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Solitary fibrous tumor of the adrenal gland – its biological behavior and report of a new case

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Abstract

Introduction: A solitary fibrous tumor (SFT) is an uncommon neoplasm of mesenchymal and probably fibroblastic origin, occurring mainly in the extremities, and pleura. However, a primary involvement of endocrine organs is rare and even exceptional when found in the adrenal gland. Hereby, we describe the 10th report of an adrenal SFT.

Case presentation: A 77-year old man was diagnosed with a lesion in the right adrenal gland during a urologic indicated computed tomography (CT). No symptoms and laboratory anomalies were reported indicating any endocrine activity. Follow up CT-scans showed progressive growth of the nodule for which the patient underwent laparoscopic right adrenalectomy. Histological examination showed a hypercellular spindle cell neoplasm with elongated nuclei and a low mitotic index. The vessels were arranged in a hemangiopericytoma-like pattern with a slight sclerosing appearance. Immunohistochemistry showed a positive staining of neoplastic cells for STAT6, CD-34 and Bcl-2. Translocation analysis using RT-PCR showed no NAB2-STAT6 fusion. The specimen was confirmed as a hypercellular variant of an adrenal SFT.

Discussion: SFT is a rare neoplasm when occurring in the adrenal gland. Differential diagnosis can be broad because of no defined pathognomonic morphological characteristics. However, NAB2-STAT6 gene fusions are considered a molecular hallmark of SFTs. Therefore, STAT6 immunohistochemistry is a valuable diagnostic tool in differentiating between SFT and histologic mimics. After diagnosing SFT, its biological behavior is difficult to predict. SFTs are mostly benign tumors. Nonetheless, a histological benign-appearing SFT can show malignant clinical characteristics impeding assessment of proper follow up. However, malignancy has not been previously reported in any adrenal SFT case report.

Keywords: Solitary fibrous tumor, Adrenal gland, Incidentaloma, Case report, Adrenalectomy

Background

Solitary fibrous tumor (SFT) is an uncommon neoplasm from mesenchymal and probably fibroblastic origin, initially described as pleural tumor (Klemperer & Rabin, 1931) but more frequently encountered at a variety of extrapleural sites including visceral organs (Morimitsu et al., 2000). However, presentation of SFT in endocrine organs is rare and even exceptional when presenting in the adrenal gland. We report, to our knowledge, the 10th case of a primary SFT in the adrenal gland and summarize what is known about its biological behavior.

Case presentation

In June 2018, a 77-year-old man visited a general practitioner with complaints of relapsing urinary tract infection. He had a medical history of Crohn's disease, paroxysmal atrial fibrillation, hypertension, and relapsing renal colic. The patient was referred to a urologist in his local hospital. There were no relevant physical examination findings. However, due to the history of

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complaints, the urologist had an abdominal computed tomography (CT) performed. This scan showed a bilateral non-obstructive nephrolithiasis without congestions and a lesion in the right adrenal gland. Both findings were present on earlier CT-scans but discarded. However, a growth of the lesion was determined, now measuring 3.5 × 2.3 cm. A follow up plan had been set up consisting of a new CT-scan in 6 months. This CT-scan showed a progressive growth of the lesion, measuring 4.1 × 3.5 cm. The absolute wash-out of the nodule correlated with an adrenal gland adenoma. Hormonal evaluation ruled out Cushing's syndrome and pheochromocytoma. The mass in the adrenal gland was considered to be a growing incidentaloma, which is an indication for adrenalectomy. The patient was referred to the surgical department of our hospital, a tertiary referral hospital for adrenal lesions. A new abdominal CT-scan showed further growth of the lesion, now measuring 4.5 × 3.4 cm (Fig. 1). A laparoscopic right adrenalectomy without complications was carried out and the patient was discharged 1 day postoperatively. On short-term follow up, there were no complications and the patient recovered well.

Concerning pathological examination, a 10 × 7.5 × 3.5 cm specimen contained an adrenal, well-circumscribed, encapsulated solid tumor mass with elastic consistency and a gray-white color. The mass measured 4.5 cm in diameter adjacent to the cortex of the right adrenal gland. The cutting surface showed some focal hemorrhagic areas. However, no evident infiltrative growth, necrosis, cystic formation or degeneration was seen. Microscopic examination of the pre-existent adrenal gland showed no necrosis or other anomalies. The microscopic aspect was described as a hypercellular neoplasm with spindled to ovoid-shaped cells divided into fascicles without any pattern. There was only a minimal amount of interstitial fibrosis present. The neoplasm showed a hemangiopericytoma-like vessel pattern with slight sclerosis. Furthermore, the neoplastic cells were uniform and elongated with polygonal vesicular nuclei, granular chromatin, sometimes a small nucleolus and small amounts of eosinophilic cytoplasm. The mitotic activity was low (mitotic index of 1 per ten high-power fields) without focal necrosis. On immunohistochemistry, neoplastic cells were positive for STAT6, CD-34, and Bcl-2. KI-67 showed a focally positive expression in accordance to the mitotic index. The markers epithelial membrane antigen (EMA), smooth muscle actin (SMA), S-100, desmin, CD-117, and MNF116 were unreactive. Beta-cathenin showed no evident nuclear expression. (Fig. 2) After this analysis, the specimen was sent for second opinion and histologically confirmed as a hypercellular variant of an SFT with low degree of mitosis and fibrosis. Translocation analysis using RT-PCR showed no NAB2-STAT6 fusion. The exact description of the protocol used for RT-PCR analysis is reported by Vogels, et al. (Vogels et al., 2014).

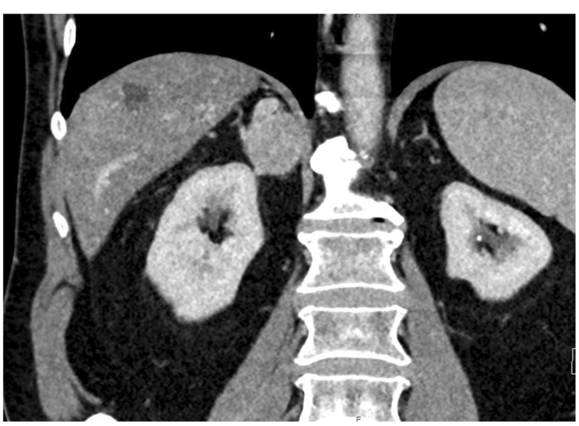

Fig. 1 Delayed contrast-enhanced abdominal computed tomography scan of the solid lesion in the right adrenal gland. The lesion is measuring 4.5 × 3.4 cm

Immunohistochemistry

Tissue fixation and processing were performed using standard methods. Immunohistochemical stainings were performed using fully automated protocols on Ultra Immunostainer (BenchMark XT, Roche, USA). Sections were stained with the following antibodies: CD34 (clone OBEnd10; Ventana Medical Systems, Tuczon, AZ), STAT6 (clone YE361; ABCam, Cambridge, UK). All stainings were visualized using 3,3′ diaminobenzidine.

Discussion and conclusions

Histologically, characteristics of adrenal and non-adrenal SFT can range from mainly cellular to fibrous features. The more fibrous end of the spectrum tends to show alternating hypercellular and hypocellular areas, where in hypercellular areas a patternless architecture of spindled to ovoid-shaped cells can be found. Cellular forms of SFT show a monotonous architecture with moderate to high cellularity and a hemangiopericytoma-like vessel pattern, consisting of thin-walled 'staghorn' branching vessels (Hornick, 2018). Morphological characteristics of SFTs independent of tumor location are not defined as pathognomonic. Therefore, the differential diagnosis can be broad. It is easy to confuse SFT with deep benign fibrous histiocytoma, cellular angiofibroma, myofibroblastoma, spindle cell lipoma, cellular schwannoma, and low-grade dedifferentiated liposarcoma. Histological features exclude the possibility of spindle cell lipoma while histologic mimics can be differentiated based on the immunohistochemical profile in which STAT6 staining is of great importance (Hornick, 2018; Fisher et al., 2015; Fletcher et al., 2013). CD34 might be a useful diagnostic

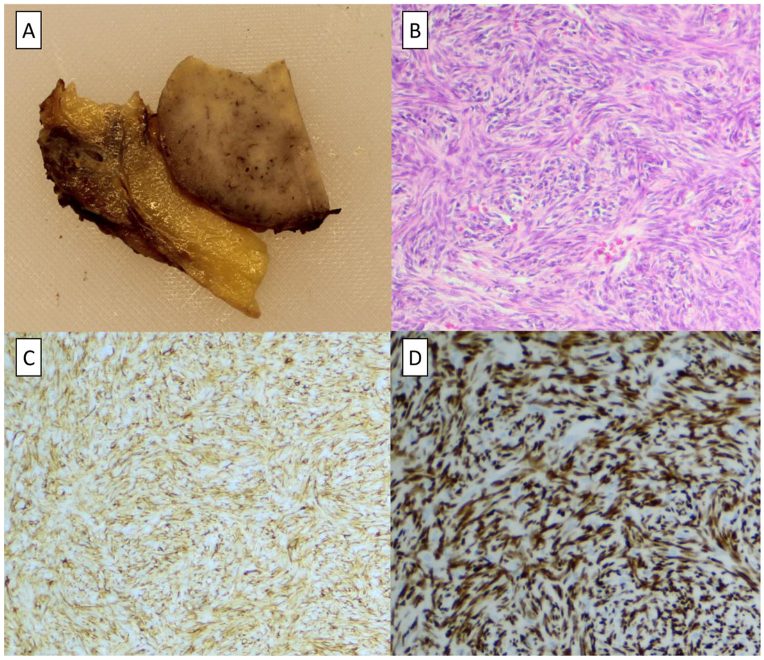

Fig. 2 Immunohistochemistry stainings of the resected lesion. **a** Resected right adrenal mass of 10 × 7.5 × 3.5 cm. **b** HE staining, showing fascicles of spindled to ovoid-shaped cells and a hemangiopericytoma-like vessel pattern, original magnification × 100. **c** Diffuse positive CD-34 immunostaining, original magnification × 100. **d** Diffuse positive STAT6 immunostaining, original magnification × 200

marker despite the lack of expression in 5–10% of all SFTs (Fisher et al., 2015). However, nuclear STAT6 expression is found in almost all SFT cases and very limited in other mesenchymal tumors. Therefore, STAT6 is an important immunohistochemical marker to distinguish SFT from histologic mimics with a sensitivity of 98% and a specificity close to 100% (Yoshida et al., 2014; Doyle et al., 2014a). Expression of STAT6 might be present in the morphologic mimics dedifferentiated liposarcoma and deep benign fibrous histiocytoma when located in the retroperitoneum and abdominal cavity which may be a potential diagnostic pitfall (Vogels et al., 2014). In 10% of dedifferentiated liposarcomas, nuclear expression of STAT6 is found, due to amplification of a STAT6-containing chromosomal region containing essential oncogenes (Doyle et al., 2014b). Besides confirmation of MDM2 and CDK4 expression using immunohistochemistry, translocation analysis of NAB2-STAT6 may be helpful (Vogels et al., 2014).

NAB2-STAT6 gene fusions are considered a molecular hallmark of SFT since it is a distinct genetic feature of SFT. This gene fusion results in nuclear STAT6 upregulation and overexpression (Chmielecki et al., 2013). Occurrence of these possibly pathognomonic gene fusions are reported in the wide range of 55 to 100% of all SFT cases and consist most commonly of NAB2 exon 4-STAT6 exon 3 and NAB2 exon 6-STAT6 exon 17 conjunction (Mohayeri et al., n.d.; Robinson et al., 2013). In this case, no NAB2-STAT6 fusion was found despite diffuse nuclear STAT6 positivity. Absence of NAB2-STAT6 fusion transcription might be explained by alternative or complex genetic rearrangements in which different exons or chromosomal rearrangements could be involved, not detectable with the used primer sequence (Vogels et al., 2014; Tai et al., 2015). Besides, there are probably unknown fusion variants that need to be revealed in the future or it might be possible that uncommon fusion variants, for example STAT6-TRAPPC5 reported by Vogels et al (Vogels et al., 2014), are not detected by RT-PCR assay. Furthermore, sufficient interpretation of RT-PCR analysis might be impeded by presence of complex breakpoints (Vogels et al., 2014).

In the vast majority, SFT independent of tumor location pursue a benign biological behavior (Gebresellassie et al., 2019). However, a broad spectrum of biological behavior is known. 10% of all SFT cases show recurrence and metastasis, even years after resection (Hornick, 2018; Treglia et al., 2014). These malignant lesions are mostly located in the mediastinum, peritoneum, retroperitoneum, and pelvis. Metastases mainly spread towards lungs, liver, and bones (Gengler & Guillou, 2005). Malignant potential is associated with metastatic disease at presentation, a tumor size of ≥15 cm, infiltrative margins, hypercellularity, nuclear atypia, a high mitotic index (≥4 per 10 HPF), and sites of tumor necrosis (Hornick, 2018; Gebresellassie et al., 2019). Additionally, NAB2 exon 6-STAT6 exon 16/17 conjunction, which is the second most common NAB2-STAT6 genotype, is associated with more aggressive clinicopathologic characteristics. This genotype/phenotype variant mostly occur in extra-thoracic SFTs, mostly seen in young patients (Hornick, 2018; Akaike et al., 2015). However, no prognostic differences in disease free-survival are seen between fusion variants (Vogels et al., 2014). Besides, correlation between morphologic findings and clinical outcome can be quite difficult. In rare cases, a histological benign-appearing non-adrenal SFT shows malignant biological behavior (Hornick, 2018). However, malignancy has not been previously reported in any adrenal SFT case report (Kuribayashi et al., 2019).

The clinical behavior of adrenal SFT is considered as slow growing without any endocrine function (Toniato et al., 2014). However, possible paraneoplastic manifestations, prognostic factors or risk factors are not identified yet (de Perrot et al., 1999). Because of these limitations in knowledge of clinicopathologic and biologic characteristics and therefore no reliable predictors of biological behavior over time, it is difficult to make an evident statement regarding follow up of an adrenal SFT (Hornick, 2018). Generally benign cases, which mostly show no characteristics associated with malignant potential, and absence of NAB2-STAT6, probably need a shorter period of follow up in case no recurrence is objectified 6 months postoperatively. However, joining of NAB2 exon 4 to STAT6 exon 2/4 are associated with mostly benign behavior (Barthelmeß et al., 2014). These cases could be eligible for shorter follow up as well. Presence of malignant potential or in case of relatively young patients, it should be considered to lengthen the period of follow up as there is still uncertainty regarding a prognosis in adrenal SFTs. However, in order to provide an appropriate follow up for an adrenal and non-adrenal SFT, it is of utmost importance to get insights in the clinicopathologic characteristics in the future.

In this case, the patient was referred to this own hospital after a postoperative appointment. The tumor was considered as non-aggressive due to low mitotic index and absence of NAB2-STAT6 fusion, and radical resection of the mass. Since these relative benign clinicopathological characteristics and older age of the patient, a limited period of follow up was set up.

Concluding, an adrenal SFT should be part of the differential diagnosis when suspecting an incidentaloma. However, no radiologic characteristics are known. Therefore, surgical resection is necessary to obtain the diagnosis SFT, which is also the appropriate therapy since its biological behavior is not quite well understood. Our case, which is to our knowledge, the 10th report of an adrenal SFT, can contribute to obtain insights in biological behavior and follow up of this rare neoplasm.

Abbreviations

Bcl-2: B-cell lymphoma 2; CD: Cluster of differentiation; CT: Computed tomography; EMA: Epithelial membrane antigen; HPF: High-power field; MNF: Myocyte nuclear factor; SFT: Solitary fibrous tumor; SMA: Smooth muscle actin; STAT6-NAB2: Signal transducer and activator of transcription 6-NGFI-A binding protein; STAT6-TRAPPC5: Signal transducer and activator of transcription 6-trafficking protein particle complex 6A

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Authors' contributions

SH wrote the manuscript under supervision of JL. IV performed histological examination of the tumor. JL and PB were the patient consultants. JL performed the surgery. All authors read and approved the final manuscript.

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Ethics approval

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Consent for publication

Patient consent was obtained for publication of this article.

Competing interests

The authors declare that they have no competing interests.

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