

Case Report

Solitary fibrous tumor with atypical features of the paravesical space: benign clinical course at the 10-years follow-up. Report of a case and review of the literature

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Summary

Extra-pleural solitary fibrous tumor (SFT) is a relatively rare soft tissue neoplasm, with only rare cases reported in the pelvic cavity. Most SFTs are histologically benign, with only a few malignant cases reported in the literature so far. We report a rare case of SFT arising in the paravesical space of a 79-year-old man. Histologically the tumor corresponds to an "intermediate risk tumor" according to a risk stratification scheme for metastatic potential, which incorporates patient age, tumor size, mitotic activity and necrosis. Notably tumor showed a benign clinical course without evidence of local recurrence after a 10-years follow-up. Tumor was composed of both spindle and epithelioid cells variably set in a fibromyxoid stroma, with focal pleomorphic, necrotic and highly mitotic (> 4 mitoses/10HPF) areas. Immunohistochemistry, showing a diffuse CD34 and STAT6 immunoreactivity, supported the diagnosis of SFT. The present case emphasizes that the clinical course of the pelvic SFTs with atypical morphological features is unpredictable on the basis of morphology alone, and thus the term "SFT with atypical features, including the risk stratification class" should be preferred to "malignant SFT".

Key words: solitary fibrous tumor, risk category, pelvis, review

Introduction

Solitary fibrous tumor (SFT) is a relatively rare soft tissue neoplasm originally described in the pleura but subsequently reported elsewhere, including the pelvic and oral cavities, kidney, breast, liver, retroperitoneum and central nervous system¹⁻⁸. Although the majority of SFTs are "histologically benign" and usually associated with an indolent clinical course, it is true that about 10-15% of "histologically malignant" SFTs (defined by the presence of ≥ 4 mitoses per 10 high-power fields, often combined with hypercellularity, cellular pleomorphism, necrosis and infiltrative margins) tends to locally recur and metastasize¹. However, some cases of histologically benign SFT may metastasize and, viceversa, histologically malignant SFT may have an indolent clinical behavior¹. In addition, although it is difficult to predict the behavior of a single tumor, it is largely accepted that, despite morphology, SFTs occurring in the retroperitoneum, pelvis, mediastinum, and meninges, tend to exhibit a

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Conflict of interest

The Authors declare no conflict of interest.

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more aggressive clinical course compared with other sites, including the pleura¹. Therefore some authors developed a risk stratification scheme for SFT based on the assessment of the following clinico-pathologic features; i) *age*: score 0 (< 55 years); score 1 (\geq 55 years); ii) *tumor size* (cm): score 0 (< 5 cm); score 1 (5 to < 10); score 2 (10 to < 15); score 3 (\geq 15); iii) *mitotic count* (/10 HPF): score 0 (0); score 1 (1-3); score 2 (\geq 4); *tumor necrosis*: score 0 (< 10%); score 1 (\geq 10%) (9). According to this scheme, it is possible to stratify SFT into three risk classes: i) low-risk (total score = 0-3); ii) intermediate-risk (total score = 4-5), high risk (total score = 6-7)⁹.

We herein report a rare case of SFT of the paravesical space in a 79-year-old man. Although the tumor showed several atypical morphological features which allowed us to classify it as “intermediate risk class for metastatic potential”⁹, the patient had a benign clinical course after 10 years from surgery. This case gave us the opportunity to provide a critical review on the “SFT of the pelvic cavity” reported in the English literature. Based on the clinico-pathologic features of patients with available follow-up, histology seems to predict clinical behavior, in that malignant/atypical features are associated with metastases in 45% of cases, whereas only 6% of SFT with conventional morphology do metastasize¹⁰⁻⁵³. However, our case supports the concept that the clinical behavior of SFT with atypical/malignant features is unpredictable for each single patient, and thus a long-term follow-up period should always be recommended.

Clinical findings

A 79-year-old man presented with a 2-month history of pelvic pain. Physical exam, including digital rectal examination, was consistent with benign prostate hyperplasia. No enlarged lymph nodes were found in the inguinal regions. Blood and urine examinations were within the normal range. Ultrasonography revealed a mass adjacent to the bladder. Computed tomography (CT) revealed a well circumscribed, 10 × 6 × 8 cm solid tumor, located in the left paravesical space, compressing the bladder (Fig. 1). The tumor borders were clear, with no evidence of direct invasion into bladder or any other organ. In addition, CT revealed neither lymph node enlargement nor distant metastases. At surgery, the tumor mass was found in the left paravesical space and it was removed with the covering pelvic peritoneum. A partial cystectomy was also performed due to the tumor adhesion to the lateral wall of the bladder. The surgical specimen was fixed in neutral-buffered 10% formalin and submitted for histolog-



Figure 1. CT showing a solid mass (T) in the left paravesical space; B: bladder.

ical examination. The post-operative course was uneventful, and pelvic pain immediately disappeared. The patient is well with no evidence of local recurrence after a 10-years follow-up period

Pathological findings

Grossly, the tumor mass appeared circumscribed and partially lined by peritoneum (Fig. 2A). The cut surface showed solid multinodular areas, gray-whitish in color, with degenerative cystic changes (Fig. 2B). Histological examination showed a uniformly hypercellular tumor with pushing margins, focally infiltrative into surrounding fat tissue (Fig. 3A). The tumor was composed, for about 70% of the entire neoplasm, of bland-looking spindle cells with fibroblastic-like appearance (scant cytoplasm, indistinct cell borders and spindly nuclei with dense chromatin), arranged into short intersecting fascicles (Fig. 3B) or haphazardly (*pattern-less*) (Fig. 3C) with interspersed brightly eosinophilic thin to thick collagen fibers (Fig. 3D) or stellate-shaped collagen bands (Fig. 3E). Frequently, hypercellular areas showed an abrupt transition into hypocellular, deeply hyalinized stroma (Fig. 3F). The remaining 30% of tumor was composed of bland-looking, medium-sized epithelioid cells with eosinophilic to basophilic cytoplasm, distinct cell borders and round to oval nuclei with small nucleoli (Fig. 4A). Most of the epithelioid cells with eosinophilic cytoplasm were closely packed (Fig. 4B) and with interspersed thin-

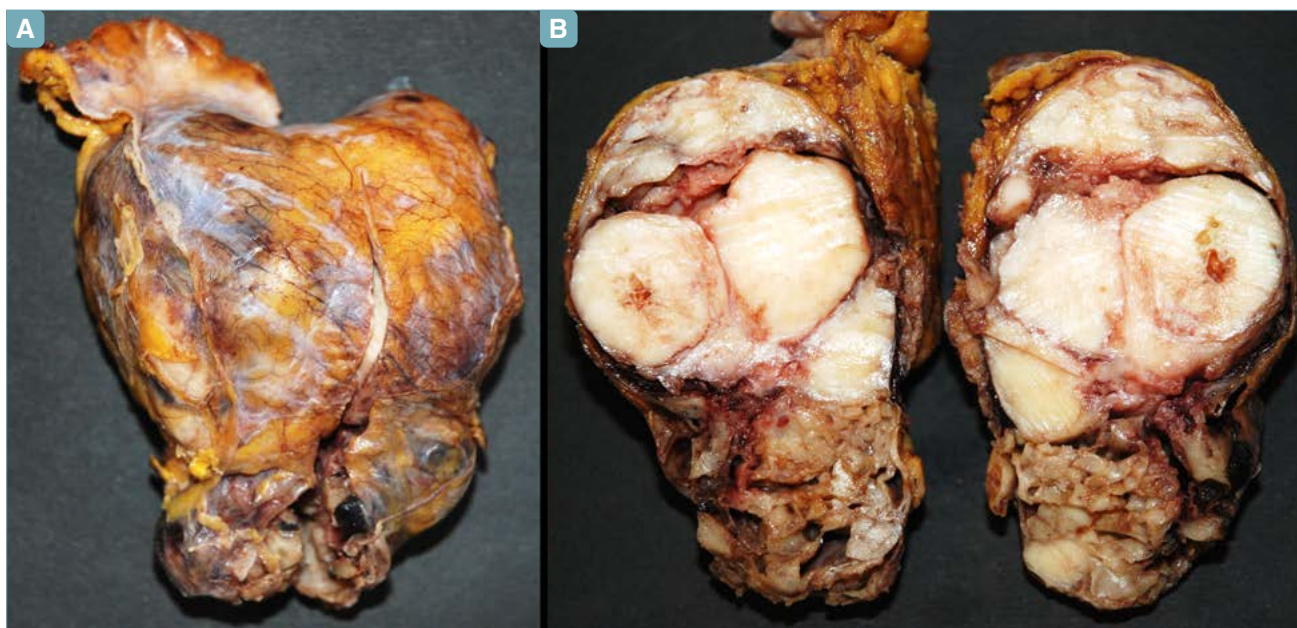


Figure 2. Tumor mass was partially lined by peritoneal surface. (B) The cut section showing a multinodular solid tumor with cystic areas.

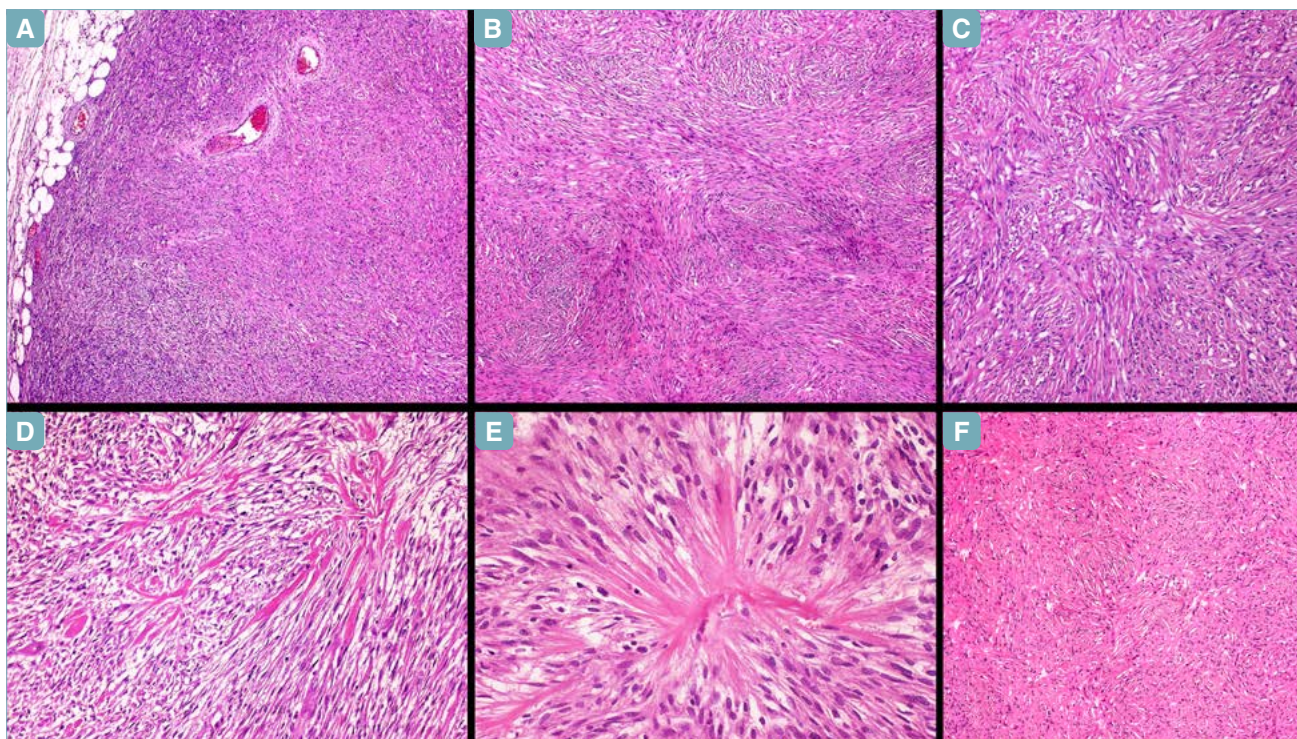


Figure 3. (A) Low-magnification showing minimally infiltrative margins. Bland-looking spindle cells arranged into intersecting fascicles (B) or haphazardly (pattern-less) (C). Thick eosinophilic collagen fibers (D) and stellate-shaped collagen bands (E) were scattered among the neoplastic cells. (F) Hypocellular fibrosclerotic areas were commonly seen.

sized collagen fibers (Fig. 4C). Like in the spindle-cell tumor component, a transition into fibrosclerotic areas was seen (Fig. 4D). Conversely, the majority of the epithelioid cells with basophilic cytoplasm were discohesive (Fig. 4E) and set in a variable abundant Alcian blue-positive myxoid stroma (Fig. 4F) showing diffuse micro- and macro-cystic changes (Fig. 4G). These stromal changes were responsible of the cystic areas easily identified at gross examination of the tumor mass (Fig. 4H). Tumor vascular component was represented by small- to medium-sized blood vessels often with perivascular hyalinization, but a hemangiopericytoma-like branching vascular pattern was lacking. Notably the most striking feature was the focal presence, limited to the spindle-cell areas, of scattered mono- or multi-nucleated giant cells with large-sized hyperchromatic and pleomorphic nuclei (bizarre cells) (Fig. 5A-C), often in association with tumor necrosis (Fig. 5D). Although mitotic count in most tumor areas was low (1-2 mitoses/10 HPF), up to 5 mitoses/10 high power field could be documented exclusively in the pleomorphic/necrotic areas. Atypical mitoses were not seen. Sarcomatous dedifferentiation, i.e. abrupt transition

from bland-looking areas into high-grade sarcomatous ones, was absent. Immunohistochemically, neoplastic cells, including pleomorphic/bizarre cells, were diffusely positive for vimentin, CD34 (Fig. 6A-C), CD99 (Fig. 6D), Bcl-2 (Fig. 6E), and only focally for EMA (Fig. 6F) and pancytokeratins (Fig. 6G). In addition, diffuse immunostaining was also obtained with STAT-6 (Fig. 6H). This latter immunomarker was not available at the time of the original diagnosis, but was tested when revising the case. No staining was obtained with S-100 protein, α -smooth muscle actin, desmin, myogenin, HMB45, SOX10, MUC4, CD31, ERG, or INI1. Based on both the morphological and immunohistochemical features, the diagnosis of “solitary fibrous tumor” was rendered. In the pathology report the following comment was added: “due to the presence of several atypical features predictive of aggressive clinical behavior, such as > 4 mitoses/10 high power field, hypercellularity, cellular pleomorphism and necrosis, the more appropriate diagnosis seemed to be “*histologically malignant SFT*” and a long-term follow-up of the patient was recommended. Based on the risk stratification scheme, recently developed by Demicco

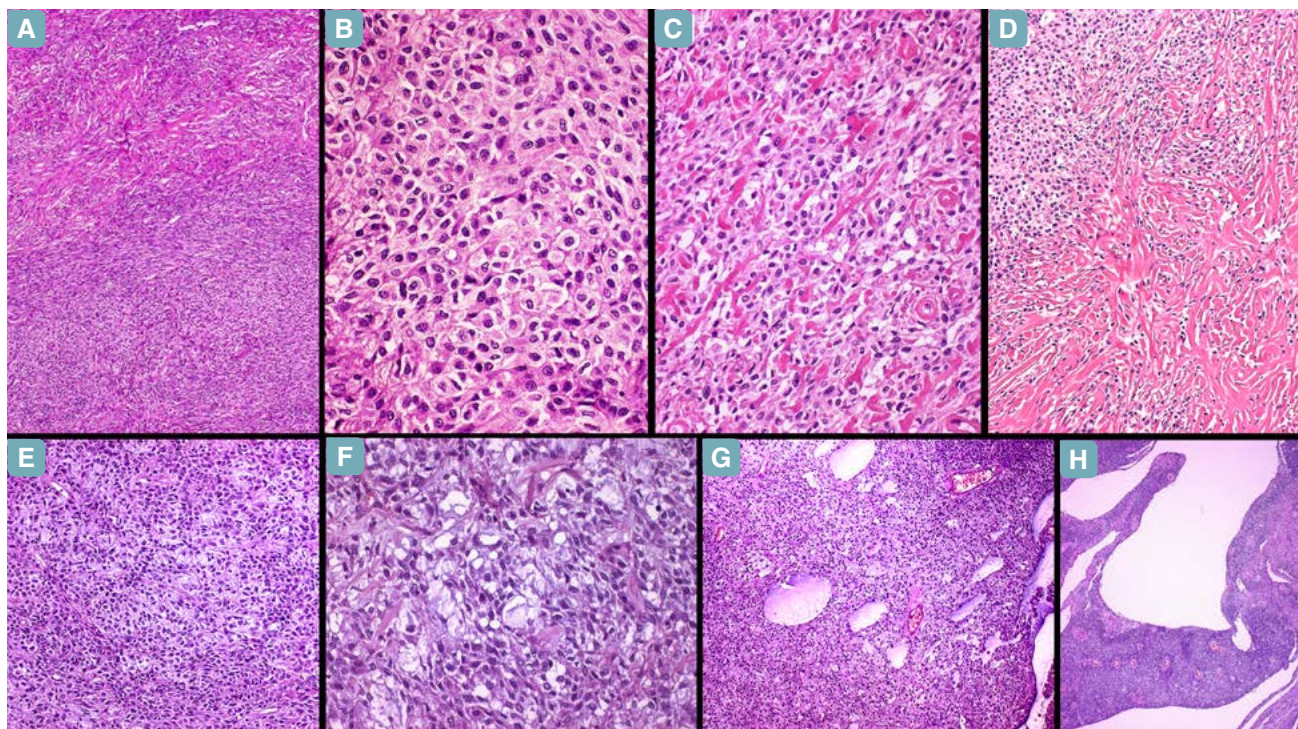


Figure 4. (A) Tumor area showing transition from spindle-cell (top of the figure) to epithelioid-cell (bottom of the figure) component. (B) Tumor area showing eosinophilic medium-sized epithelioid cells closely packed. (C) Thin eosinophilic collagen fibers were interspersed among the neoplastic cells. (D) Epithelioid-cell area blending into fibro-sclerotic area. (E) In some tumor areas the epithelioid cells had basophilic cytoplasm and were discohesive. Stroma was myxoid (F) and frequently underwent microcystic (G) and macrocystic (H) degenerative changes.

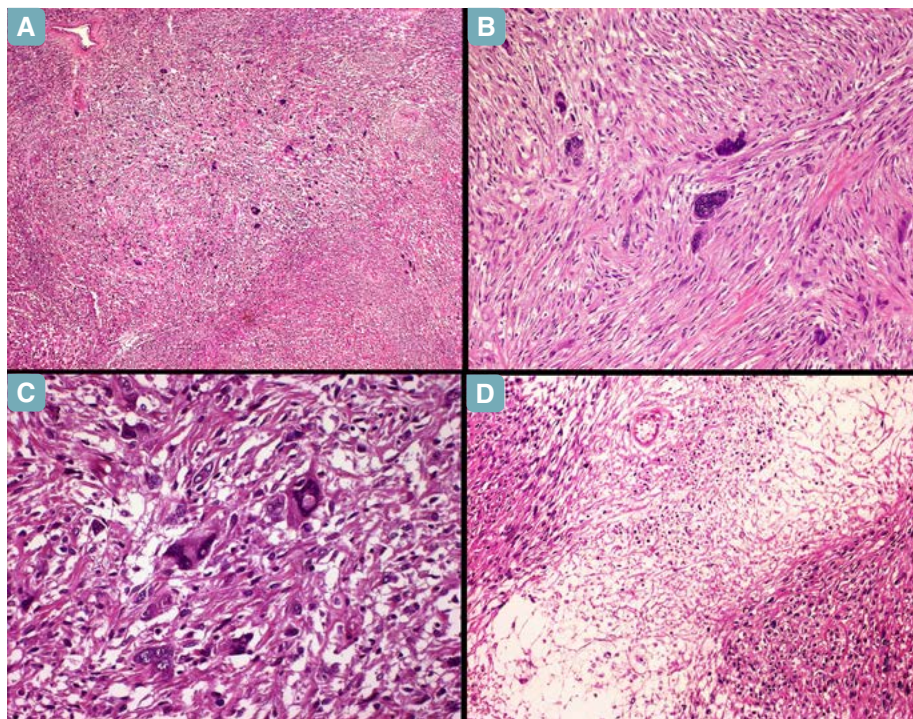


Figure 5. (A) Low-magnification showing a spindle-cell area with numerous pleomorphic/bizarre cells. (B) The pleomorphic cells were scattered among the bland-looking neoplastic spindle cells. (C) Some pleomorphic cells were multi-nucleated. (D) Tumor necrosis was evident in the pleomorphic areas.

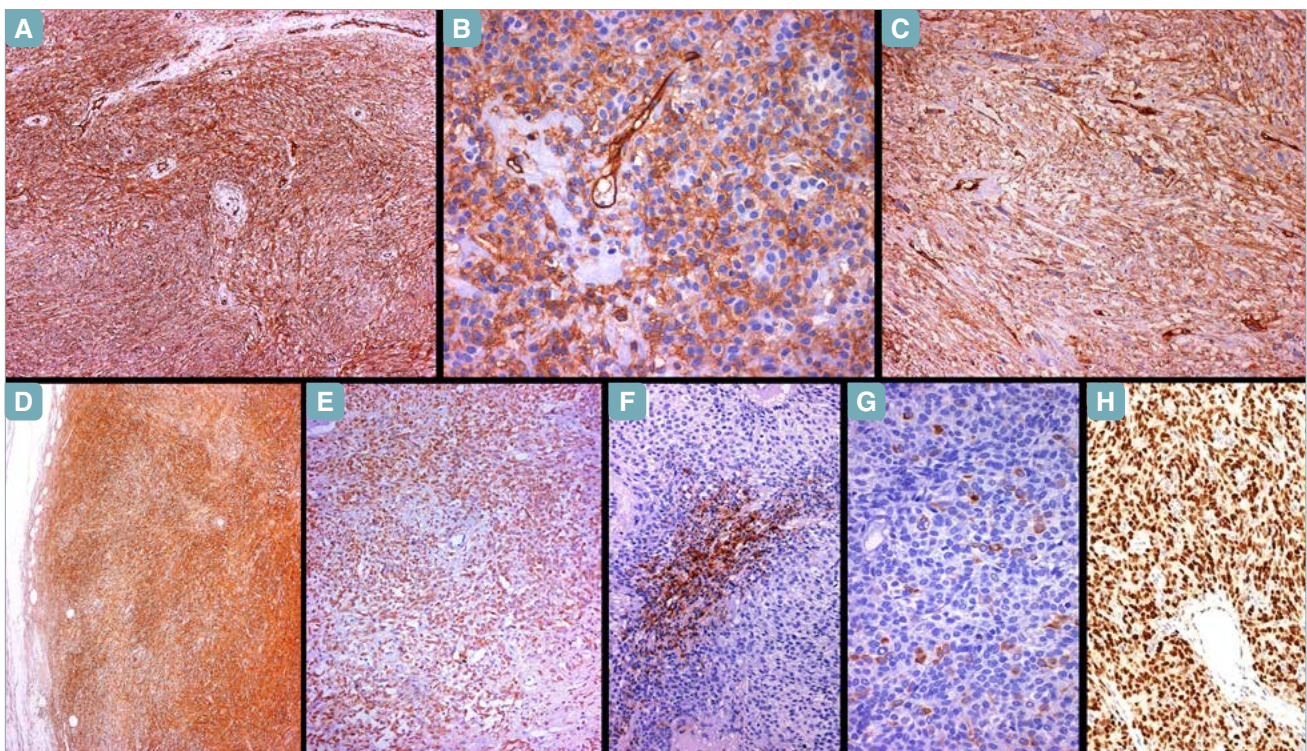


Figure 6. CD34 stained diffusely and strongly the neoplastic spindle (A), epithelioid (B), and pleomorphic (C) cells. A diffuse immunostaining was also observed for CD99 (D) and Bcl-2 (E). Only focal staining was obtained with EMA (F) and pancytokeratins (G). Diffuse nuclear staining for STAT6 (H) supported the diagnosis of SFT.

et al. ⁹, SFT was incorporated into an “*intermediate risk class*” in that a total score 5 was obtained: i) age: score 1 (age: 79 years); ii) tumor size: score 2 (10 cm); iii) mitotic count (/10HPF): score 2 (≥ 4); iv) tumor necrosis: score 0 (< 10%).

Review of the literature

The present case led us to review the literature on the clinico-pathologic features of SFT arising from the pelvic cavity. After a PubMedLINE-based search, using the following Medical Subject Headings (MESH:

“Pelvis and Solitary Fibrous Tumor”), numerous case reports and a few series were available. The cases labeled as “*abdominal/pelvic or retroperitoneal SFT*” or “*SFT apparently arising from the pelvic bones*” were excluded from the study. We were able to select 87 cases, whose main clinicopathologic features are summarized in Tables I-II ¹⁰⁻⁵³. The patients (54 males and 33 females) ranged in age from 24 to 83 years. Tumor size ranged from 4 to 30 cm. Although in most cases the authors said only that tumor was located in the pelvis, there were articles in which the site was mentioned in detail, including the paravesical, retrovesical, prevesical, rectovesical, pararectal, presacral,

Table I. Clinicopathologic features of histologically benign SFT of the pelvis: 63 cases.

References	Number of cases/ Site	Age/sex	Tumor size	Histology	Outcome
n.10	n.1 Retrovesical	68 yr/M	10 cm	Benign	NA
n.11	n.1 Pelvis n.1 Pelvis	64 yr/F 53 yr/F	5.7 cm 4.5 cm	Benign Benign	NA NA
n.13	n.1 Pelvis	49 yr/M	11 cm	Benign	NED, 3 months
n.14	n.4 Presacral/Pelvis	24-53 yr/4F	4-20 cm	Benign	NA 1 distant metastases, NA
n. 15	n.1 Ileum	33 yr/M	8.7 cm	Benign	NED, 36 months
n.16	n.1 Pelvis, prevesical	74 yr/M	11 cm	Malignant	NED, 18 months
n.17	n.1 Pelvis	58 yr/F	5.5 cm	Benign	LR, 24 months; NED, 72 months
n. 18	n.1 Paravesical n.1 Retrovesical	60 yr/M 60 yr/M	4 cm 5 cm	Benign Benign	NA NED, 24 months
n. 19	n.1 Retrovesical	39 yr/F	7.5 cm	Benign	NA
n.20	n.1 Pelvis	63 yr/M	30 cm	Benign	NED, 24 months
n. 22	n.1 Pelvis	62 yr/F	14 cm	Benign	NED, 60 months
n. 24	n.6 Pelvis	29-76 yr/4M-2F	4-18 cm	Benign	NED, 0-62 months 2 LR, 0-62 months 1 liver metastasis, 0-62 months
n.25	n.4 Pelvis	30-66 yr/3M-1F	7.9-11.7 cm	Benign	NED, 36 months
n.26	n.9 Pelvis	Median age: 56 yr/7M-2F	6.9-19 cm	Benign	1 DOD, 34 months
n.29	n.1 Pelvis	64 yr/M	10 cm	Benign	NED, 20 months
n. 31	n.1 Peri-rectal	56 yr/F	9 cm	Benign	NED, 24 months
n.32	n.2 Pelvis	48-73 yr/2F	NA	Benign	NED, 7-21 months
n. 33	n.1 Pelvis	52 yr/M	14.5 cm	Benign	NA
n.34	n.6 Pelvis	26-76 yr/3M-3F	5-15 cm	Benign	NED, 6-60 months
n. 35	n.1 Pelvis	76yr/M	17 cm	Benign	NED, 60 months
n. 36	n.1 Pelvis	52 yr/M	20 cm	Benign	NA
n. 37	n.1 Pelvis	74 yr/M	10 cm	Benign	NA
n. 38	n.1 Sigmoid mesocolon	68 yr/M	16 cm	Benign	NA
n. 40	n.1 Peri-rectal	37 yr/M	9.5cm	Benign	NED, 48 months
n. 42	n.1 Paravesical	34 yr/M	12 cm	Benign	NA
n.43	n.1 Pelvis	63 yr/F	16 cm	Benign	NA
n. 45	n.1 Paravesical	49 yr/M	10 cm	Benign	NED, 6 months
n. 46	n.1 Paravesical	46 yr/F	5 cm	Benign	NED, 25 months
n. 48	n.1 Perivesical	61 yr/M	13.6 cm	Benign	NA
n. 50	n.1 Retrovesical	64 yr/M	12 cm	Benign	NED, 3 months
n. 51	n.1 Prevesical	68 yr/M	19 cm	Benign	NED, 24 months
n. 52	n.5 Pelvis	32-48 yr/2M-3F	5-12 cm	Benign	4 NED, 2-17 years 1 LR , 6 months/AWD 12 months

Abbreviations: NA, not available; LR, local recurrence; NED, no evidence of disease; AWD, alive with disease; DOD, dead of disease.

Table II. Clinicopathologic features of histologically malignant SFT of the pelvis: 24 cases.

Reference number	Number of cases/ Site	Age/sex	Tumor size	Histology	Outcome
n. 12	n.1 Perivaginal	83yr/F	7.5 cm	Malignant	NED, 36 months
n. 21	n.1 Presacral	52yr/F	12cm	malignant	NED, 36 months
n. 23	n.1 Pelvis	70yr/F	17 cm	Malignant	DOD, 4 months
n. 24	n. 2 Paravesical n. 2 Rectovesical	47-61yr/4M	4.7-10 cm	Malignant	2 patients: LR, 0-62 months 1 patient: Liver metastases, 0-62 months
n. 27	n.4 Pelvis	31-66yr/3M-1F	NA	Malignant	2 patients: DOD, 12 months or later 1 patient: LR, 10years AWD, NA 1 patient: Distant metastases, 12 years lost follow-up
n. 28	n. 1 Pelvis	52yr/M	14 cm	Malignant	NA
n.30	n. 1 Pelvis	41yr/M	12.9 cm	Malignant	NED, 12 months
n.32	n.3 Pelvis	48-73yr/3F	16 cm	Malignant	2 patients NED, 7-21 months 1 patient Omental metastases, AWD, 12 months
n. 39	n.1 Pararectal	46yr/M	7.7cm	Malignant	LR, 6 months AWD, 12 months
n.41	n.1 Pelvis	28yr/M	18cm	Malignant	NA
n.44	n.1 Prevesical	74yr/M	11 cm	Malignant	Lung metastases AWD, 12 months
n. 47	n.1 Prevesical	61yr/M	11cm	Malignant	NA
n. 49	n.1 Pelvis	60yr/M	14cm	Malignant	NA
n. 53	n.3 Pelvis	32-71yr/2M-1F	1 case: 20 cm 2 cases: NA	Malignant	1 patient LR, 4years; NED, 5years 1 patient Distant metastases, 12 months; AWD, 24 months 1 patient Distant metastases, 24 months; AWD, 24 months

Abbreviations: NA, not available; LR, local recurrence; NED, no evidence of disease; AWD, alive with disease; DOD, dead of disease.

paravaginal spaces (Tabs. I-II). Most of the clinically reported symptoms were largely due to compression of urinary bladder and/or rectum. The majority of SFTs (63 out of 87) were histologically benign, while the remaining cases (24 out of 87) were reported to be “malignant SFTs”. Clinical follow-up was not available in 20.6% (13 out of 63 cases) and 16.6% (4 out of 24 cases) of histologically benign or malignant SFTs, respectively. In addition, the available follow-up period was relatively short for the majority of both histologically benign (3-72 months; only 1 case with a follow-up

at 17 years) or histologically malignant tumors (4-62 months; only 1 case with a follow-up at 12years). Notably tumors labeled as “malignant SFT” were associated with a local recurrence in 25% of cases (5 out of 20) and distant metastases in 45% of cases (9 out of 20). Local recurrence was reported in a wide range, from 6 months up to 10 years from surgery²⁷, while most of the distant metastases – mainly occurring in the liver and lung – were documented within the first 2 years from surgery^{23,32,44,53}. Interestingly, only one patient experienced metastatic disease at 12-years follow-up²⁷.

In contrast, tumors labeled as “benign SFT” showed a local recurrence in 8% (4 of 50) and distant metastases in only 6% of cases (3 of 50). The former was reported from 6 up to 62 months, while the latter from 34 up to 62 months after surgery.

Discussion

The pelvic cavity is rarely the site of origin of SFT, with most lesions located in the para/pre/peri-vesical spaces^{10,16,18,19,24,42,44,45-47,50,51}. Radiological imaging, as in our case, is not specific, often showing solid, nodular masses with well circumscribed borders^{14,24,25,34}. Accordingly the final diagnosis of SFT is still histologically-based. We admit that the diagnosis of SFT is straightforward in presence of a conventional morphology, while it may be challenging, especially when pathologist is facing with unusual sites and/or unusual morphological variants.

Apart from the unexpected site, it was the combination of spindle and epithelioid cells variably set in a fibro-myxoid stroma, along with pleomorphic/necrotic areas, that caused some difficulties in recognizing the present pelvic tumor as SFT. However, awareness that SFT may exhibit a wide morphological spectrum, including epithelioid cell component and variably abundant myxoid stroma, was helpful for a correct diagnostic interpretation. At the time (in 2010) of the original diagnosis, namely “*histologically malignant SFT*”, STAT6 – a specific immunomarker for SFT, resulting from an intrachromosomal inversion-derived gene fusion (*NAB2-STA6*) that drives STAT-6 nuclear expression – was not available, and thus the diagnosis was supported exclusively by a diffuse CD34 immunoreactivity, along with the lack of the expression of several other markers. We have recently performed immunohistochemical analyses that showed a diffuse nuclear staining for STAT6 in our case, thus further confirming the diagnosis of SFT.

Actually, it is well known that malignancy in SFT may develop “*de novo*” or more rarely in the form of sarcomatous dedifferentiation from a pre-existing histologically benign SFT¹. Extra-pleural SFT, including pelvic tumors, with atypical morphological features, despite adequate negative surgical margins, can show adverse events (local recurrences and distant metastases) in 6-20% of cases¹. A PubMedLINE-based search on SFT arising from the pelvic cavity retrieved 87 cases (54 males and 33 females). Most SFTs (72.4%) were histologically benign, while the remaining cases (27.6%) were reported to be “*malignant SFT*”, and most of the cases occurred in males (60.3% in histologically benign SFT; 66.6% in histologically

malignant SFT). Based on the clinico-pathologic features of patients with available follow-up, histological malignancy seems to predict adverse events in terms of local recurrence (25% vs 8% in histologically benign SFT) and distant metastases (45% vs 6% in histologically benign SFT). Tumor size, a potential unfavorable predictive feature, could not be studied in that it was not reported in most tumors with aggressive clinical course. The follow-up period of the reported cases is relatively short (with only two exceptions), and only 3 patients and 1 patient, respectively with histologically-malignant SFT or histologically-benign SFT, died of disease^{23,26,27}, while 5 metastatic patients are alive with disease at a 12-24 months follow-up^{24,32,44,53}.

The present pelvic SFT was originally classified as “*histologically malignant*” based on the coexistence of atypical features, including hypercellularity, cellular pleomorphism, increased mitotic activity (> 4 mitoses/10 HPF) and necrosis¹. Recently, the tumor was reclassified as an “*intermediate risk tumor*” for the development of metastasis by using the novel four-variable risk stratification model proposed by Demicco et al.⁹. The authors showed that their risk stratification model had 100% of sensitivity, in that all metastatic SFT evaluated (pleural and extra-pleural tumors) were classified as tumors with intermediate/high-risk class, with no reported case falling into the low-risk class⁹. Notably, our patient experienced an indolent clinical course after 10 years from radical surgery, emphasizing that the prognosis of extra-pleural SFT remains unpredictable for each single patient^{1,7}. Accordingly, we propose to abandon the use of the term “*malignant SFT*” in favor of “*SFT with atypical features*” to which the risk stratification class for distant metastasis should be included. This suggestion highlights that atypical morphological features do not necessarily reflect an adverse clinical outcome, but only a risk category (moderate- or high-risk) for distant metastases, and thus long-term follow-up of patients is mandatory.

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