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Clinical Characteristics and Outcomes of Solitary Fibrous Tumor in The Extremities: A Case Series of Six Patients

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Abstract: ***This case series reports on six patients with solitary fibrous tumor (SFT) of the extremities, ranging from 32 to 70 years old, including two males and four females. The clinical presentation, disease progression, MRI findings, histopathological examinations, and immunohistochemistry staining were analysed. All patients were positive for STAT6 markers, with two negative for CD34. The study highlights the similarities in MRI and immunohistochemistry findings among the cases, underscoring the importance of these diagnostics in establishing the diagnosis and guiding management strategies for SFT of the extremities. This study aims to analyse the clinical presentation, progression, diagnostic imaging, and histopathological features of solitary fibrous tumors in the extremities to enhance understanding and management of this rare condition.***

Keywords: Solitary Fibrous Tumor, Extremities, MRI Findings, Histopathology, Immunohistochemistry

1. Introduction

Solitary Fibrous Tumor (SFT) is a fibroblastic tumor with uncertain behaviour that can arise in any part of the body. It was initially described as a tumor originating in the pleura in 1931. (1) However, with many studies and researches were conducted, SFT are more common to occur in other parts than pleura itself such as peritoneum, meninges, and extremities.(2) SFT possesses various morphological features and may mimic other soft tissue sarcomas.

In 2020, the World Health Organization classified SFT in the category of malignant fibroblastic and myofibroblastic tumors with 20% risk of metastases. (3) Due to the rarity of the SFT of the extremities, diagnosing and managing SFT can be very challenging with the endless surgery and morbidities to the patients.

This study is significant because it provides valuable insights into the diagnostic challenges and management of SFT in the extremities, contributing to the limited literature on this rare condition.

2. Methodology and Materials

All patients with SFT of the extremities treated from year 2018 to 2023 were identified in our centre. We managed to track down six patients with complete clinical notes, including clinical symptoms, the course of the disease, magnetic resonance imaging findings, histopathological with immunohistochemistry staining, prediction of metastases, recurrence, and oncological outcome. Any patients who were lost to follow-up or incomplete data were excluded.

3. Case Presentation

Case 1
A 54-year-old man presented with bilateral thigh mass for 2 years duration with history of excision of right thigh mass more than 20 years before. Magnetic Resonance Imaging (MRI) showed right thigh mass measured 5.5cm x 9.4cm x8.5cm, encased the sciatic nerve while on the left thigh showed 3.7cmx 5.7cm x 22cm mass that located subcutaneously with deeper extension into the quadriceps muscle. He also had hard lumps on the right chest wall and at the back measuring 5cm x 3cm and 5cm x 4cm respectively.

CT Thorax showed multiple lung nodules. He received adjuvant radiotherapy post excision. However, he had recurrent swelling at the back with mass measuring 4 x 9.3cm with increasing size of lung nodules.

Case 2
A 48-year-old woman presented with a history of right hip pain and a plain radiograph showed destruction of right pubic rami and lytic lesion at L5 and S1 vertebra. She had a history of left calf intramuscular swelling for 5 years, measuring 18cm x 25cm. MRI showed both gastrocnemius and soleus were involved and the lesions was in close proximity to neurovascular bundle with extension in between the tibia and fibula bone. Biopsy of the calf swelling was extrapleural solitary fibrous tumor. She had multiple nodules at both lungs, liver and pancreas.

Case 3
A 32-year-old firefighter came with left calf swelling for 4 months duration and left hip pain for 1 week with inability to walk. There was a mass measuring 6cm x 9cm x 12cm at the posterior calf and the plain radiograph showed pathological fracture of left intertrochanteric femur. Histopathological

examinations for both lesions were taken and came back as solitary fibrous tumor. Computed Tomography (CT) of Thorax revealed multiple cannon ball lesion bilaterally.

Case 4

A 70-year-old lady with underlying solitary fibrous tumor of left gluteal region, measured 15cm x 11cm x 8cm, was excised 6 years before and came back with fracture of supracondylar and subtrochanteric of left femur. She also had multiple bone pain and back pain. Skeletal survey showed disseminated lytic lesion and bilateral lung nodules.

Case 5

A 52-year-old lady was diagnosed with malignant left fronto-parietooccipital solitary fibrous tumor and craniotomy and resection of the tumor was done twice for the local recurrent. She came to orthopaedic after three years for bilateral thigh pain. There were multiple lytic lesions on bilateral femur, with left acetabular destruction. Besides, she also had multiple scattered lytic lesions in the appendicular and axial skeletal. Prophylactic fixation with cephalomedullary devices were done bilaterally.

Case 6

A 37-year-old lady came with right thigh swelling for 8 years and rapidly increased in size for the past 2 years. On MRI images, the mass was measured 6cm x 10.8cm x 10.9 cm, appeared homogenous intermediate to muscle on T1-weighted and heterogenous intermediate on T2-weighted with avid enhancement. There was no flow-void signal to suggest high flow vascular component. Tissue biopsy revealed solitary fibrous tumor.

Summary of the Solitary Fibrous Tumor of the Extremities patients.

Case	Age	Gender	Location	Single/Multiple Lesions	Spine Involvement	Lung Involvement
1	54	Male	Bilateral Thigh Chest Wall Back	Multiple	No	Yes
2	48	Female	Left Calf Right Pubic Rami	Multiple	No	Yes
3	32	Male	Left Calf Left Femur	Multiple	No	Yes
4	70	Female	Left Gluteal Left Femur	Multiple	Yes	Yes
5	52	Female	Brain Bilateral Femur Pelvis	Multiple	Yes	No
6	37	Female	Right Thigh	Single	No	No

MRI findings showed similarity among the cases and featuring as intermediate signal on T1-weighted, hypointense to intermediate intensity on T2-weighted with avid enhancement. All cases have flow-void signal on T2-weighted that almost give clue of SFT than other sarcoma. On post contrast, the tumor appeared as non-enhancing which suggestive of myxoid component or necrosis which is absent for case 6.

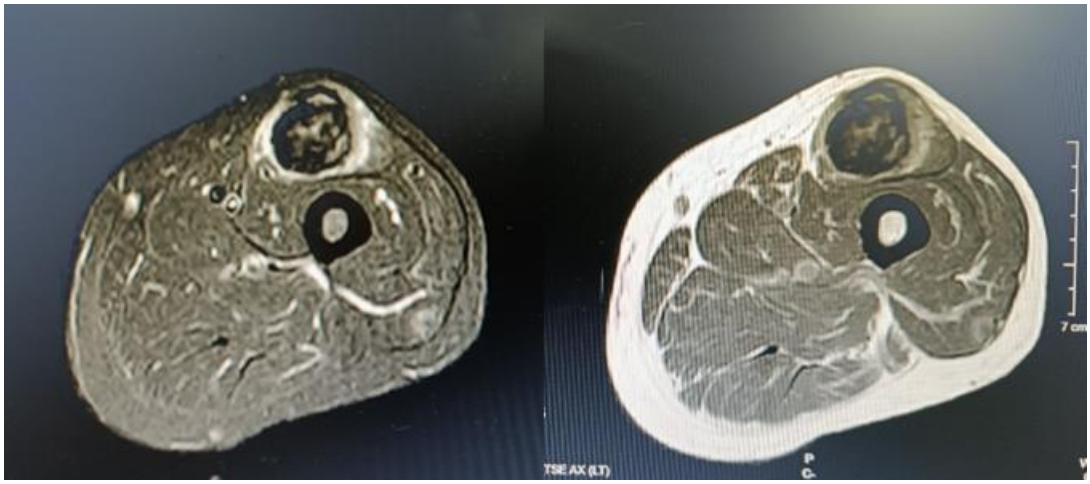

Figure 1: MRI of Case 1 – soft tissue mass at the anterior right thigh. T1-weighted FS (left side) post contrast image showed mass which infiltrate into the quadriceps muscle. T2-weighted sequence (right side) showed intermediate intensity of the mass. No bony involvement in this case.

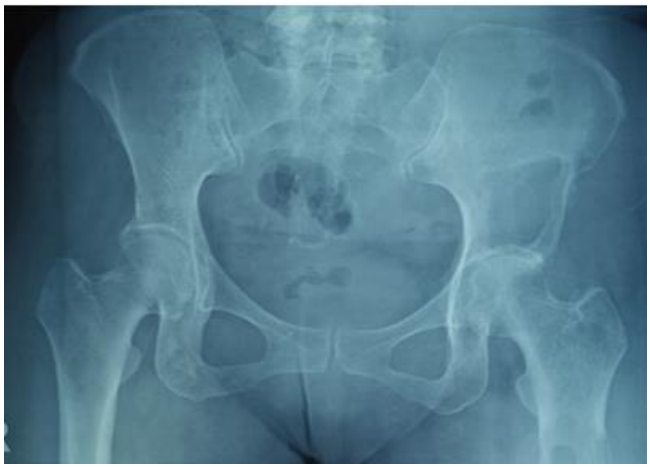

Figure 2: Pelvis Plain Radiograph of Case 5 showed large lytic lesion at the left ilium, left medial acetabular wall and bilateral proximal femur

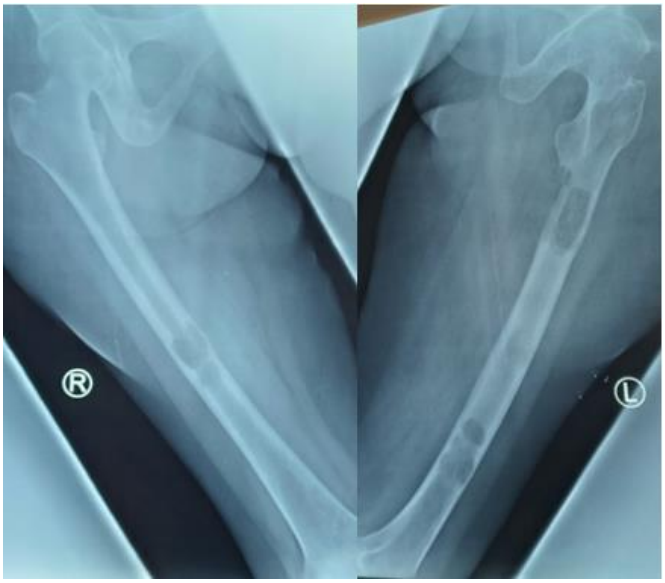

Figure 3: Plain radiograph of Case 5 showed multiple lytic lesions involving bilateral femur

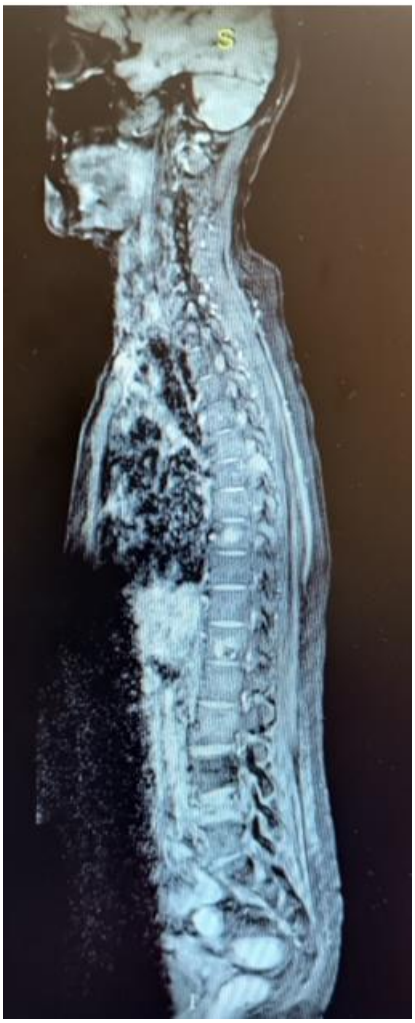

Figure 4: Magnetic Resonance Imaging (MRI) image of whole spine of Case 5 showed multiple spine level involvement. She had no neurological deficit following this

Microscopically, all cases shared the same features with the spindle to oval epithelioid cells present in patternless pattern and variable cellularity. There were also area of hyalinization and myxoid stromal change. As the previous name of SFT, pericytomas implies, there were variable sized of branching, dilated staghorn shaped vessels, imparting the pericytomatous pattern. Immunohistochemistry staining for case 1-5 were positive for STAT6 and CD34 while case 6, only STAT6 was positive.

Summary of the SFT cases and the prediction of metastases.

Case	Age (year)	Size (cm)	Mitotic Index	Prediction of metastases and mortality (points)	Metastases	RT	AA	IHC STAT6	IHC CD34
1	54	>15	3	High (5)	Yes	Yes	No	Positive	Negative
2	48	>15	1-2	High (5)	Yes	No	No	Positive	Positive
3	32	>15	21	High (5)	Yes	No	No	Positive	Positive
4	70	<15	4	High (6)	Yes	Yes	Yes	Positive	Negative
5	52	>15	7	High (6)	Yes	No	Yes	Positive	Positive
6	37	<15	0	Low (2)	No	No	No	Positive	Positive

AA-Antiangiogenic Pazopanib. RT – Radiotherapy. Mitotic Index – x/10hpf.
IHC – Immunohistochemistry staining for STAT6 and CD34 Prediction of metastases and mortality – Based on age, size of the tumor, mitotic index (3 Variable Model). Risk - Low: 0-2, Intermediate: 3-4, High: 5-6.

4. Clinical Outcome

There were only case number 5 and 6 who received thyroxine kinase inhibitor, pazopanib as adjuvant medical therapy. However, both cases unable to continue more than a year due to a limitation. Case 4 received radiotherapy for the primary lesion in the brain after the recurrence requiring craniectomy and re-excision of the tumor. To this date, cases 1-4 were

succumbed to death secondary to lungs metastases. Despite of multiple lesions in the bone including spine for case 5, she can ambulate with walking frame and partially dependent. The only case with low risk of metastases, case 6, does not show any evidence of metastases or local recurrence.

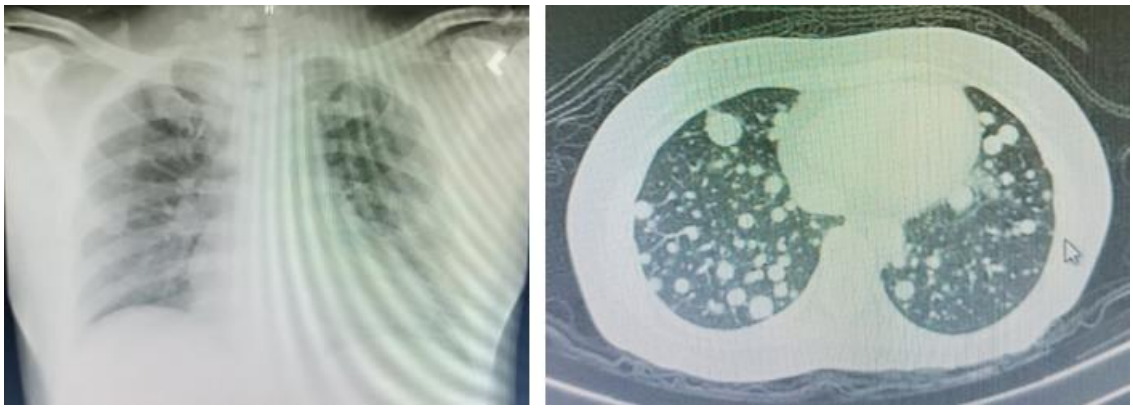

Figure 5: Chest radiograph of Case 1 (left side) – haziness of the bilateral lung fields with lung nodules. CT Thorax of Case 2 (right side) – various sizes of lung nodules, representing metastases to the lungs of SFT.

Case 1-4 had disease progression and not able to survive while Case 5 and 6 are still under follow-up.

5. Discussion

SFT is a rare neoplasm with the incidence in the extremities accounts for 8% from all SFT cases and 2% of the soft tissue neoplasm. (4) Because of the rarity, the diagnosis is often challenging. However, there were some similarities among the cases reported in this case series and previous literatures, that will be able to guide us on getting the diagnosis.

SFT of the extremities was commonly reported in between 20-70 years and in our case series, the mean age was 48.8 years (range from 32-70). A case series reported by Kanazawa group had a mean age of 47.8 years. (5)

The tumors were in the deep layer of the tissue with four cases involving bones and only two cases (Case 1 and 6) were purely soft tissue lesions. Unlike other soft tissue sarcoma, SFT appeared with intermediate signal intensity on T1-weighted sequence and heterogenous low signal intensity with flow void on T2 weighted sequence. In a larger lesion, SFT can presented with scattered avid intra-tumoral foci of hypoenhancement, which indicates regions of necrosis, cystic changes, and haemorrhage. Feeder vessels sometimes can be seen in SFT of the soft tissue. (5, 6, 7)

Tissue diagnosis can be very confusing as SFT are variably cellular, with oval to spindle-shaped nuclei and scanty cytoplasm. SFT typically have staghorn blood vessels due to pronounced vascularity known as hemangiopericytic growth pattern which also present in synovial sarcoma and hemangiopericytoma, a rare vascular neoplasm. (4, 8, 9, 10)

Based on immunohistochemistry staining, all cases were positive for STAT6. Only case 1 and 4 were negative for CD34. In getting the accurate tissue diagnosis, immunohistochemistry markers, CD34 and STAT6, play a crucial role, that strongly support the diagnosis of SFT. Besides, excellent sensitivity and sensitivity towards SFT shown by markers for NAB2-STAT6 gene fusion, although STAT6 expression also can present in other soft tissue neoplasm. (9)

From our case series, four out of six cases had metastases to the lungs, which led to their mortality. There is a literature reported that SFT can metastases to the liver, peritoneum, and retroperitoneum. (2) Three of our patients, Case 1, 2 and 3 had poor survival rate with less than a year after metastases to the lungs had developed.(8)

Even though SFT is regarded as a benign neoplasm with uncertain behaviour, the surgical treatment will be like other sarcoma, with the goal of wide resection margin, the reduce the rate of local recurrence and subsequently improves survival. (11) Unfortunately, most of our patients presented with multiple lesions, that indicates the tumor already metastases.

Adjuvant therapy such as radiotherapy is controversial which may work for local control and need further evaluation in SFT. As of other fibrous tumor, the use of antiangiogenic such as Temozolomide and bevacizumab, sorafenib, pazopanib and axitinib were believed to slow down the progress but among all, pazopanib showed the most favourable outcome. However, with the limited studies and case series of SFT treated with pazopanib, the efficacy and survival rate are still questionable and require more prospective studies and clinical trial in the future. (12)

Long term follow-up and regular surveillance is essential especially in low and intermediate risk group due to its potential for late recurrence and metastases. (9, 13)

6. Conclusion

Diagnosing and managing solitary fibrous tumors (SFT) of the extremities is challenging due to their rarity and variability in presentation. This case series demonstrates that imaging and histopathological examinations, particularly STAT6 and CD34 markers, are crucial in establishing an accurate diagnosis. Despite aggressive treatment, the prognosis remains guarded, especially in cases with metastatic disease.

Further research is needed to improve diagnostic accuracy and treatment outcomes for SFT.

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