Malignant Solitary Fibrous Tumor of the Kidney
Report of a Case and Comprehensive Review of the Literature

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Renal solitary fibrous tumors (SFTs) have been reported infrequently. We report a 76-year-old man with a left renal mass that had previously been shown radiographically to be stable, but was now growing. Grossly, the mass measured 12 cm, was poorly circumscribed, and invaded beyond the renal capsule. Approximately 10% of the neoplasm consisted of haphazardly arranged spindle cells admixed with dense collagenous bands, which is typical of benign SFT. However, the remainder of the mass was composed of pleomorphic, spindled sarcoma cells with frequent mitoses and foci of necrosis. Immunohistochemically, we observed CD34 labeling in the benign SFT component with loss of expression in the sarcomatous component, focal labeling for Bcl-2 protein in both areas, and absence of labeling for cytokeratin, renal cell carcinoma marker, S100 protein, CD117, and muscle markers in both areas. To our knowledge, this is the first reported case of malignant renal SFT, likely representing transformation from a histologically documented benign SFT component.

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Solitary fibrous tumors (SFTs) are rare mesenchymal neoplasms, occurring mainly in the pleural cavity. Since their initial description in the pleura by Klemperer and Rabin in 1931,1 SFTs have been reported to arise at nearly every site in the body.2 Although SFTs are generally benign, slow-growing neoplasms with favorable prognoses, malignant variants, best characterized in the pleura, have been reported.3-5 The cell of origin for SFTs was a subject of considerable debate for many years, but modern immunohistochemical and ultrastructural studies strongly favor a fibroblastic/primitive mesenchymal cell of origin.4 The SFTs arising in the kidney are a rare and relatively recent addition to this group of neoplasms, with 18 histologically benign cases previously reported in the literature.6-19 We report what is, to our knowledge, the first documented case of malignant renal SFT in a 76-year-old man; we discuss its clinical, light microscopic, and immunohistochemical features, and differentiate it from other pseudosarcomatous, sarcomatoid, and sarcomatous lesions of the kidney.

REPORT OF A CASE
Clinical History

A 76-year-old man with a history of multifactorial, dialysis-dependent, chronic renal failure (diabetes mellitus, hypertension, and multiple myeloma) and prostatic adenocarcinoma that had been treated by radical prostatectomy, presented with an enlarging left renal mass as identified on imaging studies. The mass was initially noted 4 years earlier on a magnetic resonance imaging scan for evaluation of spondylolisthesis, but in follow-up evaluations it was considered stable. However, 1 year prior to the current presentation, the mass had increased in size by 30%, as shown on repeat magnetic resonance imaging for L5 radiculopathy. An abdominal computerized tomographic scan obtained at the time of an episode of abdominal pain showed an enlarging 7-cm left renal mass with irregular calcifications (Figure 1) that was then considered suspicious for renal cell carcinoma (RCC). The patient underwent radical left nephrectomy without complications. Intraoperative consultation reported the mass as a high-grade malignancy, favoring sarcoma. Four months postoperatively, the patient returned with multiple small lung nodules, consistent with metastases from the primary renal tumor.

Gross and Microscopic Findings

The gross specimen included tissue from the left kidney, ureter, and adrenal gland, along with perinephric tissue, weighed 1140 g and measured 12 × 6 × 5 cm in overall dimensions. Sectioning revealed a tan-pink, focally necrotic, poorly defined mass measuring 12 × 10 × 7.5 cm that involved the inferior pole of the kidney with extension to the renal hilum. Multiple surgical margins, including the hilar margin, were grossly involved.

Microscopic examination revealed 2 distinct histologic appearances. The first, a high-grade pleomorphic sarcoma, accounted for more than 90% of the sampled tumor. This area consisted of hyperchromatic and pleomorphic spindled cells surrounding staghornlike blood vessels (Figure 2, A), with frequent mitoses (Figure 2, B) and foci of tumor necrosis. The remaining 10% was characterized by haphazard growth of wispy, bland, spindle cells with scant cytoplasm among a moderate volume of dense, ropey collagen (Figure 2, C). The latter areas showed infrequent mitoses, but were associated with dilated, angulated blood vessels. This morphology is typical of benign SFT. The high-grade malignant component extended beyond the renal capsule and was present at the Gerota fascial, ureteral, and hilar adipose tissue margins.

Immunohistochemistry

Immunohistochemically, CD34 showed variable staining, with strong labeling in the benign SFT-appearing areas (Figure 3) and absence of labeling in the more pleomorphic cells. Focal labeling

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for Bcl-2 protein was observed throughout the lesion in both components (Figure 4, A and B). The pleomorphic component did not label with antibodies to S100 protein, smooth muscle actin, HMB-45, RCC marker antigen, cytokeratins 7 and 20, cytokeratin AE1/AE3, epithelial membrane antigen, CD117 (c-Kit), CD99, or synaptophysin.

**COMMENT**

Although SFTs have been most commonly described in the pleura, they have now been recognized at diverse sites. The kidney is a relatively infrequent site for SFT, with fewer than 20 cases reported in the world literature (Table). Among the previously reported patients, there were 7 men and 11 women, ranging in age from 28 to 83 years. The tumors from these patients measured between 2.0 and 25.0 cm in greatest dimension, with 11 located in the right kidney, 5 in the left kidney, and 1 without a side specified. A single patient had bilateral lesions. Although the tumor described in our patient measured 12.0 cm in greatest dimension and was localized to the left kidney, it is significantly dissimilar to previous reports of renal SFT in multiple aspects.

To date, all renal SFTs have been histologically identical to benign lesions occurring in the pleura. They have been circumscribed tumors with alternating hypocellular areas composed of bland, spindled cells with scant cytoplasm and few mitotic figures arranged in haphazard, storiform, or fascicular patterns, intertwined with hypocellular areas displaying dense collagen fibers. Many lesions demonstrated a focal hemangiopericytoma-like growth pattern. Furthermore, a recent series of renal SFT presented in abstract form by Pierson et al reported 6 cases with low mitotic rate and without atypia or tumor necrosis. In contrast, the present lesion displayed these usual features of benign SFT only focally. Most of the neoplasm showed marked hypocellularity with significant pleomorphism, numerous mitoses, and foci of necrosis. The criteria for malignancy in SFTs, first proposed by England et al in 1989, include increased cellularity with crowded/overlapping nuclei, cellular pleomorphism, and mitotic count of more than 4 per 10 high-power fields. By this standard, we may clearly classify our case as histologically malignant.

It is well known, however, that cytologic malignancy in SFTs does not always portend an unfavorable clinical course. In the larger published series of malignant SFT of the pleura, cases with up to 10 mitoses per 10 high-power fields and marked nuclear pleomorphism that were grossly polypoid, well-circumscribed, and completely resectable, behaved in a benign fashion, and cases that were poorly circumscribed, infiltrative masses were uniformly malignant. Conversely, a few cases with benign histologic findings have either invaded the wall of the renal vein or focally extended into perirenal adipose tissue, albeit with negative surgical margins. Although there have been no large studies of extrapleural malignant SFT, one may infer from the data on pleural lesions that an easily resectable renal SFT, particularly one with bland histology, would likely behave in a benign manner. In support of this premise is the clinical follow-up available on 14 of the 18 patients previously reported, which showed 13 patients with no evidence of disease (follow-up, 2–89 months) and 1 patient dead, but not of disease. Conversely, the multiple gross and microscopic surgical margins involved in our case, along with the overtly sarcomatous structure, would predict a poor prognosis. Indeed, this patient developed radiographic evidence of pulmonary metastases 4 months postoperatively.

Another key feature of this case is the lesional growth radiographically observed over a period of years. The mass was initially noted incidentally by radiographic examination as a stable lesion; it subsequently increased in size and, during a 4-year period, progressed to a mass that was suspicious for malignancy. This history, along with the 2 histologic reports of this tumor (bland SFT-like and sarcomatous), suggest malignant transformation from a benign SFT. Additional evidence for this hypothesis comes from the immunohistochemical profile of this tumor. It is well known that although SFTs are generally negative for muscle markers, cytokeratin, and S100 protein, a large percentage show diffuse, strong positivity for CD34 and at least focal positivity for Bcl-2.

Yokoi et al have postulated 2 mechanisms for the development of malignant SFTs. The first possibility is that these malignancies occur de novo and grow rapidly, a finding they demonstrate in 3 cases from the pleural cavity. The other possible mechanism is transformation (‘‘de-differentiation’’) within a pre-existing benign SFT, which appears to be operative in our case. They note 2 pleural SFTs with similar dual histologic features to our case, which also exhibited loss of CD34 in the overtly malignant component when compared with the typical SFT architecture. The Bcl-2 positivity observed in both components of this tumor is consistent with the findings of Chilosi et al that Bcl-2 protein expression is preserved across the spectrum of SFT lesions. The collective clinicopathologic, radiographic, and immunohistochemical evidence therefore supports a diagnosis of malignant transformation of a renal SFT in the current case.

Given the unusual histologic appearance of the tumor in this case, it is important to differentiate it from a diverse group of spindle cell lesions of the kidney. Foremost among these is primary synovial sarcoma of the kidney, including lesions formerly designated cystic embryonal sarcomas, which are likely the closest mimickers of the high-grade structure seen in the current case. Synovial sarcomas typically demonstrate high cellularity and are composed of primitive spindled cells that are often arranged around dilated, entrapped renal collecting ducts.
Figure 2. Solitary fibrous tumor. A, Cellular spindled tumor with hemangiopericytoma-like growth (hematoxylin-eosin, original magnification ×100). B, High-grade sarcomatous component (hematoxylin-eosin, original magnification ×200). C, Usual solitary fibrous tumor component showing haphazard spindle cells growing among dense collagen bundles (hematoxylin-eosin, original magnification ×200).

Figure 3. Diffuse positive staining in benign solitary fibrous tumor component (CD34 immunohistochemistry, original magnification ×200).

Figure 4. Focal staining in both benign (A) and malignant (B) components (Bcl-2 immunohistochemistry, original magnification ×400).
lined by hobnail epithelium. At high magnification, the tumor cells contain plump, ovoid nuclei and indistinct cytoplasm. Mitotic figures and extensive necrosis are common features. Finding a cytokeratin-positive "cysts" (entrapped, dilated renal collecting ducts) within the tumor may be helpful diagnostically; however, these entrapped cysts are not always present and, furthermore, may be seen in other renal neoplasms such as clear cell sarcoma of the kidney and congenital mesoblastic nephroma. As with SFT, the tumor cells are often organized as solid areas displaying intersecting fascicles and/or hemangio-pericytoma-like growth.24,25 Compounding the diagnostic difficulty is the fact that synovial sarcomas are immunohistochemically negative for desmin, actin, S100 protein, and cytokeratin, and they are immunoreactive for vimentin and Bcl-2. In comparing synovial sarcoma with usual benign SFTs, the CD34-negative, epithelial membrane antigen–positive phenotype of synovial sarcoma would help distinguish them from SFT.18

It is now recognized that many lesions formerly diagnosed as hemangioepericytoma may be better classified as SFT. This phenomenon may apply to the few cases of so-called renal hemangioepericytoma previously reported in the literature, and has already resulted in reassessment of one of these lesions as an SFT.16

Congenital mesoblastic nephroma is characterized by densely packed spindled or round blue cells with numerous mitoses that may architecturally be arranged as sheets or interlacing bundles. Specific clinical and molecular features eliminate congenital mesoblastic nephroma as a possibility in this case because these tumors generally present within 3 months of birth and are virtually never seen beyond the first 3 years of life.24 Cellular congenital mesoblastic nephroma contains a unique ETV6-NTRK3 gene fusion, which distinguishes it from other spindled renal neoplasms.25–29 Primary fibrosarcoma and malignant peripheral nerve sheath tumor are rare in the kidney, but may involve the kidney secondarily. Fibrosarcomas may be indistinguishable from malignant SFT on a small amount of biopsy tissue because both feature monomorphic spindle cells with minimal pleomorphism and an elevated mitotic rate.30 Although the usual type of SFT may be distinguished from fibrosarcoma by the absence of dense cellularity and high mitotic rates,13,30 the current case shares many of these features in its dominant structure. Finding the classic "herringbone" pattern of fibrosarcoma, the absence of a hypocellular component, along with immunohistochemical negativity for both CD34 and Bcl-2, would be most useful in distinguishing fibrosarcoma from malignant SFT.17,31 Similarly, malignant peripheral nerve sheath tumors composed of wavy fascicles of spindle cells demonstrating alternating hypocellular and hypercellular areas, and showing Bcl-2 positivity in up to one third of cases,32 may be confused with the usual SFT. However,

<table>
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<tr>
<th>Source, y</th>
<th>(No. of Cases)</th>
<th>Age, y/Sex</th>
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* NED, no evidence of disease; DNOD, died, not of disease; and NA, not available.
focal expression of S100 protein and negativity for CD34 will help in their distinction.

In summary, we report the first clinicopathologically documented case of malignant SFT arising in the kidney. We note its likely origin from benign SFT and highlight its transformation to sarcoma. Although SFTs may have been included previously as a rare differential diagnosis of renal spindle cell lesions, the malignant potential demonstrated in this case makes them an important diagnostic consideration in this group.

References