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Clinicopathological characteristics of renal solitary fibrous tumor

A single institution experience

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Abstract

To analyze the clinical characteristics, treatment modalities and outcomes of adult renal solitary fibrous tumors (SFT) treated at a single institution. Demographic, diagnostic, surgical, and pathological findings of patients who had undergone radical nephrectomy (RN) due to renal SFT were collected from the database of a single institution and were retrospectively reviewed. Ten patients (6 men and 4 women) were diagnosed with renal SFT in our institution between January 1, 2000 and December 31, 2016. The mean age was 50.9 ± 8.2 years (range, 38–63 years). Of the 10 patients, 6 were asymptomatic, 2 presented with flank pain, 1 presented with abdominal discomfort, and 1 presented with haematuria. Computed tomography scans were obtained for all patients. Open RN was performed on 6 patients, and laparoscopic RN was performed on 4 patients. The mean tumor size was 10.23 ± 4 cm (range, 5.3–19 cm). Pathological diagnosis revealed that the tumors in 8 patients were benign, while those in the other 2 patients were malignant renal SFT. No recurrence occurred during a mean follow-up period of 47.3 ± 21.5 months (range, 16–85 months). Renal SFT is extremely rare, and its diagnosis may be challenging because of a lack of typical imaging manifestations. RN is a safe treatment modality for benign or low-grade malignant renal SFT, ensuring favorable outcomes.

Abbreviations: BMI = body mass index, CT = computed tomography, LRN = laparoscopic radical nephrectomy, RCC = renal cell carcinoma, RN = radical nephrectomy, RTB = renal tumour biopsy, SFT = solitary fibrous tumors.

Keywords: clinical characteristics, renal, solitary fibrous tumor, treatment modalities

1. Introduction

Solitary fibrous tumor (SFT) is a spindle cell tumor originating from mesenchymal cells. Although originally regarded as separate entities, SFT and haemangiopericytoma are now considered 1 neoplasm in the WHO classification of soft tissue tumors.[1] SFT is predominantly distributed in the pleura of the respiratory system as well as in the orbital cavities, thyroid, and sublingual gland.[2–5] The presence of SFT arising from the genitourinary system is rare,[6,7] and renal SFT is especially uncommon. Because it is an unusual renal lesion, a definite diagnosis is usually very difficult before surgery. Owing to its rarity, only a few cases have been described.[8,9] To the best of our knowledge, fewer than 60 cases of renal SFT have been reported in the English literature to date.[10,11] Furthermore, the small number of cases included in these studies limits the comprehensive understanding of renal SFT.

In the present study, we retrospectively investigated the clinical characteristics, management, and survival data of 10 adult patients with renal SFT diagnosed over 17 years at our institution. To date, our sample size represents the largest cohort of adults with renal SFT in the world.

2. Materials and methods

2.1. Patients

Clinical and radiological data were retrieved from archival files and were retrospectively analyzed. The institutional review board of the First Affiliated Hospital of Guangxi Medical University approved this study. All consecutive patients with histologically proven renal SFT treated at our single institution between January 1, 2000 and December 31, 2016 were included in the present study. Follow-up data were collected during periodic visits to the outpatient department or via telephone interviews.

Age, gender, body mass index (BMI), chief complaint, and underlying conditions were analyzed. Computed tomography (CT) scans were obtained for all patients. Each CT scan was reviewed independently by 2 experienced radiologists. Disagreements over imaging findings were resolved by debate, discussion, and consensus between the 2 radiologists. Imaging features of each scan were examined for lesion location, shape, size, number, and unenhanced and contrast-enhanced intensity and were

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Table 1

Clinicopathologic data of 10 cases of renal SFT.

No./sex/age	Side	Symptom	Tumor size, cm	BMI, m^2/kg	Treatment	Pathology	Follow-up (months)	Outcome
1/M/50	L	Ultrasound	$10 \times 9 \times 6$	24.5	ORP	Benign	36	NED
2/F/48	L	Ultrasound	$7 \times 6 \times 6$	24.3	ORP	Benign	85	NED
3/F/60	R	Hematuria	$8 \times 4 \times 3$	21.2	LRP	Benign	78	NED
4/M/47	R	Ultrasound	$9 \times 4 \times 5$	20.7	ORP	Benign	56	NED
5/F/44	R	Abdominal discomfort	$14 \times 10 \times 8$	25	ORP	Low-grade malignant	49	NED
6/M/45	R	Ultrasound	$9 \times 6 \times 5$	21.8	LRP	Benign	44	NED
7/M/61	R	Flank pain	$19 \times 12 \times 10$	22	ORP	Low-grade malignant	35	NED
8/M/53	R	Flank pain	$13 \times 12 \times 9$	23	ORP	Benign	48	NED
9/F/63	L	Ultrasound	$8 \times 6 \times 5$	21	LRP	Benign	26	NED
10/M/38	L	Ultrasound	$5.3 \times 4 \times 3$	22	LRP	Benign	16	NED

F = female, L = left, LRP = laparoscopic radial nephrectomy, M = male, NED = no evidence of disease, ORP = open radical nephrectomy, R = right, SFT = solitary fibrous tumor.

classified as hypointense, isointense, or hyperintense with respect to the adjacent normal renal tissues.

2.2. Pathology

All pathological specimens were reviewed by 2 experienced pathologists specializing in genito-urology. Pathological diagnosis, tumor size, and resection margin status were reported. Typical microscopic features of benign renal SFT, including fusiform or ovoid spindle cells and varying amounts of collagen bundles with patternless, storiform or fascicular arrangements with an occasional haemangiopericytomatous pattern were the diagnostic criteria.

Immunohistochemical markers, including CD34, CD99, bcl-2, smooth muscle actin (SMA), S100, cytokeratins (CK), desmin, epithelial membrane antigen (EMA), and human melanoma black 45 (HMB45), were measured for equivocal cases.[2,4,12] The diagnostic criteria for malignant renal SFT include increased cellularity, pleomorphism, increased mitotic activity (>4 mitoses per 10 high-power fields), hemorrhage and necrosis.[12]

2.3. Statistical analyses

Continuous data are presented as the mean and standard deviation unless stated otherwise. The statistical significance of continuous variables was evaluated using the Mann–Whitney *U* test. Statistical analyses were performed using SPSS version 16 (SPSS, Chicago, IL), with P values $<.05$ considered significant.

3. Results

3.1. Clinical findings

During the study period, 702 patients diagnosed with renal cell carcinoma (RCC) underwent partial nephrectomy (PN) or radical nephrectomy (RN). A total of 10 patients with renal SFT were identified from among 702 RCC cases treated at our institution (1.42%). All the patients underwent RN with the diagnosis of renal SFT. Their mean age was 50.9 ± 8.2 years (range, 38–63 years), and their mean BMI was 22.3 ± 1.75 kg/m^2 (range, 20–25 kg/m^2). Six patients were men and 4 were women. Three patients were asymptomatic but were incidentally diagnosed during health screening programmes or while seeking treatment for other medical conditions. The chief complaints included 2 instances of flank pain, 1 instance of abdominal discomfort and 1 instance of hematuria (Table 1).

3.2. Treatment

Open radical nephrectomy (ORN) was performed in 6 patients, and laparoscopic radical nephrectomy (LRN) was performed in 4. The mean operative time was 97.1 ± 6 and 84.75 ± 18.2 minutes ($P = .269$), and the mean BMIs were 23.25 ± 1.6 and 21 ± 0.74 kg/m^2 ($P = .022$) for the open and laparoscopic groups, respectively. Neither recurrence nor metastasis occurred during a mean follow-up period of 47.3 ± 21.5 months (range, 16–85 months; Table 1).

3.3. Imaging findings

All patients underwent CT in the pre-contrast, arterial, venous and excretory phases. Pre- and post-contrast Hounsfield unit values were obtained for 10 patients. All the cases were misdiagnosed as RCC before surgery. In the 8 patients with benign renal SFT, CT images typically showed a well-circumscribed solid homogeneous mass in the pre-contrast phase, and enhancement after contrast injection was typically intense and homogeneous in each phase (Fig. 1), partially correlating with necrosis and hemorrhage. In the 2 patients with malignant renal SFT, the CT images typically showed a heterogeneous, irregular, ill-defined boundary mass in the pre-contrast phase, while enhancement after contrast injection was typically intense and heterogeneous, simultaneously correlating with necrosis, hemorrhage, or cystic degeneration in each phase (Fig. 2). Calcification was not observed in any patient.

3.4. Histopathology

The tumors had a mean diameter of 10.23 ± 4 cm (range, 5.3–19 cm). The gross specimen of benign renal SFT was a circumscribed round mass (Fig. 3A). The cut section revealed a whirled-like grey-white or white mass with a firm or fibrous consistency (Fig. 3B). The gross specimen of malignant renal SFT showed irregular and unencapsulated mass (Fig. 3C). The cut section revealed a yellowish white to trans-grey myxoid and lobulated mass with prominent hemorrhage and necrosis (Fig. 3D). Pathological diagnoses revealed that the tumors were benign in 8 patients (Fig. 4A and B), and there were low-grade malignant SFTs in 2 patients (Fig. 4C and D). None of the patients had a positive surgical margin or invasion into the renal fat or lymphovascular system. The tumor cells of malignant and benign SFT all stained diffusely positive for CD34 (Fig. 5A and B) and bcl-2 (Fig. 5C and D). The immunohistochemical indexes were selected in accordance with the location of the primary lesion, as

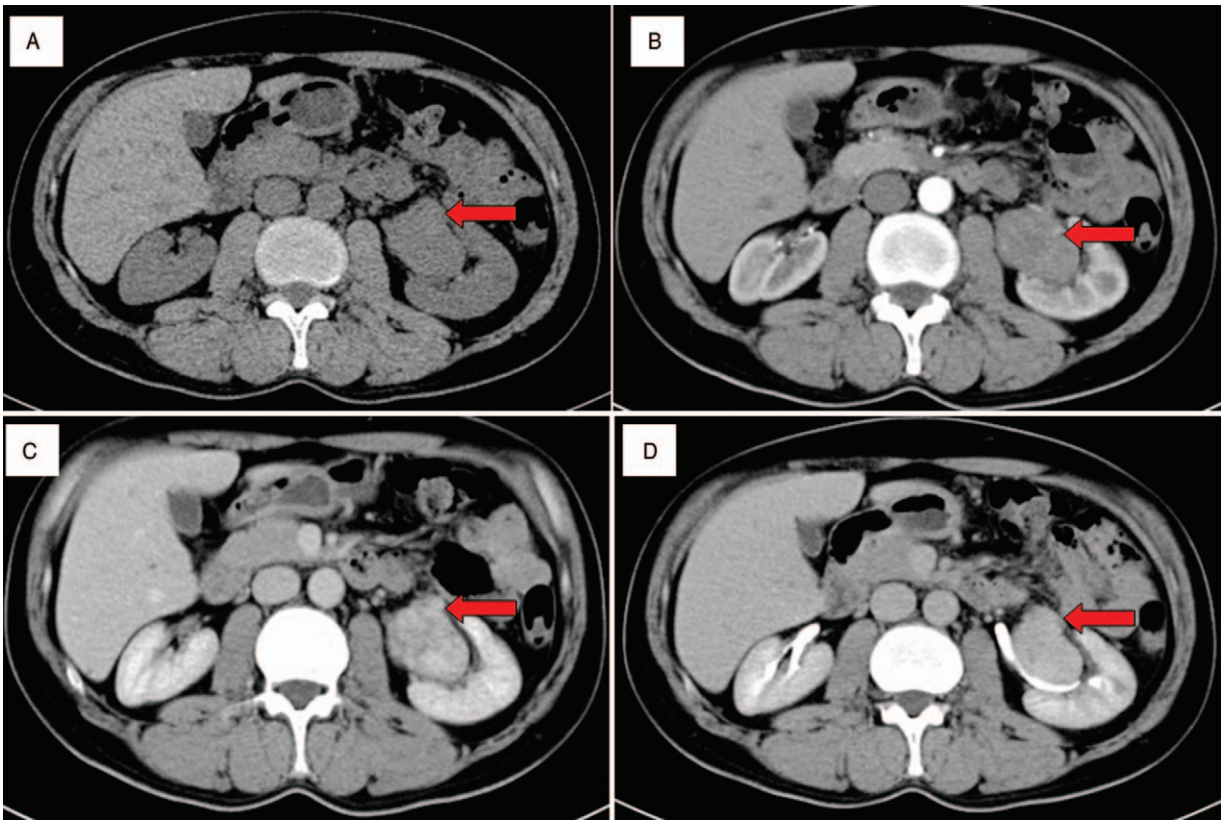

Figure 1. (A) Computed tomography image showing a homogeneous soft tissue mass (red arrow) located within the left kidney in the pre-contrast phase. (B–D) With contrast, the arterial, venous and excretory phases show a well-circumscribed, solid, homogeneous, low-enhanced mass (red arrow) in the left kidney.

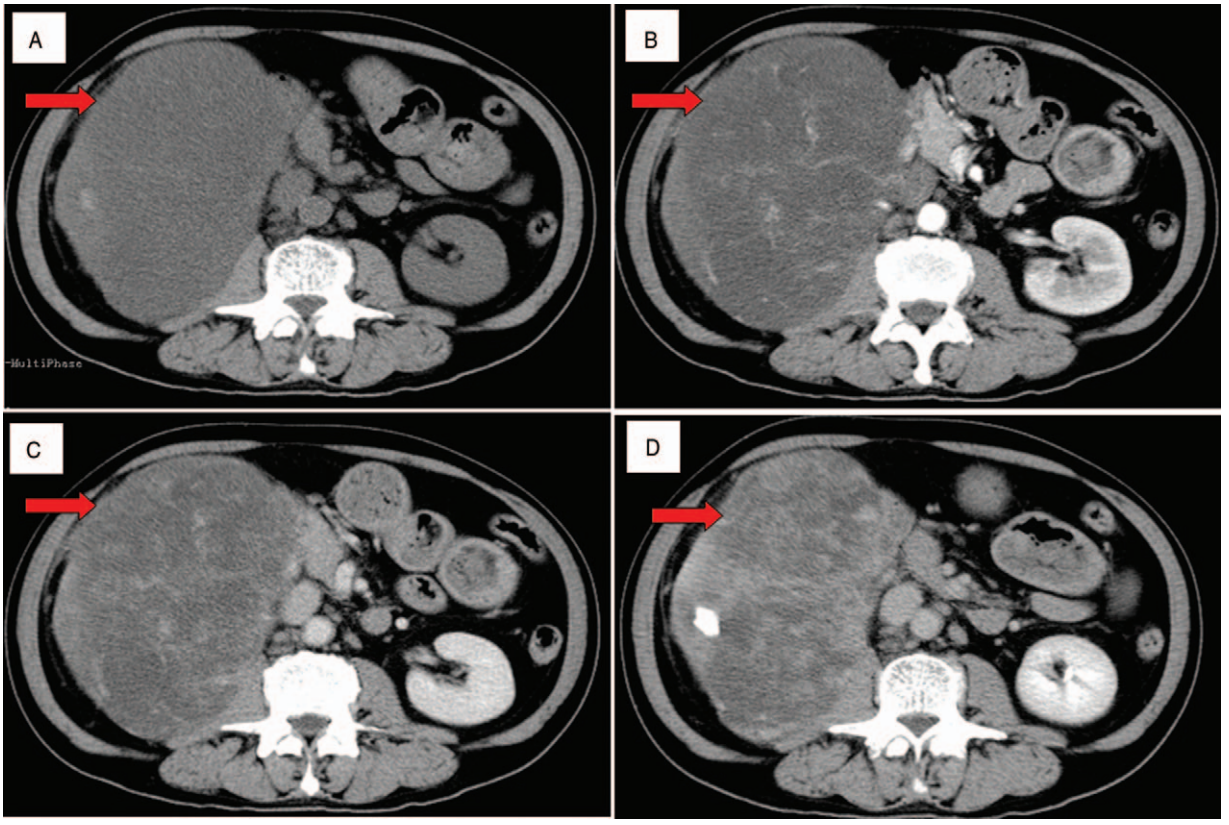

Figure 2. (A) Computed tomography image showing a heterogeneous, irregular, ill-defined boundary mass in the right kidney in the pre-contrast phase. (B–D)With contrast, the arterial, venous, and excretory phases show a solid, heterogeneous, and irregular enhanced mass in the right kidney.

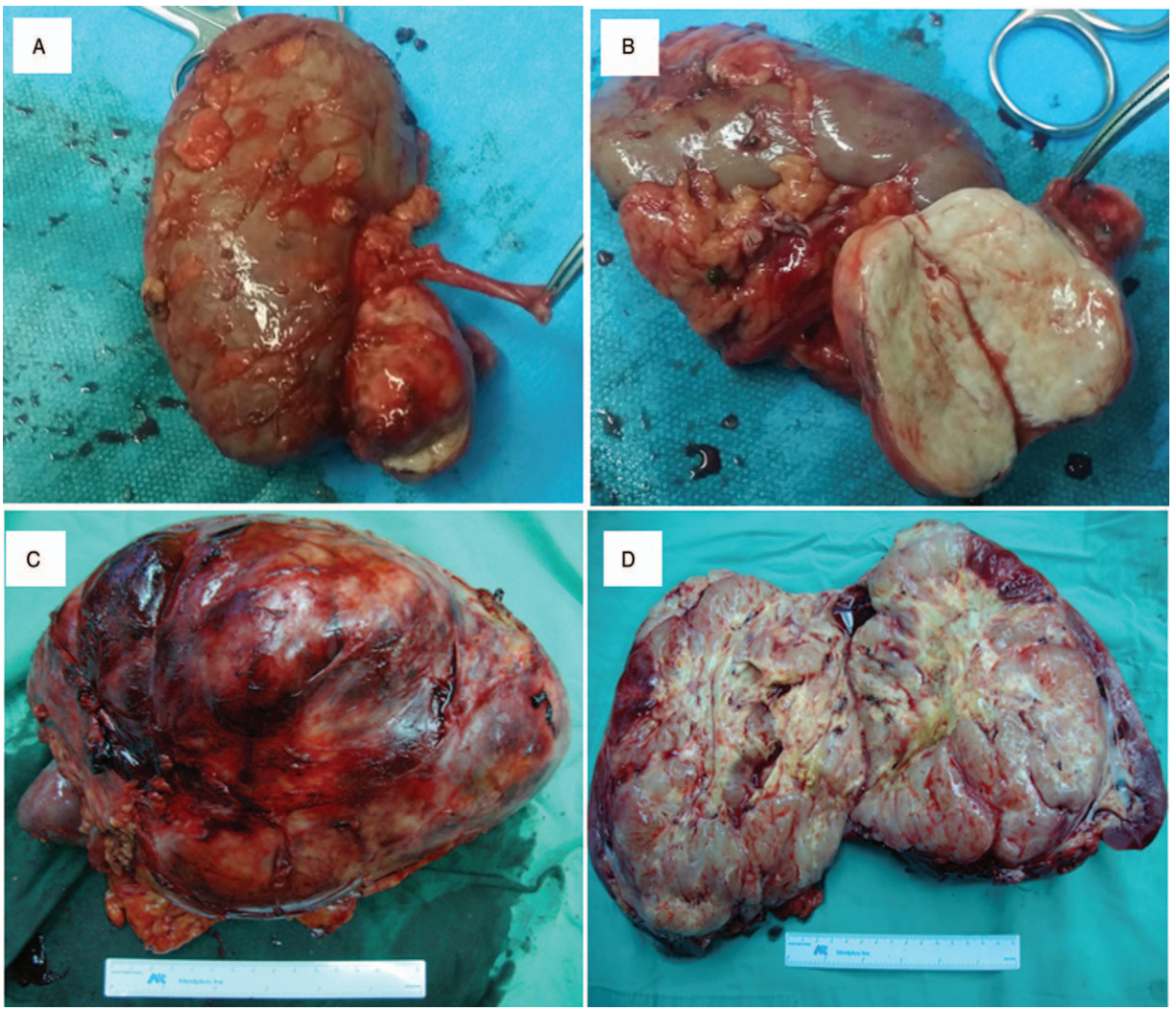

Figure 3. (A) A gross specimen of benign renal SFT, showing a circumscribed round mass. (B)The cut section showing a whirl-like grey-white mass with a firm or fibrous consistency. (C)The gross specimen of malignant renal SFT showing an irregular, ill-defined, unencapsulated mass. (D)The cut section showing a yellowish-white myxoid lobulated mass with prominent haemorrhage and necrosis.

different tissues have different specific markers. Table 2 displays the immunohistochemical results.

4. Discussion

SFT appears very infrequently in the kidney. The rarity of the tumor is a major obstacle in clinical research, and contemporary data are scarce. To the best of our knowledge, this study is the largest investigation of renal SFT and its surgical outcomes. Our results agree with previously reported demographics, radiological findings, surgical outcomes, recurrence rates, and mortality. Furthermore, the majority of cases of renal SFT were likely isolated, and therefore, the detailed incidence remains unknown.[13] In the WHO kidney tumors classification, they are described as a "fibroblastic mesenchymal tumor with malignant potential". Accordingly, our study showed that the incidence of renal SFT among the patients diagnosed with RCC was 1.42% (10/702) at our institution. As shown previously, the disease did not demonstrate a gender predominance.[10,11] The age distribution of the renal SFT patients was concentrated between the ages of 28 and 83 years (mean, 52 years); likewise, the mean age of our group was 50.9 ± 8.2 years (range, 38–63 years).

Renal SFT is primarily unilateral, and bilateral SFT has seldom been reported in the literature.[14,15] Symptoms of renal SFT usually do not differ from those of RCC, including flank or abdominal pain, and/or gross haematuria and a palpable mass. Patients generally present for consultation if larger tumors compress the adjacent organs or induce symptoms. Most cases are incidentally detected on radiological imaging including ultrasound, CT or magnetic resonance imaging (MRI). In our cohort, only 4 patients had clinical symptoms, including 2 with flank pain, 1 with abdominal discomfort and 1 with haematuria; these findings are consistent with those of other reports.

Renal SFT mimics RCC and must be included in the differential diagnosis of angiomyolipoma, fibroma, and fibrosarcoma. Renal SFT has been described as a hypoechoic or heterogeneous echoic mass with relatively well-defined margins and as a hypoechoic mass with intratumoral vascularity on Doppler ultrasonography. The typical imaging manifestation of renal SFT is a well-circumscribed, smooth, lobulated, soft tissue mass that is

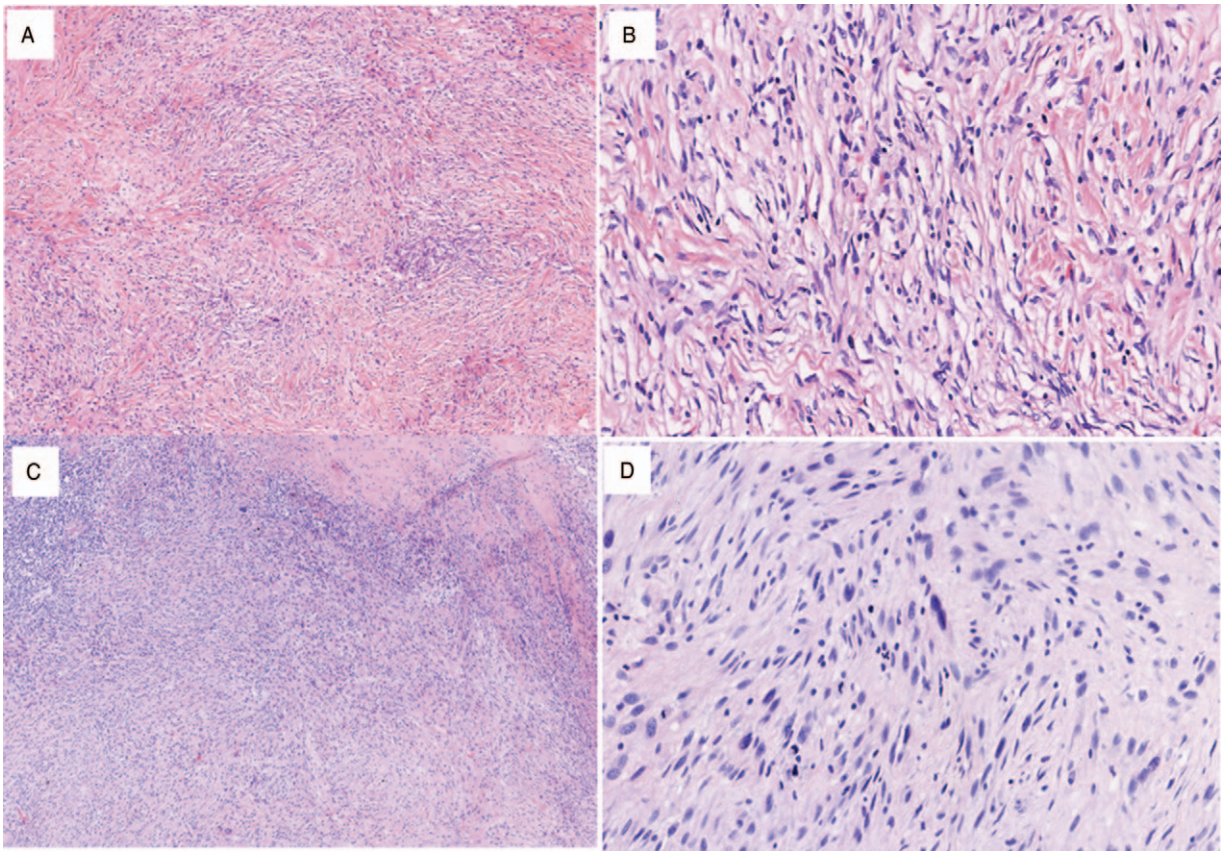

Figure 4. (A–B) Representative microscopic features of a benign SFT consisting of tightly packed round-to-fusiform cells with clear indistinct cytoplasmic borders forming ill-defined fascicles (haematoxylin–eosin staining 100×, A and 400×, B). Representative microscopic features of a malignant renal SFT showing crowded overlapping nuclei, pleomorphism, nuclear atypia, and numerous mitotic figures (haematoxylin–eosin staining 100×, C and 400×, D).

attenuated in the pre-contrast phase and is mildly or moderately increased in the post-contrast phase. The mass appears mostly homogeneous when unenhanced but may appear homogeneous or heterogeneous with enhancement.[10,11,16] Although these characteristics are nonspecific for making a differential diagnosis, it enables CT scanning to be a useful modality for preoperative diagnosis. MRI shows low or intermediate signal intensity on T1- and T2-weighted images. T2-weighted imaging of hypointense lesions reveals hypercellularity and abundant collagenous stroma. The hyperintense lesions demonstrate necrotic, myxoid, or cystic changes.[17]

The diagnosis of renal SFT is based primarily on histopathological and immunohistochemical findings. Macroscopically, renal SFT is classically solid, firm, and well circumscribed, with grey, white, or yellowish-brown cut surfaces, demonstrating partial hemorrhage and necrosis. Microscopic features include the presence of irregular beam- or vortex spindle-shaped cells. Some areas have alternating dense and sparse cells, with collagen fibers in-between, while other areas are rich in blood vessels with visible hemangiopericytoma-like structures. Cellular atypia is inconspicuous, and nuclear fission, hemorrhage, and necrosis are rarely seen. It is very important to differentiate SFT from other spindle cell tumors or sarcomatoid RCC using immunohistochemical biomarkers. The tumor cells of SFT are diffusely positive for CD34, CD99, and Bcl-2. Especially for CD34, strong-positive expression is observed in most tumor cells[4,10,11,18,19] with important diagnostic significance for SFT. However, a recent study suggested that a substantial minority of SFTs express either PAX8 or PAX2.[19] PAX8 and PAX2 are commonly used as renal tumor markers. This presents a diagnostic pitfall for renal SFT in clinical practice and demonstrates that sensitive biomarkers of SFT are urgently needed. Until recently, little research has involved the molecular genetics of SFT. Using whole exome and transcriptome sequencing, 3 groups recently identified NAB2–STAT6 gene fusions in the vast majority of SFT.[20–22] Subsequently, 2 articles reported that strong nuclear STAT6 was largely specific for SFT.[23,24] Therefore, STAT6 may be highly sensitive and an almost perfectly specific marker for SFT. Future prospective studies recruiting consecutive patients should be required to verify the presence of STAT6. Pathological features of malignant renal SFT showed indistinct boundaries with cellularity, pleomorphism, increased mitotic activity, hemorrhage, and necrosis.

Traditionally, the role of renal tumor biopsy (RTB) has been controversial because of safety and accuracy issues. Several lines of evidence have demonstrated that RTB has good accuracy and safety in diagnosing renal tumor and its subtypes before surgery due to improvements in imaging and puncture techniques.[25] As a tertiary referral center, patients in our series tended to have larger tumors (the mean diameter was 10.23 ± 4 cm). Nevertheless, because the diagnoses of renal tumors were definite (although the nature of the tumors was unknown) we did not perform RTB before surgery.

The tumor size of renal SFTs ranged from 2 to 25 cm, with a mean diameter of 8.75 cm, as shown in the series. Likewise, the

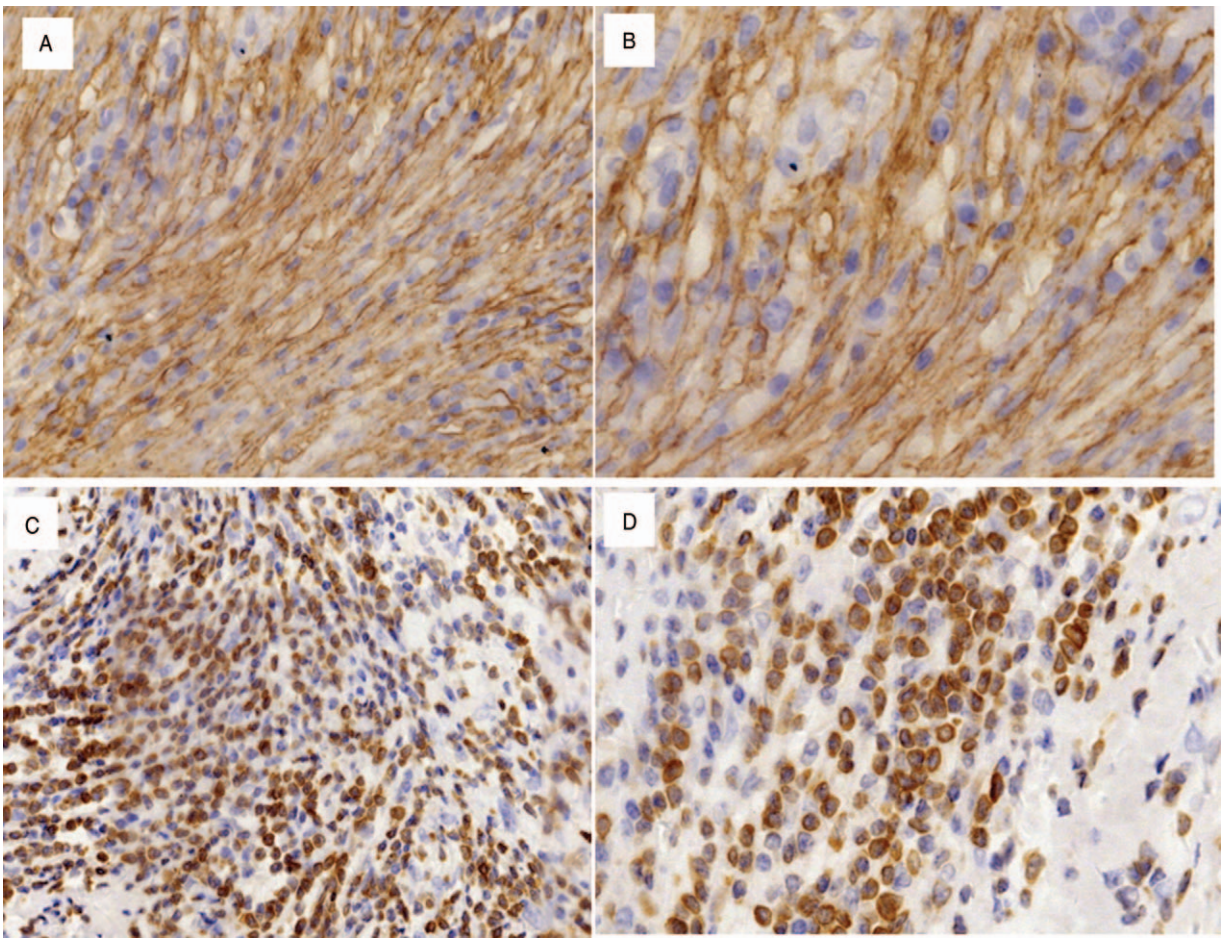

Figure 5. (A–B) Microscopic picture of a renal SFT showing diffusely positive staining for CD34 (100× A and 400× B). (C–D)Microscopic picture of a renal SFT showing diffusely positive staining for bcl-2 (100× C and 400× D).

mean tumor size in our group was 10.23 ± 4 cm (range, 5.3–19 cm). This means that it may be technically challenging to remove these tumors via laparoscopy alone. During the 15-year study period, the surgical approaches performed in our institution have changed. Earlier, few surgeons performed LRN, but it is now considered the minimal invasive treatment for RCC. Open and laparoscopic operations were chosen based on the surgeon's preference, and tumor size was not a statistically significant factor in the decision.

The natural history of untreated renal SFT has not been reported. Although the clinical symptoms and pathological diagnoses revealed that tumors in some patients were benign in other organs, postoperative recurrence or metastasis was occasionally encountered. SFT are categorized as having intermediate biological potential with a low risk of metastasis according to the 2002 WHO Classification. Clinical behavior cannot be predicted on a histopathological basis, with benign-appearing tumors exhibiting aggressive behavior, and vice versa.

Table 2

Immunohistochemistry marker expression in 10 cases of renal SFT.

No.	CD34	CD99	bcl-2	SMA	Vimentin	Actin	S100	EMA	HMA45	ki67, %
1	+	+	+	+	−	−	−	−	−	0
2	+	+	+	−	−	−	−	−	−	0
3	+	−	+	−	−	−	−	−	−	0
4	+	−	+	−	+	−	−	−	−	2
5	+	+	+	−	+	−	−	−	−	15
6	+	+	+	−	+	+	−	−	−	0
7	+	+	+	−	+	−	−	−	−	10
8	+	+	+	+	+	−	−	−	−	0
9	+	+	+	+	−	−	−	−	−	2
10	+	+	+	−	−	−	−	−	−	5

EMA = epithelial membrane antigen, SFT = solitary fibrous tumor, SMA = smooth muscle actin.

A recent large study of prognostic factors in SFT was reported by Demicco et al in 2012.[1] They concluded that a larger tumor size (>15 cm), advanced age (>55 years), and more mitotic counts (>4 high-power fields) conferred a high risk for both metastasis and death. However, the clinical behavior of individual tumors is notoriously difficult to predict. In the present study, all 10 patients who underwent complete tumor resection, including ORN or LRN, were alive during the mean follow-up of 47.3 ± 21.5 months (range, 16–85 months). In the relevant literature, the prognosis of malignant renal SFT patients was also favorable, with infrequent recurrence or metastasis.[26,27] Our findings were consistent with those of the literature. Although 2 patients with renal SFT showed low-grade malignant features, no recurrence or metastasis occurred during the follow-up period. RN for benign or malignant renal SFT was associated with a favorable prognosis according to our results.

Therefore, long-term follow-up is mandatory for patients with benign or malignant renal SFT. Future large population studies are required to enrich our understanding of this tumor type and its behavior and to improve its diagnosis and management.

In conclusion, renal SFT is a rare benign tumor. To date, there have been few large studies available on renal SFT. In this retrospective, single-institution cohort study, we evaluated the clinical outcomes of 10 patients with renal SFT in a single institution. The preoperative diagnosis of renal SFT remains difficult. Characteristic findings are not often observed in imaging studies; therefore, histological features and immunohistochemical staining may be helpful in confirming the diagnosis. Surgery is the primary treatment for benign or low-grade malignant renal SFT, and the prognosis following complete tumor resection is favorable.

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Writing – review & editing: Qin Bing.

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