risk factors and characteristics of diabetic nephropathy in patients with new-onset diabetes after kidney transplantation
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Objective: Diabetes developing de novo after transplantation (NODAT) may progress to diabetic nephropathy (DN) in certain renal allograft patients. However, few data have been collected related to the predisposing factors and clinicopathologic characteristics of DN in NODAT patients.
Method: We compared clinical and morphological features between cases with (n = 14) and without (n = 98) DN among a total of 112 NODAT patients diagnosed between 2005 and 2012.
Results: Among clinical factors, the proportion of patients with a high body mass index (>25 kg/m2) was significantly higher in DN patients than in non-DN patients. The prevalences of coronary heart disease, smoking, and hepatitis B and C viral infections; degrees of HLA mismatches; donor age and gender; and type of immunosuppression were not different between the two groups. Laboratory features showed lower serum albumin and creatinine levels in DN patients than in non-DN patients. Renal allograft histology showed increased percentages of global glomerulosclerosis and higher degrees of mesangial matrix increase, interstitial fibrosis, arteriolar hyalinosis, and arteriosclerosis yet lower "ptc" scores in DN patients than those in non-DN patients.
Conclusion: Metabolic factors may be responsible for the development of DN in NODAT patients. Renal function is not helpful in the distinction between DN and non-DN patients. However, renal graft injuries are more advanced in DN patients than in non-DN patients at the time of diagnosis.

E-PS-15-003
Living donors with proteinuria: Importance of renal biopsy
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Objective: The aim of this study is two-fold; first to investigate the importance of proteinuria in the determination of renal pathology in donors, and second to find out the importance of renal biopsy in the selection of donor for transplantation.
Method: Among 679 donors only 70 showed proteinuria. Serial 24-h urine protein and microalbumin examined, and all of them underwent renal biopsy. Renal biopsies examined by light, immunofluorescence and electron microscopy.
Results: The mean 24-h urine protein found 438 ± 302 mg/day in 70 cases. Among 70 cases with proteinuria, only 21 (30 %) had a chance to become a donor after biopsy (Group 1). Biopsy findings of these 21 cases were nonspecific. In group 2, the biopsy diagnosis was FSGS in 17, IgA nephropathy in 8, MPGN in 4, IgM nephropathy in 3, and TIN in 2, hypertensive nephropathy in 2, MGN in 1, MCD in 1, lupus nephritis in 1 and nonspecific biopsy findings in 10 cases. A significant difference found between group 1 (284,8 ± 114 mg/day) and group 2 (503 ± 333 mg/day) in regards of 24-h urine protein ($p < 0.01$). In addition significant differences was noted between group 1 (34,2 ± 59,2 mg/day) and group 2 (143 ± 275,4 mg/dl) in regards of 24-h urine microalbumin ($p < 0.01$). Only 16 patients from group 2 also showed microscopic hematuria in addition to proteinuria.
Conclusion: We suggested that proteinuria greater than 300 mg was a marker of renal disease. We concluded that microalbuminuria determination may be a more reliable marker of renal disease, and the presence of microalbuminuria should preclude donation.

E-PS-15-004
Ultrastructural findings and capillary HLA-DR expression in renal allografts with humoral, vascular and tubulointerstitial rejection: Correlation with development of transplant glomerulopathy
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Objective: We aimed to study the ultrastructural (US) findings and capillary HLA-DR expression in 52 renal allografts with acute humoral (AHR), acute vascular (AVR), acute tubulointerstitial (ATR) and chronic humoral rejection (CHR) and correlate these findings with the development of transplant glomerulopathy (TG).
Method: ATR, AVR, AHR, and CHR were found in 12 (23 %), 12 (23 %), 14 (27 %) and 14 (27 %) patients, respectively. Peritubular capillary DR (PTC-DR) and glomerular DR (GDR) expression evaluated. The lower intensity of PTC-DR was considered to indicate more extensive PTC destruction.
Results: US changes including capillary endothelial swelling and multilamellation, subendothelial widening and GBM duplication found to be highest in biopsies with AHR compared to biopsies with ATR and AVR ($p < 0.001$). The loss of PTC-DR expression, therefore, the destruction of PTC was found highest in biopsies with AHR and CHR compared to biopsies ATR and ACR. TG was developed 8,3 %, 33,3 % and 57,1 % in patients with ATR, AVR and AHR respectively ($p = 0,01$). The development of TG was 45,5 ± 9,2 months in ATR cases, 20,7 ± 8 months in AVR cases and 7,2 ± 3 in AHR cases. Capillary endothelial swelling, subendothelial widening, multilamellation, and GBM duplication showed a great impact on the development of TG. The risk of TG development

increases with decreasing expression of PTC-DR ($p < 0.001$). Therefore, the severity PTC destruction had a significant impact on the development of TG.
Conclusion: Early US changes and capillary DR expression are helpful for predicting the development of TG. This may be useful for determining the patients' with the risk of TG and chronic rejection.

E-PS-15-005
Kidney biopsy yield is contingent upon the biopsy operator and the interpreter of adequacy when evaluated at the time of the procedure
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Objective: To evaluate the yield of kidney biopsies performed by different practitioners, using different imaging modalities for guidance, and with different performers of immediate interpretation of adequacy.
Method: The number of glomeruli and arteries, and the rate of significant complications secondary to the biopsy procedure were retrospectively reviewed from 362 kidney biopsies. These parameters were compared between differing practitioners performing the biopsy (nephrologists or radiologists), differing imaging modalities for guidance (ultrasound or computed tomography), and between differing interpreters of biopsy adequacy conducted at the time of biopsy (general pathologists, renal pathologists, nephrologists).
Results: Biopsies utilizing immediate interpretation were found to have more glomeruli ($p = 0.002$) and arteries ($p = 0.019$) when the biopsy was performed by a radiologist compared to a nephrologist. There were significantly more glomeruli ($p = 0.0001$) and arteries ($p = 0.0005$) in biopsies with the immediate interpretation performed by pathologists (no difference whether general or renal pathologist) compared to nephrologists. The rate of complications did not significantly differ regardless of biopsy operator or the interpreter of immediate adequacy.
Conclusion: The yield of kidney biopsy material may depend on the practitioner conducting the biopsy and the interpreter of immediate adequacy at the time of biopsy.

E-PS-15-007
Evaluation of glomerular basement membrane and expression of TGF-beta 1 and fibronectin in renal biopsies of patients with diabetic nephropathy
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Objective: To evaluate the Glomerular Basement Membrane (GBM) thickness and expression of TGF-β1 and fibronectin in renal biopsies from patients with Diabetic Nephropathy (DN).
Method: Fifty-seven cases of diabetic patients were divided in DN group ($n = 19$) and DN superimposed group ($n = 38$). GBM morphometry, DN classification and quantification of TGF-β1 and fibronectin expression were performed.
Results: DN group showed thicker GBM than DN superimposed group. TGF-β1 immunostaining in DN superimposed group was higher in glomerular and tubulointerstitial compartments. Fibronectin expression was higher in tubulointerstitial compartment. Class III presented higher proteinuria levels than Class I and increased GBM thickness than Class I and II. Class IV had higher serum creatinine levels and lower TGF-β1 expression in glomerular and tubulointerstitial compartments than Class I. Class III presented increased glomerular fibronectin comparing to Class IV. Patients with less than 10 years of diabetes showed increased GBM thickness and significant positive correlation between GBM thickness and proteinuria.
Conclusion: GBM thickness and expression of TGF- β1 and fibronectin are related to DN pathogenesis. We conclude that the use of TGF-β1 and fibronectin in situ can be an important tool in the diagnosis of evolution and progression of DN regarding different classes of this entity.

E-PS-15-008
BK virus (BKV) associated with bladder urothelial carcinoma in a renal transplant recipient: BKV's oncogenic potential revisited
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Objective: BKV reactivation in immunosuppressed patients may cause nephropathy and organ loss in renal transplant recipients. BKV may also be associated with an increased risk of kidney and bladder carcinomas. We report a renal transplant patient with BKV nephropathy who developed a urinary bladder carcinoma 10 years post-transplant.
Method: A 60-year-old female with microscopic polyangiitis received a kidney transplant and immunosuppressive therapy. Two years later a renal biopsy showed BKV nephropathy and 10 years later a urinary bladder biopsy revealed high-grade urothelial carcinoma with giant cells. Immunohistochemistry (IHC) for SV40 was performed on both biopsies.
Results: Renal biopsy showed a dense, cortical and medullary, lymphoplasmacytic infiltrate. The tubular epithelium exhibited numerous inclusions and strong SV40 nuclear immunoreactivity. Interstitial fibrosis/tubular atrophy affected >50 % of the cortex. Glomeruli (16) showed slightly increased mesangial matrix. No Ig or complement deposits were detected. Bladder biopsy revealed a high-grade urothelial carcinoma with a multinucleated giant cell component and extensive, strong immunoreactivity for SV40 in tumour cell nuclei. Non-neoplastic urothelium was negative.
Conclusion: This case adds to a small number of kidney transplant recipients showing an association between BKV reactivation and aggressive variants of urothelial carcinoma. The strong viral immunoreactivity displayed by tumour cells lends support to BKV oncogenic potential.

E-PS-15-009
Classification and clinicopathological correlation of renal biopsies: 15 years of experience in a single centre
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Objective: Hospital de Santa Maria (Lisbon, Portugal) is a tertiary healthcare institution, with an active renal transplantation centre and a broadly experienced Nephrology Department covering all age groups. It relies on renal biopsy diagnosis, which are processed for optical and immunofluorescence microscopy in our Department and, whenever required, for electronic microscopy in another institution. We present our experience through a 15 year-long series.
Method: We performed retrospective analysis of the reports of 1220 renal biopsies, received during the 2000–2014 period and concerning 898 patients with an age range between 9 months and 89 years.
Results: An adequate sample was obtained in 717 cases. Clinical presentation was either transplant-related (26.0 %) or consisted of nephrotic syndrome (19.8 %), haematuria and/or proteinuria (17.2 %), tumour (7.5 %) or other (29.4 %), including systemic diseases and renal failure. The histopathological patterns were transplantation pathology (11.7 %), primary glomerular disease (34.3 %), secondary nephropathies (16.2 %), tubulointerstitial nephritis (4.8 %), vascular disease (2.0 %), tumour (5 %), miscellaneous nephropathies (1.9 %) and unclassified glomerulonephritis (3.5 %). No pathology was found in 13.9 % specimens.

Conclusion: To our knowledge, statistical data regarding renal pathology is scarce throughout. This is one of the largest series of a single hospital in the literature and the first in our country.

E-PS-15-010

Role of phospholipase A2 receptor (PLA2R) antibodies in patients with membranous glomerulonephritis: A prospective study on Indian cohort

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Objective: Search for a cause for Membranous glomerulonephritis (MGN) is crucial to determine its treatment and management. Primary MGN was a diagnosis of exclusion until the discovery of target antigen, PLA2R. Lack of published data from Indian population prompted this prospective study to determine the sensitivity and specificity of circulating anti-PLA2R antibodies in MGN patients by using cell based indirect immunofluorescence test (IIFT) and correlating with clinicohistopathology and response to treatment.
Method: MGN cases (n = 34) diagnosed by renal biopsy and IIFT were evaluated for serum PLA2R using IIFT on biochip containing HEK 293 cell lines transfected with cDNA coded for PLA2R and also investigated for causes for MGN. Positive cases were followed up for a period of 6 months of treatment with a repeat testing.
Results: PLA2R positive MGN cases (n = 14) had higher 24 h proteinuria (10 ± 2.46 g) with BM thickening vs 7 ± 3.8 g proteinuria in secondary MGN additionally showing mesangial hypercellularity and endocapillary proliferation. Clinical profile of both groups was same. Sensitivity and specificity were 70 and 100 %; 8 complete remission; 2 partial and 2 no response. Remission was less in PLA2R group.
Conclusion: Anti-PLA2R in serum is a good reliable biomarker for primary MGN and for monitoring its disease activity.

E-PS-15-011

Biopsy proven glomerular diseases of pregnancy: A study of 17 cases

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Objective: Although some degree of physiological changes develop in kidney function or pre-existing renal disease can be exacerbated, some women develop renal disease during the course of the pregnancy. We describe here renal biopsy data of our pregnant patients presenting with renal disease.
Method: We retrospectively searched for the kidney biopsies performed in pregnant women in our hospital database.
Results: We re-evaluated kidney biopsies of 17 pregnant women with mean age of 29.5 years. Mean gestational age at which biopsy has been performed was 13.8 weeks. Biopsy diagnoses were focal segmental glomerular sclerosis in 8 (47 %) cases (one of them is perihilar type), preeclampsia in 6 (35.2 %) cases, thrombotic microangiopathy in 1 (5 %) case, IgA nephropathy with preeclampsia in 1 (5 %) case and mesangial proliferation in 1 (5 %) case. One patient had twin pregnancy and one patient had systemic lupus erythematosus before pregnancy. Two patients had undergone therapeutic curettage in their 9th weeks of gestation and one patient has lost her baby in 25th weeks of gestation.
Conclusion: Kidney biopsy may be a difficult procedure during pregnancy, however it offers the opportunity to make a correct diagnosis, with which timely management are crucial to improve outcomes.

E-PS-15-012

OpenEHR: Generating and maintaining information models for structured data in renal biopsy reporting

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Objective: Structured pathology reports might be as useful for renal biopsy reporting as they have been for reporting cancer resection specimen. For efficient reuse in quality control, registries and research, structured reports should consist of structured data, not just structured text. Here we present a method to generate and maintain a data set for renal biopsy reporting.
Method: The openEHR specification and archetype editor were used to create the information model. The information model is managed and further developed in the multilingual open knowledge platform http://arketyper.no/ckm/en.
Results: The information model for structured renal biopsy reporting consists both of structured data and free text elements. Typical data elements are e.g. number of glomeruli (numeric) and grade of arteriosclerosis (list of internal codes). Knowledge support based on international consensus is provided for each data element allowing for consistent data input. The model is intended to be a maximum data set, which can be adapted for use in individual pathology departments. The data structure can be implemented in pathology information systems. Data can be transferred to registries using electronic communication standards in healthcare.
Conclusion: The information model is accessible in the open knowledge platform http://arketyper.no/ckm/en (http://arketyper.no/ckm/en/#showArchetype_1078.36.547) and will be optimized by a thorough collaborative review process.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-16 Neuropathology

E-PS-16-001

The WHO Grade I Collagen Forming Meningioma produces angiogenic substances: A proposed novel meningioma entity

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Objective: Meningiomas stem from arachnoid cap cells, the so-called meningiothelial cells. According to their histopathological features meningiomas are classified either as WHO grade I (the meningiothelial, fibrous / fibroblastic, transitional / mixed, psammomatous, angiomatous, microcystic, secretory and the lympholasmacyterich subtype), grade II (the atypical and the clear cell subtype) or grade III (malignant or anaplastic phenotype).
Method: We report on a case of a 62-year old female patient who was referred to hospital because of progressive obliviousness and concentration difficulties.
Results: An occipital convexity-meningioma was diagnosed and subsequently resected. Within the tumour tissue there were multiple spheroid precipitates, i.e. secretion products that turned out to consist of collagen. Part of the tumour cells displayed positive reactions for vasogenic substances, namely for vascular endothelial growth factor (VEGF) and epidermal growth factor receptor (EGFR). Correspondingly, the diagnosis "WHO Grade I Collagen Forming Meningioma" seemed to be most appropriate.
Conclusion: The "WHO grade I collagen forming meningioma" we report on produces collagen and angiogenic substances. To the best of our knowledge, no such entity has been reported on in previous literature. We propose this collagen producing meningioma as a novel WHO grade I meningioma subtype.

E-PS-16-003

Myxoid chondrosarcoma of the cerebellopontine angle: Case report

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Objective: To present a case of a 44-year old man that suffered from intermittent dizziness and headaches,and in a MRI a tumour was discovered in the cerebellopontine angle and histologically is consistent with a myxoid chondrosarcoma.
Method: The patient's information and imagenology studies were retrieved in order to present this rare tumour.
Results: Histological analysis revealed the tumour tissue fragment corresponded to cells in round nodules disposition and a few spindle shaped cells alternating with island of chondroid tissue in a myxoid backgrounds. It had no mitosis and mild atypia. Immunohistochemical markers based on S-100 were positive in tumour cells and the Ki67 was 1 %. The sample was negative for cytokeratin and carcinoembryonic antigen. A diagnosis of low grade myxoid chondrosarcoma was reported.
Conclusion: Myxoid chondrosarcoma is a rare tumour, usually found in the lower extremities, with an intermediate grade, and tendency to relapse and metastasize. Chondrosarcoma accounts for 6 % of neoplasms of the base of the skull and 0.15 % of all intracranial tumours. To the authors' knowledge, this is the ninth report of this variant reported at this location. The tumour origin is believed to be the choroid plexus, the pineal region or the dura mater. It is more frequent in males. The incidence is unknown and the prognosis is generally poor due to its local invasion.

E-PS-16-004
Meningeal Melanocytoma: An unexpected find: Case report
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Objective: Originally derived from the neural crest, melanocytes are normal constituents of the pia mater and subarachnoid. They are widely scattered across the meninges with higher density in the central area of the superior spinal cord, brainstem and skull base. Meningeal melanocytoma is an uncommon, slowly growing, well differentiated melanocytic neoplasm. It was first described in 1972 and currently accounts for less than 0,1 % of brain tumours.
Method: A 47 years old man was admitted to our hospital, accusing bilateral paresthesia of the upper limbs, often accompanied by pain. MRI revealed a T1 hyperintense craniospinal lesion of about 19/17,6/41,1 mm occupying most of the spinal canal from the foramen magnum to C2-C3 level. Neurosurgical resection was performed.
Results: The most striking feature of the tumour, both macroscopic and microscopic was that of a heavily pigmented lesion. Histopathological appearance featured nestes of slightly spindled, pigmented cells with oval nuclei and small nucleoli, often with perivascular distribution and accompanied by melanophages. No cytologyc atypia or mytotic figures were present. It was diagnosed as meningeal melanocytoma, later confirmed by immunohistochemestry. Postsurgical evolution was favorable and the patient undergoes neurological followup.
Conclusion: Primary CNS melanocytic neoplasms have intrigued pathologists for many years. When evaluating these lesions, special attention must be paid to their histologic features to distinguish melanocytoma from its malignant counterpart.

E-PS-16-005
Gliosarcoma with rhabdomyoblastic differentiation: A case report
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Objective: Gliosarcoma is a rare neoplasm of the central nervous system characterized by biphasic histological pattern displaying both glial and sarcomatous components.
Method: A 62 year-old woman presented with a left sided hemiparesia and symptoms of intracranial hypertension. On physical examination, the patient was confused with left hemiplegia. Computer tomography revealed an irregular enhancing mass lesion involving the frontal insular cortex that was thought to be consistent with a brain metastasis. A craniotomy was performed with gross total resection of the tumour.
Results: On gross examination, the tumour was grey colored with bleeding and necrotic components. Microscopic examination showed a mix of glial and sarcomatous components with large areas of necrosis. The glial component was composed of large atypical cells with numerous mitotic figures. The mesenchymal elements were composed of spindle shaped cells with elongated, excentrated, vesicular nuclei and prominent nucleoli. The glial components were GFAP positive. Mesenchymal cells were GFAP, KL1 negative, vimentin and caldesomon positive. The diagnosis of rhabdomyoblastic gliosarcoma was made . The patient passed away few days after surgery.
Conclusion: Gliosarcoma is an aggressive tumour characterized by a biphasic glial and sarcomatous pattern. However, it is not well established whether it is a variant from glioblastoma or a separate entity.

E-PS-16-006
Papillary glioneuronal tumour
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Objective: The papillary glioneuronal tumour is a relatively new entity in neuropathology. It was first described in 1996 as a "pseudopapillary ganglioneurocytoma" by Komori. In 2007 it was included in the WHO clasification with less than 40 cases reported in literature.
Method: We present the case of a 51 years old man, admitted to our hospital with left sided hemiparesis, dizziness and headaches. Neuroimaging revealed a large, well demarcated cystic tumour in the right temporal and parietal lobes. Its largest diameter was of 73 mm and it contained an inner solid component of about 15 mm. The patient was scheduled for neurosurgery and intraoperative consultation was requested, revealing characteristic neuronal and glial features. The lesion was excised and thoroughly examined by light microscopy.
Results: H-E histologic sections showed small oligodendrocyte-like tumour cells forming vasocentric papillae and solid, nodular structures with a neuropil-like matrix. The cells in this matrix ranged from oligodendroglia-like neurocites to well differentiated neurons. The final diagnosis was of a papillary glioneuronal tumour.
Conclusion: While still an uncommon find, it is important to recognize this lesion as it is a grade I neoplasm with excellent prognosis. Despite sharing many common features to other neuroglial tumours, its papillary architecture is highly distinctive. Soon after excision, our patient's condition improved with slight remission of the symptoms.

E-PS-16-007
Ganglioneuroma: An incidental tumour of the adrenal gland
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Objective: Ganglioneuroma is an asymptomatic clinically silent tumour that rarely occur in the adrenal glands. Diagnosis is often incidental because unlike other neuroblastic tumours it does not secrete excess catecholamine or steroid hormones. However, an index of suspicion with radiographic studies such as MRI, CT scan and tissue biopsy can aid early detection.
Results: Case Report: A 25-year-old female presented with 10-months history of a right flank pain and persistent headache. Pain was none radiating and dull. Clinical examination was of a well-preserved female, with a 6×5 cm non tender right flank mass, BP = 120/80 mmHg, Pulse = 88 bpm, Urea and electrolytes were within range. CT scan revealed a circumscribed mass on the upper pole of the right kidney.

Tissue biopsy showed compressed adrenal tissue by a well-circumscribed tumour composed of intersecting fascicles of spindle cells with wavy nuclear contours and interspersed by clusters of mature ganglion cells. It was diagnosed mature ganglioneuroma.
Conclusion: Adrenal ganglioneuroma is a rare serendipitous neoplasm mimicking other neuroblastic tumours due to non-specificity of symptoms. Ancillary radiographic studies such as MRI and CT scan may aid pre-operative diagnosis. However, the mainstay of diagnosis is tissue biopsy with identification mature ganglion cells with neural tissues.

E-PS-16-008
Cerebral schistosomiasis: Case report and literature review
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Objective: Schistosomiasis is a parasitic disease most incident in Africa, Southeast Asia and South America, reaching 230 million cases reported worldwide. Neuroschistosomiasis (NE) is considered a rare complication, affecting mainly the spinal cord, followed by cerebellum, with few cases affecting the brain. We report a case of cerebral schistosomiasis caused by S. mansoni with pseudotumoural presentation.
Method: A 19-year-old man presented with headache and refractory seizures. The computed tomography (CT) showed a front-parietal expansive lesion with perilesional edema suggesting astrocytoma.
Results: After excision, the histology revealed granulomas surrounding S. mansoni eggs. He was treated with praziquantel and prednisone, with clinical improvement and resolution of the lesion.
Conclusion: In NE, the eggs of the parasites migrate through the vertebral venous plexus, causing immune reaction and granuloma formation. The spinal cord is usually affected by S. mansoni and S. haematobium and acute myelopathy is the most common manifestation. Cerebral disease is most often caused by S. japonicum and the clinical presentation varies from acute encephalitis to lesions that can be mistaken for tumours, especially gliomas. NE should be considered in the differential diagnosis of lesions in the central nervous system of patients who live or have visited endemic areas.

E-PS-16-009
A rare case of hemangioblastoma of the cerebellum
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Objective: Hemangioblastoma is a rare, slow growing tumour of the central nervous system uncertain histogenesis. Hemangioblastoma occur both sporadically predominantly in the cerebellum and in association with von Hippel-Lindau syndrome.
Method: A 71 year old woman presented with a 5 month history of headache, vomiting and walking instability. Imaging studies demonstrated a cyst in the cerebellum measuring 3 cm in greatest diameter with a well-circumscribed mural nodule measuring 1,4 cm. The lesion was resected.
Results: Microscopically the nodule consisted of clear stromal cells in a rich capillary network. The stromal cells showed low mitotic rate and cells were positive for Vimentin,S100p, NSE and negative for GFAP, EMA,CD10,D240 and VEGF.A limited population of tumour cells was immunoreactive with CD56 and Inhibin A. The Ki67 index was low. Based on the previously mentioned morphologic and immunohistochemical characteristics the diagnosis of hemangioblastoma WHO grade I was posed.
Conclusion: Hemangioblastoma is an uncommon neoplasm which have rather characteristic MR imaging features. The prognosis is excellent if surgical resection can be achieved. Other neoplasms with clear cell features should also be considered in the differential diagnosis.

E-PS-16-010
A case study of a central neurocytoma
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Objective: Report a central neurocytoma case in a Brazilian male.
Method: Case description: A 20-year-old unconscious male was admitted to the department of emergency and he was diagnosed with intracranial hypertension (IH). He reported headaches during the last 6 months, and also blackouts and vomitings. The computerised tomography (CT) showed an expansive intraventricular tumour, with mass effect, and obstructive hydrocephalus. The histopathological analyse showed multiple softened and greyish material fragments measuring $2{,}8 \times 2{,}4 \times 0{,}6$ cm, with regular structures and differentiated small lymphocytes like cells, with enlarged and bare nuclei, coarse chromatin, pale and clear cytoplasm, compact arrangements with rosettes like structures, rare mitoses and occasional atypia, without necrosis or haemorrhage. The Immunohistochemistry analyse (IHA) with the peroxidase system revealed EMA, GFAP, vimentin negative, Ki-67 (+4 %), CD57 (+) and IDH1 (inconclusive), and together with other findings that were compatible with Central Neurocytoma.
Results: Discussion: Most patients present IH as initial symptom in neurocytomas. The clinical history is short and is not easy to make the differential diagnosis with other intraventricular tumours, such as oligodendroglioma and ependymoma, which was our first hypothesis. The IHA for the neuronal markers such as synaptophysin, calcineurin, neuron specific enolase and microtubule-associated with the protein 2, as well as the immuno-negativity for the glial fibrillary acidic protein and for the neurofilament proteins allowed our diagnosis. The tumour rarity and typical presentation are peculiarities in this case.
Conclusion: Neurocytomas must be remembered as a cause of IH.

E-PS-16-011
Brain stem atypical teratoid/rhabdoid tumour in a 27-yar-old male: A case report
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Objective: Atypical teratoid/rhabdoid tumour (AT/RT) is highly malignant pediatric CNS tumour associated with inactivation of the INI 1/hSNF5 gene, composed of rhabdoid cells with variable primitive neuroctodermal, mesenchimal and epithelial components. AT/RT is presenting in children under the age of 3 years, rarely in older children and sporadically in adults.
Method: A 27-yar-old male was admitted to our hospital with recent history of headache, vertigo, vomiting, rapid onset of bilateral deafness and bilateral narrowing of the visual field. MRI showed obstructive hydrocephalus due mesencephalic tumour which surrounding lamina quadrigemina and compressed aqueducts. After suboccipital craniotomy, we received grayish tissue which measured 2 cm in diameter.
Results: Hematoxylin-eosin histology revealed tumour composed of rhabdoid cells in lobular organization, surrounded by abundant stroma. Tumour cells had abundant cytoplasm and vesicular nucleus. Tumour was necrotic with rare mitoses and Ki67 up to 12 %. Tumour cells were negative for PLAP, OCT3/4, AE1/3, INI1 and immunopositive to EMA, NSE, synaptophisin, GFAP and SMA.
Conclusion: In conclusion we found that the tumour was very rare case of AT/RT in brain stem of an adult young man, the cells of which were less positive for Ki67 than is usual for these tumours.

E-PS-16-012

Choroid plexus papilloma of the fourth ventricle: A case report

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Objective: We have a rare case of a man who present a Choroid plexus papilloma (CPP) involving the fourth ventricle.
Method: Ten months ago, this patient consult the urgency of the military hospital of Tunis and was hospitalized in neurosurgery.
Results: We report a case of a 30 years old man who presented symptoms of increased intracranial pressure for 2 months. The patient did not have any medical history or family history related to brain lesion. CT scan and Brain MRI showed a lobulated hypervascular 50 × 40 × 50 mm sized mass intensely enhanced on contrast study and occupying the whole of fourth ventricle with obstructive hydrocephalous. The treatement was the surgery excision. The tumour appeared macroscopically as cauliflower-like, 40 mm sized masse, brownish and friable. Histopathology revealed a papillary tumour with a delicate fibrovascular core lined by columnar or cuboidal epithelial cells with vesicular nuclei without nuclear atypia, mitosis, and necrosis. Their appearance is very similar to normal choroid plexus.
Conclusion: CPP is a benign neuroepithelial intraventricular lesion WHO grade I account for less than 1 % of all brain tumours. It is most commonly found in children (2–6 %) and rarely in adult (0,5 %). Very few reports of CPP in adult are present in the literature.

E-PS-16-013

Epidemiology of cases presenting neuropsychiatric disorders, following a suicidal poisoning by drugs, in Morocco

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Objective: To describe and analyze the characteristics of suicide cases occurred in Morocco and presented neuropsychiatric disorders due to drug intoxication, in order to contribute to the reduction of morbidity and mortality that result.
Method: This is a retrospective study of all cases of suicide by drugs—which presented neuropsychiatric disorders -, occurred in Morocco between 1990 and 2013, and reported to the Moroccan Poison Control Centre.
Results: In 24 years, 1674 cases were reported (399 adolescents and 1275 adults). The sex-ratio (F/M) was 2,9. The psycholeptics (59 %) were the most implicated from the morbidity viewpoint, the antiparkinsonians (5,3 %) were from the lethality viewpoint. The median duration of consultation was 4 h. The most observed neuropsychiatric disorders were somnolence (33 %) and hypoesthesia (29 %). Coma had appeared with a lethality of 4,9 %. Decontamination was carried out in 57 % of cases. Twenty-two cases have kept sequelae, 11 have died. Following the odds-ratio analysis, the gender is a risk factor (a risk of 5 for males).
Conclusion: Suicidal poisoning by nervous system drugs causes severe cases which require immediate medical attention but also a heavy management. The best therapeutic approach remains prevention, so it is important to follow the anti-toxic control strategy.

E-PS-16-015

Pilomyxoid astrocytoma in an adult male: A case report

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Objective: To present a case of a pilomyxoid astrocytoma (PMA) in a 21yo male patient. PMA is a recently recognized WHO grade 2 tumour that was previously characterized as a subtype of the WHO grade 1 pilocytic astrocytoma. PMA is reported to have an average age at presentation ranging from 10 to 18 months.
Method: The patient presented to our hospital with an episode of severe headache. An MRI scan revealed a mass in the suprasellar region of the brain. Two biopsies of the tumour, each measuring 0,5 cm, were sent to our laboratory and were examined using hematoxylin and eosin slides, as well as immunohistochemical techniques.
Results: Microscopically the tumour was composed of piloid cells in a mucoid matrix, with a predominantly angiocentric cell arrangement. The lesion did not contain Rosenthal fibers or eosinophilic granular bodies. The tumour cells were positive for vimentin, GFAP, S-100 and Synaptophysin, while ki-67 was estimated at less than 3 %. These findings were compatible with the diagnosis of PMA.
Conclusion: PMA typically presents in the very young (median 10 months) and can occur in older children. They are rare in adults. To our knowledge there are only 23 adult patients with PMA reported in the English language literature.

E-PS-16-016

Are we facing Neurofibromatosis 1? An unusual combination of 2 pilocytic astrocytomas and a GIST

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Objective: Neurofibromatosis type 1 (NF1) is a multisystem disorder that's characterized by the growth of nervous system tumours. Pilocytic astrocytomas, preferably located within the optic pathway, are the major type of central nervous system (CNS) tumours in this disease but synchronous lesions, especially in unusual ages and localizations, are rare. We will report a case.
Method: A 42-year-old woman, with HIV infection, presented with seizure. The MRI revealed two synchronous CNS tumours: one in the parietal lobe and the other in the cerebellum. The previous year patient was diagnosed with a multifocal GIST of the small bowel.
Results: Both CNS tumours had morphological features consistent with pilocytic astrocytomas, as cystic morphology, Rosenthal fibers and eosinophilic granular bodies. None had BRAF or IDH1 mutations neither MGMT hypermethylation. With that unusual combination of neoplasms pathologists alerted for NF1. After that other clinical signs of NF1 were found, so a genetic test was ordered.
Conclusion: NF1's patients require a multidisciplinary follow-up where pathologists may play a role. Pathologist should always alert for NF1 when facing a pilocytic astrocytoma of optic pathway but synchronous pilocytic astrocytomas or multifocal GISTs, although not being a diagnostic criteria, should also raise suspicion.

E-PS-16-017

A case of spindle cell oncocytoma of adenohypophysis

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Objective: Spindle-cell oncocytoma (SCO) is a grade I tumour according to WHO/2007 classification. It was presumed that SCO arises from the folliculostellate cells of the adenohypophysis but recent immunohistochemical and ultrastructactural studies suggest that it derives from the pituicytes of the posterior pituitary and thus shares a common origin with pituicytomas and granular cell tumours.
Method: A 52-year-old woman presented with headache and visual disturbances. CT scan showed a tumour with suprasellar extension compressing the optic chiasm that resembled a macroadenoma. The tumour could not be easily separated from the pituitary during the surgical operation.

Results: Histological examination showed a hypervascular tumour consisted by interwoven fascicles of spindle to epithelioid cells with an oncocytic granular cytoplasm. Immunophenotypically the neoplasm was positive for S100, Galectin-3, Vimentin, EMA, Annexin-A1 and TTF-1, while it was characteristically negative for GFAP, Chromogranin, Synaptophysin, CD68, TFE-3, IDH1R132H and CD34. SDHB, ATRX and INI1 expressions were retained. Ki-67 index was 10 %.
Conclusion: The differential diagnosis of spindle-cell oncocytoma from pituicytoma is difficult and relies upon clinicopathological criteria and even ultrastractural studies to reveal the abundant mitochondria and the junctional complexes at the cell borders. Recently, some authors propose that SCO is a variant of pituicytoma.

E-PS-16-018
Angiomatous meningioma: Case report
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Objective: Menengiom is the most common intracranial tumour. It is a benign neoplasm which arises from the arachnoid cap cells of the cerebrum and the spinal cord.
Method: Angiomatous meningioma(AM) is a rare histological subtype of meningioma, constituting %2.1 of all meningiomas. Histologically, its blood vessel component exceeds %50 of total tumour area. AM is reported in two types which are microvascular and macrovascular. AM also demonstrates some distinct features compared to other benign meningiomas, such as it seems that male female ratio for AM is higher than that for general meningioma.
Results: We report a clinical case of a 77 year old woman with angıomatous menıngıoma in the cerebrum which was suspected for hemangioblastoma by radiologists.
Conclusion: Our aim is to present the histomorfological features of this uncomman variant of meningioma with different diagnosis.

E-PS-16-019
Extracraneal primary ectopic meningioma of the frontal bone: A case report and review of the literature
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Objective: Extracraneal non-dural or ectopic meningiomas are very rare, but their similitude to their intracranial more common counterpart in terms of histologic and immunophenotypic features, usually allows an accurate differential diagnosis with other head-and-neck lesions.
Method: We report the case of a 70-year-old woman presenting with a slow growing frontal subcutaneous mass, static on palpation, progressing for 6 years. Computed tomographic scan described an extracraneal soft tissue mass, contiguous with the external aspect of the cortical of the frontal bone, causing superficial erosion and sclerotic reaction. The patient underwent tumour resection.
Results: Surgical specimen was a flat 3,5 × 2,3 × 0,7 cm fragment of tan-yellow tissue comprising bone splinters. Histologic analysis showed a neoplastic lesion, composed of epithelioid and fusiform cells, with pale eosinophilic cytoplasm of syncytial appearance, round to oval uniform nuclei with delicate chromatin and occasional small solitary nucleoli. The cells formed occasional whorls and were disposed in a collagenous background. No necrosis or mitotic activity were identified. Tumour cells showed immunoreactivity to epithelial membrane antigen, S100 protein and progesterone receptors. Final diagnosis was of a grade I extracraneal fibrous meningioma.
Conclusion: This case illustrates the characteristics of these rare extracraneal lesions. In cases such as this, an intracaneal component must always be excluded.

E-PS-16-021
The role of immunohistochemistry in lymphoplasmacyte-rich meningioma
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Objective: Lymphoplasmacyte-rich meningioma is a very rare subtype of benign meningioma, which is characterized by prominent inflammatory cell infiltration with sparse meningothelial component. The incidence is less than 1 % of all meningiomas. We present a case of 45-year-old male without any systemic hematologic abnormalities.
Method: The patient was admitted at the Neurosurgery Clinic with headache, confusion, disorientation, nausea and vomiting. Neurological examination and complete blood count were normal. The MRI revealed isodense, contrast-enhanced dural mass in the right frontal parasagital region. Total tumourectomy was done and gross examination showed oval, well-circumsribed tumour with diameter of 4 cm.
Results: Microscopic analysis showed neoplasm composed of rare nests of meningothelial cells surrounded by extensive lymphocytic and plasma cell infiltrate, separated by proliferated colagenous connective tissue bands. The meningothelial cells had round to oval nuclei without clear cytoplasmic borders. Immunohistochemistry showed positive signal for EMA, PR, CD3, CD4, CD20, LCA, CD79alfa and Bcl2; focal positive signal for CD138, IgA, IgD, IgG, IgM, λ, k and negative signal for CD34, CD10,CD23. The proliferative index for Ki-67 was low (4 %).
Conclusion: Immunohistochemical analysis had a crucial diagnostic role in differentiating this rare tumour subtype from intracranial inflammatory process.

E-PS-16-022
Xanthomatous meningioma
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Objective: Meningioma is a neoplasm derived from meningothelial cells representing various histopathological features. Metaplastic meningioma is one of the rarest subtypes. Metaplastic meningioma exhibiting extensive xanthomatous changes, namely 'xanthomatous meningioma', is an extremely rare variant of meningioma.
Method: The surgical specimens were formalin-fixed and paraffin embedded. The section were stained with routinary H&E. Immunohistochemistry was performed.
Results: A 32-year-old male patient presented to outpatient clinic with dizziness. Magnetic resonance imaging revealed a mass lesion with 7,4 cm diameter in the right frontal area. Total resection of the tumour was performed. Microscopically, the tumour composed of two components. The conventional meningioma component showed polygonal cells with eosinophilic cytoplasm and round to oval nuclei. The xanthomatous component was composed of tumour cells with vacuolated clear cytoplasm and round nuclei. Immunohistochemically, epithelial membrane antigen (EMA), Vimentin and Progesterone were expressed in both the conventional meningioma and the xanthomatous component. CD68 was expressed only in the xanthomatous component.

Those xanthomatous cells had been considered as neoplastic meningothelial cells, but not macrophages, because of being positive for EMA. This case was diagnosed as xanthomatous meningioma, WHO grade 1.
Conclusion: It is important to pathologists not to misidentify xanthomatous tumour cells as macrophages.

E-PS-16-023
Posterior fossa tuberculoma in a 9-year old boy mimicking posterior fossa tumour
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Objective: Posterior fossa tuberculoma in young children without classical symptoms of fever or lethargy can initially present with neurological symptoms and mimic a tumour, both clinically and on imaging studies. A diagnosis of tuberculoma can be missed without proper history and clinical work up.
Method: A 9-year old boy presented with repeated episodes of headache of 1 month duration and unsteady gait for 1 week. CT scan and MRI showed a space occupying lesion in the posterior fossa and a malignant posterior fossa tumour was considered. A right suboccipital paramedian craniotomy and tumour excision was done. Specimen received was soft, grayish white to pale yellow, measuring in aggregate 42 mm. Entire tissue was analyzed.
Results: Histology exhibited extensive areas of caseative necrosis, surrounded by epithelioid cells, numerous Langhans giant cells, lymphocytes and occasional plasma cells. Focal areas of microgranulomas with surrounding reactive gliosis was noted. No Cryptococci or fungal element was discernible. Post operatively, a very high ESR and history of direct contact with his father, a patient treated for pulmonary tuberculosis was confirmed.
Conclusion: Intracranial tuberculomas are often mistaken as tumours in neuroimaging studies and not detected in early stages. The importance of clinical history and other ancillary investigations is reemphasized.

E-PS-16-024
An intermediate grade melanocytoma in quadrigeminal cistern
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Objective: A case of intermediate grade melanocytoma of the brain in a 42-year-old woman is presented. Primary melanocytic tumours of the central nervous system (CNS) are classified as well differentiated melanocytoma and malign melanoma. This case has been considered worth presenting as it is in the quadrigeminal cistern, it is invasive and it is rare.
Method: The surgical specimens were formalin-fixed and paraffin embedded. The sections were stained with routinary H&E. Immunohistochemistry was performed.
Results: Histological examination revealed the tumour to be composed of cells which have oval shaped to fusiform nucleus and eosinophilic cytoplasm. There were concentrated melanin pigments in some areas. Also brain invasion was detected. Immunohistochemical staining showed that the neoplastic cells were positive for Vimentin, HMB45, Tyrosinase and focally positive for S100, MelanA and KBA62. Ki67 index was found as % 0–1.
Conclusion: Primary melanocytic tumours of CNS arise from melanocytic cells in leptomeninx. They are usually seen as non-invasive masses. It is important to distinguish it from meningiomas and melanotic schwannomas. Neoplasm which has minimal atipia and brain invasion or increased mytotic activity is defined as intermediate grade. It is foreseen that it will behave more agressively.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-17 Ophthalmic Pathology

E-PS-17-001
Ocular rhinosporidiosis mimicking conjunctival squamous papilloma in Kenya: A case report
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Objective: To describe a case of ocular rhinosporidiosis that clinically mimicked squamous papilloma.
Method: Clinical examination of conjunctival mass and supravital staining with toluidine blue was done. Surgical resection of the mass was performed and it was submitted for histopathological examination.
Results: Histopathological examination revealed multiple sporangia which were filled with endospores
Conclusion: Ocular rhinosporidiosis may resemble conjunctival squamous papilloma. Vital staining with 0.05 % Toluidine blue dye did not distinguish the two lesions well.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-18 Other Topics

E-PS-18-001
Are we pathologists reducing ourselves to replaceable technicians?
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Objective: To show how the ever increasing need to use immunohistochemistry, flow cytometry and molecular diagnostic testing risks making pathologists mere technicians who render tissue diagnoses and to present some potential remedies.
Results: As an example, years ago, a lung biopsy showing adenocarcinoma would be signed out using only routine hematoxylin & eosin staining, but now increasingly requires immunostaining to confirm that it is lung primary and molecular testing for mutations conferring sensitivity to targeted therapy. Pathologists can make themselves less replaceable if they bring their diagnoses to direct encounters with patients (as a team member), decision-making conferences (such as tumour boards), policy-making meetings (like patient safety committees), clinicopathologic conferences, radiologic conferences and clinical case-based teaching in medical education. As an example, pathologists are in a unique position among medical educators to expertly edit a case presentation of lung primary adenocarcinoma to teach how the signs and symptoms relate to the radiology, microscopic pathology, treatment and prognosis.
Conclusion: Instead of withdrawing into roles of nothing more than back-room morphologist diagnosticians, pathologists can find ways of integrating their diagnoses and knowledge of pathology into patient care and medical education, ways that utilize their knowledge as physicians.

E-PS-18-002
Splenic hamartoma
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Objective: Splenic hamartoma is a rare tumour with incidence <1 % in autopsies. We present a case of a splenic hamartoma in a 56-year-old woman.

Method: The patient was asymptomatic, however there was clinical suspicion of a hamartomatous lesion. After splenectomy, the organ's weight was 200 g, measuring 12 × 9 × 6cm. Gross examination revealed a solitary, well-circumscribed, unencapsulated, redish, partially hemorrhagic tumour with maximum diameter 5.5 cm.
Results: Microscopically, structurally disorganized splenic red pulp tissue (highlighted by reticulin stain), with no organized white pulp, was observed. Sinusoidal vascular structures were present, in an inflammatory background with histiocytic predominance. The cells of the lesion were positive for CD-8 and CD-34, focally positive for CD-31, whereas Factor VIII was negative. These findings were compatible with the diagnosis of splenic hamartoma.
Conclusion: Splenic hamartoma is a tumour-like malformation most commonly representing an incidental finding. Sometimes it is difficult to differentiate a splenic hamartoma from a splenic hemangioma, which is the most common primary tumour of the spleen. A positive stain for CD-8 is helpful in such cases, as splenic hamartomas are immunoreactive for CD-8, while splenic hemangiomas are CD-8 negative.

E-PS-18-003
Metastatic thymic carcinoma: A case we should always consider in the differential diagnosis of a metastatic cancer of unknown primary site
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Objective: Thymic carcinoma frequently spreads to the pleural space, regional lymph nodes, liver and brain. However, the initial clinical presentation involving spinal metastases is extremely rare.
Method: We present a case of a 62-year old female with progressive paraparesis. The CT and the MRI showed a neoplastic lesion with an intradural component, which caused the spinal compression, and an extradural component; located on the left edge of the spinal canal at the level of the thoracic vertebrae T11-T12.
Results: Microscopically the neoplastic cells were of medium size, with scant cytoplasm, atypical dark nuclei, frequent mitoses. They were organized in solid nests. Necrosis was absent and crushing artifact was observed in some areas. The immunohistochemical study revealed positivity of the neoplastic cells for CKAE1/AE3, CK8, 34BE12, P63, CD5, while CK20, TTF1, GCDFP15, CD56, Synaptophysin, CD45(LCA), HMB45 were negative.
Conclusion: Immunohistochemical examinations using CKAE1/AE3, P63 and mainly the thymic-carcinoma specific marker CD5 were crucial for confirming the primary site in the Thymus and should be performed in all cases of cancer of unknown origin.

E-PS-18-004
Causes of death in the central region of Ghana: Threat to tourism and socio-economic development?
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Objective: The Central Region of Ghana has many world heritage sites related to the slave trade dotted along its sandy beaches. We aimed at finding out the causes of death in the Central Region of Ghana, and highlight the potential effects of these causes of death on tourism and socio-economic development.
Method: Mortality data from autopsies provide data about the causes of death in the communities of the Central Region. A retrospective descriptive study of autopsy data for the Central Region was carried out over a 2-year period in the Cape Coast Teaching Hospital the only autopsy center in the Central Region.
Results: Out of 470 autopsies performed, 72 % were males and 28 % females. 52.8 % were young adults (18–44 years). Unnatural deaths were the leading cause of death (58.7 %) most being road traffic accidents (58–30.4 % as occupants of vehicles 21.4 % as pedestrians), followed by drowning (15.9 %). 14. 3 % of deaths were due to infections followed by cardiovascular deaths (6.8 %).
Conclusion: There is a high prevalence of road traffic accidents and drowning in the Central Region of Ghana and infections remain a significant cause of death. This has a negative effect on tourism and socio-economic development.

E-PS-18-005
The useful immunohistochemical panel for differentiating solitary fibrous tumour/hemangiopericytoma
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Objective: The most recent World Health Organization (WHO) classification of the tumours of soft tissue considered the term hemangiopericytoma (HPC) obsolete, and places all such tumours within the extrapleural solitary fibrous tumour (SFT) category. In contrast, central nervous system SFT and HPC continue to be regarded as different entities in the latest version of the WHO CNS tumour classification. This study aims to highlight the helpful histological and immunohistochemical features of each of hemangiopericytoma and solitary fibrous tumour to enable reproducible classification.
Method: 25 solitary fibrous tumours and hemangiopericytoma with variable histological features and different localization were selected and then stained for CD34; BCL2; VIMENTINE and CD99.
Results: The mean age of the patients at the time of surgery was 50 years. The male-to-female ratio was 1:1.25. The most common presenting clinical symptoms were a slow growing mass. The characteristic immunoprofile of solitary fibrous tumour was BCL2+ with diffuse staining; CD99+; VIMENTIN+ and CD34+ with a diffuse and intense staining. For hemangiopericytoma, the immunoprofile was BCL2+ with focal staining; CD99+; VIMENTIN+; and CD34±.
Conclusion: Staining for CD34; BCL2; VIMENTINE and CD99 comprises a concise panel for distinguishing Solitary fibrous tumour from Hemangiopericytoma.

E-PS-18-006
Cutanosis amyloidosis: A study with Tioflavin-t and Congo-red staining
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Objective: Cutaneous amyloidosis is one of the most common localized amyloidosis. Commonly cutaneous biopsies are examined with the H&E stain. Amyloid can be also detected with several techniques such as Congo-red stain, as well as crystal violet, thioflavin, methyl violet stains, cytokeratin 5/6 stain. The goal of this study is to reevaluate the stains of Congo-red and thioflavin-t of cutanous amyloidosis.
Method: Twenty-seven cases of cutaneous amyloidosis diagnosed between 2013 and 2016 years were included the study. Congo-red staining and its typical polarization were used to diagnose amyloidosis. Original congo red stained sections were compared with decolorized and restained with thioflavin-t sections of 27 cases with cutaneous amyloidosis.
Results: 16/27 patients were female and 11 were male. While 24 cases were localised cutaneous amyloidosis, 3 were systemic. Most of the localized amyloidosis were primary localized type except one secondary amyloidosis due to the seborrheic keratosis. Thioflavin-t was stained of all cases and it was evaluated easily than Congo-red. One case was diagnosed during the study who were not stained with Congo-red before.

Conclusion: Amyloid deposits could be evaluated by using Congo-red, crystal violet or toluidine blue stains. Congo red stain is the most used method but it needs technical and laboratory experiences. Thioflavin-t or Congo-red stains under ultraviyolet light could more be helpful and sensitive. However limited number of patients was included this study, thioflavin-t staining could be an alternative or additional method for Congo-red staining in cutaneous amyloidosis.

E-PS-18-007

Can Hematoxylin and Eosin staining achieve a diagnosis of a pulmonary fat embolism?: Case report

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Objective: We illustrate an autopsy case in which the diagnosis of fat embolism was made with exclusive focus on standard staining (Hematoxylin and Eosin (H&E) staining) of pulmonary sampling.
Method: We present a case of 60 year-old female who was a victim of a traffic accident which caused a tibial closed fracture. She He was hospitalized and scheduled for a surgical operation. Clinical deterioration occurred, followed by rapid death.
Results: The external examination and the autopsy showed no specific asphyxia syndrome without any particular finding except cardiac hypertrophy. A histological examination with standard staining has been performed showed the presence of embolic fat droplets in some alveolar capillaries with a total narrowing of the vascular lumen.
Conclusion: The histological examination with H&E staining can be conclusive in case of postmortem diagnosis of fat embolism. The pulmonary sampling in such case must be exhaustive. The pathologist must be warned thus he will pay particular intention in order to find fat droplets in the capillary lumen.

E-PS-18-008

Sudden death associated with unexpected lesions of the pituitary gland

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Objective: We report the autopsy findings and the histological features of two autopsy cases, in which tumour pituitary lesions lead to sudden death.
Method: Report of two cases.
Results: First observation: A 41-year-old woman presented a sudden agitation. She dead almost 30 min after. Macroscopic autopsy findings included a heavy edematous brain associated to a large tumour arising from the sella turcica associated to a hypertrophy of the pituitary gland. Microscopic examination revealed a pituitary adenoma and an intravascular papillary endothelial hyperplasia of the cavernous sinus known else as Masson's tumour. Second observation: A 52-year-old man with a history of head ache treated symptomatically. He presented a sudden loss of consciousness and he dead few minutes after. The macroscopic findings of the autopsy included essentially heavy edematous brain with a pressure cone of the cerebellar tonsils. Also we noticed a large tumour ($3 \times 3 \times 2$cm) associated to a pink-grey hypertrophy of the pituitary gland. Microscopic examination showed homogenous pituitary hyperplasia.
Conclusion: These two cases highlight the need for a thorough postmortem investigation, including a microscopic examination of the pituitary gland.

E-PS-18-009

Sudden death due to undiagnosed Gaucher's disease: Case report and revue of the literature

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Objective: Gaucher disease is a rare, inherited metabolic disorder in which an enzymatic deficiency causes an accumulation of harmful quantities of certain fats. It is not described as a cause of sudden death.
Method: Here, we report a case of a 33 year-old- female with a medical history of valvular stenosis died suddenly in suspected circumstances.
Results: The external examination revealed brownish, reddish, yellow, and green subcutaneous hemorrhages on the torso as well as the upper and lower extremities. The autopsy showed a sclerosis and calcification of the left cardiac valve associated with an abnormally enlarged liver and spleen (hepatosplenomegaly) with a hypertrophy of the lymph nodes. A histological examination was performed showed Gaucher's cell in the splenic, hepatic and lymph node tissue. Unfortunately, the bone marrow was not collected.
Conclusion: By this observation we underline the important role of histology in solving some critical problem and the value of routinely collecting bone marrow during an autopsy to enable accurate testing and diagnosis.

E-PS-18-010

Sudden unexpected death due to undiagnosed glioblastoma: Report of two cases

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Objective: We report two cases of sudden unexpected death due to undiagnosed glioblastoma with special focus on the histological features.
Method: We report two cases.
Results: First observation: A 42-year-old woman was found dead in her house, in advancing degree of putrefaction. A medicolegal autopsy was performed showing essentially a gray discoloration of the brain with partial liquefied parenchyma. Also, a varicolored brain tumour of the right frontoparietal region was identified. It contained regions of necrosis and hemorrhage, extended to the skull bone. Histologically, although the brain parenchyma was adversely affected by the autolytic artifact, we noticed a tumourous tissue composed of mostly poorly differentiated pleomorphic astrocytic cells associated to an important degree of nuclear atypia and a large zone of necrosis. Second observation: A 64-year-old man suddenly collapsed in prison and dead some minutes after. A medicolegal autopsy was required. Pathological findings showed a heavy weighed brain. At coronal sections, the cerebral hemispheres were asymmetrical with deviation of midline structures from right toward left. In the right fronto-parieto-temporal region we noticed an enlarged spherical mass (cm $14 \times 6 \times 5$), with variegated appearance. Histologically, a small-cell astrocytic neoplasm with focal gigantocellular differentiation featuring necroses was described and a diagnosis of a glioblastoma was retained.
Conclusion: In cases with sudden death with suspected intracranial pathology the necessity of a multidisciplinary approach, including the forensic medicine and the pathologist is compulsory.

E-PS-18-011

A case of sudden unexpected death due to a granulomatous vasculitis: Necropsy findings and histological features

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Objective: Takayasu arteritis (TA) is a form of large vessel granulomatous vasculitis, mainly affects the aorta and its branches in different ways. We illustrate an exceptional case of sudden death due to TA diagnosed on the basis of histologic features.
Method: We report a case of a 19-year old girl suddenly collapsed at home and died few minutes after.
Results: In autopsy, we find a significant circumferential narrowing of the aorta and the major branches notably the carotid artery with a major symmetric hypertrophy of the heart associated to a moderate left ventricular dilatation. A histological examination was performed that confirms the myocardial hypertrophy and the massive pulmonary edema. Moreover, it specifies that this parietal vessel infiltration is panarteritis due to TA. To our knowledge, this is the first described report of such complication of TA which occurs as a sudden death with such mechanism.
Conclusion: By our case we underline that autopsy must be completed and the aorta and the branches have to be dissected and explored very thoroughly. And finally, we emphasize the important role of autopsy in explaining such threatening mechanism of some rare disease.

E-PS-18-012
The influence of intra-abdominal hypertension on the morphological status of the brain
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Objective: It is already known that increase of intra-abdominal pressure has a negative effect on the function of the gastrointestinal, respiratory, cardiovascular ans urinary tracts. Our purpose was to research the influence of intra-abdominal on the brain.
Method: The experimental research: male rats of the same age, weight, diet (n = 100). Among them: a control group (n = 10)—intact animals without affecting; comparison group (n = 90)—animals, which was artificially created by intraabdominal hypertension of different degrees (15, 25, 35 mm Hg) and different exposure times (3, 12, 24 h). The method of creation of intra-abdominal hypertension—pneumoperitoneum. We made the morphological examination of the brain tissue.
Results: We got the next results: 15 mm Hg—only pericellular swell, the general structure of the brain and cerebellum are kept; 25 mm Hg—capillarstasis, perivascular swell, plethora, gliosis of the brain tissue; 35 mm Hg—extensive zones of encephalomalacia, gliosis of the brain tissue, hemorrhages, brain depression. These changes amplified at increase in an exposition of intra-abdominal hypertension.
Conclusion: The degree of changes of the brain tissue depends on the level and time of the intra-abdominal hypertension.

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E-PS-19 Paediatric and Placental Pathology

E-PS-19-001
Caroli syndrome associated with autosomal recessive polycystic kidney disease
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Objective: Caroli syndrome is a rare genetic disorder characterized by dilatation of the intrahepatic biliary tree and congenital hepatic fibrosis. It occurs in more than 60 % of the individuals with autosomal polycystic kidney disease and appears to be inherited in an autosomal recessive manner due to a mutation of the PKHD1 gene, which is also linked to ARPKD. It has an average incidence of less than 1 case per 100,000 people, with more reported cases of Caroli syndrome than of Caroli disease.
Method: We report the case of a late preterm female infant diagnosed with autosomal recessive polycystic kidney disease and no family history of renal disorders. At gross examination we observed markedly enlarged kidneys with bosselated surface, occupying most of the abdominal cavity and containing multiple small cysts in the renal cortex and medulla.
Results: Microscopic evaluation showed radially arranged, elongated cysts, lined by cuboidal or flattened epithelium and surrounded by interstitial fibrosis. Microscopic evaluation of the liver revealed unusually numerous, irregular and dilated intrahepatic bile ducts accompanied by congenital hepatic fibrosis, highly suggestive for Caroli syndrome.
Conclusion: Although extremely rare, Caroli syndrome should be taken into consideration as differential diagnosis in neonates with jaundice, hepatosplenomegaly, dilatation of the intrahepatic biliary tree or congenital hepatic fibrosis. We emphasize the importance of high resolution ultrasonography as primary imagistic modality for evaluation of autosomal recessive polycystic kidney disease, especially during the perinatal and neonatal periods.

E-PS-19-002
Calretinin immunohistochemistry in the diagnosis of Hirschsprung disease
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Objective: To evaluate calretinin immunohsitochemistry in the diagnosis of Hirschsprung disease. The basis of which is negative calretinin immunoexpression corresponds to a diagnosis of Hirschsprung disease.
Method: 224 rectal suction biopsy tissue blocks were retrieved from the archives of Hospital Sultanah Bahiyah/ Hospital Alor Star. All 224 sections were stained with calretinin immunostain. The sections were then evaluated by three independent observers; a senior pathologist, junior pathologist and pathology trainee. Interpretations in 206 sections were compared with the gold standard of resection reports or medical records.
Results: Calretinin immunohistochemistry had a sensitivity of 97.9 % and a specificity of 90.7 %. The agreement between calretinin immunostaining and the gold standard was statically excellent [K = 0.883, 95%CI (0.236–1.00)]. Interobserver reliability between the observers yielded excellent agreement [K = 0.976].In 45 of the 224 biopsies that were initially reported as insufficient/inconclusive based on H&E staining and serial sections, the concordance of calretinin immunostaining with the gold standard was strong [K = 0.808]. The study found a false positive rate of 10 % with only one biopsy reported as inconclusive by all three observers. The final outcome for 18 biopsies were not found.
Conclusion: Calretinin immunohistochemistry has proven to be an efficient tool in the diagnosis and exclusion of Hirschsprung disease.

E-PS-19-003
Hydranencephaly: A rare type of intrauterine destructive lesion of the brain
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Objective: Hydranencephaly (HA) is a rare congenital condition of unknown etiology, in which cerebral hemispheres are absent and neonatal skull can be transilluminated.
Method: Routine USG examination was performed at the 13th and 23rd weeks of gestation. Autopsy of the neonate after termination of pregnancy was performed using routine procedures enriched with transillumination of the skull using a bright light source.
Results: First USG examination showed normal brain. Although the next USG scan revealed the pattern of empty fetal skull, this was overlooked.

Later, due to severe IUGR and polyhydramnion, the pregnancy was terminated by c.s. at the 31st week of gestation. The neonate had dysmorphic facies with normal head circumference, presented with seizures and no respiratory activity. Postnatal USG of the head revealed HA. The neonate died 56 h after delivery. At autopsy, the transillumination sign was positive. Hemispheres were formed by 1 mm thick layer of pio-glial membrane. Cerebellum and optic nerves were atrophic. Otherwise, autopsy findings were within normal limits.
Conclusion: We refer a rare case of HA, in which the injury of the brain must have developed between 13th and 23rd weeks of gestation. No infection or other possible known causes of HA were identified.

E-PS-19-004
A case of pedunculated hepatic mesenchymal hamartoma in a child
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Objective: Liver tumours are uncommon during childhood, when they show an age-dependent distribution and are mostly malignant. Hepatic mesenchymal hamartoma (HMH) is a rare benign lesion, presumably congenital, usually occuring under the age of 2. There is still no agreement upon its histogenesis, whether it represents developmental anomaly, true neoplasm or reactive lesion resulting from biliary obstruction or anomalous blood supply.
Results: A 1-year-old boy was admitted due to acute abdomen. Clinical investigation revealed a hepatic tumour (US, MR) which was surgically removed. The tumour was torquated around a stalk connected to falciform ligament, and adherent to omentum and transverse colon. Grossly, it had gray-brown, glistening, lobular surface and measured 6 × 5,5 × 4,5 cm. The cut-surface was necrotic and hemorrhagic, with only a narrow rim of preserved solid tissue at the periphery. Histologically, it was composed of abundant, myxoid and loose stroma with focally dilated bile ducts, sparse cords of hepatocytes and numerous blood vessels, some of which thrombosed. There were only a few mitotic figures, but no atypia. No extramedullary haematopoiesis was noted. The tumour margins were positive.
Conclusion: Unlike classic HMH showing multiple cysts, sometimes resembling lymphangioma, the tumour in our case was solid and pedunculated. Although the lesion is benign and should not recur, since it may rarely progress into malignancy, we believe our patient should be followed-up for a longer period.

E-PS-19-005
Megacystis Microcolon Intestinal Hypoperistalsis Syndrome (MMIHS): Case report
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Objective: Megacystis microcolon intestinal hypoperistalsis syndrome (MMIHS) is a congenital disorder characterized by abdominal and urinary bladder distension, microcolon and abnormal GI peristalsis.
Method: We report the case of a newborn with suspicious antenatal ultrasound findings: distended urinary bladder and abdomen. After the birth she was transferred to the NICU and multiple investigations were performed, including pathological examination of ileal and colonic biopsies.
Results: Complementary investigations revealed a thick walled urinary bladder, narrowing of the rectosigmoid and other anomalies. The laparostomy confirmed the malrotation of the mesentery, with right-sided jejunoileum and left-sided ileocecal valve. The histology revealed fibrous submucosa and hyperplastic ganglion cells. Muscularis propria (MP) showed a hypoplastic external layer and hyperplastic myenteric plexus. Immunohistochemistry revealed weak SMA reaction of the internal MP layer. S100 showed the hyperplastic feature of the myenteric plexus. Calretinin was negative in ganglion cells and neural fibers. The ileum showed edematous submucosa, with atrophic MP, weakly positive for SMA. Ganglion cells were present and hyperplastic in the myenteric plexus. S100 and Calretinin were positive in neural structures.
Conclusion: MMIHS is a severe disorder with poor prognosis and limited lines of treatment. The case presented revealed an interesting immunohistochemically profile, somewhat similar to Hirschprung's disease. The infant was alive 10 months after the birth, with left ileostomy and gastrostomy.

E-PS-19-008
Beckwith Wiedemann Syndrome: A 9 year retrospective analysis
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Objective: Beckwith-Wiedemann Syndrome (BWS) is rare, with an incidence of 1/14.000 newborns, mostly sporadic, with rare cases linked to anomalies of chromosome 11, characterized by overgrowth leading to an asymmetric or uneven appearance, known as hemihyperplasia. We aim to present a review of clinicopathologic correlation of BWS at our institution.
Method: We present a 9 year retrospective (2006–2015) review of BWS, performing a correlation between pre-natal ultrasonography, morphological characteristics findings and literature.
Results: The study included four cases, 2M/2F, with gestational age between 19 and 36 weeks, three from medical termination pregnancies and one from a fetal death. The characteristics found in ultrasonography were increased kidney volume in all cases; omphalocele, overgrowth, kidneys with low differentiation and macroglossia in half of cases. The characteristics features observed in autopsy were: dysplastic kidneys (75 %), increased adrenal gland (75 %) omphalocele (50 %), macroglossia (50 %), pancreatic hyperplasia (50 %), and reduction of the head perimeter (50 %). All cases, but one, have a clinical diagnose of BWS and one case have molecular confirmation (25 %), none with family history.
Conclusion: The recognition of this syndrome is an important finding for a correct genetic counseling for future pregnancies of the parents.

E-PS-19-009
Meckel Gruber Syndrome: A rare and lethal anomaly
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Objective: Meckel Gruber syndrome is a lethal autosomal recessive disorder, caused by the failure of mesodermal induction. It is characterised by meningo-encephalocele, policystic kidneys and polydactyly. Other abnormalities associated with this syndrome is cleft palate, cardiovascular disease, hepatic ductal dysplasia, oligohydramnios, genital deformations, bowed legs, microcephaly, hydrocephalus, pulmoner hipoplasia. The world wide incidence varies from 1 in 1.300 to 1 in 140.000 live births. Highest incidance was reported in Gujarati Indians.
Method: A 29-year-old patient was admitted to the hospital with gestation at 12 weeks. She had a previous healthy fullterm pregnancy. There was no history of teratogenic drugs or infectious disease. A routine ultrasonography revealed a single fetus with occipital encephalocel and bilateral polycystic kidneys. The pregnancy was terminated and a 22 g male fetus was delivered and send for autopsy. Macroscopic examination of the fetus showed polydactyly, occipital encephalocel measuring 2 × 1 cm and

bilateral polycystic kidneys. Microscopic examination of the kidneys revealed cystic renal dysplasia.
Results: The diagnosis were consistent with Meckel Gruber syndrome.
Conclusion: Meckel Gruber syndrome results in 100 % in fetal and neonatal mortality. It has a high risk of recurrence so parents should be counseled for future pregnancies.

E-PS-19-010
Small bowel cystic lymphangiomatosis: A rare tumour
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Objective: Generalized cystic lymphangiomatosis is a rare anomaly of the lymphatic system. They are generally observed in the skin, skeletal system, soft tissues and visceral organs. Rarely, lymphangiomas occur in the gastrointestinal tract especially in the distal ileal mesentery. They are considered to be a congenital dysplasia of lymphatic tissue and abnormal development of the lymphatic vessels during fetal life.
Method: A 5-year-old girl was admitted to the hospital with recurrent abdominal pain. Pysical examination and laboratory tests were in normal limits. Abdominal ultrasonography and magnetic resonans imaging revealed multipl cystic tumoural lesions which measure up to 8 cm and localized in the mesenteric region. The patient underwent partial ileal and mesenteric resection including cytic lesions. Macroscopic examination of the resected specimen showed multipl diffuse cystic lesions in different sizes containing chylosis fluid and localized in the mesentery and intramural part of the ileum. Microscopically all the cystic lesions were lined by flattened endotelium and immunohistochemically showed diffuse D2-40, focally CD31 and CD34 positive staining.
Results: The final diagnosis was lymphangiomatosis of the small bowel.
Conclusion: Although rare, intestinal lymphangiomatosis should be kept in mind in pediatric patients whose sonographic findings show cystic lesions in the abdominal cavity.

E-PS-19-012
A case of Patau syndrome combined with Congenital Adrenal Hyperplasia and cystic fibrosis
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Objective: Patau syndrome was first described in 1960 as a group of birth defects caused by trisomy of chromosome 13. The estimated incidence of trisomy 13 at the time of delivery was calculated as 1.6 per 10,000 deliveries. Congenital adrenal hyperplasia is a group of autosomal recessive disorders characterized by impaired cortisol synthesis. The incidence ranges from 1:10000 to 1:20000 births and is more prevalent in some ethnic groups, particularly in remote geographic regions. Approximately 95 % of all congenital adrenal hyperplasia cases are caused by 21-hydroxylase deficiency. Cystic fibrosis is an autosomal recessive disease caused by mutations in the CF transmembrane conductance regulator gene, on chromosome 7, prevalence is 1:2500 newborn infants.
Method: The case of a 1-month-old girl with of trisomy 13, congenital adrenal hyperplasia (21-hydroxylase deficiency) and cystic fibrosis.
Results: We find syndactyly, polydactyly, gnathoschisis, hypoplasia of the aortic tract, bicorporeal septate uterus. Histology the presence of adrenal hyperplasia. The pancreas showed extensive fibrosis, acinar destruction and dilatation of ducts. The typical acidophil content in the secretory ducts and acini of the pancreas was confirmed.
Conclusion: Thus, this case demonstrates of Patau syndrome combined with congenital adrenal hyperplasia and cystic fibrosis.

E-PS-19-013
Bilateral ovarian germ cell tumours in a patient with Swyer syndrome: A case report
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Objective: Swyer syndrome is a rare manifestation of disturbances of gonadal and sex development in which the individual has 46,XY genotype but is phenotypically a girl.
Method: We present a case of 11-year-old girl, admitted to hospital with complaints of lower abdominal pain, anorexia and subfebrile temperature. Ultrasonography revealed a large tumour of the right ovary. By laboratory investigations, the alpha-fetoprotein level in serum was 15,954 IU/ml (laboratory reference range, 0–4.6). The chromosome analysis revealed 46,XY karyotype. The patient underwent lower laparotomy and right adnexectomy.
Results: Grossly, the tumour (17 × 5 × 8 cm) was nodular, grayish-white. It had cystic areas. Histological examination revealed a mixed germ cell tumour with the reticular pattern, characteristic of yolk sac tumour. Alveolar, glandular and trabecular architecture was present. By immunohistochemistry, alpha-fetoprotein and CD117 were expressed. There were regions composed of primitive mesenchyma enclosing cysts lined by cytokeratin AE1/AE3-positive respiratory epithelium. Areas containing immature lipocytes, hyaline cartilage and ossification were also found. Prophylactic left adnexectomy was performed. The histopathological examination showed the typical features of gonadoblastoma: cells with inconspicuous cytoplasm and small round-to-oval nuclei, surrounded by ovarian-type stroma.
Conclusion: Swyer syndrome is associated with a significant risk of developing different germ cell tumours including teratomas. Prophylactic gonadectomy is recommended.

E-PS-19-014
The case report of pleomorphic anaplastic neuroblastoma with unique evaluation of carbon isotopic composition in tumour tissue
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Objective: Pleomorphic anaplastic neuroblastoma (PAN) was described for the first time as an aggressive histological type characterized clinically by advanced stage of disease with abdominal dissemination and poor response to treatment [1]. Rarity of this entity together with its unusual biology may render PAN diagnostically challenging.
Method: The patient was 3-years old boy presented with pathological mass originating from right suprarenal gland with tumour dissemination in abdominal cavity and bone marrow infiltration accompanied by elevated concentrations of catecholamines and their metabolites in the urine. The isotope ratio measurement in frozen tumour tissue, performed with the use of Sercon 20–22 Continuous Flow Isotope Ratio Mass Spectrometer (CF-IRMS) coupled with Sercon SL elemental analyzer for simultaneous carbon-nitrogen-sulfur (NCS).
Results: In microscopic examination of tumour tissue pleomorphic and anaplastic cells were fund as well as necrosis and microcalcifications. Immunophenotype of tumour cells appeared not clear. Neuron-specific enolase and Protein Gene Product 9.5 were positive, neuroblastoma 84 marker was found in single tumour cells only. Myogenic differentiation protein presence and myogenin cytoplasmatic reaction were also observed. Proliferation Ki-67 index was 60 %. The isotope ratio measurement in frozen tumour tissue have revealed the following results: the stable carbon isotopes ratio 13C/12C (δ13C) was −27.25 ‰.
Conclusion: Stable isotope ratio measurement is an unique procedure in oncology. The method meets the highest requirements concerning measurement quality and credibility. Striking low values of carbon stable isotope ratios in PAN tissue in presented case may also be related to its aggressive clinical behavior in presented case and helpful in individual patients' treatment consideration.

E-PS-19-015

Erdheim-Chester disease—Case report

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Objective: Erdheim-Chester disease (ECD) is a sporadic non-Langerhans cell histiocytosis, first described as "lipoid granulomatosis" by Jakob Erdheim and William Chester in 1930. It is a very rare disease that typically affects middle-aged patients and has a significant male predominance. In paediatric age is extremely rare.
Method: We report a case 4-years-old child that presents extensive lesion in the base of the skull, with destructive behaviour of osteolytic type and tissue component, with associated diabetes insipidus—clinical suspicion of Langerhans cell histiocytosis.
Results: Histopathological evaluation of biopsies revealed infiltrating lesion by histiocytes with a foamy cytoplasm, with positive staining for CD68 and negative for CD1a, Langerin and S100 protein. Genetic study confirmed BRAF V600E mutation, and patient began therapeutic with dabrafenib.
Conclusion: ECD is a very rare disease, especially in paediatric age, and it is associated with high mortality rates. BRAF V600E mutation was recently described in about 50 % of patients with ECD which lead to worldwide therapeutics with BRAF inhibitors, that proved to be very beneficial with increase in survival rates.

E-PS-19-016

A very rare tumour of infancy

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Objective: Melanotic neuroectodermal tumour of infancy (MNTI) is an extremely rare, pigmented neoplastic entity of neural crest origin. More than 90 % of these tumours occur in the head and neck region, especially the maxilla, during the first year of life. However its presentation since birth and intracranial extension is more exceptional.
Method: We report the case of a 1-month-old girl who presented a cranial swelling since birth rapidly growing. Radiologic investigations showed a richly vascularized mass with extra and intracranial extension. Those clinical and radiologic findings were suggestive of juvenile hemangioma. The child underwent complete surgical excision.
Results: Histopathological examination revealed the tumour consisted of the two cell components. The first type was small round cells with high nuclear to cytoplasmic ratio consistent with neuroblastic cells. The second type was large polyhedral cells containing melanin. The Ki67 index was 90 %. No adjuvant treatment was proposed after surgery.
Conclusion: MNTI is considered to be a benign tumour with good prognosis and rarely behaves as a malignant the clinical behavior of this tumours may be distinguished by the pathological findings.

E-PS-19-017

Infantile digital fibromatosis: A case report

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Objective: Infantile digital fibromatosis (IDF) is an uncommon benign proliferation of myofibroblasts in the dermal tissue on the digits and toes with a marked tendency for recurrence. The tumour may often resolve spontaneously. We discuss through this case report clinicopathological features of this tumour.
Method: We report a 2-year-old girl without notable medical history, who presented three firms nodular lesions of the 4th and 5th fingers of the left hand appearing since 3 months.
Results: Macroscopic examination revealed 3 white nodules with a smooth surface. Microscopically, the dermis and the subcutaneous tissue contained a benign proliferation made of non atypical myofibroblasts with a fascicular pattern. The tumour cells were placed on a hyaline collagen matrix highly vascularized. The trichromatic Masson staining revealed many inclusion bodies in the cytoplasm of neoplastic fibroblasts.
Conclusion: The IDF is a rare benign tumour of childhood, characterized by a good prognosis. Despite the spontaneous regression reported in the literature, surgical excision is the best treatment for these tumours.

E-PS-19-018

Neonatal neuroplastoma of abdominopelvic sympathetic ganglia mimicking teratoma: An autopsy case report

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Objective: Neuroblastoma is the commonest solid tumour of childhood derived from neural crest ectoderm that occur either in the adrenal gland or associated sympathetic ganglia. Here, we presented an unusual presentation of neuroblastoma arising from the sympathetic chain.
Method: We reported an autopsy case of abdominopelvic neuroblastoma occurring in a 37-week-old newborn male who died on the second day because of cardio-respiratory failure.
Results: The complete autopsy demonstrated moderate ascites, pleural and pericardial effusions, congested and oedematous lungs, hypertrophic cardiomyopathy, hepatomegaly, splenomegaly and a globular tumour in the abdominopelvic region compressing the left kidney which showed a pyelo-calyceal hydronephrosis. The tumour was well-circumscribed with smooth external surface, had a firm consistency, and measured $8 \times 6 \times 5$ cm. On cut section, the tumour appeared heterogeneous with peripheral focal hemorrhagic areas. On microscopic analysis, the tumour was composed of lobules of small round cells with hyperchromatic nuclei and scanty cytoplasm. Rare mitotic figures were observed. At few places, the tumour showed neuropil and schwannian stroma. On the basis of these findings, diagnosis of poorly differentiated neuroblastoma was considered.
Conclusion: The presented case highlights the significance of detailed histological analysis in neonatal neuroblastomas with unusual presentation.

E-PS-19-019

Presacral mature cystic teratoma: Part of Currarino triad

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Objective: The Currarino triad is a relatively unknown hereditary disorder, composed of an association of a congenital anorectal stenosis (or another type of low anorectal malformation), an anterior sacral defect, and presacral mass. The triad may be incomplete but the sacral bony defect is considered to always be present. The sacral mass may be a teratoma, an anterior sacral meningocele, an enteric cyst, dermoid, or a combination of these. Rare cases of malignant transformation were described. Constipation is the most common presenting symptom.
Method: Case report with literature review.
Results: A newborn female with a vestibular fistula and chronic constipation. During follow up she needed periodic rectal dilatations. When was 3 years-old she started non-responding to laxative therapy and imaging exams revealed a presacral mass, hemisacrum and anorectal stenosis. Posterior sagittal anorectoplasty and tumourectomy of the presacral mass were then performed, which pathology evaluation was compatible with a mature cystic teratoma.

Conclusion: Apart from the mandatory rectal examination in patients with severe chronic constipation, an imaging complementary study of the pelvic region may help to diagnose the Currarino triad. Pathology support is essential for the precise diagnose of the presacral mass and exclusion of any malignant transformation.

Monday, 26 September 2016, 07.00–19.00, Hall 11.3
E-PS-20 Pulmonary Pathology

E-PS-20-001
Colloid adenocarcinoma of the lung: A case report and review of the literature
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Objective: The 2015 World Health Organisation classification of lung tumours defines colloid adenocarcinoma as "an adenocarcinoma in which abundant mucin pools replace air spaces". This category now includes those cystic neoplasms which were previously classified as 'mucinous cystadenocarcinoma'. We present a case of a colloid adenocarcinoma of the lung, which was entirely cystic in nature.
Method: A 73 year old woman presented with a 4 month history of a dry cough. A CT scan of the chest showed a 9.3 cm cystic lesion in the right lower lobe. The patient underwent a right lower lobectomy.
Results: Macroscopically, a 93 mm thin-walled, uniloculated cyst was identified, filled with mucinous material and abutting the pleura. Histologically, the cyst was lined partly by atypical mucinous epithelium, which expressed CK20 and CDX2, and partly by benign ciliated columnar epithelium, which expressed CK7.
Conclusion: Fewer than 100 cases of pulmonary colloid adenocarcinoma have been reported in the literature. The most important issue for the pathologist is to distinguish whether these tumours represent a primary pulmonary neoplasm or a metastasis. Immunohistochemical staining of colloid adenocarcinoma is variable and may not be helpful. Therefore, clinical and radiological correlation remains vital in the management of such patients.

E-PS-20-003
Pathohistological apects of pulmonary Langerhans cell histiocytosis
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Objective: To analyze the pathohistological findings, demographic data, as well as clinical symptoms of patients with pathohistologically confirmed pulmonary Langerhans cell histiocytosis (PLCH).
Method: We retrospectively analyzed biopsy material obtained by bronchoscopy and open lung biopsy, as well as medical charts of 13 patients in which PLCH was diagnosed during the 15-year period.
Results: PLCH was found in 9 (69.3 %) women and in 4 (30.7 %) men. The average age of patients was 34.7 years (the youngest was 20 and the oldest patient was 64 years old). The main clinical symptoms were cough (76.9 %) and chest pain (61.5 %). Eleven (84.6 %) patients were smokers. In most cases, PHLC histologically corresponded to the cellular phase of the disease (46.1 %), whereas the proliferative phase was present in 5 (38.4 %), and fibrotic one in 2 (15.5 %) patients. Immunohistochemical analysis showed positivity of Langerhans cells for CD1a and S-100 in all examined cases, while cells were positive for CD68 in 9 cases. In 6 patients (46.2 %), there was a regression of the disease, and in 7 (53.8 %) patients the illness progressed in spite of the applied therapy.
Conclusion: For definitive diagnosis of PLCH pathohistological analysis with immunohistochemical confirmation of Langerhans cells is necessary.

E-PS-20-004
Differential diagnosis and criteria of prognosis immunophenotype of the neuroendocrine tumours of the lung
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Objective: Neuroendocrine tumours of the lung(NETL) make up 20–25 % of tumours of the respiratory tract. It is not always possible on the predict clinical behavior to basis of morphological features.
Method: The research is based on biopsy and surgical materials from 152 patients, aged 53 ± 13 years. There were 49(32 %) typical carcinoids(TC), 32(21 %) atypical carcinoids(AC), 60(39 %) small cell carcinomas(SCLC) and 11(8 %) large cell carcinomas(LCNEC).
Results: In the NET of the lung the expression of TTF-1 and cytokeratins 7 and 19 was explored. The expression of cytokeratins 7 and 19 were most often observed in LCNEC -70 and 91 % of cases, more rarely in SCLC-42 % and 66.7 % of cases and even more rarely in AC-46 % and 53.3 % of cases and only in 6 % and 18.2 %-TC. The expression of cytokeratin19 was more frequently detected in LCNEC than in SCLC and AC($p < 0.05$). The frequency of the expression of TTF-1 in TC was significantly less than in AC and LCNEC,SCLC($p = 0.004$), 7.1 % of cases, compared to 64 %, 83 %,78 % of cases in AC,SCLC and LCNEC respectively.
Conclusion: The results indicate that the expression of cytokeratins 7 and 19, TTF-1 in TC and AC allows to mark out to the group of risk of more rapid progression and metastasis.

E-PS-20-005
Uncommon diagnosis of pleuropulmonary tumour: Woman 35 years old with progressive dyspnea. Case report and experience of the 12 de octubre hospital in 20 years (Madrid, Spain)
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Objective: Diagnose a pleuropulmonar mass in a woman of 35 years old, who went to the hospital for progressive dyspnea, detecting in a test image a left pleural mass of 12.9 × 14.6 × 9.9 cm, with cystic areas. Second focus of 5 × 2,7 cm adjacent to the internal mammary artery, being metabolically inactive with PET CT.
Method: Left thoracotomy was performed, which evidenced tumour implants in diaphragmatic, visceral and parietal pleura. Pleural biopsy was performed and then pleuroneumonectomy.
Results: Histological sections showed cellular proliferation, arranged forming nests or sheet consisting monomorphic spindle cells, infiltrating lung, pleura and chest wall part, with isolated mitosis. No necrosis was observed. With immunohistochemical study the cellularity was positive for keratins AE1AE3, EMA and BCL-2. FISH was performed subsequently observed translocation (X, 18). The diagnosis was monophasic synovial sarcoma pleuropulmonary.
Conclusion: Pleuropulmonary synovial sarcoma represents less than 0.5 % of all lung tumours, with a recurrence rate of 75 and 42 % death of patients at 2.5 years. A review of medical archives of "12 de octubre" hospital from 1995 to 2015 have been diagnosed 5 cases, 80 % of monophasic type, 60 % in men and smokers, 2 of them diagnosed incidentally and passing away 40 % of patients.

E-PS-20-007
A rare case of pulmonary cribriform adenocarcinoma
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Objective: To describe the case of a middle-aged male with an incidental pulmonary cribriform adenocarcinoma and to review the literature on this entity.
Method: A 50 year old gentleman, who was being followed up for a pericardial cyst discovered in 2012, was found to have a 10 mm left upper lung nodule on follow-up computed tomographic assessment in 2014. This lesion grew from 10 to 17 mm by the end of 2015 and thereupon, both the pericardial cyst and the lung lesion were excised. The tumour histologically exhibited a predominantly cribriform appearance, with mucin-filled acinar structures set in a desmoplastic stroma, together with a focal thyroid-like appearance. Diffuse TTF1 and CK7 positivity together with CK20, thyroglobulin, calretinin, synaptophysin, keratin 5/6 and calponin negativitiy confirmed the pulmonary origin of the tumour.
Results: The patient is well, with no evidence of recurrence.
Conclusion: Pulmonary cribriform adenocarcinomas are exceedingly rare and are often misdiagnosed as metastatic tumours. They are currently considered a subtype of acinar adenocarcinoma. They occur predominantly in older male smokers and do not seem to harbour epidermal growth factor receptor mutations, although other mutations, including mutations in KRAS, ALK1 and ROS1, have been isolated. Their behaviour is, as yet, unclear.

E-PS-20-009
Detection of Aldehyde Dehydrogenase [AlDh1] Cancer Stem Cell (CSC) marker in lung cancer and its correlation with patient prognosis
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Objective: Cancer stem cell markers are a group of pleuripotent cells actively dividing in an uncontrollable manner and are recognized by specific landmarks on their membrane as glycoprotein's or in the cytoplasm as enzymes or in the nucleus, e.g. ALDH1,CD-44, CD-133 etc. AIM-To detect CSC ALDH-1 in lung cancer and its clinicopathological correlation for prognostication.
Method: Biopsies from 36 fresh previously untreated lung cancer patients visiting [ELMC&H & KGMU, Lucknow were taken. The biopsies were analyzed by using Haematoxylin and Immunohistochemistry for ALDH1 [Daco].
Results: In 36 samples analyzed, 35 were Non Small cell carcinoma [NSCLC]and 1 was Small cell carcinoma lung. On applying ALDH1 [IHC], 28 were positive (golden brown staining) and 08 were negative. Out of the 28 IHC positive cases all were NSCLC while out of the 08 negative cases 1 was SCLC and 07 NSCLC. Staging of lung cancer was performed in 29 out of the 36 positive cases. In the 29 cases staged, 68.9 % were in stage III+IV, 30.9 % in stage II+I. Seven cases could not be staged due to lack of CT findings.
Conclusion: Presence of ALDH1 may indicate a poorer prognosis if a lung carcinoma detected in early stage demonstrates ALDH1 by IHC.

E-PS-20-010
Pulmonary hyalinizing granuloma with Castleman's Disease: A rare case report
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Objective: Pulmonary Hyalinizing Granuloma (PHG) is an uncommon lung disease suggested to be associated with exaggerated immune response to an antigenic stimuli.
Method: We present the second case in the literature of PHG with Cattleman's Disease who was admitted with diarrhea and dry cough.
Results: Radiological investigation of 20 years old male revealed bilateral multiple pulmonary nodules, mediastinal, hiler and mesenteric lymphadenomegalies. Histologic examination of pulmonary nodule and pre tracheal lymph nodule revealed PHG and Castleman's Disease, respectively.
Conclusion: PHG can be misdiagnosed as metastasis or other benign diseases radiologically. Histopathologic evaluation should be performed for the correct diagnose of PHG and the associated immunological disease.

E-PS-20-011
ALK gene rearrangements in non-small cell lung cancer Kazakhstan patients
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Objective: Chromosomal rearrangements of ALK gene has been identified in 3.3 % of lung adenocarcinomas and define a distinct molecular subgroup of non-small cell lung carcinomas (NSCLC) that may benefit for available/investigational targeted therapies. Fluorescence in situ hybridization (FISH) technique is considered to be standard procedure for the evaluation of ALK gene translocations; however, immunohistochemistry (IHC) could be a promising alternative mode of screening for detection of mutant ALK protein.
Method: A total of 46 NSCLC samples were tested for ALK protein expression using CD246 ALK antibody (ALK1 clone). All IHC strong positive cases have been screened with FISH to confirm probable rearrangement by using ALK Break Apart FISH Probe Kit.
Results: Six adenocarcinomas (13 %) were identified with ALK immunoreactivity (H-score ≥ 100). Among these tumours, five showed predominantly solid pattern and in the remaining two—one was papillary pattern of growth. Concordance between IHC strong positive cases and FISH was 83.3 % (5 of 6).
Conclusion: More sensitive, available and less expensive ALK IHC is recommended as screening. For All IHC positive cases to confirm ALK gene rearrangements FISH analysis is recommended. Proportion of patients with tumours positive ALK protein IHC and FISH is higher than in published data.

E-PS-20-012
Immunohistochemical expression of various mucins in resected lung adenocarcinomas
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Objective: Differential diagnosis between primary TTF-1 negative adenocarcinomas of the lung and metastatic ductal adenocarcinomas of the pancreas can be challenging. Therefore, we investigated the immunohistochemical expression of various mucins in resected primary adenocarcinomas of the lung and compared data to known expression patterns of mucins in pancreatic ductal adenocarcinomas.
Method: We collected 215 cases of resected adenocarcinomas of the lung and explored the immunohistochemical expression of TTF-1, MUC1, MUC2, MUC4, MUC5AC and MUC6. Positive mucin expression was evaluated as percentage of positive cells and results were compared with positive or negative expression of TTF-1. Because up to 63 cases were not evaluable and due to the subsequent smaller sample size, statistical evaluation was limited and data was analyzed by descriptive means only. Analysis was performed by SPSS 21.
Results: MUC1 was evaluable in 165 cases (100 %) and showed expression in all tumour cells in 86.7 % of cases (143/165). MUC2 was positive in 0.6 % (1/162). 17.9 % of the cases (27/151) were positive for MUC4 in all tumour cells and completely negative in 45 % of cases (68/151).

MUC5AC was positive in all tumour cells in 6.9 % of cases (12/173) and completely negative in 38.7 % (67/173). MUC6 was negative in 88.9 % of cases (169/190). 40.7 % and 80 % of all TTF-1 negative carcinomas were negative for MUC5AC (11/27) and MUC6 (24/30), respectively.
Conclusion: MUC5AC and MUC6 may be helpful in the differentiation between primary TTF-1 negative adenocarcinomas of the lung and metastatic ductal adenocarcinomas of the pancreas.

E-PS-20-013
Relation of EGFR and KRAS mutation status with phosphorylation of EGFR in lung adenocarcinomas
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Objective: EGFR protein expression in lung adenocarcinomas is variable, and independent of EGFR mutation-status. Phosphorylation sites of the EGFR-internal domain function as positive or negative activity modulators. Tyr845, for example, promotes cell survival, while Tyr1068 and Tyr1148 activate MAPK. Since there is no information, if phosphorylation occurs randomly or selectively, we decided to analyze EGFR phosphorylation in pulmonary adenocarcinomas in correlation with EGFR and KRAS mutations.
Method: Tissue microarrays (TMA) were produced. One TMA with 74 adenocarcinomas (37 with EGFR mutations). Another TMA with 65 mucinous adenocarcinomas (35 with KRAS mutations, EGFR mutation negative). Antibodies for phosphorylated EGFR at 845, 1045, 1068, 1148, and 1173 were used. Percentage of the positive tumour cells and intensity of the staining were recorded and expressed as H-score. For downstream signaling pathways one specific protein was selected and analyzed by immunohistochemistry (GAB1, GRB2, PLCgamma, DOK2, pERK, PI3K, NFkB, STAT1, STAT3).
Results: In EGFR mutated adenocarcinomas the phosphorylation on Tyr845, Tyr 1068 and Tyr1148 occurred in significant higher proportion of tumour cells compared to EGFR-wild type tumours. In KRAS-mutated adenocarcinomas a higher phosphorylation was observed on Tyr845 in comparison to KRAS-wild type tumours, while on Tyr1045 and Tyr1065 it was lower in KRAS-mutated tumours. (All results statistically significant).
Conclusion: Pulmonary adenocarcinoma use different phosphorylation sites on the EGFR simultaneously, however single phosphorylation sites are used preferentially by either KRAS- and EGFR-mutated adenocarcinomas compared to wild-type adenocarcinomas. This results in activation of different signaling pathways and functional differences between EGFR- and KRAS-mutated adenocarcinomas.

E-PS-20-014
Primary extraskeletal osteosarcoma of the pleura mimicking mesothelioma: A case report
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Objective: Primary extraskeletal osteosarcoma is an extremely rare malignant neoplasm of pleura. Histopathologically the tumour is characterized by neoplastic osteoid, bone and occasional chondroid matrix.
Method: Multiple pleural nodules were found on a chest computed tomography of a 64-year-old man with dry cough complaints. Two nodules were excised through left thoracotomy on a clinically and radyologically suspicion of mesothelioma.
Results: Pathologic examination of the biopsy specimen revealed malignant mesenchymal tumour consistent with osteosarcoma. The patient underwent adjuvant chemotherapy and died 12 months after surgery. Pleural metastasis should be considered first for patients who present with pleural osteosarcoma. However, there was no osteosarcoma found in the other organs in our case.
Conclusion: We present a case of primary extraskeletal osteosarcoma of the pleura for its rarity. Clinical, radiological and histopathological correlation should be done before making the diagnosis.

E-PS-20-015
mTOR expression is associated with high survival in small cell lung carcinoma patients
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Objective: SCLC is the most aggressive pulmonary carcinoma, with median survival from 2 to 4 months. Long-term prognosis is poor and 5–10 % have a 5 years survival. The discovery of highly specific and potent mTOR inhibitor rapamycin and its derivatives, increased the interest of the scientific community to this target. This study aimed to correlate mTOR expression in SCLC biopsies and correlate with patients survival index.
Method: A total of 39 representative and well preserved biopsies of 7 women and 32 men with small cell lung cancer were randomly incorporated in this study. Chemotherapy treatments were identified from medical records (first-line treatment: etoposide+carboplatin; and second-line treatment: ciclofosfamine+etoposide+epirubicin). Immunohistochemical staining was performed with Bond-Max auto-stainer and mTOR (Ser2448) clone was applied.
Results: Mean survival was 205 days and only 8 patients (20.5 %) remained alive 1 year after diagnosis. Patients expressing positive mTOR had high survival rates ($p = 0.01$). Patients with positive mTOR or negative ERCC1 expression had longer survival when treated with carboplatin+etoposide ($p < 0.05$) (unpublished data).
Conclusion: In this study patients with positive mTOR had significantly longer survival, indicating mTOR possible prognostic and chemotherapy target value for SCLC patients. Furthermore, ERCC1 and mTOR expression evaluation can also be useful for long-term prognosis to be applied on routine.

E-PS-20-016
LRP and MRP-1 (Multidrug Resistance phenotype) are expressed in all histological patterns of lung adenocarcinomas
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Objective: Lung cancer is frequent and has high mortality rate. Multidrug Resistance (MDR) phenotype can be evaluated by Multidrug Resistance Protein 1 (MRP-1) and Lung Resistance-related Protein (LRP) expression. The author's objective was to evaluate MDR phenotype in lung adenocarcinomas (ADC).
Method: A series of 45 adenocarcinomas were studied by immunohistochemistry. Streptavidin Biotin protocol was applied for LRP antibody (Novocastra, clone 9D6) and MRP-1 antibody (Novocastra, clone 33A6). Intensity and percentage of stained cells were registered. Wilcoxon-Mann-Whitney was performed using STASTISTICA 7 software.
Results: Acinar pattern was present in 42 (93,3 %) cases, bronchioloalveolar pattern in 25 (55,5 %) cases, solid pattern in 18 (40 %) cases, papillary pattern in 7 (15,5 %) cases, and micropapillary pattern in 15 (33,3 %) cases. Lymph node metastasis were observed in 13 cases (28,9 %). LRP and MRP-1 expression were higher in all the ADCs compared to non tumoural tissue. No differences were found when comparing

histological patterns, between primary tumour and metastasis, or according to smoking habits, gender and age.
Conclusion: MRP export organic anions and are related to cytotoxic and antiviral drugs resistance. LRP expression is related to cisplatin resistance. Lung adenocarcinomas show MRD phenotype acquisition, demonstrated by MRP-1 and LRP overexpression. This evidence may have implications in drug resistance.

E-PS-20-017
Efficacy of the UroVysion kit for the diagnosis of malignant pleural effusion
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Objective: To validate the UroVysion kit for the diagnosis of malignant pleural effusion (MPE) in pleural fluid (PF) samples.
Method: PF samples from cancer patients with positive cytology (n = 26) and ones with benign etiology (n = 7) were analyzed by the UroVysion kit (Abbott Molecular, Illinois, USA) which is composed by labeled probes that hybridize with the centromeric region of chromosomes 3, 7, 17 and locus 9p21 p16 INK4A. These regions are considered targets for the development of metastases. Cut-off values were established for each probe.
Results: MPE included cases of non-Hodgkin lymphoma (n = 4), lung (n = 11) and breast (n = 11) cancer. Cases were considered aneuploid if monosomy or polisomy was observed in at least two of the probes analyzed. With this criterion all cases were correctly classified.
Conclusion: The UroVysion kit detected aneuploidy in all cases of MPE regardless of tumour origin. The relevance of the use of FISH probes in PF samples is to provide an early diagnosis of MPE, especially in cases of suspicious cytology. To test the accuracy and confirm the results, it still needs to enlarge the MPE cases with negative and inconclusive cytology.

E-PS-20-018
Frequency of genetic abnormalities in malignant pleural effusion
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Objective: To evaluate the most frequent genetic alterations in cases of malignant pleural effusion (MPE) by the Urovysion kit.
Method: In 26 cases of MPE (4 lymphomas, 11 lung and 11 breast cancer metastases) we analyzed the genetic abnormalities observed in the chromosomes 3, 7, 17 and locus 9p21 p16 INK4A by the Urovysion kit (Abbott Molecular, Illinnois, USA), a FISH kit used for diagnosis of bladder cancer in samples of urine.
Results: Cr3: Monosomy:65.4 %; Trisomy:100.0 %; Tetrasomy:15.4 % and Polisomy: 3.8 % Cr7: Monosomy:76.9; Trisomy:92.3 %; Tetrasomy:30.8 % and Polisomy: 23.0 % Cr17: Monosomy:92.3 %; Trisomy:100.0 %; Tetrasomy:34.6 % and Polisomy: 26.9 % Cr9p21: Monosomy:40.0 %; Trisomy:70.0 %; Tetrasomy:0 % and Polisomy: 0 %
Conclusion: Monosomy and trisomy were the most frequent chromosomic abnormalities observed in all chromosomes. The chromosome 17 was one that showed up the biggest number of abnormalities regardless the origin of primary tumour.

E-PS-20-019
Pulmonary pleomorphic giant cell carcinoma: A case report
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Objective: Pulmonary pleomorphic carcinoma, an uncommon malignant lesion of the lung is a subset of sarcomatoid carcinoma. The World Health Organization defines pleomorphic carcinoma as a poorly differentiated NSCC namely a squamous cell carcinoma, adenocarcinoma, or undifferentiated NSCC that contains at least 10 % spindle and/or giant cells or a carcinoma consisting only of spindle and giant cells.
Method: We report a case of a 69-year-old, tobacco smoker with pulmonary pleomorphic carcinoma. Chest computed tomography (CT) showed an inhomogeneous enhancing mass in the superior segment of the left upper lobe and revealed a solitary osteolytic mass in L5 disc-space. Partial tumour resection was performed.
Results: Histologically, the tumour was consisted mostly of polygonal pleomorphic cells and some non-cohesive multinuclear giant cells. No gland formation or other differentiating features were observed. Immunohistochemically, tumour cells were positive for vimentin, pancytokeratin (KerAE1/AE3), low molecular weight cytokeratin (Ker8/18), thyroid transcriptional factor-1 (TTF-1), high molecular weight cytokeratin (Ker34βE12) and p63 protein. Tumour cells were negative for CK5/6, Melan-A and HMB-45.
Conclusion: These tumours are rare accounting for less than 1 % of all lung cancers and have an extremely poor prognosis compared with other non-small cell lung cancers.

E-PS-20-020
Lung adenocarcinoma pattern recognition is relevant for chemotherapy resistance evaluation: Relevance of ERCC1 expression
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Objective: ERCC1 (excision repair cross-complementing 1) is involved in DNA damage repair. Knowledge concerning repair mechanisms is important to better understand chemotherapy response. Authors aimed to study ERCC1 expressionin lung adenocarcinomas (ADC), according to histological patterns.
Method: A series of 45 lung ADCs were studied. Immunohistochemistry (IHC) was performed according to Streptavidin-Biotin protocol for ERCC1 antibody. Intensity and percentage of stained cells were registered. Wilcoxon-Mann–Whitney was performed using STASTISTICA 7 software.
Results: Acinar pattern was present in 42 (93,3 %) cases, bronchiolo-alveolar pattern in 25 (55,5 %) cases, solid pattern in 18 (40 %) cases, papillary pattern in 7 (15,5 %) cases, and micropapillary pattern in 15 (33,3 %) cases. Lower ERCC1 expression was identified in acinar (p = 0,0016) and papillary (p = 0,019) patterns, compared to non-tumoural tissue. Papillary pattern showed lower expression compared to solid (p = 0,043) and BA/lepidic patterns (p = 0,044). Female gender had higher ERCC1 expression (p = 0,000846).
Conclusion: Results indicate that DNA repair is not impaired in micropapillary, solid and BA/lepidic patterns. Lower ERCC1 expression in acinar and papillary patterns demonstrates less DNA repair pathway activation. ERCC1 expression has been associated with chemotherapy resistance, as for cisplatin and these patterns seem to be less prone to cisplatin resistance as DNA repair mechanisms are implicated in chemotherapy resistance.

E-PS-20-021
Mitotic count is not a significant prognostic factor in stage Ia lung adenocarcinoma
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Objective: A new WHO classification of lung neoplasms was launched in 2015. No grading system for lung adenocarcinoma (LA) is internationally accepted. We investigated the prognostic value of growth patterns, mitotic count, nuclear atypia, peritumoural lymphatic, vascular and airway spread, necrosis, the Kadota grading system and the modified Sica scoring system.
Method: Between 2004 and 2013, 183 resected stage Ia LA could be matched with information on overall survival. The reviewed parameters were evaluated with Kaplan-Meier analysis, Log-Rank test, multivariate Cox regression and the ROC curve test.
Results: Sensitivity (74–52 %) and specificity (44.7–57.5 %) were low for mitotic counts. Growth pattern ($p = 0.038$), nuclear atypia ($p = 0.022$), and vascular ($p = 0.001$) and airway ($p = 0.038$) spread were significant markers in the univariate model. We found no difference between low and intermediate grades in either the Kadota or the Sica system. By Cox regression, growth pattern ($p = 0.001$) and vascular invasion ($p = 0.01$) were independent prognostic markers.
Conclusion: Growth pattern and vascular invasion were independent prognostic factors in stage Ia LA. A high mitotic rate does not necessarily confer bad prognosis. We suggest that LA grades should be assigned as low (in situ, minimally invasive, lepidic, acinar and papillary carcinoma) and high (solid and micropapillary).

E-PS-20-023

Adventitial remodeling of experimental pulmonary hypertension induces myofibroblast-produced collagen V in a Th17-pathways-related manner

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Objective: Pulmonary hypertension is a complex disease characterized by profound pulmonary artery adventitia (PA) remodeling. Our aim was to examine the hypothesis that fibro-proliferative and inflammatory changes of the PA adventitia are related to the presence of myofibroblast activation that induce Collagen V expression in a dependent IL-17 signaling manner.
Method: Wister male rats were sacrificed 21 day after treatment with monocrotaline (MCT;$n = 5$) compared to controls (CTR;$n = 5$). Right ventricular pressure; HE and picrossirius red staining, immunohistochemistry for IL-17-related markers and "in situ" immunofluorescence for smooth muscle actin (SMA) and collagen types I and V, electron microscopy and fibronexus morphometry were used.
Results: The right ventricular pressure and right cardiac hypertrophy index was higher in MCT than CTR group ($p < 0{,}05$). A significant increase of PA adventitia thickness (9-times vs CTR), total collagen (20 % vs CTR), collagen I (3-times × CTR), collagen V (4-times vs CTR), fibroblasts + SMA expression (2-times vs CTR), plasmatic membrane of myofibroblast (4-times more fibronexus vs CTR), IL-17, IL-6 and TNFβ were observed.
Conclusion: Myofibroblast-mediated collagen V expression andTh-17 signaling downstream of IL-17 may hold therapeutic value for treatment of PH.

E-PS-20-024

Mucoepidermoid carcinoma—a case report

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Objective: Mucoepidermoid carcinoma (MEC) of the lung is a rare subtype of lung cancer that is sub-classified into low and high grade, based on histological features.
Method: We report the case of a 47 year old man. CT scan incidentally showed a cystic mass in favor of a hydatid cyst. The patient had a left upper lobectomy with lymph node dissection. Histological examination concluded mucoepidermoid carcinoma of low grade.
Results: Mucoepidermoid carcinoma is a salivary gland-type tumour that consists of mucin-secreting cells, squamous or squamoid cells, and intermediate-type cells. About 50 % of the tumours occur in patients aged less than 30 years. There is no association with smoking. Computerized tomography of the chest shows a well-defined, centrally located endobronchial mass. A histopathological subclassification into low-grade and high-grade types has been proposed. High grade tumours are rare, and the diagnosis should be determined after careful exclusion of adenosquamous carcinoma. A lack of TTF1 and napsin A in a MEC may also be useful for differential diagnosis. MAML2 rearrangement is exclusively seen in MEC.
Conclusion: Primary pulmonary MEC represents a rare type of lung cancer. Patients with low-grade MECs, generally have a good prognosis after primary surgical resection. In contrast, high-grade pulmonary MECs are aggressive malignancies.

E-PS-20-025

Frequency and histopathological features of granulomas in resection specimens of lung tumours

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Objective: The incidence and significance of lung tumours is increasing in worldwide. Granulomas without any clinical signs or symptoms may be seen randomly in lymph nodes or lung parenchyma. This study aims to find frequency and histopathological features of granulomas within parenchyma and lymph nodes of resected lung tumours in our institution.
Method: Of the 134 cases of resected lung tumours from the surgical database of our institution from 2011 to 2016, 15 cases had granulomas. H&E stained slides were evaluated to identify detailed histomorphological features of granulomas.
Results: The patients were 4 females and 11 males ranging from 44 to 77 years (median 62 years). The diagnosis of lung tumours was adenocarcinoma ($n = 7$),squamous cell carcinoma ($n = 3$), large cell neuroendocrine carcinoma ($n = 2$), pleomorphic carcinoma ($n = 2$),and atypical carcinoid ($n = 1$). All of the specimens had lymph node dissection. There were granulomas only in lymph nodes of 9 cases, only in parenchyma of 4 cases, and both in lymph nodes andadn parenchyma of 2 cases. Both granulomas and metastatic tumour were seen in same lymph node station in 1 case. Necrosis in granulomas was detected in 3 cases. Some of the granulomas of 2 cases had fibrosis. EZN stain was applied to 5 cases, one of them represented bacillus.
Conclusion: Granulomas are identified in 11 % of our cases. The lymph nodes and parenchyma of the lung tumour specimens may contain granulomas which could be a sign of infectious or inflammatory pathology.

E-PS-20-026

Principles of clynic-morphologic verification of bronchoalveolar tumour

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Objective: Among rare forms of interstitial disseminated diseases of lungs, intravascular sclerogenic bronchoalveolar tumour is the most difficult for diagnostics; in majority of cases it is detected accidentally, which is caused by absence of pathognomonic clinical features.
Method: Methods: histological material is obtained by minimally invasive videothoracoscopic access. Tinction with hematoxylin and eosin for

synoptical study, under Masson's method, with the aim to detect the intensity of sclerotic processes.
Results: Thoracobiopsy results showed, that together with remained lung tissue, there are structureless homogeneous formations, represented with vitreous connective tissue, where the separate petrification focuses are found, similar formations fill the lumens of alveolas and bronchias, sometimes they include vesicular structures. In zones of pathological formations and hyalinosis, immured deformed bronchias with epithelium metaplasia were found, lumens are spasmed. In lung parenchyma presence of multiple angiomatosis focuses is shown, at that vessels turned to strange form, some of them were filled with «chylous» content, others were plethorical, arteriovenous anastomosis was found. In subpleural zone of lung tissue vessel proliferation of different size was found, with fibrinoid degeneration of their walls andperivascular lymphoid infiltration with background of fibrosis. Walls of lung arteries are thickened irregularly, muscular layer is hypertrophic. At tinction of tissue material under Masson, hyalinized structure include the connective tissue, partially stained in shades of blue and violet, which certifies the presence of fibrosis process.
Conclusion: Described clinical observation shows that adoption of computer tomography and diagnostic videothoracobiopsy of lung into clinical practice gives the ability of morphological verification of rare forms of lung pathology, which allows excluding the diagnostic mistakes, differentially choose the pathogenetic therapy and estimate the disease prognosis.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-21 Soft Tissue and Bone Pathology

E-PS-21-001
Atypical lipomatous tumour of larynx, closely simulating a spindle cell lipoma: A case report
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Objective: In practice, there is frequent histological overlap between atypical lipomatous tumour and a spindle cell lipoma. In the literature, there are few cases reports of this tumour arising in different locations like salivary glands, oral cavity and gingiva. However, rarely it has been described in the larynx.
Method: Case report.
Results: A 58-year-old women presented with difficulty in swallowing. On examination an exophytic tumour was seen involving the supraglottis and piriform fossa bilaterally. Debulking surgery was perfomed and multiple tissue fragments were sent for histological analysis. Histologically, the neoplasm showed features closely resembling spindle cell lipoma, being composed of mature adipose tissue associated with bland spindle cells interspersed within the collagen bundles. No atypical lipoblasts or florette cells were seen. On Immunohistochemistry, the spindle cells stained positive with CD34. The differential diagnosis included a spindle cell lipoma and atypical lipomatous tumour (well differentiated liposarcoma). Based on the histological features, the former was more favoured. However to further support the diagnosis, FISH analysis was performed for MDM2 amplification. Surprisingly, there was very convincing MDM2 amplification, in keeping with a atypical lipomatous tumour closely simulating a spindle cell lipoma.
Conclusion: Atypical lipomatous tumour is a slow growing, infiltrative, and non-metastasizing neoplasm that is microscopically and diagnostically challenging (2). It rarely arises in larynx and has to be distinguished from a spindle cell lipoma which can closely resemble it morphologically. FISH analysis for MDM2 amplification should be considered in the cases with overlapping features to differentiate atypical lipomatous tumour from a benign spindle cell lipoma.

E-PS-21-002
Vascular tumours in Kano, Nigeria: A histopathological review
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Objective: Vascular tumours range from benign hemangiomas to lesions that are locally aggressive but infrequently metastasize, to relatively rare, highly malignant angiosarcoma. There is a paucity of studies on vascular tumours in Nigeria. The objective of this study is to determine and document the relative frequency and pattern of these tumours in our locality.
Method: The materials consisted of tissue blocks, glass slides and duplicate copies of histopathology reports of patients whose soft tissue biopsy specimens were received in the Department of Pathology of Aminu Kano Teaching Hospital in the of Nigeria, over a period of 10 years. The method employed included retrieving the histopathology request forms, from where clinical data such as age, gender and site of affectation were obtained. The corresponding retrieved archived haematoxylin and eosin slides were reviewed by the Authors and the diagnoses were confirmed. The tumours were classified based on WHO typing of vascular tumour.
Results: Vascular tumours accounted for 16.0 % of all cases of soft tissue tumours. The mean age was 29 years with bimodal age peaks in the 2nd and 3rd decades. The male to female was 1.1:1. The head and neck region was most affected (22.3 %). The benign, malignant and intermediate tumours constituted 68.0, 28.8 and 3.2 % respectively. Lobular capillary hemangioma (40.0 %) was the predominant benign histologic subtype recorded while haemangiopericytoma (2.3 %) and Kaposi sarcoma (21.6 %) constituted the most frequent intermediate and malignant entities respectively.
Conclusion: Vascular tumours constitute a significant proportion of soft tissue tumours in our environment. They showed a bimodal peak age of incidence without a significant sex predilection.

E-PS-21-005
Clear cell sarcoma of the big toe: An uncommon case
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Objective: Clear cell sarcoma is a rare malignant tumour affecting primarily young adults. This is a melanin-producing soft tissue sarcoma which arise in the deep soft tissue of the distal extremities associated with tendons and aponeuroses. Clear cell sarcoma was described first by Enzinger in 1965 and molecular genetic analysis is highly recommended since the t(12;22) that characterizes clear cell sarcoma has been identified in malignant melanoma.
Method: A 33 year old men presented with a 6 month history of a slow growing lobulated gray-white mass in the left big toe measuring 3,4 cm in greatest diameter. The mass was resected. Sections from the mass were studied by means of morphology and immunohistochemistry.
Results: Histological examinations confirmed a diagnosis of clear cell sarcoma. Immunohistochemically the neoplastic cells were positive for S100p,Melan A, HMB45,P16 and negative for EMA,CK7,CK19,Pankeratin,actin,desmin,FXIIIA. The cytoplasm contained large amounts of intracellular glycogen (PAS+).
Conclusion: The overall prognosis of clear sarcoma is poor. Tumour, size necrosis and local recurrence have proved to be the most robust prognostic factors. Complete surgical resection remains the optimal treatment for this aggressive chemoresistant tumour.

E-PS-21-006
Ossifying fibromyxoid tumour of soft parts: A malignant variant
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Objective: Ossifying fibromyxoid tumour of soft parts (OFMT) is a well recognised mesenchymal neoplasm of uncertain lineage, first described by Enzinger et al. in 1989. Rarely have cases been reported as malignant. As a result of its controversial origin and uncertain biological behaviour, some do not recognise malignant OFMT. Criteria for malignancy have not yet been defined and universally accepted: there is still confusion and uncertainty between pathologists how to recognise a malignant variant of OFMT. We report a patient with history of typical OFMT that developed multiple metastases. We propose that the Folpe and Weiss criteria, modified to include S100 expression, are used to recognise and characterise malignant OFMT.
Method: 9 years following initial diagnosis of OFMT, the patient presented to the sarcoma clinic with a solid lesion in the right calf. Biopsy confirmed OFMT and further imaging including CT, MRI and CT-PET identified six other, distant and radiologically similar lesions.
Results: Primary tumour (2006): Histologically it was pseudocapsulated with monomorphic rounded cells proliferation and extensive bone formation. Mitotic index: 4 mitoses x10HPF. IHC profile: positive expression for Vimentin. Negative expression for S100, Desmin, CD34, Bcl 2 and CK's. Metastases histology(2015): Histologically it was similar to the previous tumour. IHC profile showed positive expression for CD10 and negative expression for S100, SMA, and Desmin. Overall in view of the clinical history, was regarded as a metastasis.
Conclusion: We confirm the existence of an OFMT with distant metastases and using Folpe and Weiss criteria, we demonstrate the presence of malignancy.

E-PS-21-007
Pathology of lipoma arborescens and its clinical significance
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Objective: Lipoma arborescens (LA) is an uncommon intra-articular lesion of the synovium, characterized by villous proliferation of the synovium and replacement of the subsynovial tissue by mature fat cells. Whether LA is neoplastic or not is still not entirely clear. The aim of the study was to evaluate the disease process in LA, with respect to the clinical parameters, and histopathological and immunohistochemical features.
Method: Case files of LA diagnosed on histopathology between 2010 and 2016 were collected, to study the case history, and tissue sections were reviewed for the histomorphological and immunohistochemical analysis.
Results: Seventeen cases of LA diagnosed on histopathology were included in the study, of which one occurred in the hip and the rest were localized to the knee. One patient with psoriatic arthritis has bilateral knee lesion. Four of the cases were primary LA and the rest had significant past history (osteoarthritis, psoriatic arthritis and rheumatoid arthritis). On histopathological examination, all case showed villous proliferation of the synovium with infiltration with mature adipocytes and focal lymphocytic infiltration. All tissue samples of LA were HMGA2 negative.
Conclusion: Our results support the hypothesis that LA is a reactive proliferative condition in response to chronic irritation, injury or inflammation.

E-PS-21-009
Epithelioid hemangioendothelioma, diagnostic challenge in small biopsy
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Objective: Epithelioid hemangioendothelioma (EHE) is a malignant angiocentric vascular neoplasm composed of cords of epithelioid endothelial cells in a distinctively myxohyaline stroma and characterized by translocations resulting in either WWTR1-CAMTA1 or YAP1-TFE3 fusion gene.
Method: A 76 year-old male patient presented with a multiple vertebral and pelvic lytic lesions without primary known, also had bone pain and constitutional syndrome. Bone marrow biopsy was performed, histopathology showed a bone marrow cellularity and hematopoietic devoid of fat, composed of cords and strands of epithelioid cells with variable amounts of palely eosinophilic, often glassy cytoplasm and occasional intracytoplasmic vacuoles (vascular chanel formation), embedded in a myxohyaline stroma, with scant mitotic activity. No necrosis was identified.
Results: On immunohistochemical analysis, the neoplastic cells were positive for: CD31, CD34, ERG, vimentin, CAMTA-1, CKAE1-AE3 (focal). And negative for: EMA, TTF1, CD99, CD117, S-100, PSA, desmin. The lession was diagnosed as an EHE.
Conclusion: - In the most recent WHO Classification of Tumours of Soft Tissue and Bone, EHE is classified as a malignant vascular neoplasm because of its significant potential for local recurrence and metastasis in approximately 25 % of cases. -Recurrent translocations involving chromosomal regions 1p36.3 and 3q25 resulting in the formation of a fusion between WWTR1 and CAMTA1 in 90 % of cases. -A small subset <5 % have a YAP1-TFE3 fusion gene, wich often correlates with a distinct morphologic appearance.

E-PS-21-010
Undifferentiated pleomorphic sarcoma of the parotid gland
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Objective: Undifferentiated pleomorphic sarcoma (UPS) it is an aggressive sarcoma, although no etiological factors have been recognized. UPS most commonly occurs in the extremities, trunk and retroperitoneum, but primary lesions of the parotid gland occur infrequently.
Method: A 70 year-old female patient presented with a 1,5-month history of a slowly enlarging but asymptomatic left-sided neck mass. Fine-needle aspiration revealed cellular evidence of a spindle cell neoplasm with features suggestive of sarcoma. Incisional biopsy was performed, histopathology demonstrated enlarged cells with round to oval vesicular nuclei most of wich contained a small nucleolus. The cytoplasm was slightly eosinophilic. Multinuclear giant cells were often observed (CD68+), mitotic figures were also abundant, and there was no necrosis. Vascular invasion was identified (CD34+). Residual atrophic ducts were scattered in the tumour adjacent gland tissue.
Results: On immunohistochemical analysis, the neoplastic cells were positive for: Vimentin, EMA, α1- antichymotrypsin. And negative for: CKAE1/AE3, S-100, melan-A, HMB-45, CD45, CD99, CD117, SMA, desmin, CD31, CD34, D-240, sinaptofisin, CDX2, GCDFP15, mammaglobin, calponin, CD10. The mass was diagnosed as an UPS of the parotid gland. The patient died 1 month after diagnosis.
Conclusion: - In the most recent WHO classification, UPS is considered a diagnosis of exclusion. It represents no more than 5 % of an adult soft tissue sarcomas. -UPS of the parotid gland is considered an uncommon malignancy. -The treatment of choice for the primary site is surgical resection with cervical lymphadenectomy for advanced tumours. Postoperative radiation therapy is recommended in view of the high rate of local recurrence.

E-PS-21-011
Kaposiform hemangioendothelioma: A case report
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Objective: Kaposiform hemangioendothelioma is a rare locally aggressive vascular tumour of intermediate malignancy. It occurs nearly exclusively during childhood. Adult cases have been reported recently.
Method: A 36 year old woman that is presented with a superficial cutanous lesion on her arm. On histologic examination there is a tumoural lesion that was charachterized by vascular structure with irregularly shaped and randomly distributed. Some of the tumour cells were with vesicular and some of them were with hyperchromatic nucleus and with eosinophilic cytoplasm. Necrosis was not observed. There was only one mitosis in 10 HPF. In immunohistochemical staining, tumour cells were positive with CD34, CD31, SMA and were negative with HHV8. According to these histologic and immunohistochemical findings; our diagnosis was " kaposiform hemangioendothelioma".
Results: Kaposiform hemangioendothelioma in adults are different from those in children. Although % 75 of kaposiform hemangioendothelioma presented with cutanous involvement, numerous anatomic location can be seen. Because of its invasive growth pattern and no- self healing tendency kaposiform hemangioendothelioma is classified as intermediate (borderline) malignancy.
Conclusion: We are reporting this case because of its rarity in adults and also because of difficulties in differential diagnosis with other vascular tumours that have similiar histological features.

E-PS-21-012
Undifferentiated pleomorphic sarcome
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Objective: Analyse undifferentiated pleomorphic sarcoma (UPS) case of a 6-years old boy admitted to the hospital, with mass on the right cheek as a chief complaint. One year ago he has an excision and an encapsulated, firm, size (4,5x3,5x2,5) cm, and gray-white mass were obtained.
Method: Clinical data analysis, macroscopic, histophatologic and immunohistochemical examination.
Results: The section revealed solid foci and variably gelatinous. Histological examination showed an uncircumscribed mass composed of spindle cells with pleomorphic nuclei, clumping chromatin, some are vesicular, some are coarse chromatin and had prominent nucleoli. The cells had eosinophilic and foamy cytoplasm. Other foci showed bizarre, binucleated or multinucleate tumour giant cells, some with excentric nuclei. Among the tumour cells, the wide fibrous tissue were noticed with hyalinisation and myxoid changes. Immunohistochemical examination revealed strong positivity of CD99 and vimentin, some cells showed middle positive for EMA and Desmin, patchy positive for EA1/3, negative for Myogenin, CD 34, and S100.
Conclusion: we report a case of undifferentiated pleomorphic sarcoma. The final diagnosis were made based on clinical, macroscopic, histophatologic and immunohistochemical finding.

E-PS-21-013
Chondrolipoma arising in the wrist: A case report
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Objective: Chondrolipoma is a rare form of lipoma showing cartilaginous metaplasia. It usually arise in the connective tissue of the skeletal system, breast, pharynx and nasopharynx. We report a case of chondrolipoma developing in the wrist.
Method: The patient was a 58-year-old female with a slowly growing mass in the right wrist for 1 year. She suffered from seropositive rheumatoid arthritis, but did not complain of pain and any history of trauma. MRI study showed a 2.8 × 2.3 × 1.6 cm sized mass at the dorsomedial side of the right wrist joint, encased by extensor compartment 2 tendon. Signal changes were those of fat, and several nodules of T1 low and T2 intermediate to high signals were noted within the mass. Excision was done.
Results: Grossly sections revealed yellow fatty surface with several white nodules. Histologically the tumour was composed of mature fat tissue with intervening fibrous tissue. Lipoblasts were absent. White nodule was mature hyaline cartilage, surrounded by thick fibrous tissue. Immunohistochemical examination for S-100 protein was positive to the fat cells and chondrocytes, but negative in the cartilage-covering fibrous tissue. The diagnosis of chondrolipoma was done.
Conclusion: We report this case by its rarity, pathogenesis and differential points to chondroid lipoma, soft tissue chondroma and synovial chondromatosis.

E-PS-21-014
Phosphaturic mesenchymal tumour, an important cause of adult-onset osteomalacia: A case report
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Objective: Phosphaturic mesenchymal tumour(PMT) is a rare soft-tissue neoplasm that results in tumour-induced osteomalacia. About 300 cases have been described in the literature, 16 located in the spine. Here we describe a spinal case.
Method: A 37-year-old man presented with generalized joint pain and pathological fractures of right femoral neck and calcaneus. Laboratory investigations revealed hyphosphatemia, normocalcemia, low levels of 1,25-dihydroxy vitamin D and elevated levels of alkaline phosphate(AP). DXA scan showed a bone mineral density within the osteoporotic range. Thoracic CT scan disclosed a mass in L1 body and right vertebral pedicle. The lesion was biopsied and, subsequently, resected.
Results: Histopathological examination revealed a tumour composed of bland spindle and epithelioid cells in a myxoid matrix. Thin-walled blood vessels were present, some with ectatic, tortuous outlines. Osteoclast-type giant cells and mature adipocytes were additionally found. Immunohistochemical staining was negative for pan-cytokeratins, CD34 and desmin and focally positive for SMA and S100 protein. PMT was diagnosed. After surgery, symptoms gradually improved and serum phosphorus and AP levels normalized.
Conclusion: PMT is an important cause of osteomalacia in the adult and must be considered in the differential diagnosis. Recognition of its histological features is critical, as complete tumour resection leads to cure in most cases.

E-PS-21-015
Expression of estrogen receptor and evaluation of histological degeneration scores in hypertrophied ligamentum flavum
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Objective: The most common spinal disorder in elderly is lumbar spinal stenosis (LSS), resulting partly from ligamentum flavum (LF) hypertrophy. Its pathophysiology is not completely understood. The present study wants to elucidate the role of estrogen receptor (ER) in hypertrophied LF.
Method: LF samples of 38 patients with LSS were obtained during spinal decompression. Twelve LF samples from patients with disk herniation served as controls. H&E and Elastica stains and immunohistochemistry for ER were performed. Proportion of fibrosis, loss and/or degeneration of elastic fibers and proliferation of collagen fibers were assessed according to the scores of Sairyo and Okuda. Group differences in ER, Sairyo and Okuda scores between patients and controls, additional orthopedic diagnoses and sex were assessed with the Mann–Whitney-U-test.

Results: There was a tendency towards higher expression of ER in LF fibrocytes in the hypertrophy group ($p = 0.065$). ER expression was significantly higher in patients with osteochondrosis ($p = 0.049$). There was no statistically relevant correlation between expression of ER and sex ($p = 0.326$). Sairyo and Okuda scores were more severe for the hypertrophy group, but in general not statistically relevant.
Conclusion: LF hypertrophy may be accompanied by higher expression of ER; further, larger studies are needed to clarify this context.

E-PS-21-016
Spindle cell rhabdomyosarcoma of unusual location: Case report
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Objective: Here we report rare variant of embryonal rhabdomyosarcoma—Spindle cell rhabdomyosarcoma in 6 years old girl, clinically presented as a abscess of perianal region. During surgery tumour with severe perifocal edema and inflammation was found.
Method: Resected tumour nodules 4.5X3.0X3.0 and 2.5X1.5X1.5 in size were well circumscribed. On cut surface soft, homogenous, yellow-white tissue was found. Routine H&E stain and immunohistochemistry (with anti- Desmin, Vimentin, CD117, CD56, S100, aSMA, Synaptophysin, CD34, CD99, Ki67 antibodies (Leica, Germany)) was performed.
Results: Microscopically tumour had heterogeneous structures, consisted of spindle cell proliferations arrayed in fascicles or whorls—growth pattern more similar to leiomyosarcoma. Malignant cells had elongated nuclei with blunted ends, small nucleoli, and eosinophilic cytoplasm. Sparse multinucleated cells was found. Mitotic figures, including atypical forms was >5 in 10 HPF. No collagenouse deposition between cells. Inflammatory infiltrate was heterogeneous, with higher degree at the periphery. Tumour contained variable-sized, thin-walled blood vessels. Immunohistochemically tumour cells expressed Desmin, Vimentin, CD117, CD56, CD99 (focal staining) and was negative for S100, aSMA, Synaptophysin, CD34. Ki67 labeled more than 50 % of tumour cell nuclei.
Conclusion: Tumour was classified as spindle cell rhabdomyosarcoma (SOIP - embryonal rhabdomyosarcoma, well-differentiated type).

E-PS-21-017
Differential diagnosis problems in a three case series of chordoma
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Objective: Chordomas are rare, slowly growing neoplasms of bone that arise from embryonic remnants of the notochord. These tumours typically occur in the axial skeleton.
Method: Between November 2015-April 2016, in our department, were rendered three new diagnoses of chordoma with sacral, intracanalar and skull base locations. The pacients were 42, 55 respectively 75-years-old, the oldest one being male.
Results: In all of the three cases, the tissue fragments received had a white-gray colour and soft or elastic consistency. The tumour showed a lobular growth pattern of round to ovoid cells, with pale eosinophilic cytoplasm growing in cords and clusters in a basophilic myxoid stroma. Variable amount of phisaliphorous cells were present. Nuclei were generally small, cytologically bland, some of them indented by intracytoplasmatic vacuoles. Despite of bland morphology, significant infiltration of bone and/or adjacent soft tissue was noticed in each case; tumour cells were positive for AE1AE3, EMA, S100 and showed scarce positivity for Ki67, thus confirming the diagnosis.
Conclusion: In spite of low grade appearance, chordoma is an aggressive lesion with high risk of local recurrences and metastastatic potential which has to be differentiated from other chordoid lesions, with different treatment and prognosis such as chordoid meningioma, chordoid glioma or metastatic carcinoma.

E-PS-21-019
Importance of differential diagnosis in clear cell chondrosarcoma: A case report
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Objective: Clear cell chondrosarcoma (CCC) is a rare variant of chondrosarcoma, most commonly encountered in the proximal part of the femur or humerus, being considered a low-grade malignancy with high survival rates comparing with chondrosarcoma or chondroblastic osteosarcoma.
Method: We present the case of a 41-year-old man having a large femoral tumour proximally located. Surgical excision and total hip replacement was performed.
Results: Resection specimen included an 11/8/4 cm tumour extending from the femoral head and greater trochanter to the upper portion of the diaphysis. Histopathology revealed groups of cells with round, hypertrophic, centrally located nuclei, some with prominent single/multiple nucleoli, clear/pale-pink cytoplasm and distinct cytoplasmatic membranes. Cartilaginous areas and numerous woven bone trabeculae with osteoclast-like giant cells were present. Mitotic figures were rare. Tumour cells were positive for S100 and negative for AE1AE3, SMA and CD34, thus supporting the chondroblastic origin of the tumour. Based on morphology and immunophenotype a final diagnosis of CCC was established.
Conclusion: Differential diagnosis of CCC imply exclusion of several entities belonging to various spectrum of diseases such as chondrosarcoma, chondroblastic osteosarcoma, chondroblastoma, osteoblastoma and metastatic clear cell renal carcinoma. Correct diagnosis is mandatory since CCC has a better prognosis than others malignancies with similar morphology.

E-PS-21-020
Key microscopic findings for distinguishing benign notochordal cell tumour from chordoma
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Objective: The concept of benign notochord cell tumour (BNCT) was established recently and BNCT was listed on WHO classification of bone tumours in 2013. It is still challenging to distinguish precisely between BNCT and well differentiated chordoma because their histologic findings are quite similar each other. To know morphologic key features for distinguishing BNCT from chordoma we examined their histologic sections and then tried to differentiate between BNCT and chordoma components in lesions that are diagnosed "chordoma arising in BNCT" on imaging study.
Method: HE-stained sections of BNCTs and chordomas found in our file were carefully examined under microscope.
Results: Histologic findings of BNCT and well differentiated chordoma overlapped. BNCT-like components in chordoma, however, made a transition to typical chordoma histology and chordoma shows fine fibrous capsules and/or septa with/without vasculature in addition to lobular architecture, intercellular myxoid matrix, and bone destruction. Hence, the border of chordoma seems very smooth. In contrast, the border of BNCT seems slightly zigzag along the contour of adjacent marrow adipocytes.

Conclusion: The findings discovered in this study can contribute to distinguish BNCT from well differentiated chordoma and to differentiate between BNCT and chordoma components in "chordoma arising in BNCT".

E-PS-21-021

Extraskeletal osteosarcoma of the forearm: A case report

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Objective: Extraskeletal osteosarcoma (ESOS) is a rare malignant mesenchymal tumour composed of neoplastic cells producing bone osteoid. It accounts for about 1–2 % of all soft-tissue sarcomas.
Method: We report a case of a ESOS involving the forearm, assessing its clinical, radiological and microscopic features.
Results: A 57 year-old man presented with an enlarging mass on the lateral-volar aspect of the right forearm. CT-exam demonstrated a well-demarcated soft-tissue mass with no connection to the bone. A biopsy was performed, the morphological examination revealing a spindle-cell proliferation with high cytological atypia and a increased mitotic rate, arranged in a storriform pattern, with a non-specific immunohistochemical profile. Following surgical excision, the tumour was found to exhibit neoplastic osteoid-matrix formation and chondroid differentiation. Immunohistochemical profile exhibited diffuse positivity for SMA, CD99 with focal S-100 staining in the chondroid area and negative staining for CD34, CK7, AE1-AE3, CDK4, CD57 and p53, therefore excluding other malignancies such as synovial sarcoma, fibrosarcoma, malignant fibrous histiocytoma and dedifferentiated liposarcoma. Based on the histological features, immunohistochemical profile and radiological aspect, a diagnosis of ESOS was made.
Conclusion: ESOS represents a rare and challenging diagnosis, requiring extensive histological examination correlated with the radiological findings.

E-PS-21-022

Desmoid type fibromatosis: Report of 7 cases

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Objective: Desmoid type fibromatosis is rare soft tissue tumour. The objective of our study is to investigate the epidemiological, clinical and histological features of 7 cases of desmoid tumour.
Method: It is a retrospective analysis about 7 cases of desmoid tumour collected in our service during 10 years. Settings concerning sex, age, localisation, size and histology were precised in each case.
Results: Six cases were female and one was male. The most represented age group was between 40 and 60 years. Two cases was localized in the cervical region, two cases in the abdominal wall, one case in the inguinal area, one case in the right thigh and one case in the right hypochondria. The size varied between 2 and 12 cm. All cases showed a variably cellular proliferation composed of spindle cells arranged into fascicles with dense collagen separating the tumour cells. The cells lack nuclear pleomorphism and mitotic figures were rare. Characteristically there is infiltaration of muscle tissue.
Conclusion: **Desmoid tumour is a benign slowly growing soft tissue tumour with potential local recurrence and invasive growth, requires prolonged surveillance. The Treatment of choice is large surgical resection. Radiotherapy has been shown to improve local control of aggressive fibromatosis.**

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-22 Thymic and Mediastinal Pathology

E-PS-22-001

Rare mediastinal tumour: Well-differentiated liposarcoma. Case description

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Objective: Among the rare tumours diagnosed in our department figure liposarcomas. These tumours are extremely hard to diagnose without IHC coloration because the histological picture they present is difficult to differentiate from other histological entities. We will present the case of a 28-year-old young man admitted to the cardiovascular surgery department on February 15, 2016 and diagnosed with mediastinal tumour and generalized myasthenia gravis.
Method: Macroscopic examniation shows two fragments: 1. An 1.5/1.5/1-cm, discoidal tumoural fragment, no incapsulation, hard consistency, yellow-brown-reddish in colour with brownish central areas; 2. An 8/6/2-cm thymus, surrounded by, and intricate with adipose tissue in its mass. The following colorations were performed in order to confirm the diagnosis: HE, VG, Argentic Impregnation, PM (Movat Pentachrome), and immunohistochemically: S 100, CD 34, SMA, Desmin, CK7, AE 1/3, CD 45 and Ki-67.
Results: The histological aspect showed tumoural proliferation with fusiform cells having elongated, focal, hyperchromatic nuclei and multivacuolized cytoplasm arranged in a fibrillary and myxoid collagen matrix. The lesion includes a polymorphous inflammatory unfiltrate and an area of bone differentiation. Intercell reticulin network evidenced by argentic impregnation. The following results are obtained immunohistochemically: S 100 positive, diffuse in the lesions, CD 34 positive in vessels and focal in stroma cells, SMA positive in vascular walls, CK7 negative, AE1/3 negative, CD45 positive in the inflammatory infiltrate, Ki-67 positive, approx. 1–3 %.
Conclusion: Histopathological aspects and IHC tests advocates for diagnosis of the well-differentiated liposarcoma (atypical lipomatous tumour), code ICD - O 8850/1. The specificity of the case comes from its association with thymolipoma.

E-PS-22-003

Thymic carcinomas: A clinicopathologic review of 9 cases

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Objective: Thymic carcinomas constitute 22 % of primary thymic epithelial neoplasms.
Method: We present a single institution series of 9 thymic carcinomas between 2012 and 2016.
Results: Of the thymic carcinomas, there were 6 men and 3 women (ages 25–77 years, mean 58). The histologic types were 5 squamous, 1 small cell neuroendocrine, 1 large cell neuroendocrine, 1 clear cell, and 1 undifferentiated thymic carcinoma. Of the 9 cases, five were resections, with tumour stages of pT2 (1 case), pT3 (3 cases) and pT4 (1 case). All of these tumours were incompletely excised. Immunohistochemistry for CD117 showed positivity in only the squamous carcinomas (4/4). CD5 was positive in all of the squamous carcinomas (4/4) and the one case of undifferentiated thymic carcinoma (1/1). The undifferentiated carcinoma was positive for TTF-1, CK8/18, and synaptophysin (focal). Pax-8 was only positive in the 1 case of undifferentiated thymic carcinoma (1/1). Of 6 patients with follow-up, the patient with clear cell thymic carcinoma developed spinal metastases; one patient with squamous cell thymic carcinoma had drop metastases and was placed on hospice care; and the others were alive with no evidence of disease.

Conclusion: Thymic carcinomas are locally aggressive with potential for metastasis. Immunohistochemical stains for CD117 and CD5 were positive in all squamous carcinomas in this series, potentially useful in determining site of origin.

Monday, 26 September 2016–Thursday, 29 September 2016, Hall 11.3
E-PS-23 Uropathology

E-PS-23-002
The significance of BerEP4 and cytokeratin 19 expressions in epithelial tumours of kidney and renal pelvis
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Objective: Epithelial tumours of kidney and renal pelvis can be problematic due to their overlapping morphologic features. The purpose of this study was to assess potential contributions of BerEP4 and Cytokeratin 19 (CK19) expressions in this context.
Method: A total 57 cases consisted of 9 chromophobe (ChRCC), 18 clear cell (CCRCC), 12 papillary (PRCC) and 2 unclassified renal cell carcinomas, 2 hybrid oncocytic chromophobe tumours (HOCT), 1 multilocular cystic renal cell neoplasm (MCRCN), 7 urothelial carcinoma of renal pelvis (UC-RP), and 6 renal oncocytomas (RO) were stained against BerEp4 and CK19 antibodies.
Results: ROs demonstrated predominantly BerEP4 expression, but no CK19 expression. Unlike ROs, ChRCCs showed CK19 expression, but no or focal BerEP4 expression. This distinctive opposite expression pattern was highlighted in HOCTs. CCRCCs showed variable expression patterns for both antibodies. PRCC demonstrated diffuse and strong CK19 and BerEp4 expressions in a variable proportion. Unlike CCRCC, MCRCN showed BerEP4 expression, but no expression for CK19. Unclassified RCCs showed strong CK19 and weak BerEP4 expressions in epithelioid areas, but no or scattered CK19 and BerEp4 expressions in spindle cell areas. UC-RP showed diffuse and strong CK19 expression, but no or focal BerEP4 expression.
Conclusion: This study revealed that 1) BerEP4 and CK19 expressions are variable and distinctive in epithelial tumours of kidney and renal pelvis, 2) an immunoprofile of BerEP4 (+)/CK19 (−) is favor of RO unlike ChRCC, 3) PRCC, type 1 expressed both biomarkers, and 4) although RCC subtypes express CK19 in a variable proportion, diffuse and strong CK19 expression is favor of UC-RP.

E-PS-23-003
Relationship among with gleason scores, age, serum prostate specific antigen and prostate volume in prostatic adenocarcinomas and prostatic adenomyomatöz hyperplasia
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Objective: To assess the relationship between prostate volume (PV), prostate specific antigen (PSA), Gleason scores (GS) and age in prostatic adenocarcinomas (PA) and prostatic adenomyomatöz hyperplasia (PAH).
Method: The study included a total of 46 cases of prostate. 22 of them were PA, 24 of them were PAH. The youngest case was 46 years old, the oldest case was 83 years old in PA. GS ranged from 4 to 10. PV ranged from 21 to 135. PSA values ranged from 1 to 1122. The youngest case was 50 years old, the oldest case was 86 years old in PAH. PV ranged from 36 to 111. PSA values ranged from 1 to 16.
Results: Statistically, there were significant correlations between psa and GS ($p = 0.031$) in PA cases. However, There were not significant correlations between PSA and age ($p = 0.121$) and age and GS ($p = 0.824$). There were not significant correlations between PV and age ($p = 0.175$) and PSA and PV ($p = 0.110$). There were not significant correlations among age and PSA and PV ($p = 0.468$, 0.693, 0.346 respectively) in PAH.
Conclusion: Relationship between PSA and GS may be more significant correlation within prognostic parameters in PA.

E-PS-23-004
Synchronous tubulocystic cell carcinoma and papillary renal cell carcinoma in end-stage renal disease
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Objective: Tubulocystic renal cell carcinoma (TCC) represents less than 1 % of renal carcinomas and is a new entity recognized by WHO classification (2016). For decades considered a "low-grade collecting duct carcinoma", its tubular differentiation was evidenced by immunohistochemical and ultrastructural studies. A possible relationship with Papillary Renal Cell Carcinoma (PRCC) based on similarities and synchronous papillary lesions has been investigated. We present a synchronous TCC and PRCC in the context of end-stage renal disease (ESRD).
Method: A 58 years-old male presented with fever, hematuria and lumbar pain post-TURP. TC showed hydronephrosis and renal atrophy of the left kidney without obstruction. Renogram revealed a non-functioning left kidney and a nephrectomy was performed.
Results: Macroscopic examination revealed two cortical separated tumours: a 2 cm, unencapsulated, spongy tumour and a close but independent, white and irregular lesion with 0,6 cm. Microscopically these tumours corresponded to a TCC and a type 1 PRCC, respectively.
Conclusion: A pathogenetic relationship between TCC and PRCC has been explored by several groups. TCC shares cytogenetic chromosomal gains with PRCC. However, by gene expression profiling discordant results were obtained. Only three TCC in ESRD are reported in the literature. This is the second synchronous TCC and PRCC diagnosed in ESRD.

E-PS-23-005
Immunohistochemical expression of cell adhesion molecules in urothelial carcinomas
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Objective: Cell adhesion molecules (CAM) are required for maintaining a normal epithelial phenotype. Abnormalities in CAM expression have been related to cancer progression. This study aimed to analyze e-cadherin, p-cadherin and b-catenin expression in urothelial carcinomas and to correlate them with clinicopathologic data.
Method: Thirty-six paraffin tissue blocks from corresponding urothelial carcinoma cases were selected. Tissue microarrays were constructed using three cores of each case. Immunostains were performed using antibodies for e-cadherin, p-cadherin and b-catenin. The immunohistochemical results were correlated with conventional clinicopathological parameters.
Results: All cases were usual urothelial carcinomas without any other specification. Patients'age ranged between 47 and 84 years old (mean age 67.3 years). Nineteen cases (19/36, 52.8 %) were of high grade and one third of the tumours were infiltrative. Expression of e-cadherin and p-cadherin was observed in 54.3 and 41.2 % of the cases, respectively. There was no association between CAM expression and tumour size, grade, infiltration or aggressive behaviour. A positive association was observed between e-cadherin and p-cadherin expression ($p = 0.002$). The majority of the cases (72.2 %) expressed b-catenin.

Conclusion: E- and p- cadherins are usually co-expressed in urothelial carcinomas and are not associated with adverse clinicopathological parameters. Expression of b-catenin is a common feature of urothelial carcinomas.

E-PS-23-006

Low-grade metastases from Clear Cell Renal Cell Carcinomas (CCRCC): A study of E- and N- Cadherin expression in 19 cases

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Objective: Low-grade metastases of CCRCC are observed in clinical practice We have tested E-Cadherin and N-Cadherin in the primary and metastatic tumours of 19 CCRCC patients.
Method: Nineteen CCRCC with low-grade metastases have been retrospectively collected and representative formalin-fixed paraffin-embedded samples of both primary and metastatic tumours retrieved in each case for microscopic evaluation. Tissue microarrays were performed for the immunohistochemical analysis.
Results: Males predominated in the series (12M/7F) Tumour size between 2 and 12 cm. Twelve cases were organ-confined and seven non-organ confined. Metastases were all G1 or G2. One case metastasized three times and two cases did it twice. Elapsed time from primary to metastasis oscillated between 0 and 204 months. Twelve patients died of disease . Three patients are alive with disease and four are alive without disease. E-Cadherin expression was lost in 15 primaries and 16 metastases while N-Cadherin was expressed only in one primary and two metastases. Cadherins switching (E-Cadherin negative/N-Cadherin positive) was not detected in the primaries while reversal switching (E-Cadherin positive/N-Cadherin negative) was observed in two metastases.
Conclusion: Metastases of CCRCC may show a low-grade. EMT and MET are considered crucial processes in tumour invasiveness and metastatic seeding, respectively.

E-PS-23-007

Immunohistochemical co-expression of ERG & CK5 in prostatic neoplasms for diagnostic efficacy in Indian subcontinents

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Objective: Immunohistochemical co-expression of ERG and CK5 markers in Prostatic Neoplasms and correlation with clinicopathological parameters.
Method: We evaluated 30 cases including BPH, BPH with PIN and prostatic carcinoma. To using routine H & E stain and both ERG & CK5 antibodies using immunohistochemistry as per standard protocol.
Results: Out of 11 cases of BHP one case showed both intraluminal ERG positivity and CK5 positivity. Diagnosed a case of PIN. Rest of BHP cases are CK5 positive & ERG negative as BHP cases. Out of 9 cases of BHP with PIN changes, two cases showed ERG positivity & CK5 negativity confirmed adenocarcinoma prostate. Two cases showed both ERG and CK5 positivity as PIN cases. Rest were confirmed as BHP. Out of 10 adenocarcinoma prostate cases only 7 cases show ERG positivity & CK5 negativity in tumour areas confirmed as adenocarcinoma. Rest 3 adenocarcinoma prostate cases show ERG positive & CK5 positive confirmed as PIN. There is no positive correlation with clinical parameters.
Conclusion: Sensitivity and specificity of ERG and CK5 in prostatic adenocarcinoma were 70 and 100 % respectively. ERG and CK5 co-expression confirms the diagnostic efficacy of prostatic neoplasms.

E-PS-23-009

Mucinous tubular and spindle cell carcinoma: Report of two cases. Problems with differential diagnostic

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Objective: Mucinous tubular and spindle cell carcinoma (MTSC) is a rare variant of renal tumour. Here we report two cases of this infrequent tumour and their diagnostic problems.
Method: The collected specimens were fixed with 10 % formalin and embedded in paraffin blocks, which were cut into 4-μm slides, and stained with hematoxilin-eosin, and the antibodies AMACR/P504S, CK34betaE12, CK7 and EMA. Alcian blue staining was also performed.
Results: Two cases, male and female, 58 and 46 years old respectively, were studied. Tumour size were 6,5 and 4 cm. Preoperative CTs demonstrated tumours are hypovascularized and well demarcated, different from other renal neoplasms. The first were treated with radical nephrectomy and the second with tumourectomy. No postoperative therapy was given. There was no evidence of recurrence and metastasis after a 12 and 17 months follow-ups.
Conclusion: 1- MTSC is a renal epithelial neoplasm with tubular formations merging with bland spindle cells and a myxoid stroma. It accounts for <1 % of all renal neoplasms. 2- Mean age is 58 years old and there is a female predilection. 3- The distinction between MTSC and a solid variant of papillary renal cell carcinoma is important because of the prognostic significance. 4- MTSC has an indolent clinical-course, but there are a few cases with metastasis.

E-PS-23-013

Renal hydatid disease mimicking renal cell carcinoma: A rare entity

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Objective: Hydatid disease (HD) is an endemic parasitic enfestation in several Mediterranean countries and constitutes an important health problem. It may arise in any organ, however isolated kidney involvement represents 4 % of the confirmed cases. Preoperative diagnosis of renal HD is difficult even in an endemic zone. Our aim is to emphasize the importance of this rare tropical disease in order to encourage physicians to consider this entity in differential diagnosis of a renal mass.
Results: A 67-year-old female patient presented with complaints of left flank pain. The medical history was unremarkable. Physical examination revealed a mild costovertebral angle tenderness. Routine hematology and biochemical tests showed a mild leukocytosis (18,78 K/uL). BUN, urea and creatinine levels were normal. Computed tomography (CT) revealed a multilobular cystic renal mass of 4,7 × 4,2 × 2,8 cm in size in the left kidney, which was suspicious for renal cell carcinoma (RCC). The patient underwent a radical nephrectomy and a pathologic diagnosis of renal HD was reached. Thorax and cranial CT revealed no sign of HD. The patient was given a medical treatment of oral albendazole.
Conclusion: It should be noted that renal HD is rare entity that may easily be confused with multicystic RCC, radiologically.

E-PS-23-014

Ovarian - type epithelial tumours: A rare case of papillary serous tumour of low malignant potential of the testis

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Objective: Serous papillary tumours of the testis and adjacent tissues are very rare neoplasms resembling surface epithelial tumours of the ovary and mostly represent a surprising finding in diagnostic procedures. The

aim of this case report was to evaluate the histopathological and immunohistochemical features of these rare tumours.
Method: We present the case of a 71-year-old man with a left testicular mass measuring 4.5 cm. Under the assumption of a testicular malignant tumour inguinal orchiectomy was performed.
Results: Histopathological examination revealed testicular parenchyma presenting a cystic lession with intracystic blunt papillae lined by columnar epithelium, with hyperchromatic nuclei, areas of hobnail cells and very rare mitoses. A focus of microinvasion was present. The underlying stroma had a fibrilar ovarian-like aspect. Immunohistochemistry showed the expression of CK7, EMA, PLAP, WT1, CA 125 and ER, while Calretinin was positive in isolated cells, and CEA, MOC 31, CK20 were negative. Ki-67 value was 10 %. Final diagnosis was serous papillary tumour of the testis with low malignant potential—ovarian type.
Conclusion: Serous papillary tumour of ovarian-type in the testis should be considered when the diagnosis of malignant mesothelioma is suspected. The microscopic appearance combined with the immunoprofile of the tumours are helpful for differential diagnosis.

E-PS-23-015
Wt1, a reliable marker for angiogenesis in clear cell renal cell carcinomas
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Objective: The tumour microenvironment comprises numerous signaling molecules and pathways that influence the angiogenic response. As angiogenesis is essential for tumour growth and metastasis, controlling tumour-associated angiogenesis is a promising tactic in limiting cancer progression. WT1 is an important regulator of cancer growth via modulation of tumour vascularization.
Method: A tissue microarray with 48 different cases of clear cell renal cell carcinomas (CCRCC) was performed with respective normal renal tissue as controls. Tumoural angiogenesis was assessed by immunohistochemical studies against WT1 and CD31 molecules (a reliable endothelial marker) (Roche). Samples were imaged using a 40X objective lens. ImageJ, a digital image analysis software, was used to quantify the percentage of positivity.
Results: A strong WT-1 cytoplasmic stain was invariably observed in the endothelial cells from all cases and controls. None of cases showed WT1 in tumoural cells. Angiogenesis was significant observed in cases against controls by WT1 and CD31 expression. A strong correlation was found between WT1 and CD31 expression. No significant associations were determined between clinical variables and angiogenesis in CCRCC.
Conclusion: WT1 is a reliable marker for angiogenesis. There is a strong correlation between WT1 and CD31 expression. Angiogenesis is not associated with clinical variables in CCRCC.

E-PS-23-016
Primary renal Ewing sarcoma / primitive neuroectodermal tumour: A case report
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Objective: Ewing sarcoma/primitive neuroectodermal tumour (ES/PNET) belongs to a group of small round cell tumours defined by alterations in the EWSR1 gene. Primary renal ES/PNET is uncommon and has worse prognosis than ES/PNET arising in other sites. We present a case of primary renal ES/PNET and discuss its clinicopathological features.
Method: A case of primary renal ES/PNET is described, with a review of the literature.
Results: A 39-year-old female underwent nephrectomy for a 13 cm mass in the inferior pole of the right kidney. Grossly, the tumour was a well-circumscribed, solid and cystic mass with extensive necrosis. Microscopically it was composed of sheets of small cells with round nuclei, fine chromatin and scant cytoplasm, with occasional peritheliomatous growth. Immunohistochemistry showed strong membrane positivity for CD99. Rearrangements of the EWSR1 gene were found by fluorescence in situ hybridization, confirming the diagnosis of renal ES/PNET. The patient was treated with post-operative chemotherapy and no evidence of disease was found after 2 years of follow-up.
Conclusion: Although rare, primary ES/PNET represents a diagnostic challenge and should be considered in the differential diagnosis of renal malignancies in young adults. Complementary studies are fundamental to differentiate it from similar renal small cell tumours, like blastematous nephroblastoma or neuroblastoma.

E-PS-23-017
Primary myxoid chodrosarcoma of the penis: Case report
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Objective: We report a case of myxoid chondrosarcoma in 67 years old man presented with 6 cm penile mass.
Method: After radical penectomy, specimen was handled in usual fashion manner. Pathohistological examination was performed by H&E staining, histochemical and immunohistochemical studies.
Results: Diagnosis was made on a morphologic basis, proven by the histochemical and immunohistochemical studies. Morphologically, tumour consisted of pleomorphic cells with large, hyperchromatic nuclei and myxoid stroma positive for Acian blue. Immunohistochemical studies showed malignant cells positive for Vimentin, Alfa SMA, NSE, Synaptophysin, S-100, EMA, and negative for CKAE1/3, CD34, CD31, CD68, CD57, Desmin, HMB45, ALK1.
Conclusion: Exstrasceletal myxoid chondrosarcoma of the penis is very rare tumour. This case presents that an exstrasceletal chondrosarcoma shows ultrastructural evidence of neuroendocrine differentiation and neuroendocrine immunophenotype. Nevertheless, surgery is the main treatment modality, but the prognosis is poor.

E-PS-23-018
Primary renal well-differentiated neuroendocrine tumour: A case report
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Objective: We present a primary well-differentiated neuroendocrine tumour of the kidney, which is an exceedingly rare entity and frequently misdiagnosed as other kidney cancers. The behavior of this tumour is not well known due to the small number of reported cases.
Method: A 52-year-old woman presents with an incidental finding of a mass in the left kidney.
Results: We received a radical nephrectomy specimen with a 6,2 cm well defined tumour. Histologically it was composed of nests and trabeculae of cells with round nuclei with salt and pepper chromatin. Immunohistochemically the cells were positive for cytokeratins AE1 / AE3 and 8/18, CD56, chromogranin, synaptophysin; they were negative for CDX-2 and TTF-1. Of the 15 lymph nodes found, four had metastasis.
Conclusion: Neuroendocrine carcinomas may originate in a wide variety of organs, including those that do not usually contain neuroendocrine cells. To the best of our knowledge, less than 100 cases of well-differentiated neuroendocrine tumours of renal origin have been reported in the literature. Patients with advanced disease have been known to survive for long periods of time even

in the presence of tumour spread. Our patient is alive and disease free 16 months after the radical nephrectomy.

E-PS-23-019

Metastatic urothelial carcinoma of the prostatic urethra to the right testis

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Objective: To report a rare case of an urothelial carcinoma of the prostatic urethra presenting as a testicular tumour.
Method: A 64-year-old man presented with hematuria and a palpable mass to the right testis. AFP and bhCG were within normal range and a right orchiectomy was performed.
Results: Macroscopically, the testis was grayish, solid, hard. Microscopically, a malignant, poorly differentiated tumour was observed, with mostly intratubular and focally intertubular growth throughout the testis, resembling embryonal carcinoma. A detailed immunohistochemical approach showed negativity for Vimentin, PLAP, CD117, bhCG, AFP, InhibinA, CD30, NSE, CK20, PSA, CD57 and positivity for p53, CKAE1/AE3, CK7, CK34bE12, p63, AMACR and uroplakin. A month later, transurethral resection of the prostate was performed, due to urinary obstruction. Microscopically, an invasive high-grade urothelial carcinoma was diagnosed. Because of the similar microscopical and immunohistochemical characteristics of both tumours, the tumour of the testis was diagnosed as a metastasis of the aforementioned urothelial carcinoma.
Conclusion: Despite the rarity of documented cases of metastatic urothelial carcinoma to the testis, especially with prominent intratubular growth, the bladder and pelvis should not be overlooked as possible sources. They may simulate primary testicular neoplasms, even in patients with known extratesticular primaries, but information in this topic is limited.

E-PS-23-020

Paraganglioma of the urinary bladder

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Objective: We present a urinary bladder paraganglioma in a 38-year-old man.
Method: The patient presented with palpitations, headaches, perspiration and abdominal pain 2 min after urination. A 24 h urine test showed high levels of noradrenaline and normetanephrine, while catecholamines, adrenaline, dopamine, metanephrine and VMA were within normal range. Computed tomography showed a lesion at the posterior bladder wall which was locally excised.
Results: We received a nodular greyish tumour with median diameter 4.5 cm. Microscopically, the neoplasm was located among smooth muscle cells, with high cellularity and solid, trabecular, pseudorosettes focally and classic Zellbalen (alveolar) architecture. The cells had abundant, amphophilic cytoplasm with median to severe nuclear pleomorphism and focally, giant, multinucleated cells. Mitoses were scarce (0-1/10 High Power Fields). The neoplastic cells were positive for neuroendocrine markers and negative for CKAE1/AE3 and p63 and the presence of sustentacular cells was confirmed with S100.
Conclusion: Paragangliomas of the urinary bladder are derived from paraganglion cells in the bladder wall. They account for less than 0.05 % of bladder tumours. They usually show clinical symptoms with hypertension, hematuria, headaches and syncope which are associated with urination ("micturition attack"). Young age, hypertension, micturition attacks and invasion through the bladder wall may indicate increased potential for malignant behaviour.

E-PS-23-021

Neuroendocrine carcinoma of the bladder

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Objective: we present two cases of Small cell carcinoma (SCC) of the urinary bladder, a rare but distinct neuroendocrine neoplasm that accounts for less than1% of all urinary bladder cancers.
Method: Two patients, a 70 year-old woman and a 50 year-old man both chronic smoking, who was admitted to the medicine with history of gross hematuria. Cystoscopy showed a white tumour occupying the bladder.
Results: Pathological diagnosis revealed a Small cell carcinoma of the urinary bladder.
Conclusion: Neuroendocrine carcinoma of the urinary bladder is very rare and it is predominantly a disease of elderly Caucasian men with a median age of 73 years often reveled with macroscopic haematuria. Diagnosis is confirmed with transurethral resection for tissue sampling. Macroscopically, SCC may appear as a large solid, isolated, polypoid, nodular mass. Histologically, all tumours are invasive at presentation. They consist of small cells with nuclear molding, scant cytoplasm and nuclei containing finely stippled chromatin. Mitoses are present. Necrosis is common. Roughly 50 % of cases have areas of urothelial carcinoma and exceptionally squamous cell carcinoma and/or adenocarcinoma. This is important, because the presence of these differentiated areas does not contradict the diagnosis of SCC. The diagnosis is supported by positive immunostaining for CD56, synaptophysin, and chromogranin. The differential diagnosis is metastasis, lymphoma, lymphoepithelioma-like or plasmocytoid carcinoma and a poorly differentiated urothelial carcinoma

E-PS-23-022

Renal glomus tumour: Diagnostic challenges of this rare entity of the kidney

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Objective: Glomus tumours were first described by Masson in 1924 as a benign mesenchymal tumour that arises from the subcutaneous tissue of the extremities. It can be rarely seen in visceral organs like kidney. We described an extremely rare primary renal glomus tumour which has only nine reported cases in the literature.
Method: A 51 years old woman admitted to the hospital with abdominal pain. USG and MRI findings revealed a cystic lesion located at the lower pole of the left kidney. The lesion was cystic and 46 mm in diameter with 16 × 10 mm and 30 × 10 mm solid nodules in it. The lesion was excised by partial nephrectomy.
Results: Macroscopically, the mass was well circumscribed, multicystic and measuring 70 × 50 × 40 mm in size. Microscopic examination revealed sheets of bland cells with round to oval nuclei and a moderate amount of eosinophilic cytoplasm. There was no atypical mitosis and necrosis. Immunohistochemically, there was strong positivity with vimentin, SMA, CD34, collagen and laminin. On the other hand EMa, keratin, CD10, CD117, HMWK, p63, pax-8 and GATA-3 were completely negative.
Conclusion: We presented the morphological and, immunohistochemical features of the glomus tumour to differentiate it from the other renal tumours on the basis of the literature.

E-PS-23-023

Renal mucinous tubular and spindle cell carcinoma combined with papilary renal cell carcinoma, type I—one tumour or two? A case report

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Objective: Mucinous tubular and spindle cell carcinoma (MTSCC) is an unusual tumour of kidney. Cases of MTSCC combined with papillary renal cell carcinoma type I. (PRCC-T1) has been described, bringing into question relationship of both entities. Here we present an additional case.
Method: A 62-year-old lady underwent nephrectomy for left kidney tumour measuring 60 × 50 × 50 mm. Five smaller tumours up to 13 mm and several serous cysts up to 30 mm were scattered around main tumour. Histopathological evaluation and immunohistochemical staining for CK18, CD10, RCC and AMACR was performed.
Results: The largest tumour was predominantly PRCC-T1, WHO/ISUP grade 3, with areas of necrosis and papillary, tubular or solid architecture. There was second component of the tumour composed of uniform spindle cells intermingled with cords or small tubules of cuboidal cells. Cells were embedded in myxoid, Alcian-blue positive matrix; a finding consistent with diagnosis of MTSCC (WHO/ISUP grade 3). Transition between both tumours was apparent focally. There was strong positivity of RCC and weak expression of CK18 in PRCC-T1 component, contrasting with no expression of RCC and strong positivity of CK18 in MTSCC component. PRCC-T1 was strongly positive for AMACR, while MTSCC component stained only weakly in focal pattern. CD10 expression was negative. Smaller tumours in surroundings were papillary adenomas without any remarkable features.
Conclusion: MTSCC and PRCC-T1 may share morphological and immunohistochemical features. Although rare, the tumours with both morphologic components are described. The data from previous genetic studies reported in literature suggests that at least a part of such cases are rather PRCC-T1 with unusual growth pattern than real collision tumour.

E-PS-23-024

Assessment of the changes in tumour grade, size, and pT of bladder tumour in residual and recurrent tumours referred to Hasheminejad Kidney Center from 2003 to 2011

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Objective: The present study aimed to assess changes in tumour grade, size, and pT in resampling of initial tumours as residual and recurrent tumours.
Method: This study was conducted on 154 patients with bladder cancer who referred to Hasheminejad Kidney Center from 2003 to 2011. Residual and recurrent tumours were considered as the presence of tumour in second TUR-B specimens performed within 8 weeks after the first one and more than 8 weeks respectively.
Results: The grade of tumour in 7.7 % of residual and 17.6 % of recurrent tumours changed from low to high. Increasing the primary tumour size from less than 3 cm to more was found in 15.4 % and 13.2 % of residual and recurrent tumours. Changing pTa to pT1 occurred in 6.8 %, pTa to pT2 in 3.4 % and pT1 to pT2 in 10.2 % of residual tumours. Also in recurrent tumours changing pTa to pT1 occurred in 12.1 %, pTa to pT2 in 1.5 % and pT1 to pT2 in 6 %.
Conclusion: There is a possibility of changing the grade, size and pT in residual tumours because of incomplete sampling. The grade change in recurrent tumours may be due to new mutations and changes in size and pT indicate tumour progression.

E-PS-23-025

Testicular fibroma of gonadal stromal origin: A rare tumour

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Objective: Benign intratesticular fibrous proliferations are rare and most arise from the paratesticular region. Testicular fibroma of gonadal stromal origin is much more rarer. According to the recent WHO classification they are classified under the sex cord/gonadal stromal tumour. The tumour presents as slow-growing, sometimes painful mass which is not associated with hormonal alteration.
Method: A 52-year old male presented with scrotal pain lasting for 1 month. There was no history of trauma, urologic or hormonal symptoms. The ultrasonography revealed mildly heterogeneous well-circumscribed mass in the left testis. The patient underwent left radical orchiectomy. Macroscopic examination showed testicular paranchymal mass measuring 2.1 × 1.5 × 1.5 cm which has white solid cut surface. Microscopically the tumour composed of uniform bland spindle cells within collagenous stroma. The mitotic activity was 0-1/10 HPF. Atypia and necrosis were absent. There was no associated minor sex cord elements. Immunohistochemically tumour cells were positive with SMA and vimentin, very focally positive with S-100, CD99 and CD34. Desmin and inhibin were negative. The Ki67 proliferating index was %1.
Results: Histopathologic diagnosis was testicular fibroma.
Conclusion: Testicular fibroma of gonadal stromal origin is a rare benign neoplasm which must be kept in mind in the differential diagnosis of benign intratesticular fibrous proliferations.

E-PS-23-026

Nephrogenic adenoma: A report of three cases

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Objective: Nephrogenic adenoma of the urinary bladder (UB) is a rare lesion associated with nonspecific symptoms and may microscopically be confused with many malignant lesions of the UB. We present three cases of nephrogenic adenoma of UB.
Method: Three male patients underwent transurethral resection (TUR) of a previous confirmed bladder mass in two cases and urethral mass in one case, by imaging techniques. Standard procedure for histopathologycal analysis and immunohistochemistry was performed.
Results: Two of the patients had previous history of chronic infection and one of them had previous prostatectomy. Two of them presented with dysuria and urinary frequency and the third patient had hematuria. One surgical specimen (utehral one) was a polipod lesion with diameter of 1,3 cm, and the another two consisted of urinary "chips" from bladder TUR. Microscopically small tubules, looking similar to mesonepric tubules, lined by a single layer of bland cuboidal cell with clear cytoplasm ant small nuclei were found. In one case some of the tubules were cysticaly dilated and some contained basophilic secretion. The stroma was edematous and rich of inflammatory cells. All three cases were CK7, EMA and PAX 2 positive.
Conclusion: The accurate diagnosis of nephrogenic adenoma is important because it can mimic malignant lesions.

E-PS-23-027

Two rare paediatric renal tumours mimicking Wilms' tumour of the kidney

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Objective: The most common pediatric renal tumour is Wilms' tumour which occurs between 6 months and 3 years of age. Specific syndromes and clinical presentations are also associated with Wilms' tumour. However there are some rare entities that are in the differential diagnosis of Wilms' tumour. Clear cell sarcoma of the kidney and rhabdoid tumour are two rare renal tumours which account %2-3 of all malignant pediatric kidney tumours. We report here two renal neoplasms with a clinical suspicion of Wilms' tumour.
Method: First case is a 10 month's old male patient with inguinal diaper dermatitis and diarrhea. Abdominal computerized tomography (CT) revealed a large 11 cm sized right renal mass with heterogeneous enhancement. The patient underwent right nephrectomy with an initial diagnosis of Wilms' tumour. Wilms' tumour diagnosis was ruled out with microscopical and immunohistochemical findings. End diagnosis was a clear cell sarcoma.
Results: Second case was a 2 years old male child with complaint of abdominal flank mass and hematuria. Abdominal CT showed a left sided 10 cm sized renal mass. Initial diagnosis was Wilms' tumour. A hipodens lesion on the liver and bilateral pulmonary metastasis were seen on CT. Rhabdoid tumour of the kidney was the final diagnosis with lack of INI1 immunostaining.
Conclusion: Clear cell sarcoma and rhabdoid tumour should be considered in the differential diagnosis when dealing with a pediatric tumour. Loss of INI1 immunostaining, absence of epithelial, mesenchymal components and lack of WT1 immunostaining, pale H&E staining of the tumour cells or identifying the rhabdoid features of the tumour should alert the pathologist for these rare entities.

E-PS-23-028
Prostate cancer with aberrant diffuse p63 expression: A case report
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Objective: Prostate carcinomas showing aberrant diffuse-nuclear p63 expression are extremely rare. This protein is strongly expressed in prostatic basal cells and absent from usual-type acinar prostate cancers.
Method: A 71 -year-old male patient presented with lower urinary tract symptoms for of 1-month duration and his prostate-specific antigen (PSA) level was 8.6 ng/mL. A ten-quadrent transrectal ultrasonography-guided prostate needle biopsy was performed.
Results: Transrectal needle biopsy of the prostate detected atypical, small prostatic glands suspected for adenocarcinoma at 2 cores. These atypical glands were diffusely strongly positive for p63 in the secretory cells, negative for HMWCK, positive for AMACR, positive for PSAP, and negative for GATA-3. The diagnosis was prostatic adenocarcinoma, Gleason score 4 + 3 = 7, with aberrant diffuse p63 expression. The patient underwent a radical prostatectomy and the final diagnosis was prostatic adenocarcinoma, Gleason score 3 + 4 = 7, stage pT2a.
Conclusion: The differential diagnosis of p63-positive prostatic adenocarcinomas includes urothelial carcinoma with microglandular pattern, basal cell proliferations, such as basal cell hyperplasia or basal cell carcinoma. Particularly, pathologist need to be aware of this rare and unusual phenomenon which is taken from needle biopsy.

E-PS-23-029
Clear cell (Tubulo) papillary renal cell carcinoma: Case report
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Objective: Clear cell (tubulo) papillary renal cell carcinoma is a distinct subtype of renal cell carcinoma first described in the setting of end stage renal disease.
Method: Histologically, the tumour cells are cuboidal to low columnar cell with clear cytoplasm and papillary and tubulo-papillary configuration. Immunohistochemically, tumour cells generally show diffuse expression for cytokeratin 7, CA9 (cup-shaped pattern), HIF-1, GLUT-1 and high molecular weight cytokeratin, but negative for AMACR, RCC Ma and TFE3. CD10 is negative or focally positive in most tumours. Genetically, this tumour has no characteristics of clear cell RCC or papillary RCC. These tumours appear to be indolent in nature, with no current documented cases of metastatic spread. The aspects of disease concept and clinical behavior are to be fully elucidated.
Results: A 61-year-old male presented with flank pain of 2 years durations. He gave a history of an open prostatectomy 6 years ago. Ultrasound and computer tomography of Abdomen showed stones in the right ureter and calyces. The patient was performed right nephrectomy due to non functional kidney. The renal mass was revealed incidentally during the pathological examination. İmmunohistochemically, tumour cells showed diffuse expression for cytokeratin 7 but were negative for AMACR.
Conclusion: As this a very rare tumour, we presented this case.

E-PS-23-031
High-grade urothelial carcinoma with areas of trophoblastic differentiation: Report of two cases arising in the upper urinary tract
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Objective: Urothelial carcinoma with trophoblastic differentiation is a rare and highly malignant neoplasm. A variable proportion of syncytiotrophoblast and cytotrophoblast cells with positive β-hCG immunohistochemical expression, along with nests of transitional cell carcinoma, are characteristic of this particular entity.
Method: Case 1: 69-year-old male with macroscopic hematuria. A 9 cm necrotizing mass was detected in the left kidney by ultrasound and CT. Case 2: 61-year-old male with macroscopic hematuria. A 4 cm mass was detected in the left kidney by ultrasound.
Results: Both cases showed similar histological features. Nests of high grade transitional cell carcinoma, as well as areas with syncytiotrophoblast cells were detected. β-hCG was intensely positive in syncytiotrophoblast cells. In addition, transitional cells showed CK7 and CK20 immunostaining.
Conclusion: Urothelial carcinoma is the most common malignant neoplasm of the renal pelvis. It tends to be multifocal, it is more common in males and occurs more frequently at an advanced age. Multiple risk factors are associated: cigarette smoking, industrial carcinogens and chronic irritation, as well as genetic factors. Urothelial carcinoma with trophoblastic differentiation is a rare condition and it is associated with highly malignant clinical behavior. Increased β-hCG serum and/or urine levels are the first symptom in some patients.

E-PS-23-032
Metastasis of testicular seminoma in the bladder: Case report
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Objective: Metastases of testicular seminoma (TS) to the urogenital system are rarely reported, with only a few cases involving the bladder.
Method: We present the case of a 55-year-old man admitted to the Urology Department for hematuria and a bladder cancer suspicion. A transuretral resection was performed and the morphological features suggested a malignant tumour infiltrating the bladder wall, composed of nests of polygonal tumour cells with abundant cytoplasm, separated by fibrous septa with lympocytes. The overlying urothelium was normal. Considering this morphology,

unusual for a bladder cancer, but suggestive of a testicular seminoma, immunohistochemistry was performed.
Results: Tumour cells expressed PLAP, CD117, OCT4, and were negative for CK7, CK20, p63. The morphological features and the immunohistochemical profile led to a diagnosis of TS metastasis in the bladder. Reviewing the medical history, we found that 2 years before the patient had undergone orchiectomy for pure seminoma with multiple metastases. During this period the patient was lost of view.
Conclusion: Although very rare, metastases of TS in the bladder should be kept in mind when facing a bladder tumour with unusual morphology. In our case, the patients' medical history prompted to differentiate between a TS metastasis in the bladder and an extragonadal seminoma.

E-PS-23-033
Human Herpes virus-8 related Kaposi Sarcoma of the ureter after renal transplantation
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Objective: Post-transplantation Kaposi sarcoma is a well known complication due to the immunosuppressive agents. It is mainly seen in the skin but rarely visceral organs are also affected like lung, liver, gastrointestinal tract and lymph nodes. However there are only 4 cases of Kaposi sarcoma originated from the ureter in the literature.
Method: A 52 years old man received a lived related kidney transplantation from his brother in our hospital. Hydronephrosis was seen at the transplant kidney with the USG after 10 months. MRI showed lymph nodes around the ureter and surgery was done for tissue diagnosis. After the diagnosis of mesenchymal tumour with intraoperative frozen section, that part of ureter was resected.
Results: Microscopic examination revealed a spindle cell neoplasm under the epithelium of the ureter. The tumour was composed of nodules of spindle cells and slit-like vascular spaces with erythrocytes. The mitotic activity was increased also. Immunohistrochemistry showed positive staining with vimentin, Fli-1, CD31, ERG and HHV-8. On the other hand keratin, EMA, S-100, desmin and CD34 were negative. Kaposi sarcoma was diagnosed according to the histological and immunohistochemical features.
Conclusion: Post transplant Kaposi sarcoma of the ureter is extremely rare and must be kept in mind that can arise even at the visceral organs.

E-PS-23-034
Primitive neuroectodermal tumour of kidney: A rare case report from Iran
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Objective: Primitive neuroectodermal tumour (PNET) of kidney is a rare neoplasm with aggressive behavior and poor prognosis. Correct diagnosis leads to proper therapy.
Method: We report a 21 year old man complaining of right flank pain and gross hematuria. Microscopic examination of H&E slides, IHC studies and PCR study of paraffin embedded blocks are evaluated.
Results: CT scan revealed right renal mass. Microscopic examination of renal mass biopsy showed a small round cell tumour. IHC studies showed negative immune reactions for CK7, CK20, CD56, chromogranin, synaptophysin, CD45, CD3 and CD 20 but NSE and CD99 were positive in tumoural cells. Real time PCR on paraffin block proved the presence of t (11–22) translocation (EWS-FL1 fusion transcript) which confirmed the diagnosis of PNET. The patient underwent neoadjuvant chemotherapy and radical nephrectomy. Microscopic examination of radical nephrectomy showed only therapy related changes with no tumour residue. The patient is symptom-free until now.
Conclusion: Only two cases of renal PNET were previously reported from Iran. Macroscopically many of the cases are located in the medullary/pelvic region like. For definite diagnosis, IHC studies are required which show more than 90 % positivity for CD99. Cytogenetic analyses can be helpful showing EWS gene and ETS translocation.

E-PS-23-035
The nested variant of the urothelial carcinoma: A case report
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Objective: The nested variant of urothelial carcinoma is rare neoplasm that is characterized by irregular nests and/or tubules of mildly atypical urothelial cells infiltrating the lamina propria and/or muscularis propria.
Method: A case of the nested variant of urothelial carcinoma of the bladder is presented with differential diagnosis.
Results: A 50-year-old man presented with hematuria. Physical examination no abnormal findings. Cystoscopic examination revealed that trigone, and right lateral wall of the bladder were replaced by mass approximately 3,5 cm in diameter. The tumour was macroscopically resected. Microscopically, tumour cells are infiltrated into part of the mucosal urothelium, lamina propria, and muscularis propria. Few mitotic figures were seen. Immunohistochemically, the tumour cells showed diffuse CK 7, and focal CK20 expression. Chromogranin was not expressed. After a follow up period for 6 months the patient free from recurrence.
Conclusion: Nested variant of urothelial carcinoma must be differentiated from the benign proliferative lesions of urothelium, such as von brunn nests, cystitis cystica and glandularis, nephrogenic metaplasia, inverted papilloma and paraganglioma. Despite its bland cytological features it behaves aggressively with invasion, metastasis and death being common.

E-PS-23-036
Endometriosis localized to ureteral wall mimicking urethelial carcinoma
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Objective: Endometriosis is the presence of functional endometroid tissue in ectopic foci outside of uterine cavity. Extragenital endometriosis rarely involves the urınary system. It ıs usually diagnosed in women aged between 30 and 35 years. İt is uncommon and even more likely to remain undiagnosed in postmenopausal women.
Method: A 51-year-old postmenopasual woman, presented with pelvic pain worsening in the last 6 months. The gynecological examination was not remarkable. She was diagnosed with severe left hydronephrosis and hydroureter secondary to left ureteral obstruction resulting in 20 % left renal function. Computer tomography mass in left urethral distal segment with homogenous contrast uptake that appeared postcontrast series. cystoscopy in the left ureter, 3-cm polypoid mass was seen which fills the lumen. A cold cup biopsy was taken.
Results: Histopathological examination; of biopsy specimen revealed benign endometrial gland and stroma underlining the normal urothelium. Immunohistochemical studies were performed for estrogen receptor, CK7, CK20 and CD10. The endometrial glands were positive for Estrogen receptore and CK7 while the endometrial stroma was positive for CD10. Ck20 staininggn not observed.
Conclusion: Urinary tract endometriosis is observed in 1–2 % of women with endometriosis. Ureteral involvment may lead to obstruction progressive hydroureteronephrosis and renal loss. Polypoid endometriosis is a rare manifestation of endometriosis that may be mistaken for a neoplasm on clinical, intraoperative, or pathologic assessment.

E-PS-23-037

Metachronous soft tissue tumours: Perivascular epithelioid cell tumour (PEComa) of the urinary bladder and gastric stromal tumour (GIST)

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Objective: PEComas are rare mesenchymal tumours composed of cells that express both myogenic and melanocytic markers making their diagnosis difficult. The urinary bladder is an extremely rare location for PEComa. The association of urinary bladder PEComa with another type of mesenchymal tumour is quite unusual. The aim of the present paper is to present a rare case of PEComa of the urinary bladder in a patient previously diagnosed with gastric GIST.
Method: A 66 years-old woman, with multiple comorbidities, including a gastric polypoid tumour (in 2004), was admitted in the hospital for investigation of an incidentally discovered bladder tumour.
Results: The 12 mm resected bladder tumour with mesenchymal appearance on routine stain presented the following IHC profile: positive reaction for HMB45 and SMA, lack of reactivity for CK, EMA, S100, Des, ALK, CD117 and CD34. The resected gastric tumour (2004) was diffusely and strongly positive for CD117 and CD34. The patient remained disease-free 6 month after surgery for bladder lesion with no evidence of tumour recurrence or new neoplasms.
Conclusion: Mesenchymal tumours detected metachronously in patients with history of GIST should be evaluated in order to confirm or to exclude metastatic GISTs, but may represent distinct lesions. The possibility, although very rare, of a urinary bladder PEComa should be considered and as a consequence a wide IHC panel must be performed in order to avoid erroneous diagnosis.

E-PS-23-038

Primitive Neuroectodermal Tumour (PNET) of the kidney: A case report

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Objective: Primitive neuroectodermal tumours (PNETs) are a group of small round cell tumours and presumed to be of neural-crest origin. PNET can rarely arise outside the nervous system except for bone and soft tissue. The kidney is a rare primary location for these tumours and approximately 50 cases of renal PNET (rPNET) have been reported in the literature. We describe a case of rPNET and review its clinical and histologic features.
Method: The surgical specimens were formalin-fixed and paraffin embedded. The sections were stained with routinary H&E. Immunohistochemistry was performed.
Results: The patient was 50-year-old man and underwent left radical nephrectomy. On gross examination, the tumour measured 6 × 5 cm in dimensions, with cystic areas and necrosis. Microscopically tumours consisted of small sized, round-oval shaped primitive cells with irregular nuclei and scanty cytoplasm, and presented rosette formation in some areas. Immunohistochemical stains were positive for vimentin and MIC-2(CD99). Microscopic and immunohistochemical findings were compatible with rPNET.
Conclusion: Though a rare entity, due to its aggressive nature rPNET should be included in the differential diagnosis of renal tumours especially in children and young adults.

E-PS-23-039

Correlation of AMACR and ERG expression with preoperative PSA levels and morphological features of the prostate cancer

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Objective: To study a correlation of AMACR and ERG expression with PSA levels and morphological features of the prostate cancer.
Method: We studied a material of needle biopsy and radical prostatectomy from 702 prostate cancer patients (2009–2015). The expression of AMACR and ERG was estimated with the use of immunostaining. For the statistical analysis the software Statistica8.0 and MedCalc12.4.0 was used.
Results: The correlation of preoperative PSA levels with Gleason first component and Gleason score on needle biopsy and with Gleason score and TNM parameters in radical prostatectomy was identified. However, dispersive analysis didn't reveal significant differences of prostate cancer morphological features in patients groups with threshold values (ng/mL) PSA < 1, PSA = 1–4 and PSA > 4. ERG expression was detected only in cases with a PSA > 4. But the significant correlation of AMACR and ERG expression, PSA level and morphological features wasn't identified in radical prostatectomy material. A high PSA level was an important factor of tumour spread prognosis. So, PSA levels ≥16,08 ng/mL predicted a high risk of extraprostatic invasion and PSA ≥ 26,75 and ≥29,85 ng/ml—the presence of lymph node and distant metastases, respectively.
Conclusion: Preoperative PSA levels correlated with Gleason score and TNM and had an important clinical significance as a prediction factor of extraprostatic invasion and metastasis . At the same time, prostate cancer from patients with PSA ≤ 4 ng/mL was ERG-negative, but wasn't a less aggressive compared with that from patients with PSA > 4 ng/ml by morphological features.

E-PS-23-040

A rare case of scrotal leiomyosarcoma

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Objective: Leiomyosarcoma (LMS) is a malignant mesenchymal neoplasm thought to have originated from smooth muscle. They account for approximately 7 % of soft tissue malignancies. LMS's are generally seen in middle-aged and elderly patients, often located in uterus or gastrointestinal organs and constitute the majority of sarcomas developing from large vessels in the retroperitoneum. Male genitourinary LMS's are rare. We report an unusual case of scrotal leiomyosarcoma.
Method: A 62 year old male presented with mass in the right scrotum. Clinical preoperative findings were consistent with lipoma. An exicisional biopsy was performed. Macroscopically there was solid nodular mass with 2.5 × 2 × 1.5 cm dimensions. Cut surface was yellow in color with centrally creamy white area. In the microscopical examination, the lesion was a mesenchymal neoplasm composed of spindle cells with cigar shaped nuclei and eosinophilic cytoplasm. There were nuclear pleomorphism and focal necrosis. Neoplastic cells displayed diffuse smooth muscle actin and caldesmon expression immunohistochemically. Desmin and EMA were focally positive. Stains for Pan-cytokeratin, S-100, CD34 and CD68 were negative. Ki-67 proliferation index was 50 %.
Results: The final diagnosis was high grade LMS.
Conclusion: LMSs can lead to significant clinical difficulty due to its wide differential diagnosis and rarity.

E-PS-23-041

Hypoglycemia and hypertension associated with bilateral metastatic renal hemangiopericytoma

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Objective: Hemangiopericytoma (HPC) classified as a soft-tissue vascular tumour arising from pericytes, which arranged around capillaries and postcapillary venules and modulate blood flow and permeability.

Consequently, HPC may occur anywhere capillaries found. Renal HPC was uncommon and to the date, only 2 cases of bilateral metastatic renal HPC have reported. A considerable proportion of patients exhibits hypertension, hypoglycemia or additional paraneoplastic syndromes.
Method: We report an uncommon case of bilateral metastatic renal HPC accompanying hypoglycemia and hypertension in a 52-year-old male. He had a history of mandibular HPC, and subsequent lung metastasis noted include bilateral renal HPC 5 years after initial presentation.
Results: To our knowledge, this is the third reported case of bilateral metastatic renal HPC. After bilateral nephrectomy and the complete resection of the tumour the patient's blood pressure and blood glucose level returned to normal also with the influence of chemotherapy. During 2 years after surgery and chemotherapy, the patient had no evidence of hypertension and hypoglycemia. Whereas after 3 years the patient had come with stubborn hypoglycemia. Radiologic examination of the whole body revealed multiple metastasis both in liver and lung. Therefore, pazopanib therapy given to the patient for tumour recurrence and steroid therapy added for the control of stubborn hypoglycemia. The patient died 1 year after the second recurrence of the disease.
Conclusion: The present case indicated that surgery with chemotherapy provides satisfactory outcomes and appears to control the paraneoplastic syndromes in renal HPC. Furthermore, the present case showed the strong effect of corticosteroid therapy, which ameliorated symptoms of hypoglycemia.

E-PS-23-042
Prostatic metaplasia of the urinary bladder
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Objective: To review a peculiar reaction in urinary bladder associated with inflammatory changes and poorly understood pathogenesis, developing benign glandular foci of metaplastic prostatic tissue.
Method: Two cases of prostatic metaplasia of the urinary bladder were studied from a males of 37 and 68 years of age. Both were located at the dome of the bladder, with a size of 4 and 3 mm. One of them was closely situated to a small foci of superficial papillary urotelial carcinoma. Immunohistochemical studied was perform to assess the prostatic nature of the lesions.
Results: Lesions were composed by closely packed glandular acini lined with two cell types, flat basal cells and cylindrical luminal cells. Nearby von Brunn nest could be seen and a glandular change evolving into the clearly developed prostatic glands. Prostate specific antigen (PSA) was intensely positive, with p63 expression in basal layer. Cytokeratin 7 and 20 expression was seen with heterogeneous pattern. Alpha-methylacyl-CoA-racemase was weakly positive in one case.
Conclusion: A few cases of ectopic prostatic tissue are describe in bladder wall. The metaplastic change we present in transition with inflammatory reaction and von Brun nests is probably an underreported change similar to the other metaplastic lesions commonly seen in the bladder.

E-PS-23-043
A rare case of solitary fibrous tumour of the adrenal gland
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Objective: We describe a new case of solitary fibrous tumour (SFT) of adrenal gland with clinical presentation, radiologic studies, histopathologic features and provide a review of the relevant literature.
Method: We report a rare localization of SFT.
Results: A 52-year-old woman consulted for a right low back pain, without palpable mass. CT scan showed an adrenal well limited mass, measuring 11 cm which wasn't secreting on biology. The patient underwent a right adrenalectomy. At macroscopic examination, the mass was a well limited and encapsulated with a fleshy texture. It was lobulated and showed edematous, congestive and necrotic changes. Histological examination revealed a well-demarcated proliferation made of fairly monomorphic spindle cells arranged in short bundles or sometimes storiform and often without particular organization. The general appearance is heterogeneous with presence of densely cellular territories, alternating abruptly with less cellular territories of hyaline fibrosis or edematous or myxoid areas. The set is supplied by a vascular network where branched vessels sometimes adopting a staghorn morphology. There wasn't a significant pleomorphism or mitotic activity. The necrosis was rather ischemic. By immunohistochemistry, tumour cells expressed intensely and diffusely CD34.
Conclusion: The clinical course of SFTs has always been a problem. The malignancy criteria vary depending on the series and tumour location. The pleomorphism, hypercellularity and mitotic index (>4 mitoses per 10GCF) are mainly the indicators of a poor prognosis.

E-PS-23-044
Metastasis of colorectal carcinoma to kidney with in-situ growth pattern mimicking primary renal/urothelial neoplasm
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Objective: Metastases of cancer to kidney are unusual finding. Here we report a case of metastatic colorectal adenocarcinoma with in situ involvement of renal pelvis mucosa and collecting ducts thus simulating collecting duct carcinoma or primary enteric type adenocarcinoma arising in urothelium.
Method: A 61-year-old man with history of colorectal cancer underwent nephrectomy for left kidney tumour measuring 20 mm in diameter. Tumour involved cortex and medulla. Histopathological evaluation and immunohistochemical staining for CK7, CK20, CDX2, PAX8, beta-catenin and GATA3 was performed.
Results: The tumour was composed of well-formed or cribriform glands of intestinal type adenocarcinoma and invaded cortex and medulla. Desmoplastic stroma and areas of necrosis were apparent. The tumour grew underneath urothelium or lined focally pelvic mucosa with abrupt transition to the normal urothelium. Some renal tubules were lined with dysplastic columnar epithelium, resembling in-situ carcinoma. There was expression of CK20, CDX2 and beta-catenin (weak membranous positivity) in the main tumour, in-situ tubular component and tumoural lining of the pelvis. PAX8 and CK7 was expressed in surrounding renal tubules or urothelium, no expression in tumour nor in situ component was seen. GATA3 was expressed in urothelial lining of the pelvis only. The diagnosis of metastatic colorectal carcinoma was established, excluding the possibility of collecting duct carcinoma or primary enteric type adenocarcinoma arising in urothelium.
Conclusion: It is important to remember the possible involvement of pre-existing epithelial structures in metastatic cancer. Such a finding may mislead the diagnosis and falsely point to primary cancer of the involved organ—in our particular case the kidney.

E-PS-23-045
Primary localized amyloidosis of the bladder which mimics neoplasia
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Objective: Amyloidosis is a disorder with mainly extracellular deposition of misfolded protein. It can be primary, secondary or hereditary and the deposits can be systemic or localized. Amyloidosis of the bladder is a rare condition and generally localized. It mimics urothelial carcinoma clinically, cystoscopically, and radiologically.

Method: 63 years old woman was admitted to our hospital with macroscopic hematuria in 2013. On computed tomography, posterolateral and superior part of the bladder wall showed 2 cm thickness which was suspicious for tumour. Cystoscopy showed irregulary areas in the posterolateral side of the bladder. Curetted material was obtained by transurethral resection of bladder.
Results: Biopsies revealed dense homogenous eosinophillic material in the lamina propria which stained orange red on congo red stain and showed apple green birefringence on polarization. There was no evidence of urothelial carcinoma or carcinoma insitu. There were no signs of systemic amyloidosis at the time of diagnosis and during the 36 months of follow-up.
Conclusion: Amyloidosis of the bladder is a rare condition which can be easily confused with urothelial carcinoma because of its appearance on imaging as well as on cystoscopy. Histological examination is a requirement for definitive diagnosis.

E-PS-23-047
Mantle cell lymphoma of the prostate—a report of case
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Objective: Mantle cell lymphoma of the prostate, primary or secondary, is rare. Less than a hundred cases have been reported in the literature. This scarcity is causing the delay in diagnosis usually done at the advanced stage of the tumour.
Method: We report the case of a 67 year old man with no medical history, the history of his symptoms back to 4 months before admission by the installation of dysuria. Ultrasound revealed a prostatic hypertrophy. The patient had a resection by bladder size. Histological examination concluded prostatic localization of a mantle cell lymphoma, confirmed by immunohistochemical study.
Results: Mantle cell lymphoma of the prostate is often discovered incidentally at autopsy or after surgery. The primary involvement of the prostate is rarely reported unlike secondary locations. The average age is 62 years. The clinical symptoms are nonspecific. Imaging is also nonspecific. The diagnosis is histological based on prostate biopsy. This is a malignant non-Hodgkin lymphoma Small cell, cells are monomorphic with sometimes indented nuclei. Tumour cells usually express CD20, CD5 and Cyclin-D1.
Conclusion: The prostate localization of mantle cell lymphoma is unusual and rare. Therapeutic consensus is not established. In first line, the teams propose chemotherapy in combination or not with radiotherapy.

E-PS-23-048
An unusual case of T-cell lymphoma of male urethra
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Objective: Primary T-cell lymphoma of male urethra is an extremely rare location for this type of cancer. We report the case of a 68 years old male patient who presented to the hospital with urinary obstruction symptoms that started 2 months prior. Clinical exam describes an urethral obstructive mass. Therefore, segmental penile urethrectomy is performed.
Method: Surgical specimen was grossly examined and processed in the pathology department. Hematoxylin eosin and van Gieson colored slides were examined under the microscope. CD3, CD25, CD30, CD20 and Tdt markers were used for immunohistochemistry study.
Results: Histopathology exam reveals a diffuse neoplastic proliferation with lymphoid features. The cells are medium sized, pleomorphic with vesicular nuclei, 2–3 small nucleoli and high mitotic index. The tumour involves male urethra and infiltrates cavernous bodies. The patient doesn't complaints about other signs and symptoms. Lab and imagistic results are within normal range. Tumour cells are positive for CD3 and CD25, with negative results for CD 30 and Tdt.
Conclusion: Primary T-cell lymphoma of male urethra is a rare form of cancer with less than 5 cases reported in the literature. The tumour is extremely aggressive and can extend to the surrounding structures in a short period of time stressing the need for prompt diagnosis and therapy.

E-PS-23-049
Adrenal myelolipoma: A study of five cases
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Objective: Adrenal myelolipoma (ML) is a rare benign tumour, which is usually incidentally discovered. It was first described by Gierke in 1905. It represents 5 % of all adrenal gland tumours. It is composed of mature adipose tissue and bone marrow elements. ML is usually unilateral and rarely bilateral.
Method: We report five cases of adrenal ML over 10 years from 2006 to 2016. A retrospective study was done by reviewing medical records. Demographic, imaging and clinicopathologic features are presented.
Results: All patients were women. The mean age was 45 years, with ages ranging from 23 to 59 years. Four patients were diagnosed incidentally with a unilateral ML. The fifth patient presented bilateral ML revealed by flank pain. Initial diagnosis was based on imagery. All patients underwent a surgical resection. Definitive diagnosis was made by pathologic findings that showed adrenal gland tumour comprising mature adipose tissue with bone marrow elements. Follow-up of all patients showed no recurrence.
Conclusion: The origin of ML remains unclear. Some theories have been discussed, including remnants of foetal bone marrow or misplaced haematopoietic cells. It is confirmed by histopathologic examination. Surgery becomes necessary for symptomatic cases or large tumours that cannot be reliably diagnosed.

E-PS-23-050
Primary sclerosing epithelioid fibrosarcoma of the kidney in a young patient: Case report and review of the literature
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Objective: Primary sclerosing epithelioid fibrosarcoma of the kidney (PSEFK) is a recently described neoplasm occurring in a wide range of ages. We describe a case of a 12-year-old girl in which the diagnosis was difficult, mostly due to the age of presentation and unfamiliarity with the entity.
Method: The clinicopathological features of a case of PSEFK are described, with a review of the literature.
Results: A 12-year-old girl underwent nephrectomy for a 5 cm right renal tumour. Grossly, it was firm and well circumscribed. Histologically it was a spindle and epithelioid cell tumour with eosinophilic or clear cytoplasm, moderate atypia and a densely hyalinised stroma with entrapped hyperplastic renal tubules. Mesoblastic nephroma and mixed epithelial-stromal tumour were considered initially, but upon review of the literature, PSEFK was recognized as the most likely diagnosis. Positivity for MUC4 and the presence of rearrangement of the EWSR1 gene confirmed the diagnosis. Seven other cases have been described to date, one of them with similar histological features.
Conclusion: PSEFK can occur in younger patients. The presence of entrapped hyperplastic renal tubules may be reminiscent of biphasic

neoplasms, but increased awareness of the entity and complementary diagnostic tools may help in its correct classification.

E-PS-23-051

Histopathological features in undifferentiated germinative testicular tumours

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Objective: Primary non-Hodgkin's lymphoma of the testis is an uncommon disease and that represent 1–2 % of all non-Hodgkin lymphomas. It accounts for about 9 % of testicular neoplasms. Histologically, 80 % to 90 % of primary testicular lymphomas are diffuse large-cell type with B cell phenotype, but isolated cases of other histological subtypes have been described such as Burkitt and burkitt's-like types in 10–20 % of cases, mainly in HIV+ patients.
Method: In many cases, the frequency and histologically type of those tumours can be confused with undifferentiated embryonar testicular carcinoma. In both situations the prognosis is unpropitious, but lymphoma needs radiotherapy before and after surgery depending by stage. Embryonar carcinoma of testis is treating by chemotherapy in conventional-dose of cytostatic.
Results: In this paper we present a case report with primary non-Hodgkin testicular lymphoma in one 34 years old patient. The particularities of case are the age of patient and tumour morphological features witch can be confused with undifferentiated seminoma.
Conclusion: This paper demonstrates the usefulness of immunohistochemistry in pathology diagnoses especially in locating rare diseases at several levels.

E-PS-23-054

Evaluation of cellular transformation and tumour aggressiveness factors expression in urinary bladder lesions in relation to bilharziasis

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Objective: Evaluation of CD44 and EGFR genes expression as markers of aggressiveness factors expression in urinary bladder lesions in relation to bilharzasis.
Method: Urinary bladder biopsies were subjected to histopathological examination, Immunohistochemical and FISH technique.
Results: Our results showed that cases of bilharzial cystitis showed significantly higher percentages and higher scores of CD44 expression compared to non-bilharzial cystitis ($p < 0.01$). Bilharzia (TCC+SCC) cases showed significantly higher scores of both EGFR and CD44 expression, compared to non-Bilharzial (TCC+SCC) cases. EGFR protein and gene were upregulated in malignant urothelial lesions namely TCC and SCC, with significant correlation with grade of neoplasia. CD44 expression was also upregulated in urothelial bladder lesions especially SCC and was correlated positively with both the grade and stage of malignancy. All examined control, cystitis and adenocarcinoma cases showed negative results for EGFR gene activation by FISH technique. All cases of bilharzial TCC showed positive gene expression which is considered significant when compared with other non-bilharzial TCC ($p < 0.01$). No significant difference in gene expression was detected between bilharzial and non-bilharzial cases of SCC ($p > 0.05$).
Conclusion: Grouping cases of (TCC+SCC), showed a significantly higher scores of both EGFR and CD44 expression in bilharzial patients compared to non-bilharzial patients, pointing to the possible role of bilharzial infection in progression of cancer and can be used as a markers. TCC subgroups showed variable expression of EGFR and CD44, denoting possibly different molecular backgrounds.

E-PS-23-055

MiT family translocation-sssociated renal cell carcinoma: A single institution experience

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Objective: MiT family translocation renal cell carcinomas (TRCC) are malignant neoplasms that are mostly seen in young adults or children. They were first published in the 2004 WHO classification as Renal Carcinomas Associated with Xp11.2 translocations /TFE3 gene.
Method: There are many types of TFE3 and TFEB transcription factor gene fusions that cause TRCC. Different histologic patterns can be seen in this tumours; but the major component is usually clear cells with papillary structures and cell islands encircled with thin walled capillaries.
Results: We have collected our 4 TRCC cases that were diagnosed between the years 2010 and 2015. Of these 4 cases only 1 is a female and the ages of the patients are between 6 and 16. None of our patients had a history of cancer or familial background with tumours. All of our patients were in advanced stage such as 2 patients stage 3 and 2 patients stage 4.
Conclusion: MiT family translocation renal cell carcinomas can be seen in adults also but they are mostly pediatric tumours. They have different histologic appearances like papillary, alveolar, tubular, etc. They have to be in mind while distinguishing renal cell carcinoma subtypes.

E-PS-23-056

Corticomedullary mixed tumour of the adrenal gland: A case report

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Objective: Corticomedullary mixed tumours are rare primary benign tumours of the adrenal gland and approximately 20 cases have been reported in the literature. Herein, we describe a case of corticomedullary mixed tumour of the adrenal gland and review its clinical and histological features.
Method: The surgical specimens were formalin-fixed and paraffin embedded. The sections were stained with routinary H&E. Immunohistochemistry was performed.
Results: A 36-year-old woman presented with hypertension, obesity and hepatomegaly. Abdominal magnetic resonance imaging showed a left heterogeneous incidental adrenal mass and patient underwent a left adrenalectomy. On gross examination, resected tumour was a single well-circumscribed ovoid mass measuring 4.5×4 cm and confined within the normal adrenal gland with cystic areas. Histological examination showed a single tumour mass composed of an admixed population of adrenal cortical and medullary cells. Immunohistochemical studies were positive both for cortical cells (inhibin-α and synaptophysin) and medullary cells (Chromogranine A). Microscopic and immunohistochemical findings were compatible with corticomedullary mixed tumour of the adrenal gland.
Conclusion: Corticomedullary mixed tumour of the adrenal gland is very uncommon and usually discovered on histological examination.

E-PS-23-059

Highly proliferative FGFR3-positive bladder tumours: A special subgroup?

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Objective: Activated FGFR3-signaling in bladder tumours is mainly associated with non-invasive low grade tumours and favorable outcome. However, there are FGFR3-overexpressing tumours showing high tumour cell proliferation. Our study aims to decipher the relevance of FGFR3-overexpression and proliferation for histopathological grading and risk stratification.
Method: N = 81 (n = 21 pTa, n = 59 pT1-4, n = 1 pTx) morphologically high grade tumours were analyzed for immunohistochemical expression of FGFR3, Ki67, p53 and keratin 20. Additionally, hotspot mutation analysis of FGFR3 and TP53 and FISH for FGFR3 amplification and break apart events was performed.
Results: We found FGFR3 point mutations in 47.6 % (10/21) of pTa and 49.2 % (29/59) of pT1-4 tumours. Only one sample had FGFR3 gene amplification and 11.3 % (8/71) showed >15 FGFR3 break apart events. 27.6 % (16/58) of analyzed tumours exhibited TP53 mutations, and one sample showed FGFR3/TP53 mutation. In Kaplan-Meier analysis patients with combined FGFR3-Ki67 overexpression tend ($p = 0.066$) to show a shorter recurrence-free survival (mean RFS: 11.6 months ± 2.8) when compared to all other combinations of protein expression (mean RFS: 20.7 months ± 4.3).
Conclusion: By now, our results encourage classification of highly proliferative FGFR3-overexpressing tumours as high grade tumours. However, further studies are necessary for addressing the impact of FGFR3-Ki67 overexpression on tumour progression and overall survival.

E-PS-23-060
Parameatal urethral cysts in prepubertal males
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Objective: Cyst formation in the parameatal area of the urethra is an uncommon entity. It was first reported in two males in 1956 by Thompson and Lantin. Benign and usually asymptomatic, these cysts have limited mention in available medical literature.
Method: We report a case of a 20 year-old male having a spherical, cystic swelling 0.8 cm in size at the external urethral meatus.
Results: The diagnosis of parameatal urethral cyst was made and the cyst was excised. Histopathological examination revealed a monolocular cyst lined with transitional cells. The postoperative period was uneventful.
Conclusion: Parameatal cysts are a benign, usually asymptomatic condition that may contain a variety of epithelial types. The cysts may resolve spontaneously in neonates but are also easily excised with minimal risk of recurrence.

E-PS-23-062
One adenocarcinoma metastising to another: A rare case of prostate/lung tumour to tumour metastasis
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Objective: To report an unusual case of a prostate adenocarcinoma metastising to an occult lung adenocarcinoma.
Method: A 70-year-old male presented with signs and symptoms of acute heart failure. He had a 9-year history of prostate adenocarcinoma (Gleason 7) treated with radiotherapy and hormonotherapy. The patient had poor compliance to the therapy and the disease relapsed, showing osteolytic lesions and a rise in seric prostate specific antigen (1416 ng/ml).
Results: Echocardiography showed a massive hemopericardium, which cytologic examination revealed epithelial malignant cells negative for PSA, but unexpectedly positive for TTF-1 and CK7 immunostains. These findings, together with the imaging results, were highly suspicious of an occult primary lung carcinoma, so an atypical lung ressection was performed. Histologically, two components were identified: one cribriform, PSA positive, TTF1 and CK7 negative; the other predominantly solid, PSA negative, TTF1 and CK7 positive. These distinct properties were diagnostic of a primary lung adenocarcinoma being metastised by a prostate adenocarcinoma.
Conclusion: To our knowledge, this is one of the few reports of a tumour to tumour metastasis, namely a prostatic adenocarcinoma metastising to a lung adenocarcinoma. Pathologists should be aware of this phenomenon, especially when an initial pathology exam defies the rationale of a clinical case.