Uro 09

BLADDER CARCINOGENESIS AND ECOGENETICS: A STUDY ON THE ROLE OF N-ACETYLTRANSFERASE POLYMORPHISM AND VARIOUS RISK FACTORS IN BLADDER CANCER

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Together with cultural habits like cigarette smoking and abuse of certain drugs and artificial sweeteners, various environmental and occupational chemicals (arylamines and related compounds) are estimated to attribute about 50-60% of human bladder cancer incidents. In this respect,activity of N-acetyltransferase (E.C. 2.3.1.5) plays an important role in the detoxication of these carcinogenic substances. The interindividual variation in hepatic enzyme activity is considerable; the genetically determined trait leads to a bipartition in slow and rapid acetylators (H.W. Goedde, Internist 15,27,1974).
In the present study, the acetylator status and anamnestic risk factors like smoking, occupational exposure to carcinogenic chemicals and drug abuse of more than 100 North German patients with bladder carcinoma were investigated. Recently, several similar studies have been published from other countries displaying the significance of slow acetylation for bladder carcinogenesis (D.A.P. Evans, L.Z.Eze, E.J.Whibley, J.med. Genet. 20,330,1983).
A highly significant association between acetylator status and bladder cancer was also confirmed in our study (61.9% of the patients compared to 42.9% in the healthy control group). Smokers (82 patients; 78.1%) exhibited a slight excess of slow acetylators. The percentage of slow phenotype in patients stating occupational exposure to potential bladder carcinogens (n=27; 25.7%) was significantly higher compared to the whole patient group (70.4%). 18 patients (17.1%) used analgetics or artificial sweeteners over a period of more than 5 years. Staging and grading data revealed more frequently superficial and highly differentiated tumours among slow acetylators, especially among smoking patients with an additional occupational risk factor.

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Uro 10

COMBINED IMMUNOHISTOCHEMICAL STUDIES AND PROLIFERATION KINETIC ON UROTHELIAL ATYPIAS AND CARCINOMAS IN THE SAME MATERIAL.

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Combined immunohistochemical studies and proliferation kinetic were performed on identical slides of atypias and carcinomas of the urinary bladder mucosa. Those studies were designed to investigate a possible correlation between histological, immunohistochemical, and cell kinetic characteristics.
71 tissue specimens that had already been treated autoradiographically, were also examined immunhistochemically.
Labelling index inreases from 1,4% in slight to 20% in marked urothelial atypia. CEA reaction in slight atypia is slight or moderate, slight, moderate or distinct in moderate atypia, and moderate to distinct in carcinoma in situ. TPA always shows moderate to distinct reactions. Cell kinetically, urothelial carcinomas, yield similar graduations. They were positive for CEA in 70% and for TPA in 100%. In G 0 and G I carcinomas negative and slightly positive reactions predominate, poorly differentiated lesions yield predominantly distinct reactions. In all grades, TPA ranges from slight to distinctly positive. As in cell kinetic analyses, there is a relation ship between differentiation grade and stage for CEA expression. This does not apply for TPA.
The results permit us to draw conclusions on the different biological and histogenetic behavior of urothelial carcinomas and atypias. There are undoubtedly differences in the behavior of papillary exophytical and solid invasive carcinomas in terms of both cell kinetics and immunohistochemistry.

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DIFFERENT TREATMENT STRATEGIES IN PATIENTS WITH METASTATIC BLADDER CANCER

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In the last two years, several papers were published about high remission rates in patients with metastatic bladder cancer treated with polychemotherapy. Most of the patients however are more than 55 years old and often in poor clinical condition, so intensive chemotherapy might be not tolerated very well. To find out, whether median survival time could be extended by treating these patients chemotherapy, and whether side-effects are tolerable.
Group A no therapy (n=7); Group B Combination chemotherapy (n=6) Cisplatinum 100 mg/m^2 d.1, Methotrexate 40 mg/m^2 d.1 and 8, Bleomycin 30 mg d. 1 and 8; Group C Combination chemotherapy (n=14) Cisplatinum 100 mg/m^2 d.1, 5 Fluorouracil 1000 mg/m^2 25^h continous infusion. Repetition in both chemotherapy groups d.21. The three groups were comparable concerning site of metastases,age, performance status. 25 men and 2 women were allocated to the arms of the study, mean age was 61.3 years (range 44-75).
Results Group B complete remission 2, partial remission 2, minor response 2. Main side-effects were: severe mucositis and bone-marrow hypoplasia with septicemia in 2 patients. Group C complete remission 4, partial remission 2, minor response 3, no change 2, progression 1. Main side-effects were: mild mucositis.
Median duration of response to chemotherapy was in both groups 7 month (range 2-13). Mean survival time was in group A 6 month, in group B and C 10.5 month.
Conclusions The remission-rates in Group B and C are similar, but the Cisplatinum/5 Fluorouracil combination was superior concerning side effects.

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URINARY BLADDER CANCER RESPONDS TO CHRONO-CHEMOTHERAPY.

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Locally advanced (stage C and D_1) transitional cell carcinoma of the urinary bladder (TCCB) usually causes death within two years. Metastatic disease (stage D_2) kills patients (pt) within a few months. We have treated 43 pt with stage D_2 TCCB. Of 35 pt evaluable for response, 1/3 had failed prior radiation therapy, and half of them had undergone prior cystectomy. 13 additional, previously untreated pt with stage C (4) or D_1 (9) TCCB had adjuvant therapy following radical cystectomy. Nine monthly cycles of doxorubicin 60 mg/m^2, followed 12 hours later by cisplatin at 60 mg/m^2 were given. This schedule was randomly begun at either 6 am or 6 pm.
57% of the pt with metastatic disease responded objectively for at least 3 months. 8 of the 20 responders had complete disappearance of cancer (CR, 20%). The median duration of CR was twice that of nonresponders ($p<0.05$). Median survival for pt with CR was 27 months (mo) (range 11-93+ mo) compared to 10 mo (range 4-25) for partial responders. Three of the complete responders are alive and well without evidence of disease at 29, 48, and 93 mo after the initiation of chemotherapy, off all chemotherapy for 14 mo to 7 years. 11 of 13 adjuvant patients (eight of whom received the full nine courses of treatment) are alive and free of disease after a median follow-up of 30 mo (range 7-50+ mo). These patients have been off all anticancer therapy for a median span of 15 mo.

Full doses of this 2-drug combination given over a relatively long span and using chronobiological schedules have yielded good treatment results. The fact that 3 patients with biopsy-proven metastatic TCCB have been taken off all chemotherapy without disease recurrence may portend its chrono-chemotherapeutic curability.

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