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CASE REPORT

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Solitary fibrous tumour of the adrenal gland associated with pregnancy

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Abstract Solitary fibrous tumour (SFT), first described as a pleural lesion, has been reported in several extrathoracic sites over the past 10 years. We describe a SFT of the left adrenal gland incidentally discovered in a 23-year-old, 22-week pregnant woman and characterised by a rapid growth during the third trimester of pregnancy. Elevated serum and urinary levels of cortisol and elevated blood levels of delta 4 androstendione and 17-OH progesterone were observed. After spontaneous delivery, the patient underwent laparoscopic resectioning of the mass and of the left adrenal gland from which the tumour was apparently originating. The kidney was not involved, and no other abdominal tumours were found. Histological and immunohistochemical features were typical of SFT of pleura and other locations. Only one case of adrenal SFT is on record, and the adrenal gland is to be added to the long list of extrathoracic locations of SFT. The association with pregnancy was a previously unrecognised event in SFT. The focal expression of progesterone receptors in the tumour cells may be related to pregnancy. This observation prompted an analysis of steroid hormone receptors in SFT of classical sites (pleura). Two of five cases had focal progesterone receptors too, a finding which deserves further investigations in a much larger series of SFTs.

Keywords Solitary fibrous tumour · Adrenal gland · Pregnancy · Immunohistochemistry

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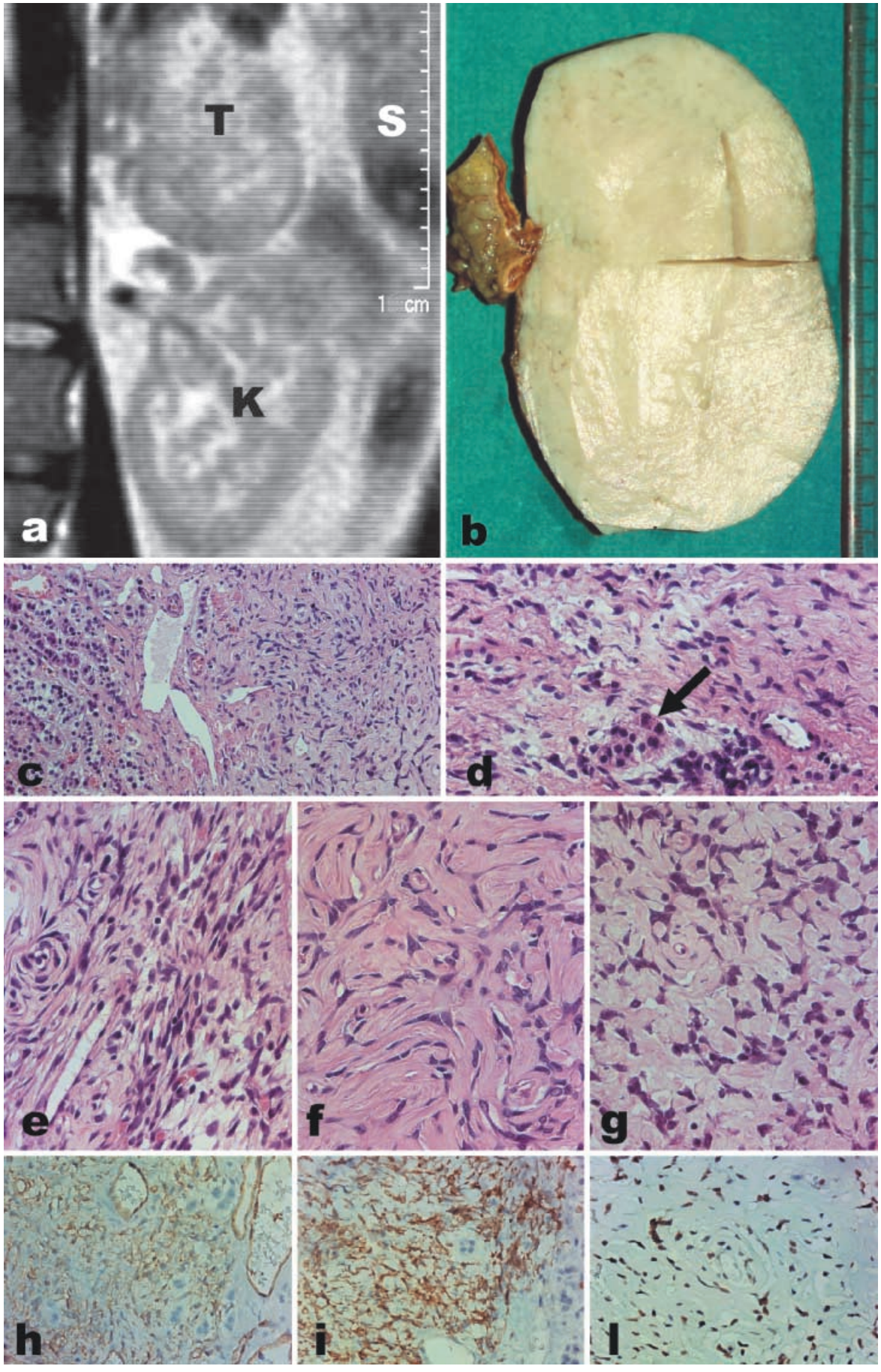
Introduction

Solitary fibrous tumour (SFT) is a spindle cell tumour which occurs most frequently in the pleura and other serosal surfaces. If encountered in soft tissues, the diagnosis of this neoplasm may be difficult because of the confusion with a great variety of soft tissue neoplasms [24]. First described in 1931 by Klemperer and Rabin [17] as localised fibrous mesothelioma, the name, the histogenesis, the biologic behaviour and the criteria of diagnosis of this tumour have been the subject of much debate. Subsequently, it has been referred to as subserosal fibroma, pleural fibroma, localised benign mesothelioma, submesothelioma and localised fibrous tumour of the pleura [1]. It was considered of mesothelial, submesothelial or non-mesothelial origin [1, 16, 23]. At the present time, it is known that such a tumour does not display the immunohistochemical or ultrastructural features of mesothelial differentiation, but shows non-specific features of fibroblastic differentiation [3, 7, 8, 23] and appears to have a characteristic immunophenotype irrespective of its location [14]. SFT has been described in locations unrelated to serosal surfaces, including the liver and lung parenchyma, mediastinum, nose and paranasal sinuses, upper respiratory tract, orbit and thymus [13, 14, 24, 25]. Only one case of adrenal location of SFT is on record [22]. We describe an additional case of adrenal SFT diagnosed in a young woman during pregnancy and show a focal expression of progesterone receptors in the tumour cells. This prompted an analysis of a small series of SFTs of classical sites (pleura) and of a control group of uterine leiomyomas for their steroid hormone (oestrogen and progesterone) receptor status.

Clinical history

In a 23-year-old, 22-week pregnant woman, a 6-cm abdominal mass was incidentally discovered during ultrasonographic monitoring of pregnancy. It was a well-demarcated mass, located in the retroperitoneum in close association with the left adrenal gland.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Past medical history was unremarkable, and the patient had not undergone previous operations. Elevated serum and urinary levels of cortisol and elevated blood levels of delta 4 androstendione and 17-OH progesterone were observed. The mass was not excised, and its growth was monitored in the course of the pregnancy, showing a rapid increase in volume from 6 cm to approximately 9 cm during the third trimester of pregnancy. After spontaneous delivery, a magnetic resonance image confirmed the presence of a single retroperitoneal solid mass measuring 9 cm in its largest diameter, which was close to but independent from the upper pole of the left kidney and of the apparent adrenal origin (Fig. 1a). A laparoscopic adrenalectomy was performed. A large whitish solid mass compressing and partially infiltrating the left adrenal gland was excised. No macroscopic signs of local infiltration or renal involvement were observed. No other abdominal masses were found.

Materials and methods

The tumour was fixed in 10% buffered formalin and processed for conventional histological examination. Paraffin sections (5-µm thick) adjacent to those stained with haematoxylin and eosin were collected onto poly-L-lysine-coated slides and processed for immunohistochemistry. The following antibodies were used in this study: CD34 (monoclonal Q-Bend-10, diluted 1/50; BioGenex, San Ramon, Calif.), bcl-2 (monoclonal 124, diluted 1/50; Dako, Glostrup, Denmark), MIC-2 (monoclonal 013, diluted 1/100; Signet Laboratories, Dedham, Mass.), vimentin (monoclonal V9, diluted 1/30; Dako), cytokeratin (monoclonal KL1, diluted 1/50; Immunotech, Marseille, France), alpha smooth muscle actin (monoclonal 1A4, diluted 1/150; Dako), S-100 protein (polyclonal, diluted 1/3000; Dako), Ki-67 (monoclonal Mib-1, diluted 1/10; Immunotech), oxytocin receptor (diluted 1/2500; kind gift of Prof. Bussolati, Torino, Italy), oestrogen receptor (monoclonal 1D5, diluted 1/75; Dako), progesterone receptor (monoclonal 1A6, diluted 1/15; BioGenex).

Five cases of pleural SFTs (from female patients, mean age 55 years) and five control cases of uterine leiomyomas (mean age 49 years) were retrieved from the pathology file of the University of Turin and analysed for their steroid hormone receptor status using the same antibodies to oestrogen and progesterone receptors listed above.

Heat-induced antigen retrieval, based on three 3-min microwave passages at 750 W, was applied for CD34, Ki-67, cytokeratin and MIC-2 immunostainings using 10 mM citrate buffer (pH 6.0). For bcl-2, oestrogen and progesterone receptors reactions, an ethylene diamine tetraacetic acid (EDTA) buffer (pH 8.0) was used. All immune reactions were developed with a standard, streptavidin-based procedure followed by diaminobenzidine as a chromogen. Appropriate positive (tissues known to express the antigens) and negative (by omitting the primary antibody) controls were introduced for all of the above immunostainings.

◀ **Fig. 1** **a** Magnetic resonance image of a solid, apparently well-demarcated tumour (*T*) located in the left adrenal region close to, but separated from, the upper pole of the kidney (*K*) and spleen (*S*). **b** Macroscopically, the tumour was a grey–whitish homogeneous solid mass of 9 cm in its largest diameter, apparently capsulated and partially infiltrating the adrenal gland. **c, d** Microscopically, a spindle cell growth infiltrating adrenocortical cells was observed. Highly cellular areas of spindle cells in a delicate stroma (**e**) or cords of elongated cells in a densely hyalinised background (**f**) were the most prominent growth patterns. Occasionally, roundish cells having plump nuclei were growing in a sclerotic stroma (**g**). The tumour cells were diffusely immunoreactive for CD34 (**h**) and bcl-2 (**i**). A focal positivity for progesterone receptors was also observed (**j**)

Pathological findings

Grossly, the tumour measured 9×6 cm, weighed 85 g and was a well-circumscribed, almost entirely encapsulated, solid mass (Fig. 1b). At one pole of the tumour, the adrenal gland was compressed and partially infiltrated. On the cut surface, the tumour had a homogeneous grey–whitish fibrous appearance, with no evidence of haemorrhage, necrosis or cystic degeneration.

Microscopically, the tumour was surrounded by a thin incomplete fibrous capsule and was characterised by bundles of spindle to plump cells growing in a collagenous matrix. The neoplastic cells partially infiltrated the adrenal gland (Fig. 1c), entrapping groups of adrenocortical cells (Fig. 1d). The cellularity varied from place to place with alternating collagen-rich and tumour cell-rich areas. The predominant pattern of growth was that of spindle cells in short fascicular, storiform and irregular arrangements in a hyaline or collagenous background (Fig. 1e). In some areas, extensive hyalinisation was present with a sclerosing appearance (Fig. 1f). Occasionally, polygonal cells were arranged in small groups in a collagenous stroma (Fig. 1g). Irrespective of the shape, the tumour cells had poorly defined, pale eosinophilic cytoplasm and an elongated or roundish, hyperchromatic nucleus with inconspicuous nucleoli. Nuclear pleomorphism was focally recognised in individual cells. No mitotic activity was found. The proliferative activity, assessed by anti-Ki67 antibodies in areas of highest labelling density, was 6%.

The tumour also had the characteristic prominent vascularity with numerous small to mid-sized vessels scattered throughout. The vessels caused a haemangiopericytoma-like appearance, including elongated, branching or dilated, thin-walled vessels. No areas of haemorrhage, necrosis or inflammatory infiltration were ever observed.

Immunohistochemically, the tumour cells were diffusely positive for vimentin, CD 34 (Fig. 1h), bcl-2 (Fig. 1i) and MIC-2. The progesterone receptor (Fig. 1j) and oxytocin receptors were focally expressed. All other markers tested (see Materials and methods) were unreactive.

The small series of pleural SFTs was negative for oestrogen receptors and focally positive for progesterone receptors in two of five cases only. All control uterine leiomyomas were intensively positive for oestrogen and progesterone receptors, as expected.

Discussion

In the present study, we have described an additional case of SFT of the adrenal gland. The morphological and immunophenotypic profile of this tumour was similar to that of the only other adrenal SFT published so far [22] and to those of classical pleural SFT.

Extrathoracic locations of SFT have been increasingly described in the literature, and the proposed mesothelial origin of such tumour is no longer supported by either

Table 1 Reported solitary fibrous tumour in a retroperitoneal location. *NOS* not otherwise specified

Site	Authors	References
Retroperitoneum NOS		
1	Nielsen et al.	[20]
2	Nielsen et al.	[20]
3	Ibrahim et al.	[15]
4	Brunnemann et al.	[2]
5	Vallat-Decouvelaere et al.	[25]
6	Vallat-Decouvelaere et al.	[25]
7	Vallat-Decouvelaere et al.	[25]
Kidney		
1	Piazza et al.	[21]
2	Gelb et al.	[12]
3	Brunnemann et al.	[2]
4	Brunnemann et al.	[2]
5	Fain et al.	[9]
6	Fain et al.	[9]
7	Fain et al.	[9]
8	Fukunaga et al.	[10]
9	Fukunaga et al.	[10]
Adrenal		
1	Prevot et al.	[22]
2	Present case	

topographical or phenotypic characteristics. SFT is a soft tissue tumour of mesenchymal (fibroblastic?) origin, which can develop in any part of the body as demonstrated by the heterogeneous distribution of the tumour in soft tissues and parenchymal organs.

The adrenal location is very rare, although several cases have been observed in the retroperitoneum and the pelvis. Moreover, several examples of intrarenal or perirenal SFTs have been reported (Table 1). A minor proportion of such cases had malignant evolution [11]. Therefore, SFT is to be taken into consideration in the differential diagnosis of spindle cell tumours of the retroperitoneal region. There is a relatively large group of tumours that can be mistaken for SFTs and may develop in such a region. This includes, of course, a number of mesenchymal tumours of fibroblastic origin (fibromatosis, fibrosarcoma, malignant fibrous histiocytoma, synovial sarcoma) or having smooth muscle or nervous differentiation (leiomyoma, peripheral nerve sheath tumours, leiomyosarcoma, rhabdomyosarcoma). Liposarcoma and lipomas may have spindle cell components but are generally recognised by the presence of scattered lipoblasts within the tumour. Vascular tumours, such as haemangiopericytoma, may also mimic SFT due to the rich vascularity and herring bone-like vessels in SFT. Intraparenchymal locations of SFT (adrenal and kidney) further increase the mimickers of this tumour entity, since sarcomatoid renal carcinomas, mesoblastic nephroma and kidney angiomyolipoma may display a prominent spindle cell growth pattern. In the adrenal gland, spindle cell tumours are rare. Pseudocysts with solid areas due to fibrous organisation and spindle cell nodule resembling ovarian stroma [5, 19] are even rarer occurrences, to be considered in the differential diagnosis. To correctly identify a SFT, the morphological features are relatively well established, although this tumour was typically described in the past as having a "patternless" pattern of growth. In addition, the immunohistochemical profile is also very characteristic. Although no individual marker is absolutely specific for SFT, the combined expression of CD34, bcl-2 and CD99 (MIC-2) definitely points towards a diagnosis of SFT.

The present case met all of the morphological and immunohistochemical criteria proposed for SFT of the pleura and of extrathoracic locations. The tumour was a solid, well-circumscribed mass, which apparently originated from the adrenal gland from which it was undissectable. The absence of kidney involvement and of other abdominal tumours supports an origin from the adrenal gland.

The tumour had a remarkable growth in the course of the last trimester of pregnancy. During ordinary ultrasonographic scans to monitor pregnancy, it was discovered that the patient bore a large 6-cm tumour in the supra-renal region. Elevated serum and urinary levels of cortisol and elevated blood levels of delta 4 androstendione and 17-OH progesterone were also observed. At the 22nd week of pregnancy, the mass was incidentally discovered and closely monitored until spontaneous delivery occurred. In a 3-month period, the tumour increased by approximately 3 cm but had no features of infiltrative growth or of malignancy. An intermediate proliferative activity index (6%) was found, which was higher than classical benign pleural SFTs. In fact, in the case series of Hanau [14], the percentage of Ki-67 positive nuclei was low in all benign SFTs with values of 0–2%, while histologically malignant and highly cellular tumours showed higher nuclear scores (mean 30%, range 20–40%). Chilosi et al. [6] reported no proliferative potential in benign SFT, but no data were provided for malignant SFTs.

The role of pregnancy in the growth of tumours in general is not fully understood; however, it is known that hormonal conditions may favour the growth of soft tissue tumours such as leiomyomatosis peritonealis disseminata [18]. This tumour may present multiple localisation with dimension up to various centimetres with regression after pregnancy. In the present case, progesterone receptors were focally expressed in tumour cells, suggesting a possible direct hormonal influence on the tumour cell proliferation during pregnancy. The growth regulatory mechanisms of SFT in particular and of mesenchymal tumour in general are not fully understood, and this association may well be incidental. The expression of progesterone receptors in the present case and a similar report in meningeal SFTs [4] prompted an analysis of a small series of SFTs of classical (pleural) location. Interestingly, two of five cases tested also showed a focal positivity for progesterone receptors in female nonpregnant patients. This finding deserves further investigations on a larger series of SFTs from different sites.

In conclusion, we have described the second case of adrenal SFT. Its morphological features and immunophe-

notype were those of classical SFT, but the extremely rare location, the focal expression of progesterone receptors and its rapid growth in association with pregnancy made the case worth reporting. In agreement with the observation of Prevot et al. [22], the adrenal gland is to be added to the long list of extrapleural locations of SFT.

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