Solitary fibrous tumor of the urinary bladder: report of a case with long-term follow-up and review of the literature

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Abstract. – Solitary fibrous tumor (SFT) is a neoplasm typically arising in the pleura. Yet, extrapleural cases have been described and are a common cause of diagnostic pitfalls, especially when met in unusual sites. We report the clinical and pathological features of a case of SFT arising in a rather unusual site, the urinary bladder, the seventh reported to date in the English literature and the first with long term follow-up. Differential diagnosis from other spindle cell neoplasms of the bladder can be problematic. Prognosis of this neoplasm is obscure and long-term follow-up is required for all cases of solitary fibrous tumor. Solitary fibrous tumor is a rare mesenchymal tumor of the urinary bladder, but should always be considered in the differential diagnosis of spindle cell neoplasms encountered in the lower genital tract.

Key Words:

Urinary bladder, Mesenchymal neoplasm, Solitary fibrous tumor.

Introduction

Solitary fibrous tumor (SFT) is a well recognized entity of the pleura[1,2]. It has received a variety of names in the past, including fibrous mesothelioma and localized mesothelioma which indicated a mesothelial origin[1]. However ultrastructural and immunohistochemical findings are more consistent with a mesenchymal origin[2-4]. Another feature pointing against mesothelial origin is that this tumor has been reported in many extrapleural sites with no mesothelial lining, such as the orbit[5,6], nasal cavity[7,8] central nervous system[9,10], major salivary gland[11], thyroid gland[12,13], periosteum[4], kidney[14], soft tissues[15], prostate[16], and urinary bladder[16-20]. SFT involving the urinary bladder is extremely rare – only six cases have been reported up to date in the English literature[16-20]. Follow-up in these cases varied from 1 to 18 months (mean: 10.6 months). We report the clinical and pathological features of SFT arising in the urinary bladder of a 59-year-old woman with a follow-up period of 77 months. SFT should enter the differential diagnosis when dealing with a mesenchymal tumor of the urinary bladder. Prognosis of extrapleural SFT cannot be predicted with certainty on histologic grounds[2]. Careful follow-up is needed for all cases.

Clinical History

A 59-year-old white woman presented with intermittent hematuria. Physical examination was unremarkable. Cystoscopy revealed a protruding, fleshy mass at the dome and the posterolateral wall of the urinary bladder, measuring 7 cm in greatest diameter. Transurethral resection was performed, but was incomplete. The pathology diagnosis was solitary fibrous tumor of the urinary bladder. A radical cystectomy with an orthotopic ileal bladder substitution was then carried out. She received no further treatment. There is no evidence of recurrence 77 months (6.4 years) after the initial diagnosis.

The surgical specimens (transurethral cutterings and cystectomy specimen) were fixed in 10% formalin. Gross examination of the urinary bladder revealed a submucosal mass that focally eroded the mucosa. Representative sections

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were embedded in paraffin and stained with hematoxylin-eosin. For immunohistochemical analysis the avidin-biotin complex technique was employed. Clone and sources of the antibodies used are shown in Table I. Diaminobenzidine was used as the chromogen. Nuclei were counterstained with hematoxylin.

Laboratory Findings

On gross examination the bladder tumor was a well circumscribed unencapsulated polypoid mass, measuring $8.5 \times 6.5 \times 4.5$ cm. The cut surface was white, solid and had gelatinous areas.

Microscopic examination revealed a cellular neoplasm composed of spindle cells and moderate amounts of collagen arranged in a disorderly or random pattern (patternless pattern) (Figure 1). Less frequently a hemangiopericytoma-like pattern was noted. It consisted of closely packed tumor cells arranged around open, irregular, branching capillaries and larger vessels. Hypercellular areas occasionally alternated with less cellular foci, within a myxoid stroma. Rarely the tumor cells were arranged in fascicles. The neoplasm was located in the submucosal connective tissue and infiltrated the muscularis propria of the bladder.

**Table I.** Clone and sources of the antibodies used.

CD34	QBEnd/10, BioGenex, San Remon, USA
CD31	JC/70A, EmergoEurope, Hague, Netherlands
Vimentin	V9, BioGenex, San Remon, USA
Actin	BioGenex, San Remon, USA
Smooth Muscle Actin (SMA)	A4, BioGenex, San Remon, USA
Desmin	33, BioGenex, San Remon, USA
AE1	BioGenex, San Remon, USA
AE3	BioGenex, San Remon, USA
bcl2	124, Dakocytomation, Carpinteria, Denmark
CD99	12E7, Dakocytomation, Carpinteria, Denmark
S100 protein	15E2E2, BioGenex, San Remon, USA
CD68	KP1, Dakocytomation, Carpinteria, Denmark
CD117/c-kit	104D2, Dakocytomation, Carpinteria, Denmark
CD246	ALK1, Dakocytomation, Carpinteria, Denmark
Ki67	MIB1, Dakocytomation, Carpinteria, Denmark
p53	D07 BioGenex, San Remon, USA

Nuclei of the tumor cells were thin and elongated with tapered ends and had inconspicuous nucleoli and evenly distributed chromatin (Figure 1). Cytoplasm was faintly eosinophilic with poorly defined borders. The cells demonstrated no significant pleomorfism (Figure 1). Mitosis were rare (< 1/10HPF).

Immunohistochemcical studies showed diffuse staining of the tumor cells for CD34, CD99, and vimentin (Figure 2). Scattered cells stained for
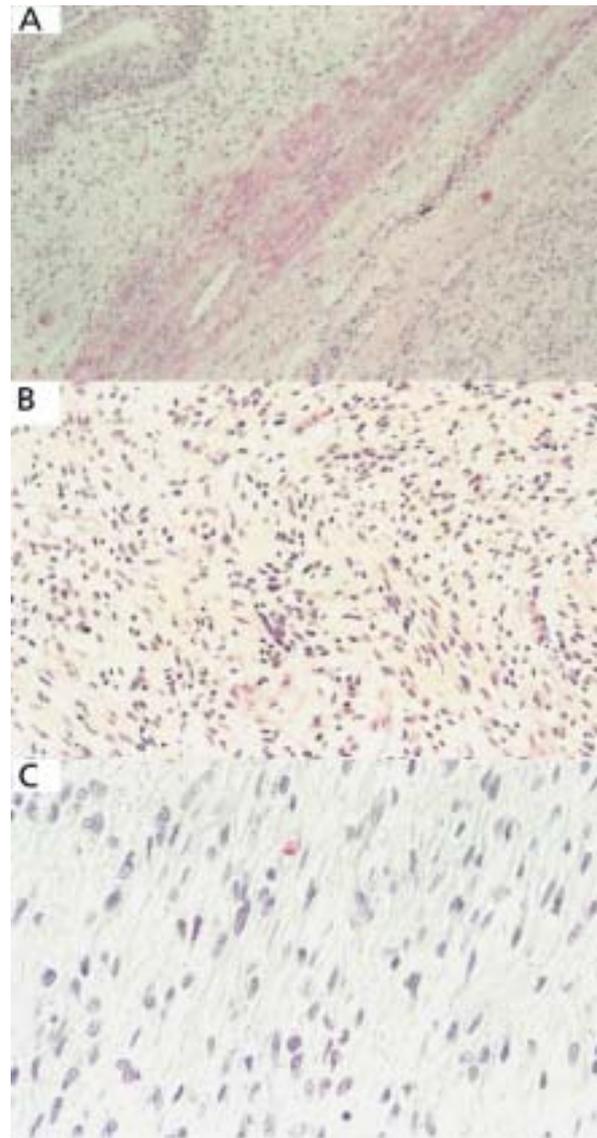
Figure 1. *A,* The neoplasm infiltrates the muscularis propria of the urinary bladder. Note the urothelium on the upper right of the photo (H/E, × 100). *B,* The tumor cells are arranged in a patternless pattern (H/E, × 200). *C,* Nuclei of the tumor cells are thin and elongated with tapered ends, inconspicuous nucleoli and evenly distributed chromatin and demonstrate no atypia (H/E, × 400).
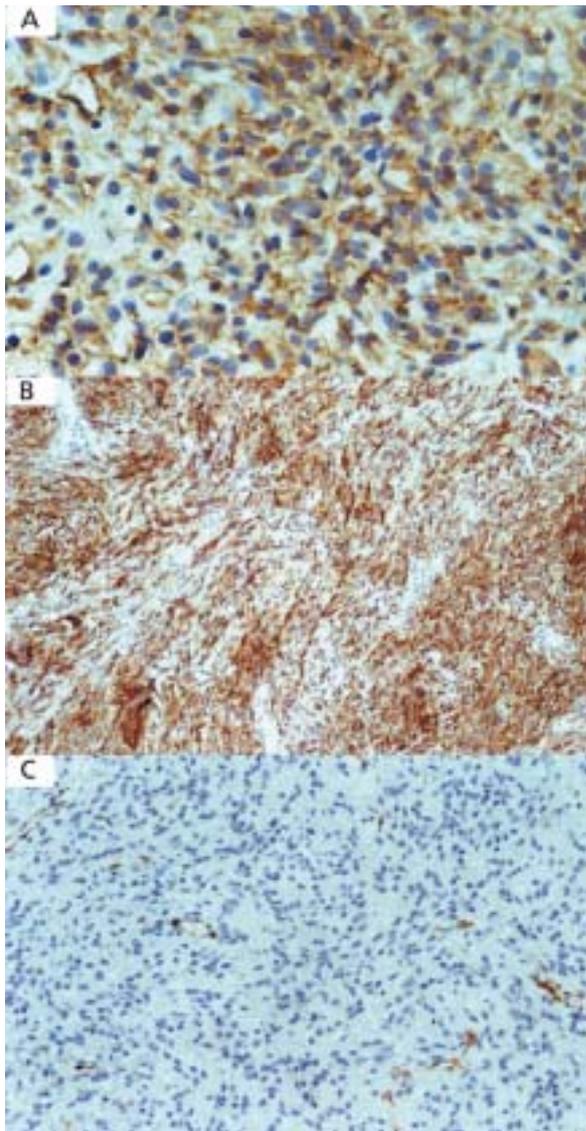
Figure 2. *A,* Tumor cells stain positively for CD34 (H/E × 200). *B,* Diffuse staining of the tumor cells for CD99 (H/E × 100). *C,* Tumor cells are negative for actin. Vessels serve as an internal positive control (H/E × 100).

CD68. Ki67 revealed positive nuclear staining of < 1% of the tumor cells. No immunoreactivity was observed for the other markers tested.

Discussion

SFT is a neoplasm typically arising in the pleura[1,2]. Yet several extrapleural cases have been reported, including the thyroid gland[12,13], orbit[5,6],

nasal cavity[7,8], central nervous system[9,10], major salivary gland[11], periosteum[4], soft tissues[15], kidney[14,21], prostate[16], and urinary bladder[16-20], indicating that SFT should always be kept in mind when facing a mesenchymal tumor even in unusual locations. To our knowledge this is the seventh case of SFT arising in the urinary bladder and the first with follow-up that exceeded 18 months.

Grossly the tumor is well demarcated and occasionally encapsulated[2]. SFT in the urinary bladder presents as a polypoid intravesical mass, frequently covered by an intact mucosa[16-20]. Microscopically the tumor is characterized by a variety of growth patterns, the most common being the "patternless pattern"[2]. This is characterized by spindle cells arranged randomly in a collagen background. Cellularity varies within the same tumor, exhibiting hypocellular and hypercellular areas[1-3]. Vasculature consists of irregular branching capillaries and larger vessels, thereby imparting a hemangiopericytoma-like appearance[2,3]. Some cases have varying proportions of myxoid stroma, as was seen in our case[2,15,16].

Immunohistochemically SFT reacts with vimentin and CD34, the later being a highly sensitive marker for this neoplasm[5,22]. Still there have been reported a few cases that were CD34 negative[22]. Bcl2 is another marker that is regarded as sensitive for SFT[10,19,20]. Our case was negative for bcl2. Negativity for bcl2 has been reported before[23]. The tumor cells can be variably positive for CD99[16,24], EMA[24], SMA[4,6,22,24], desmin[2,6,22] and are negative for cytokeratins, CD31 and S-100 protein[15,16,22,25].

Treatment of solitary fibrous tumor of the urinary bladder varies. Cystoprostatectomy, wide excision and transurethral resection have been used[16-20]. All the reported cases pursued an innocent course, even though some of them exhibited moderate[20] or vigorous[18] cellular atypia. Our case was treated with cystectomy, due to the large size of the tumor mass (major diameter 8,5 cm), that made transurethral resection inadequate and wide excision impossible.

SFT usually pursues a benign course. However they have a potential to recur or metastasize[2,23,24]. Increased cellularity, pleomorfism and mitoses > 4/10HPF are considered to be indicators of malignant SFT[2]. Clinically benign cases exhibit neither of these features[2]. However there have been reported cases of clinically malignant SFT (exhibiting recurrence after complete excision or metastases) showing a benign histology[2,23,24].

Therefore it is difficult to predict with certainty the clinical behavior of SFT based on histology. Cellularity, pleomorfism and increased mitotic counts can be applied to intrathoracic and extrathoracic SFT as predictive features of malignancy bearing in mind that these tumors can recur or metastasize even in the absence of them. As a result careful and long-term follow up is required for all cases of SFT.

The differential diagnosis of SFT includes a variety of neoplasms due to the wide range of morphology and the combination of growth patterns that can be seen. SFT of the urinary bladder should be distinguished from inflammatory myofibroblastic tumor[26-29], leiomyosarcoma/leiomyoma[30-32], sarcomatoid carcinoma[33] and hemangiopericytoma[5,10]. Most of these entities can be distinguished on histologic grounds or with the aid of immunohistochemistry. Inflammatory myofibroblastic tumor, also known as inflammatory pseudotumor, is characterized by prominent myxoid matrix, lymphocytic infiltration, reactivity for ALK1 and lack of CD34 expression[26-29]. These features help the differential diagnosis, albeit myxoid stroma can be seen in SFT[2,15,16], as was in our case, but is rarely prominent. In leiomyoma and leiomyosarcoma the cells are arranged in interlacing fascicles, have abundant eosinophilic cytoplasm and exhibit strong, diffuse immunoreactivity for SMA and desmin[30-32]. Dinstiction of sarcomatoid carcinoma from SFT is usually easy, since the former displays atypical spindle cells with large hyperchromatic nuclei, increased mitotic activity and is positive for cytokeratins, features that are rarely, if even, seen in SFT[33]. Differential diagnosis from hemangiopericytoma is extremely difficult, since they share the same microscopic and immunohistochemical features. It has been proposed that hemangiopericytoma is characterized by patchy and weak CD34 immunoreactivity, contrasting with the diffuse, strong pattern of SFT, as it was seen in our case[5,10]. Reticulin staining is also of important help in the differential diagnosis[10]. However the delination of hemangiopericytoma as a separate entity has become obsolete and these tumors are now regarded as SFTs[34].

Pleural SFT seems to derive from the submesothelial mesenchyme, since both submesothelial stromal cells and neoplastic cells express CD34[5]. The consistent absence of CD34 immunoreactivity in mesothelioma[5] and normal mesothelial cells[35] and the sporadic occurrence of SFT in extrapleural sites with no mesothelial lining further argues against a mesothelial origin of the tumor. Similarly, extrapleural SFT probably arises from adjacent fibroblasts, as has been proposed for periosteal SFT arising from periosteal fibroblasts[4]. In urinary bladder, the CD34(+) fibrocytes found in the deep lamina propria and the tunica muscularis[36] are a potential candidate for giving rise to this neoplasm.

In summary, we present a case of SFT arising in a rather unusual site. The clinical outcome of this neoplasm is unpredictable on histological grounds. Complete excision of the neoplasm is necessitated and can be achieved by wide excision or transurethral resection. Cystectomy is saved for larger tumors that cannot be adequately treated with these methods. Our case was managed by cystectomy due to large tumor size. The neoplasm exhibited a benign histology and pursued a benign clinical course on long-term follow-up. Careful long lasting follow-up is recommended for all cases of SFT.

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