Histol Histopathol (2022) 37: 43-50

http://www.hh.um.es

Histology and Histopathology
From Cell Biology to Tissue Engineering

ORIGINAL ARTICLE **Open Access**

Clinicopathological analysis of retroperitoneal solitary fibrous tumours: a study of 31 cases

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Summary. A solitary fibrous tumour (SFT) is a mesenchymal tumour that exhibits fibroblast differentiation and rarely occurs in the retroperitoneum. The main purpose of this study was to explore the clinical manifestation, histopathological features and biological behaviour of retroperitoneal SFT. From 2011 to 2020, 31 patients were hospitalized and diagnosed with retroperitoneal SFTs. We summarized and analysed the morphological features, immunophenotype, treatment and prognosis. Patients (13 M; 18 F) ranged in age from 25 to 79 years with a mean age of 53.6 years. The main symptoms included an abdominal mass (48.4%) and abdominal discomfort (25.8%). The mean maximum diameter of the tumours was 12.9 cm (range, 4-40 cm). Histopathologically, there were 17 classic cases and 14 hemangiopericytoma-like cases. The tumour cells were positive for STAT6 (96.8%), CD34 (96.8%), CD99 (93.5%) and BCL-2 (90.3%). All patients were treated with complete surgical excision, and 3 of the patients also received chemotherapy. After a median follow up period of 44 months (range, 6 to 107 months), 2 patients died. Patients in the high- or intermediate-risk group were prone to metastasis and/or recurrence. The sites of metastases and/or recurrences involved the liver, bone and pelvis. The Ki-67 labelling index in the high-intermediate risk group (median, 10%) was significantly higher than that in the low-risk group (median, 3%). The retroperitoneal SFT demonstrates an indolent clinical course, and patients from the high- or intermediate-risk group require close follow-up. A Ki-67 labelling index ≥10% may be used as an important reference for prognosis.

Key words: Solitary fibrous tumour, Retroperitoneal, Clinicopathological characteristics, Recurrence, Metastasis, Prognosis

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DOI: 10.14670/HH-18-392

Introduction

Solitary fibrous tumours (SFTs) are heterogeneous mesenchymal tumours exhibiting variable clinical and biological characteristics (Demicco et al., 2020). SFT was first reported to occur in the pleura (Klemperer and Coleman, 1992), and it was later confirmed that it can also occur at any anatomic site including the head and neck (Smith et al., 2017), trunk (Ge et al., 2016), and lower extremities (Chuang et al., 2016). However, an SFT in the retroperitoneum is extremely rare, and the existing literature on SFTs is limited (Yoh et al., 2014). Owing to its rarity, retroperitoneal SFTs are not fully understood.

SFT was defined as a fibroblastic tumour characterized by a prominent, branching, thin-walled, dilated vasculature and *NAB2-STAT6* gene rearrangement by the 2020 WHO classification of soft tissue and bone tumours. Most SFTs are histologically benign, but approximately 12-22% of cases are malignant (Campbell and Antippa, 2006). Although adverse outcomes were associated with mitotic activity, tumour necrosis and size, histologically benign SFTs have been reported to metastasize and/or to recur (Gold et al., 2002). Therefore, it is challenging to evaluate the biological behaviour of the SFT.

Of note, morphologic and immunophenotypic

Abbreviations. SFT, solitary fibrous tumour; F, female; M, male; SE, surgical excision; CT, chemotherapy; RT, radiotherapy; ZSJQ-BIO, Zhong Shan Jin Qiao-Biology; N, No; Y, Yes; FISH, Fluorescence in situ hybridization; HPFs, high power fields

overlap with other spindle cell sarcomas in the retroperitoneum often makes the diagnosis of SFT difficult. Until recently, some studies have identified *NAB2-STAT6* gene fusions and STAT6 overexpression in the vast majority of SFTs (Doyle et al., 2014b; Chuang et al., 2016). The application of these auxiliary examinations made it possible to accurately diagnose SFTs. Moreover, focusing on these histological parameters, including atypical, cellular, and mitotically active parameters, would enable us to promptly consider this diagnostic possibility and to predict its prognosis. There have been a few studies on the clinicopathological correlation in SFTs (Demicco et al., 2012; Feasel et al., 2018). However, the present study is the largest one to investigate the clinical manifestation, morphology, immunophenotype, diagnosis, biological behaviour and prognosis of this unusual entity.

Materials and methods

Patient enrolment

Patient files from the Department of Pathology of the authors and colleagues who participated in this study during the period from March 2011 to April 2020 were retrospectively reviewed. This retrospective review was conducted with a protocol approved by the Ethics Committee of the hospitals. The clinical data from the institutional archives and Electronic Medical Record System were collected and analysed anonymously, including the patient age, sex, vital status, date of the last follow-up, primary tumour site, site of metastasis and recurrence, and chemotherapeutic and surgical interventions. Cases with incomplete clinical data or no follow-up information were excluded from this study. All patients were definitively diagnosed with SFT by postoperative pathological and immunohistochemistry examination. Routine haematoxylin and eosin slides were reviewed by two experienced pathologists, and immunohistochemical examinations and fluorescence in situ hybridization (FISH) were performed for diagnosis and differential diagnosis. Histopathological variables were evaluated, and a tumour risk stratification model for metastasis or recurrence was established according to the 2020 WHO classification of soft tissue and bone tumours.

Immunohistochemistry and fluorescence in situ hybridization (FISH)

Immunohistochemistry was performed on 4 mm-thick formalin-fixed paraffin-embedded tissue sections according to the manufacturer's instructions. The panel of primary antibodies was as follows: STAT6, CD99, BCL-2, CD34, vimentin, S-100, SMA, CD117, DOG-1, Ki-67 and MDM2 (antibody information is detailed in Table 1). Specifically, immunoactivity for STAT6 was evaluated using the following scale described by Doyle et al (the positive proportion was scored as "1+ for <5%, 2+ for 5-25%, 3+ for 26%-50%, 4+ for 51%-75%, and 5+ for >75%", and the staining intensity was scored as "0 for no staining, 1 for light yellow, 2 for yellowish brown, and 3 for brown"). The expression patterns of the other primary antibodies are also listed in Table 1. In addition, all cases in this study underwent an *MDM2* gene amplification test in order to exclude dedifferentiated liposarcoma.

Statistical analysis

Significant differences between groups were determined using one-way analysis of variance (one-way ANOVA). A $p<0.05$ was considered statistically significant. Analyses were conducted with Prism 7.0 (GraphPad Software, Inc.).

Results

Clinical characteristics

Thirty-one cases were identified in the pathology archives and Electronic Medical Record System (Table 2). The patients included 13 males and 18 females aged from 25 to 79 years with an average age of 53.6 years at diagnosis. The patients' symptoms varied and were non specific, and included a palpable mass (n=15),

Table 1. List of antibodies.

Antibody	Positive part	Dilution	Clone	Company	Retrieval
STAT6	Nucleus	Prediluted	EP325	ZSJQ-BIO, China	EDTA ph8.0
CD99	Cytoplasm/membrane	Prediluted	HO36-1.1	ZSJQ-BIO, China	EDTA ph8.0
BCL-2	Cytoplasm/membrane	Prediluted	EP36	ZSJQ-BIO, China	EDTA ph8.0
CD34	Cytoplasm/membrane	Prediluted	EP88	ZSJQ-BIO, China	EDTA ph8.0
Vimentin	Cytoplasm	Prediluted	EP21	ZSJQ-BIO, China	EDTA ph8.0
S-100	Nucleus/cytoplasm	Prediluted	15E2E2+4C4.9	ZSJQ-BIO, China	EDTA ph8.0
CD117	Cytoplasm/membrane	Prediluted	SC168	ZSJQ-BIO, China	EDTA ph8.0
SMA	Cytoplasm	Prediluted	UMAB237	ZSJQ-BIO, China	EDTA ph8.0
MDM2	Nucleus/ cytoplasm	Prediluted	1E6&17B3	ZSJQ-BIO, China	EDTA ph8.0
Ki-67	Nucleus	Prediluted	MIB1	ZSJQ-BIO, China	EDTA ph8.0

ZSJQ-BIO, Zhong Shan Jin Qiao-Biology

abdominal pain (n=7), abdominal distention (n=1), dysuria (n=1) and extremity weakness (n=1). However, 6 of the 31 patients (19.4%) had no symptoms at all, and the tumours were discovered incidentally during physical examination. The tumours had different adjacent structures involving the pancreas, kidney, psoas major, bladder, rectum, liver, ureter, ileum, intestine, omentum and ovary. All patients underwent surgical resection, and 2 of them also received chemotherapy or chemoradiotherapy (case 9 received a chemotherapy with ifosfamide and nedaplatin, and case 31 received ifosfamide plus radiotherapy). The tumour size ranged from 4 to 40 cm with a mean maximum diameter of 12.9 cm. Of note, there were three masses in case 3 and two masses in cases 29 and 31.

Pathologic features

Macroscopically, the tumours were usually large in size and slightly hard in texture. The appearance of the tumours was grey-red, with no evident haemorrhage or necrosis on the cut surface. The histopathologic features, including cell density, cellular atypia and necrosis, and mitoses, of each case are summarized in Table 3. The entire morphologic spectrum of retroperitoneal SFTs was presented in our series, including 14 cases of cellular SFT and 17 cases of classic SFT. Microscopically, the cellular variants were composed of ovoid, monomorphic cells with various staghorn-like vessels. The classic variants demonstrated sparse tumor cells haphazardly arranged in coarse collagen fibres (Fig. 1). Mitotic activity ranged from 0 to 6 mitotic figures/10 high-power fields (HPFs) (mean, 1.7/10 HPF). Twenty-two cases were diagnosed as borderline SFT, and 9 cases (1, 3, 4, 9, 12, 18, 23, 29 and 31) were diagnosed as malignant SFT according to the criteria for malignancy: striking hypercellularity, mitotic rates, and necrosis.

Immunohistochemical and FISH studies

The immunohistochemistry results of each marker are shown in Table 4. Thirty of the 31 cases of SFT (96.8%) showed nuclear staining for STAT6, which was usually diffuse (5+ in 21 cases; 4+ in 7 cases; and 3+ in 2 cases) and intense (strong in 22 cases; moderate in 7 cases; and weak in 1 case). Tumour cells were positive for vimentin (31/31, 100%), CD34 (30/31, 96.8%), CD99 (29/31, 93.5%) and BCL-2 (28/31, 90.3%) (Fig.

Table 2. Clinical data of 31 patients with retroperitoneal SFT.

Case no. /gender/age	Symptom	Adjacent structure	Treatment	Maximum diameter/cm	Recurrence/ Months	Metastasis/ months/location	Follow up/ months
1/F/55	Palpable mass	Pancreas, Kidney	SE	40	Yes/6	No	44, alive
2/F/49	Palpable mass	Bladder	SE	9	No	No	44, alive
3/F/48	Abdominal distention	Right kidney	SE	20, 8 and 3	No	No	47, alive
4/M/57	Palpable mass	Bladder, Rectum	SE	20	No	No	71, alive
5/M/57	Abdominal pain	Left kidney	SE	15	No	No	100, alive
6/M/56	Abdominal pain	Bladder	SE	16	No	No	99, alive
7/M/55	Abdominal pain	Liver	SE	16	No	No	44, alive
8/M/32	Asymptomatic	Left upper retroperitoneum	SE	18	Yes/48	Yes/48/Liver	107, alive
9/F/64	Abdominal pain	Ureter，Rectum	SE+CT	11	Yes/24	Yes/24/Liver and bone	92, died
10/M/58	Palpable mass	Ileum	SE	5	No	No	58, alive
11/M/78	Palpable mass	Intestine	SE	21	No	No	24, died of lung cancer
12/M/51	Abdominal pain	Bladder	SE	10	No	No	28, alive
13/F/52	Asymptomatic	Right kidney	SE	6.5	No	No	75, alive
14/F/62	Asymptomatic	Intestine	SE	4	No	No	100, alive
15/F/57	Asymptomatic	Omentum	SE	4	No	No	18, alive
16/F/46	Palpable mass	Omentum	SE	6	No	No	31, alive
17/F/25	Abdominal pain	Bladder, Ureter	SE	11	No	No	57, alive
18/F/66	Abdominal pain	Ovary	SE	16	No	No	73, alive
19/F/53	Asymptomatic	Ureter, Rectum	SE	6	No	No	28, alive
20/F/46	Asymptomatic	Bladder, Omentum	SE	5	No	No	43, alive
21/M/59	Palpable mass	Bladder	SE	17	No	Yes/65/psoas major	69, alive
22/F/60	Palpable mass	Bladder	SE	7	No	No	56, alive
23/M/45	Palpable mass	Bladder	SE	9	No	No	49, alive
24/F/43	Palpable mass	Bladder	SE	11	No	No	35, alive
25/M/61	Palpable mass	Ureter	SE	14	No	No	30, alive
26/F/60	Palpable mass	Sigmoid colon	SE	13	No	No	28, alive
27/M/61	Dysuria	Bladder	SE	15	No	No	14, alive
28/F/36	Palpable mass	Rectus abdominis，Bladder	SE	15	No	No	14, alive
29/F/79	Extremities weakness	Ileum, appendix	SE	8, 6	No	No	12, alive
30/M/36	Palpable mass	Bladder	SE	12	No	No	6, alive
31/F/55	Palpable mass	Pancreas, Kidney	SE+CT+RT	20, 10	Yes/6	Yes/12/ Liver	39, alive

F, female; M, male; SE, surgical excision; CT, chemotherapy; RT, radiotherapy.

2). Almost all the tumours were negative for SMA (0/31), CD117 (0/31), desmin (1/31) and S-100 (1/31). MDM2, a useful marker for the diagnosis of dedifferentiated liposarcoma, was also negatively expressed in 31 cases of retroperitoneal SFT (data not shown in Table 4). The immuno¬histochemistry for the Ki-67 labelling index showed 1% to 30% positive for nuclear of tumours cells (median, 5%), and it was 10% or higher in 35.5% of cases. In addition, there was no *MDM2* gene amplification in any of the cases by FISH.

Follow up information

Thirty-one patients underwent complete follow up for 6 107 months (median, 44 months). By the last follow-up, 2 patients died (one patient died of extensive metastasis of the SFT and the other died of lung cancer), and 29 patients were alive. Of the 29 surviving patients, 3 cases (cases 8, 9 and 31) presented with liver metastasis and local recurrence, and case 9 also presented with bone metastasis. Two patients presented with local recurrence (case 1) or metastasis (case 21). The status of each patient at the last follow up is summarized in Table 2.

Risk stratification and the Ki-67 labelling index

All cases were classified by the risk stratification criteria according to the 2020 WHO classification of soft tissue and bone tumours. Total scores based on age, size, and the mitotic index were used to evaluate the risk for progression (Low: 0-2, Intermediate: 3-4, and High: 5-6). Of the 31 cases, 9 cases, including 5 histopathologic features of malignancy were high risk (9/31), 11 cases including 3 histopathologic features of malignancy, were intermediate risk (11/30), and 11 cases (11/30), including 1 histopathologic feature of malignancy, were low risk (Table 5). In the high-risk group, 2 patients (cases 9 and 31) developed liver and/or bone metastases and 2 patients had local recurrence, with a median follow-up period of 45.5 months (range, 12 to 100 months). In the intermediate-risk group, 1 patient developed liver metastasis, with a median follow-up period of 44 months (range, 6 to 107 months). However, no patients from the low-risk group developed metastasis or recurrence, with a median follow-up period of 44 months (range, 18 to 100 months).

The median of Ki-67 levels of the low-, intermediate-, and high-risk groups were 3% (range, 1% to 10%), 3% (range, 1% to 20%) and 15% (range, 1% to 30%), respectively. The median Ki-67 level of the high-risk group was significantly higher than that of the

Table 3. Histopathologic Features of retroperitoneal SFT.

No	Morphologic Features	Cell density	Cellular atypia	Mitoses (No./10HPF)	Necrosis
1	Classic	Medium	High	1	N
2	Cellular	High	High	0	N
3	Classic	Medium	High	6	Y
4	Cellular	High	Medium	0	Y
5	Classic	High	High	4	N
6	Cellular	High	High	0	N
7	Classic	Low	Low	0	N
8	Classic	High	High	1	N
9	Cellular	High	High	5	Y
10	Classic	Medium	Low	0	N
11	Cellular	High	High	0	N
12	Cellular	High	Medium	3	N
13	Classic	Low	Low	0	N
14	Classic	Low	Low	0	N
15	Cellular	High	Medium	0	N
16	Cellular	High	Medium	2	N
17	Classic	Medium	Low	0	N
18	Cellular	Medium	Low	0	N
19	Cellular	High	Medium	2	N
20	Cellular	High	Medium	0	N
21	Cellular	High	Medium	5	Y
22	Classic	High	Medium	2	Y
23	Classic	Medium	Medium	1	N
24	Classic	Low	Low	0	N
25	Cellular	High	High	5	N
26	Classic	Medium	Medium	0	N
27	Classic	Medium	Low	0	N
28	Classic	Medium	Medium	4	Y
29	Cellular	High	High	5	Y
30	Classic	Medium	Medium	2	N
31	Classic	Medium	High	5	Y

N, No; Y, Yes.

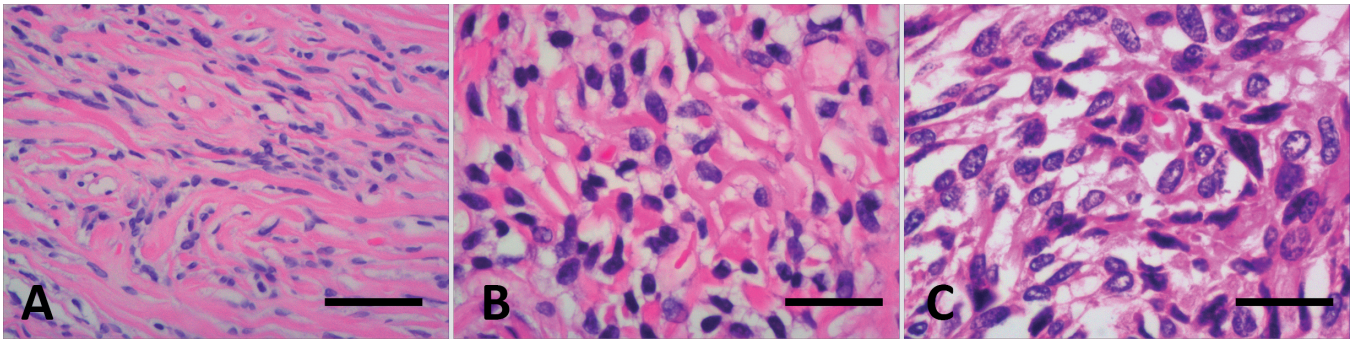

Fig. 1. Histologic illustration of retroperitoneal SFT with low **(A)**, intermediate **(B)** and high **(C)** risk. Scale bars: A, 100 μm; B, 50 μm; C, 25 μm.

Table 4. Immunohistochemical phenotype of retroperitoneal SFT.

No	STAT6	CD99	BCL-2	CD34	Vimentin	S-100	SMA	Desmin	CD117
1	5+	+	+	+	+	-	-	-	-
2	5+	+	+	+	+	-	-	-	-
3	5+	+	+	+	+	-	-	-	-
4	4+	-	+	+	+	-	-	-	-
5	4+	+	+	+	+	-	-	-	-
6	5+	+	+	+	+	-	-	-	-
7	5+	+	+	+	+	-	-	-	-
8	5+	+	+	+	+	-	+	-	-
9	4+	+	-	+	+	-	-	-	-
10	5+	+	+	+	+	-	-	-	-
11	5+	+	+	+	+	-	-	-	-
12	5+	+	-	+	+	-	-	-	-
13	5+	+	-	+	+	-	-	-	-
14	5+	+	+	+	+	+	-	-	-
15	5+	+	+	+	+	-	-	-	-
16	5+	+	+	+	+	-	-	-	-
17	4+	+	+	+	+	-	-	-	-
18	4+	+	+	+	+	-	-	-	-
19	5+	+	+	-	+	-	-	-	-
20	5+	+	+	+	+	-	-	-	-
21	5+	+	+	+	+	-	-	-	-
22	5+	+	+	+	+	-	-	-	-
23	5+	+	+	+	+	-	-	-	-
24	3+	+	+	+	+	-	-	-	-
25	3+	+	+	+	+	-	-	-	-
26	4+	-	+	+	+	-	-	-	-
27	5+	+	+	+	+	-	-	-	-
28	-	+	+	+	+	-	-	-	-
29	5+	+	+	+	+	-	-	-	-
30	4+	+	+	+	+	-	-	-	-
31	5+	+	+	+	+	-	-	-	-

Table 5. Risk stratification and the Ki-67 labelling index of retroperitoneal SFT.

Case	Total score	Risk stratification	Ki-67(%)
1	5	High	3%
2	1	Low	5%
3	5	High	30%
4	4	Intermediate	10%
5	6	High	1%
6	4	Intermediate	3%
7	4	Intermediate	3%
8	4	Intermediate	20%
9	5	High	30%
10	2	Low	5%
11	4	Intermediate	3%
12	3	Intermediate	20%
13	1	Low	3%
14	1	Low	1%
15	1	Low	1%
16	1	Low	1%
17	2	Low	1%
18	4	Intermediate	10%
19	1	Low	10%
20	1	Low	3%
21	6	High	15%
22	3	Intermediate	5%
23	2	Low	5%
24	2	Low	3%
25	5	High	10%
26	3	Intermediate	1%
27	4	Intermediate	3%
28	5	High	8%
29	5	High	30%
30	3	Intermediate	1%
31	6	High	15%

The total score of each case was calculated according to the 3-tiered model proposed by Demicco et al. Risk stratification: Low 0-2, Intermediate 3-4 and High 5-6.

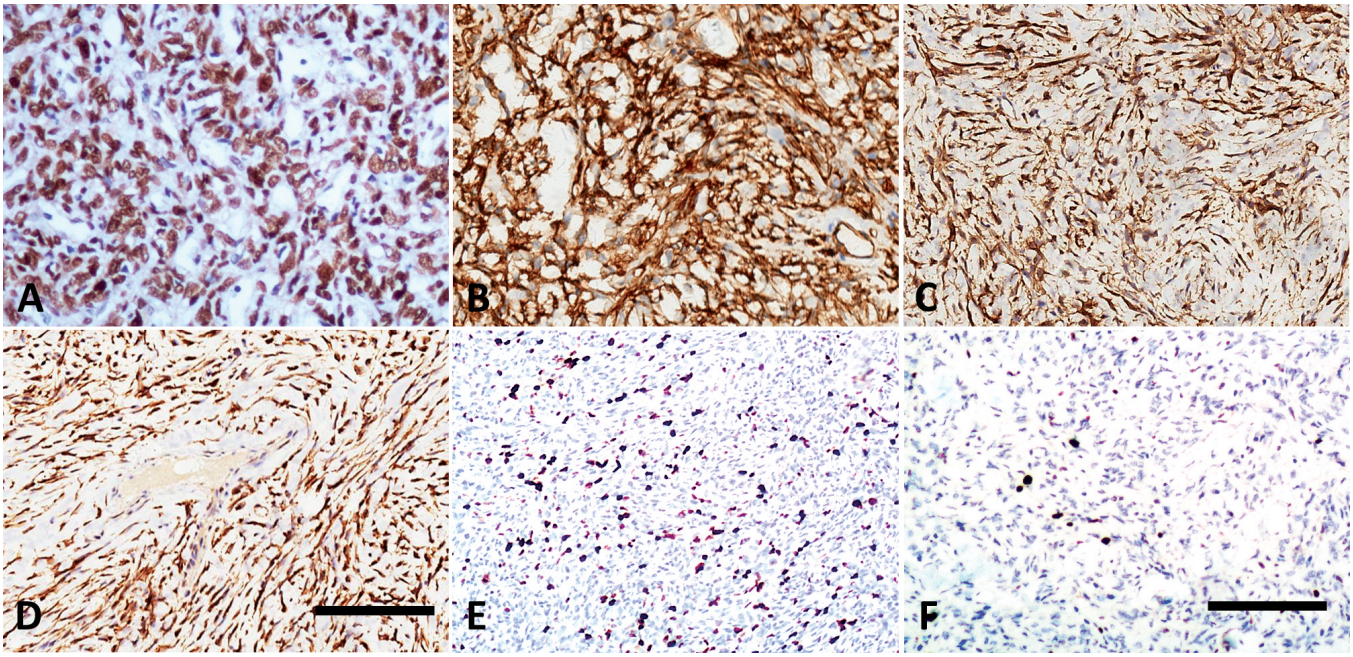

Fig. 2. Immunohistochemistry examination showing that the tumours were positive for STAT6 **(A)**, CD34 **(B)**, BCL-2 **(C)**, CD99 **(D)**, Ki67 >10% **(E)** and Ki67<10% **(F)**. Scale bars: A-D, 25 μm; E-F, 100 μm.

intermediate- and low-risk groups (P<0.05 and P<0.01, respectively). However, Ki-67 levels were not significantly different between the intermediate- group and low-risk groups (P>0.05). Interestingly, the Ki-67 level in the high-intermediate risk group (median, 10%) was still significantly higher than that in the low-risk group (P=0.034).

Discussion

A SFT is a fibroblast differentiation tumour with uncertain biological potential that seldom occurs in the deep soft tissues, particularly the retroperitoneum. Since hemangiopericytoma was classified into the entity of solitary fibrous tumour in the 2013 WHO classification of soft tissue tumours, the morphological spectrum of the tumour was greatly expanded. The present study reviewed 31 cases of SFT in the retroperitoneum, an uncommon location that lacks a large series of case reports.

According to previous studies (Demicco et al., 2012; Rajeev et al., 2015), retroperitoneal SFTs usually occurred in middle aged patients, especially those aged 50-60 years old. However, SFTs can also occur in young patients such as in the present study. Consistent with these findings, the variation in gender ratio was slight. The maximum diameters of the SFTs were usually large, with 64.5% of cases ≥10 cm. The symptoms varied depending on the location of the lesion, and 74.2% of patients (23/31) presented with non-specific physical symptoms of abdominal discomfort. It was observed that 71% of cases (5/7) with tumour sizes less than 6.5 cm caused no clinical symptoms. Therefore, this subgroup of cases is often incidentally discovered during physical examination. The main reason why retroperitoneal SFTs are difficult to detect may be due to the large cavity and the hidden growth pattern of the tumour. SFTs of the skin, extremities and other sites present with obvious signs, and symptoms of mass lesions are likely to be diagnosed early. Patients with retroperitoneal SFTs tend to have a larger size than those that occurring in other sites. Tumour size ≥10 cm was considered an important basis for benign and malignant judgements or a predictor of worse outcome for metastasis (England et al., 1989; Gold et al., 2002; Demicco et al., 2012; van Houdt et al., 2013).

STAT6, fused with the NAB2 gene forming the NAB2-STAT6 fusion gene on chromosome 12q13, is regarded as a highly specific and sensitive marker of SFT. Previous studies demonstrated that STAT6 protein was positively nuclear expressed in 98% of SFTs (Doyle et al., 2014b; Feasel et al., 2018). In addition, SFTs are also positive for CD34, BCL-2, CD99 and vimentin. However, these markers often lack specificity. CD34, a marker frequently used for the diagnosis of SFTs, has been shown to be positive in other mesenchymal neoplasms such as gastrointestinal stromal tumours, dermatofibrosarcoma protuberans and adipocytic tumours. Furthermore, frequent expression of CD99 and BCL-2 has also been reported in many spindle cell tumours (Hirakawa et al., 1996; Doyle et al., 2014b). The immunohistochemistry results of the present study demonstrated that STAT6 and CD34, which were shown to be better than other markers, were recommended for the use of diagnosis of retroperitoneal SFTs. This finding is the same as that selected by a series of 26 cutaneous SFTs studied by Feasel et al. (2018). However, some studies have confirmed that dedifferentiated liposarcoma, one of the primary histologic differential diagnoses, is also positive for STAT6 (Doyle et al., 2014a; Creytens et al., 2015).

According to the literature, liposarcoma is the most common mesenchymal tumour of the retroperitoneum, accounting for 32% of tumours located in this space (Lee et al., 2011; Lochan et al., 2011). Dedifferentiated liposarcoma, one of the most common histological subtypes, had both clinical and histologic overlap with SFT. In terms of age at onset, there was no difference between SFT and dedifferentiated liposarcoma (Hong et al., 2010). Moreover, both of these types of tumours in the abdominal cavity had similar clinical manifestations and imaging findings. Interestingly, STAT6, located at 12q13, was also confirmed to be amplified in dedifferentiated liposarcoma (Doyle et al., 2014a). However, STAT6 protein expression analysed by immunohistochemistry showed weak intensity in dedifferentiated liposarcoma (Doyle et al., 2014b). Histopathologically, retroperitoneal dedifferentiated liposarcoma and SFT tend to be low to intermediate tumours. Therefore, this clinical information and results can sometimes pose a challenge in the diagnosis of SFT. Given the specific expression of CDK4 and MDM2 in dedifferentiated liposarcoma, the examination of these markers by immunohistochemistry or MDM2 amplification are necessary for differential diagnosis (Binh et al., 2005; Kammerer-Jacquet et al., 2017).

In addition, extra-gastrointestinal stromal tumours (E-GISTs) and aggressive fibromatosis were considered when confronted with tumours centred on the retroperitoneum. Characteristics of spindle cells, sclerosing collagen, hypercellularity, and mucoid degeneration can also be observed in GIST. In addition to positive expression of CD34, GISTs showed strong positivity for CD117 and DOG1 markers, which were usually negative in SFTs. Aggressive fibromatosis arises as a slowly growing palpable mass that is usually asymptomatic. Histopathologically, tumours were composed of elongated, slender, spindle-shaped cells. In some cases, apparent nuclear hyperchromasia or cytological atypia may help exclude aggressive fibromatosis. It is worth noting that β-catenin was strongly nuclear positive in 70%-75% of aggressive fibromatosis, and it was also expressed in 40% of SFTs (Ng et al., 2005).

The prognosis of patients with retroperitoneal SFT was favourable. Patients who underwent complete tumour resection showed 93.5% of survival after the follow-up period of 6-107 months, except for one patient

who died directly from widespread metastasis of SFT at 92 months after the first surgery. Although tumours located in the mediastinum, abdomen, pelvis and retroperitoneum tend to behave more aggressively than those in the superficial sites, the mean of Ki-67 labelling index (8.3%) in the present study still suggested that retroperitoneal SFT was a low-grade soft tissue tumour. Our study demonstrated that the metastasis and/or recurrence rate of retroperitoneal SFT was only 16.1% (5/31), which was much lower than that of other sarcomas in the retroperitoneum (Lee et al., 2011; Lochan et al., 2011). These data were still within the range of the 10% to 30% reported in the literature. Extrapleural SFTs are usually more aggressive than pleural SFTs, particularly in cases occurring in the mediastinum, pelvis, and meninges (Ronchi et al., 2018). Up to 10% of pleural SFTs were malignant (Travis et al., 2015). Our research also confirmed that the proportion of retroperitoneal malignant SFTs (29%) was significantly higher than that of pleural SFTs. However, the cases of recurrence or metastasis were completely from the high- and intermediate-risk groups. Eighty percent of cases (4/5) in the study recurred or metastasized within 2 years. Some cases with obvious malignant morphological characteristics showed no metastasis or recurrence, although it had been followed up for a long time. Therefore, the sharp use of borderline or malignant terms may not accurately reflect the metastatic potential of tumours.

The Ki-67 labelling index is often used to predict the prognosis of malignant tumours. However, there have been no relevant reports on the Ki-67 levels associated with the prognosis of SFT in the retroperitoneum. In the present study, immunohistochemistry results for Ki-67 levels revealed that the tumour cells proliferative index in the high- and high-intermediate risk groups was higher than that of the low-risk group (median Ki-67%: 15% vs 10% vs 3%). Although the proportion of recurrence or metastasis in the high-intermediate risk group was significantly higher than that in the low-risk group, there were still some cases whose prognosis was difficult to predict. Therefore, we recommended that some patients with high Ki-67 expression in this group should be followed up closely for a long time to avoid overtreatment. Based on the statistical results, Ki-67 ≥10% can be used as an important auxiliary reference for the prognosis of patients in the high-intermediate risk group. However, a more accurate cut-off value still requires longer follow-up. Previous studies demonstrated that metastatic sites of SFT were frequently observed in the liver, bone and lungs (Vallat-Decouvelaere et al., 1998). Our study also found that retroperitoneal SFT metastasized to the liver, bone and pelvis, although only in 11.8% of cases. Tumours located in the mediastinum, abdomen, and retroperitoneum tend to be more aggressive than tumours located in superficial sites (Jo and Fletcher, 2014). Indeed, Feasel et al. (2018) demonstrated that cutaneous/subcutaneous SFTs showed no recurrence or metastasis, and 2 cases of histologically malignant SFT were included. The main reason may be that this series of cases was low risk according to the risk stratification criteria. However, a case in the high-risk group from our study showing apparent histological malignancy with 3 large masses exhibiting no metastasis or recurrence after 4 years of follow-up. Therefore, longer follow-up and larger studies are still needed. Gold et al. (2002) reported that histologically benign SFTs recurred and metastasized many years after primary resection. In view of this unpredictable behaviour of SFTs, we recommend long-term close follow-up, especially for patients in the intermediate- and high-risk groups, rather than simply using benign and malignant diagnoses to indicate clinical risk.

Surgery was recommended as a first-line therapy for retroperitoneal SFTs (Rajeev et al., 2015). Although chemotherapy and radiation therapy have proven effective in some cases (Stacchiotti et al., 2013; de Lemos et al., 2019), the low rate of recurrence or metastasis of retroperitoneal SFT makes it seemingly unnecessary to use them to improve outcomes.

In summary, we present the largest series of retroperitoneal SFTs with STAT6 confirmation by immunohistochemistry to date. Given the significant morphologic and immunophenotypic spectrum of SFT overlap with other neoplasms, a panel of markers is necessary for diagnosis and differential diagnosis on the basis of morphology. Although the prognosis is favourable, patients with retroperitoneal SFT classified into high- and intermediate-risk groups are prone to metastasis or recurrence and require long follow-up. A Ki-67 labelling index ≥10% may be used as an important reference for tumour recurrence or metastasis.

Acknowledgements. This work was supported by the Guangxi Natural Science Foundation (grant nos. GUIKEAD19110071). National Natural Science Foundation of China (grant nos. 81470110) and Guangxi College Students' Innovative entrepreneurial Training Plan Program (grant nos. 20190601019, 20190601017 and 20190601098). This study was also supported by High-level Hospital Construction Research Project of Maoming People's Hospital.

Author Contributions. Xiaolu Yuan made the final diagnosis and wrote this article. Lei Zhang and Yuan Liu performed the follow-up work. Xuming Wang, Lei Zhang and Jianguo Wei collected the clinical data. Yu Chen did the statistical analysis. Jianguo Wei revised the article. All authors contributed to and approved the final version of the manuscript.

Ethics approval and consent to participate. The present study was approved by the Ethics Committee of Maoming People's Hospital.

Competing interests. The authors declare that they have no competing interests.

References

Binh M.B., Sastre-Garau X., Guillou L., de Pinieux G., Terrier P., Lagace R., Aurias A., Hostein I. and Coindre J.M. (2005). MDM2 and CDK4 immunostainings are useful adjuncts in diagnosing well-differentiated and dedifferentiated liposarcoma subtypes: A comparative analysis of 559 soft tissue neoplasms with genetic data.

Am. J. Surg. Pathol. 29, 1340-1347.

Campbell N.A. and Antippa P.N. (2006). Solitary fibrous tumour of the pleura. Heart Lung Circ. 15, 400-401.

Chuang I.C., Liao K.C., Huang H.Y., Kao Y.C., Li C.F., Huang S.C., Tsai J.W., Chen K.C., Lan J. and Lin P.C. (2016). NAB2-STAT6 gene fusion and STAT6 immunoexpression in extrathoracic solitary fibrous tumors: The association between fusion variants and locations. Pathol. Int. 66, 288-296.

Creytens D., Libbrecht L. and Ferdinande L. (2015). Nuclear expression of STAT6 in dedifferentiated liposarcomas with a solitary fibrous tumor-like morphology: A diagnostic pitfall. Appl. Immunohistochem. Mol. Morphol. 23, 462-463.

de Lemos M.L., Kang I. and Schaff K. (2019). Efficacy of bevacizumab and temozolomide therapy in locally advanced, recurrent, and metastatic malignant solitary fibrous tumour: A population-based analysis. J. Oncol. Pharm. Pract. 25, 1301-1304.

Demicco E.G., Park M.S., Araujo D.M., Fox P.S., Bassett R.L., Pollock R.E., Lazar A.J. and Wang W.L. (2012). Solitary fibrous tumor: A clinicopathological study of 110 cases and proposed risk assessment model. Mod. Pathol. 25, 1298-1306.

Demicco E.G., Fritchie K.J. and Han A. (2020). The WHO Classification of Tumours Editorial Board. Solitary fibrous tumour. WHO Classification of Tumours Soft Tissue and Bone Tumours, 5th ed. Lyon. IARC Press. pp 104-108.

Doyle L.A., Tao D. and Marino-Enriquez A. (2014a). STAT6 is amplified in a subset of dedifferentiated liposarcoma. Mod. Pathol. 27, 1231-1237.

Doyle L.A., Vivero M., Fletcher C.D., Mertens F. and Hornick J.L. (2014b). Nuclear expression of STAT6 distinguishes solitary fibrous tumor from histologic mimics. Mod. Pathol. 27, 390-395.

England D.M., Hochholzer L. and McCarthy M.J. (1989). Localized benign and malignant fibrous tumors of the pleura. A clinicopathologic review of 223 cases. Am. J. Surg. Pathol. 13, 640-658.

Feasel P., Al-Ibraheemi A., Fritchie K., Zreik R.T., Wang W.L., Demicco E., Saeb-Lima M., Goldblum J.R., Rubin B.P., McKenney J.K., Ko J.S. and Billings S.D. (2018). Superficial solitary fibrous tumor: A series of 26 cases. Am. J. Surg. Pathol. 42, 778-785.

Ge W., Yu D.C., Chen G. and Ding Y.T. (2016). Clinical analysis of 47 cases of solitary fibrous tumor. Oncol. Lett. 12, 2475-2480.

Gold J.S., Antonescu C.R., Hajdu C., Ferrone C.R., Hussain M., Lewis J.J., Brennan M.F. and Coit D.G. (2002). Clinicopathologic correlates of solitary fibrous tumors. Cancer 94, 1057-1068.

Hirakawa N., Naka T., Yamamoto I., Fukuda T. and Tsuneyoshi M. (1996). Overexpression of bcl-2 protein in synovial sarcoma: A comparative study of other soft tissue spindle cell sarcomas and an additional analysis by fluorescence in situ hybridization. Hum. Pathol. 27, 1060-1065.

Hong S.H., Kim K.A., Woo O.H., Park C.M., Kim C.H., Kim M.J., Chung J.J., Han J.K. and Rha S.E. (2010). Dedifferentiated liposarcoma of retroperitoneum: Spectrum of imaging findings in 15 patients. Clin. Imaging. 34, 203-210.

Jo V.Y. and Fletcher C.D. (2014). Who classification of soft tissue tumours: An update based on the 2013 (4th) edition. Pathology 46, 95-104.

Kammerer-Jacquet S.F., Thierry S., Cabillic F., Lannes M., Burtin F., Henno S., Dugay F., Bouzille G., Rioux-Leclercq N., Belaud-Rotureau M.A. and Stock N. (2017). Differential diagnosis of atypical lipomatous tumor/well-differentiated liposarcoma and dedifferentiated liposarcoma: Utility of p16 in combination with mdm2 and cdk4 immunohistochemistry. Hum. Pathol. 59, 34-40.

Klemperer P. and Coleman B.R. (1992). Primary neoplasms of the pleura. A report of five cases. Am. J. Ind. Med. 22, 1-31.

Lee S.Y., Goh B.K., Teo M.C., Chew M.H., Chow P.K., Wong W.K., Ooi L.L. and Soo K.C. (2011). Retroperitoneal liposarcomas: The experience of a tertiary asian center. World J. Surg. Oncol. 9, 12.

Lochan R., French J.J. and Manas D.M. (2011). Surgery for retroperitoneal soft tissue sarcomas: Aggressive re-resection of recurrent disease is possible. Ann. R. Coll Surg. Engl. 93, 39-43.

Ng T.L., Gown A.M., Barry T.S., Cheang M.C., Chan A.K., Turbin D.A., Hsu F.D., West R.B. and Nielsen T.O. (2005). Nuclear beta-catenin in mesenchymal tumors. Mod. Pathol. 18, 68-74.

Rajeev R., Patel M., Jayakrishnan T.T., Johnston F.M., Bedi M., Charlson J. and Turaga K.K. (2015). Retroperitoneal solitary fibrous tumor: Surgery as first line therapy. Clin. Sarcoma Res. 5, 19.

Ronchi A., Cozzolino I., Zito Marino F., Accardo M., Montella M., Panarese I., Roccuzzo G., Toni G., Franco R. and De Chiara A. (2018). Extrapleural solitary fibrous tumor: A distinct entity from pleural solitary fibrous tumor. An update on clinical, molecular and diagnostic features. Ann. Diagn. Pathol. 34, 142-150.

Smith S.C., Gooding W.E., Elkins M., Patel R.M., Harms P.W., McDaniel A.S., Palanisamy N., Uram-Tuculescu C., Balzer B.B., Lucas D.R., Seethala R.R. and McHugh J.B. (2017). Solitary fibrous tumors of the head and neck: A multi-institutional clinicopathologic study. Am. J. Surg. Pathol. 41, 1642-1656.

Stacchiotti S., Tortoreto M., Bozzi F., Tamborini E., Morosi C., Messina A., Libertini M., Palassini E., Cominetti D., Negri T., Gronchi A., Pilotti S., Zaffaroni N. and Casali P.G. (2013). Dacarbazine in solitary fibrous tumor: A case series analysis and preclinical evidence vis-a-vis temozolomide and antiangiogenics. Clin. Cancer Res. 19, 5192-5201.

Travis W.D., Brambilla E., Burke A.P., Marx A. and Nicholson A.G. (2015). Introduction to the 2015 world health organization classification of tumors of the lung, pleura, thymus, and heart. J. Thorac. Oncol. 10, 1240-1242.

Vallat-Decouvelaere A.V., Dry S.M. and Fletcher C.D. (1998). Atypical and malignant solitary fibrous tumors in extrathoracic locations: Evidence of their comparability to intra-thoracic tumors. Am. J. Surg. Pathol. 22, 1501-1511.

van Houdt W.J., Westerveld C.M., Vrijenhoek J.E., van Gorp J., van Coevorden F., Verhoef C. and van Dalen T. (2013). Prognosis of solitary fibrous tumors: A multicenter study. Ann. Surg. Oncol. 20, 4090-4095.

Yoh T., Sata R., Kobayashi A., Wada S., Nakamura Y., Kato T., Nakayama H. and Okamura R. (2014). A large retroperitoneal malignant solitary fibrous tumor. Int. Surg. 99, 414-418.

Accepted November 8, 2021