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ORIGINAL ARTICLE **CME**

Synovial Sarcoma: Epidemiology, Prognosis, and Imaging in a Tertiary Referral Centre

KH Tsang[1], WSW Chan[1], MK Chan[1], KC Lai[1], ACL Chan[2]

Departments of [1]Radiology and Imaging, and [2]Pathology, Queen Elizabeth Hospital, Jordan, Hong Kong

ABSTRACT

Objectives: *To review the disease pattern of synovial sarcoma in a tertiary sarcoma centre in Hong Kong.*

Methods: *Patients with a histological diagnosis of synovial sarcoma from June 2000 to June 2014 were recruited. Patient data were collected using the electronic Patient Record System and available images were reviewed using the Picture Archiving and Communication System. Kaplan-Meier analysis was performed for overall survival. Multivariate Cox regression was performed to evaluate potential prognostic factors.*

Results: *A total of 45 consecutive patients with a mean age of 39 years and male-to-female ratio of 1:1.05 were recruited. Tumours were evident in the lower extremities in 28 (62%) cases, in the upper extremities in four (9%), and elsewhere in 13 (29%). The mean duration of symptoms to diagnosis was 1.5 years. The mean tumour size was 7.0 cm. Metastatic disease was present in 11 (24%) patients at initial diagnosis. The most common site of metastasis was the lung. Nineteen patients died of synovial sarcoma during follow-up. The median survival time was 7.5 years. Tumour size of >5 cm (hazard ratio [HR] = 10.06; 95% confidence interval [CI], 1.30-78.15; p = 0.027) and presence of metastasis at diagnosis (HR = 5.56; 95% CI, 1.20-25.77; p = 0.028) were significant adverse prognostic factors after adjustment for age, gender, tumour location, histological subtypes, and adjuvant therapy.*

Conclusion: *Tumour size of >5 cm and presence of metastasis at diagnosis were identified as adverse prognostic factors.*

Key Words: *Epidemiology; Magnetic resonance imaging; Sarcoma, synovial; Survival analysis; Tomography, spiral computed*

中文摘要

香港一所三級醫院內的滑膜肉瘤病例回顧：流行病學、預後和影像學

曾劍鴻、陳施媛、陳文光、黎國忠、陳澤林

目的：回顧香港一所三級醫院內的滑膜肉瘤病例。

方法：2000年6月至2014年6月期間根據組織學確診為滑膜肉瘤的患者均納入研究範圍。使用電子病歷系統收集患者數據和影像資料。根據Kaplan-Meier分析得出總生存率，再使用多因素Cox比例風險模型評估潛在的預後因素。

Correspondence: *Dr KH Tsang, Department of Radiology and Imaging, Queen Elizabeth Hospital, Jordan, Hong Kong.*
Email: tsang_kh@yahoo.com.hk

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結果：共45名患者被納入研究範圍，平均年齡39歲，男女比例為1:1.05。28例（62%）腫瘤在下肢，4例（9%）在上肢，13例（29%）在其他部位。從出現症狀至確診的時間平均為1.5年。平均腫瘤大小7.0 cm。11例（24%）的患者在初次診斷時已發現有轉移。肺是最常見的轉移部位。隨訪期間19例因滑膜肉瘤死亡；患者中位生存期7.5年。調整年齡、性別、腫瘤部位、病理類型和輔助治療後顯示腫瘤大於5 cm（風險比 = 10.06；95%置信區間1.30-78.15；p = 0.027）以及初次診斷時有轉移現象（風險比 = 5.56；95%置信區間1.20-25.77；p = 0.028）為顯著不良預後因素。

結論：滑膜肉瘤大於5 cm以及初次診斷時有轉移現象均是不良預後因素。

INTRODUCTION

Synovial sarcoma is an uncommon soft tissue tumour, accounting for 2.5% to 10.5% of all primary soft tissue sarcomas.[1-6] It is the fourth most common soft tissue sarcoma according to the Armed Forces Institute of Pathology. The tumour is usually seen in adolescents or young adults and there is no definite sex predilection.[4] Various studies have been carried out but local data are generally lacking. Several prognostic factors have been identified but results are inconsistent with the exception of tumour size of >5 cm that has been shown to have an adverse effect on prognosis. We aimed to study the epidemiology of synovial sarcoma in a local sarcoma centre, and to identify adverse prognostic factors as well as to review the imaging findings. A literature search was performed and the findings were compared with our local study.

METHODS

All patients with a histologically proven diagnosis of synovial sarcoma from June 2000 to June 2014 in a regional hospital in Hong Kong were consecutively recruited in this study. Patient age, gender, presenting symptoms, duration of symptoms, tumour location, tumour size, and presence of metastasis at initial presentation were reviewed using the electronic Patient Record System (ePR). Incidence of disease recurrence, and site and duration of first recurrence were recorded. The number of deaths was also reviewed. Available images were reviewed using the Picture Archiving and Communication System and the ePR. Imaging findings were discussed.

Statistical Analyses

Kaplan-Meier analysis was performed for overall survival. Patient age, sex, tumour size, tumour location, metastasis at presentation, and histological subtypes were subjected to univariate and multivariate Cox proportional-hazards regression analysis. Statistical analyses were performed using the Statistical Package for the Social Sciences (Windows version 22.0; SPSS Inc, Chicago [IL], USA). This study was approved by the departmental review board of the author's institution.

RESULTS

A total of 45 consecutive patients were included. No patient was lost to follow-up. The mean age was 39 years (range, 11-88; median, 36 years), with a male-to-female ratio of 1:1.05. Tumours were located in the lower extremities in 28 (62%) patients, upper extremities in four (9%) patients, and elsewhere in 13 (29%) patients.

The mean duration of symptoms from presentation to diagnosis was 1.5 years. The mean size of the tumour when measured at its greatest dimension was 7.0 cm (range, 1.3-22 cm). Presence of a mass or swelling was the most common presenting symptom. Pain at the site of the tumour was reported in 16 (36%) patients. The mass usually increased in size gradually. Sometimes only pain was present without notification of a mass lesion. A history of prior trauma was reported in four (9%) patients.

Metastatic disease was present at initial presentation in 11 (24%) patients. The lungs were the most common site of metastasis and affected nine (82%) patients. One (9%) patient had bone metastasis to lumbar vertebra and another (9%) had distant lymph node metastasis at presentation.

Recurrent disease was present in 13 (29%) patients. The mean time of recurrence was 3 years. The lung was the most common site of tumour recurrence, present in six (46%) patients. Local recurrence occurred in three (7%) patients. Other less common sites of recurrence included the stomach, pancreas, spleen, lymph nodes, and skin.

The mean follow-up time was 44.8 months. Nineteen

patients died of synovial sarcoma during follow-up period. The median survival was 7.5 years.

Of the 45 patients, magnetic resonance images (MRIs) were available for 15, of whom six had also undergone computed tomography (CT). Another six patients had CT imaging but no MRI.

Synovial sarcoma usually had a well-defined lobulated appearance and was heterogeneous on T2-weighted imaging. Triple signal intensity was observed in 33% (5 of 15) of patients on MRI. Haemorrhage manifested as T1 hyperintense foci was seen in 47% (7 of 15) of cases on MRI. A cystic component was seen in 53% (8 of 15) of patients and fluid-fluid level was noted in 20% (3 of 15). Bone and neurovascular infiltration was present in 27% (4 of 15) and 13% (2 of 15) of patients, respectively. Of the 12 patients who had CT performed, intra-tumoural calcifications were identified in 33% (4 of 12).

Histologically, there are three main subtypes of synovial sarcoma: monophasic, biphasic, and poorly differentiated. Monophasic was the most common subtype in our cohort, accounting for 49% (22 of 45), the other two subtypes accounted for 20% each (9 of 45 each). In five (11%) patients, subtype was unspecified.

The 5-year overall survival rate in our series was 50% and the 10-year overall survival was 44% (Figure 1).

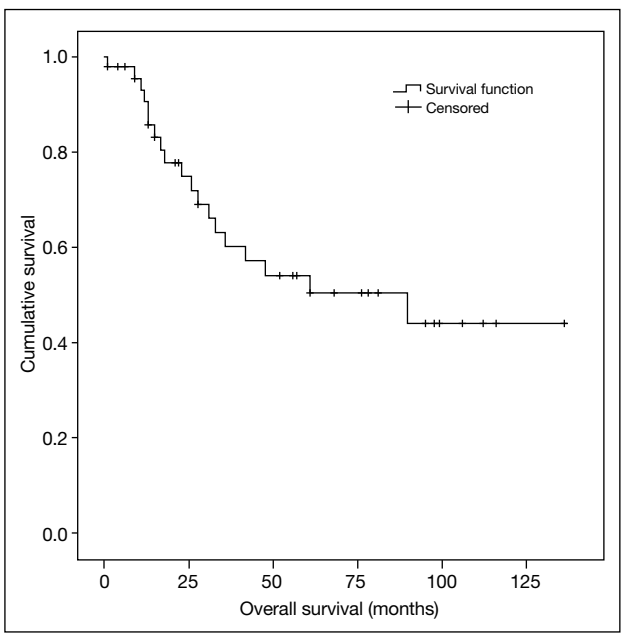

Figure 1. Overall survival of the 45 patients with synovial sarcoma.

Univariate analysis (Table 1) showed that tumour size >5 cm, presence of metastasis at presentation, and poorly differentiated subtype were associated with poorer overall survival ($p = 0.006$, $p < 0.0001$, and $p = 0.034$, respectively; Figure 2).

Multivariate Cox regression analysis identified tumour size of >5 cm ($p = 0.027$, hazard ratio [HR] = 10.06, confidence interval [CI] =1.30-78.15) and metastasis at presentation ($p = 0.028$, HR = 5.56, CI = 1.20-25.77) as significant adverse prognostic factors for overall survival (Table 2).

DISCUSSION

Synovial sarcoma accounts for approximately 10% of all soft tissue sarcomas.[1-6] Synovial sarcoma is a misnomer, named after its microscopic resemblance to normal synovium. Despite its name, these lesions do not arise from synovium, but are thought to originate from primitive mesenchymal cells. They undergo differentiation to resemble synovial cells and show dual epithelial and mesenchymal differentiation.[3,7-9]

Synovial sarcoma occurs most frequently in adolescents and young adults, with the majority of patients

Table 1. Patient characteristics and univariate analysis of factors influencing overall survival.

Variable	No. (%) of patients* (n = 45)	p Value
Mean age (years)	39	0.231
Sex		
Female	23 (51)	0.704
Male	22 (49)	
Tumour size (cm)		
≤5	18 (40)	
>5	27 (60)	0.006
Tumour location		
Extremity	32 (71)	0.369
Non-extremity	13 (29)	
Metastasis at presentation		
No	34 (76)	
Yes	11 (24)	<0.0001
Histological subtype		
Monophasic	22 (49)	
Biphasic	9 (20)	0.237
Poorly differentiated	9 (20)	0.034
Radiotherapy		
No	16 (36)	
Yes	29 (64)	0.065
Chemotherapy		
No	28 (62)	
Yes	17 (38)	0.682

* Except otherwise stated.

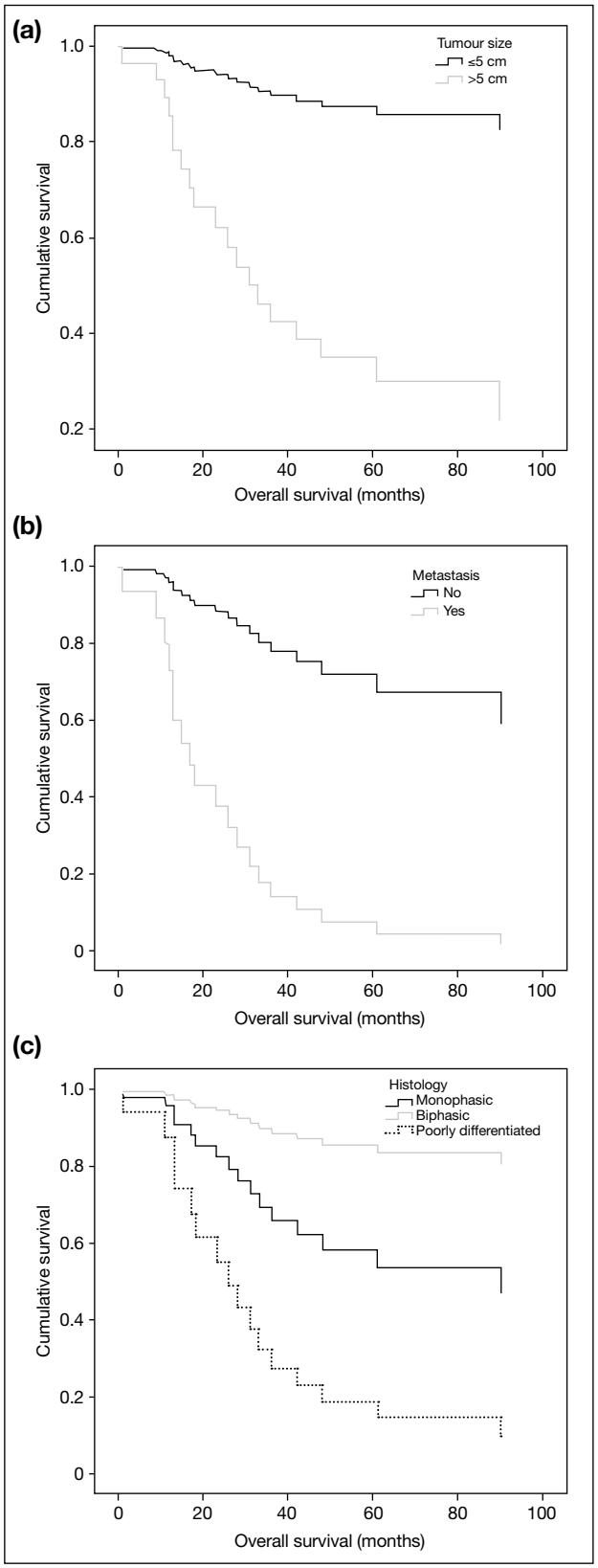

Figure 2. Univariate analyses: (a) tumour size on overall survival (OS) shows significant difference; (b) metastasis at presentation on OS shows significant difference; and (c) histological subtypes on OS shows significant difference for poorly differentiated tumour as compared with monophasic subtype.

Table 2. Multivariate analysis for overall survival.

Variable	p Value	Hazard ratio	95% Confidence interval
Age	0.391	0.98	0.93-1.03
Sex	0.158	0.35	0.08-1.50
Tumour size >5 cm	0.027	10.06	1.30-78.15
Tumour location	0.083	4.55	0.82-25.27
Metastasis at presentation	0.028	5.56	1.20-25.77
Histological subtype	0.320	2.20	0.46-10.45
Adjuvant therapy	0.055	0.21	0.41-1.04

presenting at 15 to 40 years of age.[4] The tumour can occur at any age, however, including the newborns and the elderly. There has recently been a case of synovial sarcoma reported in a 32-week premature infant in Japan.[10] In our series, the youngest patient was aged 11 years and the oldest aged 88 years.

Gender predilection varies in different publications. Both a slight male and a female predominance have been reported,[11,12] although other studies have shown no sex predilection.[3,4] In our series, no significant gender difference was noted.

Synovial sarcoma usually occurs close to joints, tendons and bursae, and rarely arises from the joint cavity.[2,4] The most common presentation is a palpable mass or swelling. The duration of symptoms before diagnosis varies widely, from weeks to decades with a mean of about 2 to 4 years. The mean duration of symptoms was about 1.5 years in our study.

Size of the lesion also varies and usually shows a slow initial growth pattern. The long duration of symptoms and initial slow growth of synovial sarcomas may give a false impression of a benign process.[4,13] Pain and tenderness at the site of the mass is frequently reported and some patients present with pain but no palpable mass.

A literature search revealed that the extremities are the most common primary site of synovial sarcoma. The lower extremities, especially the thigh, are most often affected, accounting for 60% to 70% of cases.[3,4] About 16% to 25% of cases occur in the upper extremities.[4] It is usually seen within 5 cm of the joint (60-75%), uncommonly seen intra-articularly (5-10%).[4] Other less commonly affected sites include the head and neck region (3-5%); trunk, thorax and chest wall (7%); retroperitoneum (0.3%); and pelvis (8%).[4,14-16]

In our study, the extremities accounted for 71.1% of cases, in which the thigh was the most common site (26.7% of all cases). The tumour occurred more commonly in the head and neck region compared with the literature, which was present in 5 cases (11.1% of all cases). It was also seen slightly more commonly in the thoracic region (13.3%).

Metastases have been reported in 16% to 25% of patients at initial presentation.[4,17,18] The lung was reported to be the most frequent metastatic site in 94% of those with metastasis,[4,17-19] which echo our results.

In the literature, 5-year survival ranged from 25% to 75% and 10-year survival from 11% to 63%[20]; these are comparable to our study of 5- and 10-year survival of 50% and 44%, respectively.

Various prognostic factors have been identified in previous studies although only tumour size (>5 cm)

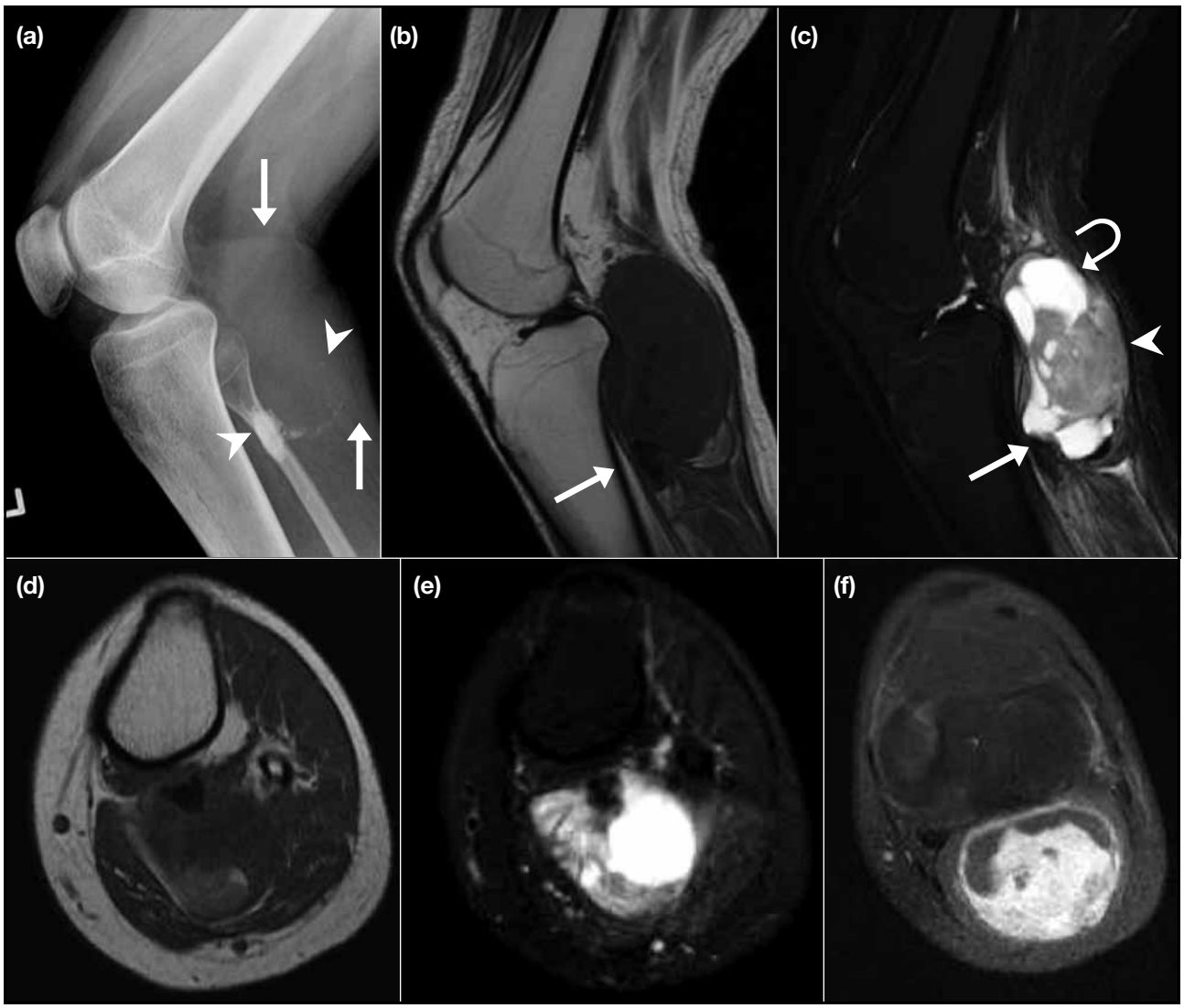

Figure 3. Synovial sarcoma in a 22-year-old male who presented with a painful popliteal fossa mass. (a) Lateral radiograph of the left knee shows a vague soft tissue mass (arrows) in the popliteal fossa with amorphous calcifications (arrowheads). No bony erosion is seen. (b) Sagittal T1 image shows the mass has a signal intensity lower than that of the fat and muscle. Foci of calcifications (arrow) are seen as areas of low signal intensity. (c) Sagittal T2 image with fat suppression shows the mass has a triple signal pattern with areas of low, intermediate, and high signal intensity presumably due to the presence of calcification (arrow), cellular component (arrowhead), and haemorrhage / necrosis (curved arrow). (d) Axial T1, (e) axial T2 fat-suppressed, and (f) axial T1 post-contrast images show heterogeneous contrast enhancement of the solid component.

has been consistently associated with a negative outcome.[11-13,19-22] Our study was consistent with such finding: tumour size of >5 cm was a significant adverse prognostic factor in multivariate analysis (HR = 10.06, $p < 0.05$). Metastasis at presentation was another significant prognostic factor identified in our study (HR = 5.56, $p < 0.05$). Several other studies have reported a similar finding.[20,23]

The prognostic significance of histological subtype remains controversial. We noted that poorly differentiated subtype was associated with the worst prognosis, followed by monophasic subtype, although no significant difference was shown in multivariate analysis.

Imaging Features

MRI is the imaging modality of choice to determine local extent of synovial sarcoma due to its superior contrast resolution. The tumour typically appears as a juxta-articular lobulated mass. Internal septa and multiple fluid-fluid levels may be seen.[5] On T1-weighted MR images, the tumour is hypointense to subcutaneous fat. Signal intensity is similar to or slightly higher than that of muscle on T1-weighted images.[2,4,5] The tumour is markedly heterogeneous on T2-weighted image and has been described as triple signal due to the presence of calcification (low signal), cellular component (intermediate signal), and haemorrhage / necrosis (high signal). Triple signal is reported in approximately 30% of cases[2-4,24] (Figures 3 and 4).

Area of haemorrhage, seen as fluid-fluid levels or foci of high-signal intensity on T1- and T2-weighted MR images, is noted in up to 47% of cases.[4] Bone involvement, either cortical destruction or marrow invasion, can be shown in MRI (Figure 5). A small synovial sarcoma, especially those <5 cm, is usually well defined and may mimic a less aggressive process[25] (Figures 6 and 7).

CT usually shows a lobulated well-defined heterogeneous soft tissue mass with density similar to or slightly lower than that of muscle.[4,14,26] Heterogeneous contrast enhancement is usually observed (Figure 5). CT is useful for detection of tumour calcifications and bony destruction. Calcifications are seen on CT images in 27% to 41% of cases.[4,26,27] Calcifications may also be seen in metastatic deposits, especially those in the lung (Figure 8).

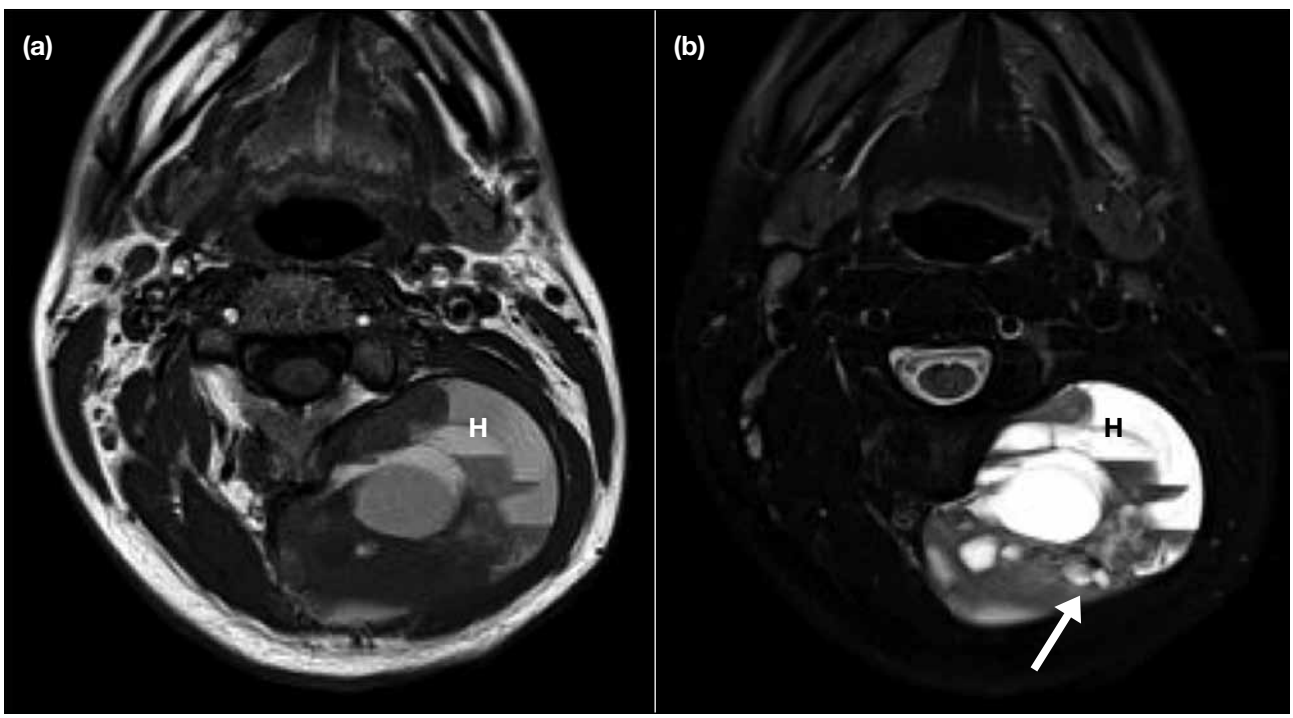

Figure 4. Synovial sarcoma in the left posterior neck region. Triple signal intensity and fluid-fluid levels are seen. (a) Axial T1 and (b) axial T2 fat-suppressed images show areas of haemorrhage with fluid levels (H). Small calcified foci are also noted (arrow).

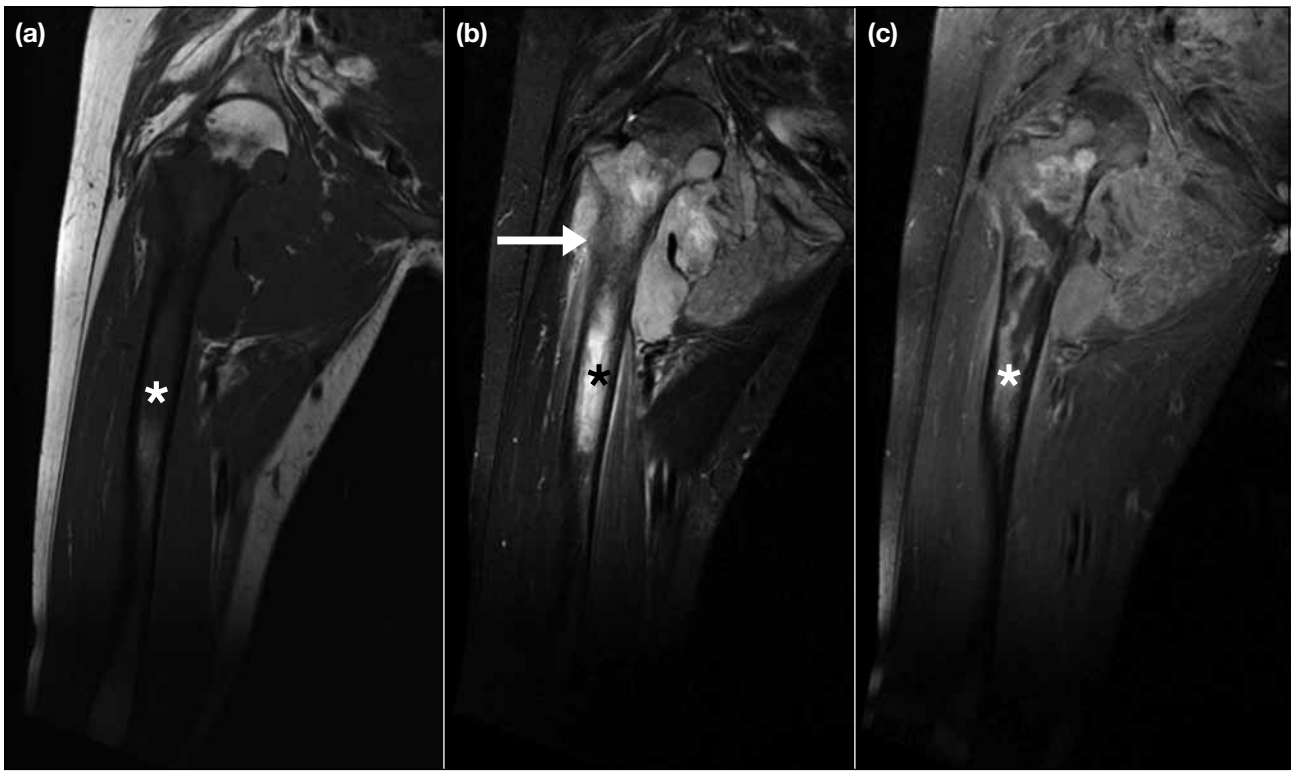

Figure 5. Synovial sarcoma in the right hip region of a 34-year-old female with extensive bone infiltration. (a) Coronal T1-weighted, (b) coronal T2 fat-suppressed, and (c) coronal post-gadolinium T1 fat-suppressed images show local invasion of the right proximal femur with cortical breach (arrow). Marrow signal changes (*) with contrast enhancement are also noted signifying bone marrow invasion.

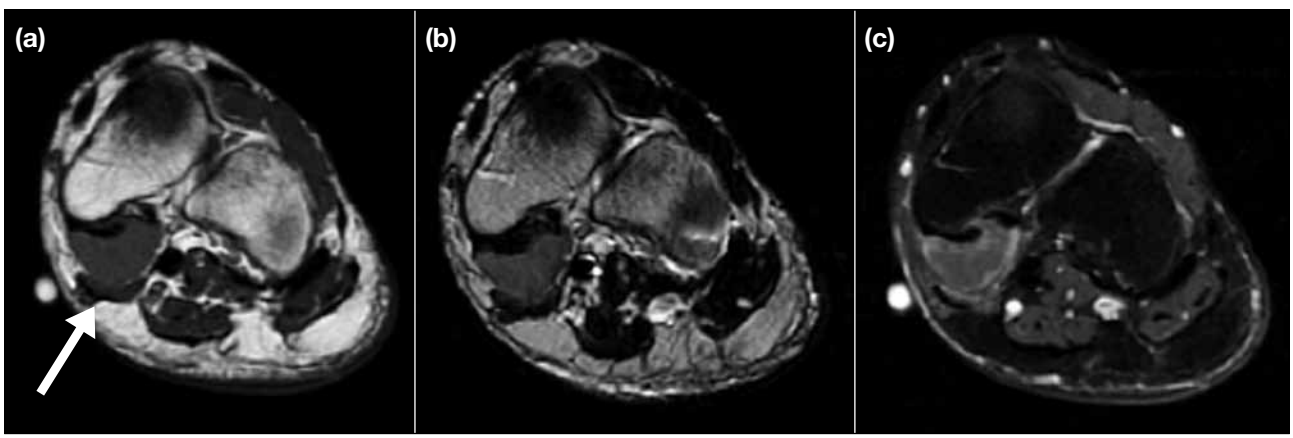

Figure 6. Synovial sarcoma in a 37-year-old male who presented with left medial plantar foot swelling for 2 years. (a) Coronal T1-weighted (T1W), (b) coronal T2-weighted (T2W), and (c) coronal post-contrast T1W with fat suppression images of the left foot show a well-defined mass lesion (arrow) in the medial plantar aspect with homogeneous low signal intensity in both T1W and T2W sequences. Peripheral rim enhancement is noted. No abnormal single intensity is detected in adjacent bone, muscles, and tendons. Together with the long presenting history, features may mimic a non-aggressive process.

Radiographs appear normal in about 50% of cases of synovial sarcoma, particularly those with a small lesion.[4] Nonetheless, it can be shown as a large spheroid well-defined soft tissue mass adjacent to the joint. Amorphous punctuate calcification or ossification can be seen in up to 30% of cases.[2,4] These calcifications are often eccentric or peripheral in location. Cases with extensive calcification have

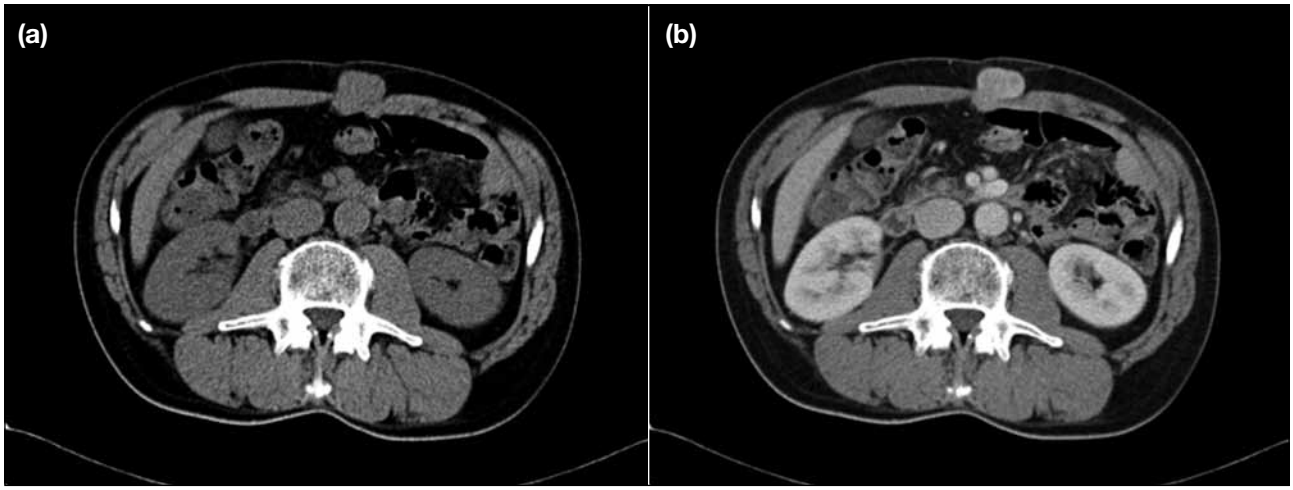

Figure 7. A 66-year-old male presented with an anterior abdominal mass for 3 years with no pain and progressive increase in size. The mass was histologically proven to be synovial sarcoma. (a) Pre-contrast and (b) post-contrast computed tomography scans show a small lobulated mass in the anterior abdominal wall abutting the rectus sheath. The mass has attenuation slightly lower than that of the adjacent muscles with heterogeneous contrast enhancement. The small size and, more particularly, a well-defined margin absolutely do not mitigate against a malignancy.

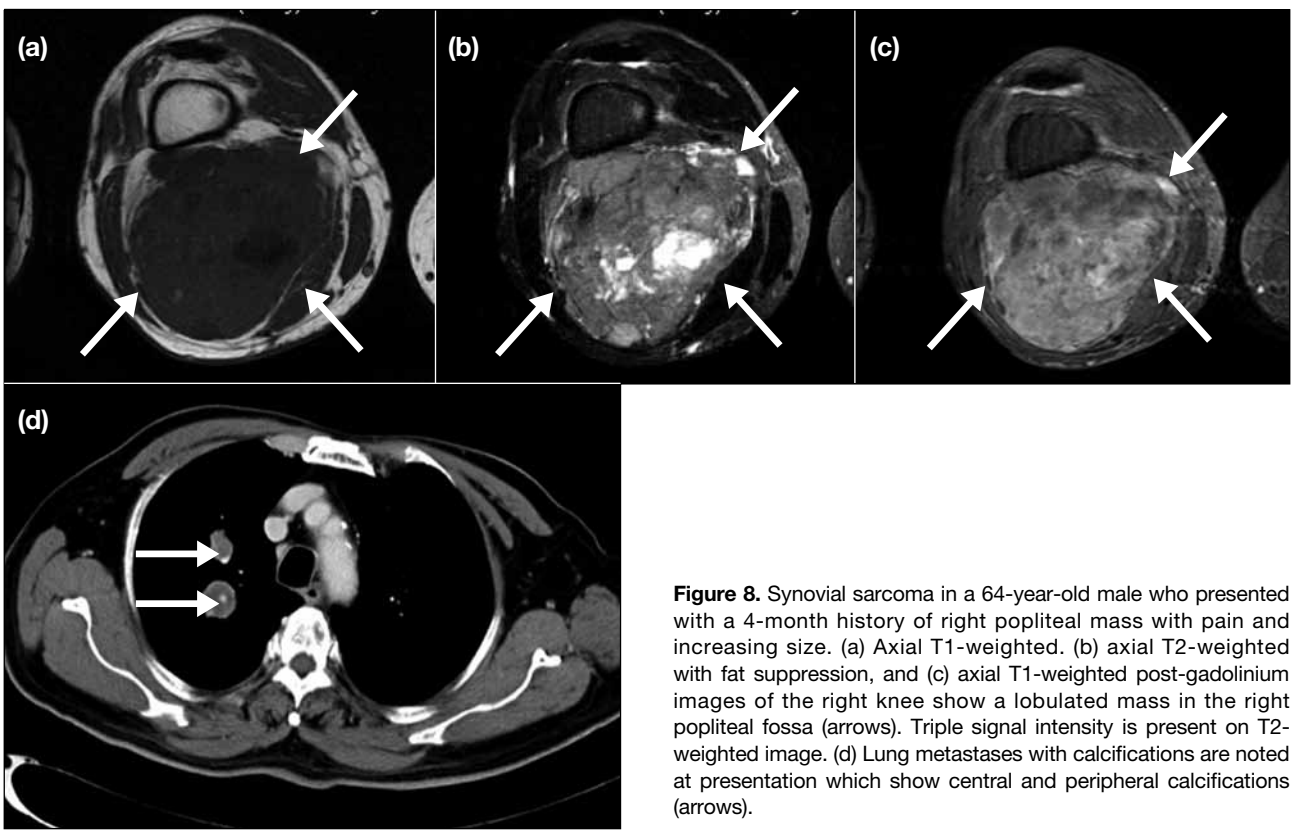

Figure 8. Synovial sarcoma in a 64-year-old male who presented with a 4-month history of right popliteal mass with pain and increasing size. (a) Axial T1-weighted. (b) axial T2-weighted with fat suppression, and (c) axial T1-weighted post-gadolinium images of the right knee show a lobulated mass in the right popliteal fossa (arrows). Triple signal intensity is present on T2-weighted image. (d) Lung metastases with calcifications are noted at presentation which show central and peripheral calcifications (arrows).

been reported to have a better prognosis in some series.[2,4,28]

The major drawbacks of our study in general included its retrospective nature, relatively small sample size, and single-centre study. Imaging analysis of our study was limited by the small number of available imaging studies for our patients.

CONCLUSION

Synovial sarcoma is an uncommon soft tissue tumour. Tumour size of >5 cm and metastasis at initial presentation were identified as significant adverse prognostic factors.

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