

How Satisfactory is Management of Soft Tissue Sarcoma out of a Sarcoma-Center? Six-Case Experience

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Abstract

Background

Soft tissue sarcoma (STS) is a diverse group of rare tumors arising from connective tissues anywhere in the body and at any age with a high fatality due to frequent pulmonary metastases. Due to rarity of the disease, it is difficult to collect good number of patients and most studies describe few cases.

Methodology

In this paper, 6 male Iraqi patients (14-68 yr old) with STS (4 in extremities and 2 in trunk wall) are reported.

Results

Five patients (83.3%) had a slowly growing mass of long duration (3-18 yr). The youngest patient had bilateral pulmonary metastases and malignant pleural effusion shortly after resection of primitive neuroectoderm tumor (PNET) of the thigh. MRI and/or CT scan was performed in 4 patients. Fine needle aspiration cytology (FNAC) was done twice revealing a diagnosis of undifferentiated sarcoma in one patient while it was inconclusive in the second. Five patients had biopsies with 3 accurate diagnoses. There were 3 rare tumors [alveolar soft part sarcoma (ASPS), PNET and fibromatosis]. Wide surgical excision (WSE) was used in 5 patients whereas forequarter amputation was necessary for a huge fibrosarcoma involving subclavian vessels and humerus. Postoperative radio or chemotherapy was offered for 4 patients. Local recurrence (LR) was noted once in fibromatosis, twice in extremity liposarcoma and 8 times in trunk wall liposarcoma (all prior to radiotherapy).

Conclusion

Patients with STS out of a sarcoma center can be satisfactorily managed by a surgical team with adequate experience providing that standard guidelines are followed.

Key Words

Soft tissue sarcoma, trunk wall, extremities, wide surgical excision.

Introduction

Soft tissue sarcomas (STS) are rare tumors arising from connective tissues throughout our body [1] [2]. They account for <1% of the diagnosed cancers [1]. Due to their rarity, it is often difficult to get a sufficient sample size of STS and therefore; most reports describe few patients [3]. Depending on the tissue of origin, there are many histological types; some of them are common [4]-[8] while others are rare or very rare [4] [5] [9]-[10]. Despite their rarity, STS could be highly fatal due to the development of pulmonary metastases [1].

The clinical features of STS are variable due to their different sites of origin. However, it is recommended that "any patient with a soft tissue mass that is increasing in size, bigger than 5 cm or is located below the deep fascia, with or without pain, should be referred to a diagnostic centre as a suspected case of STS" [6]. Imaging is vital in the evaluation of patients and the preferred modality is MRI [6]. Tissue diagnosis, on the other hand, can be obtained by a core-needle and/or a well-planned incisional biopsy [6]. Whatever the histologic type of STS, all are positive to Vimentin (a marker of connective tissue origin) but negative to Cytokeratine and epithelial membrane antigens (markers of epithelial tissue) [11].

Wide surgical excision (WSE) with limb preservation is the backbone of STS therapy; amputation is occasionally required. Radiotherapy can reduce local recurrence (LR) in low-grade STS while chemotherapy is used for certain histologic types such as rhabdomyosarcoma in children and synovial sarcoma in young age groups [11].

Soft TS is ideally managed by an experienced multi disciplinary team in a specialized sarcoma center. These tumors are so rare that a surgeon may see one case of STS per year [3]. Accordingly, such "occasional sarcoma surgeon" hardly gains the necessary experience. What about patients who have no access to such centers? Can we offer them a satisfactory management? In this article, 6 patients with STS managed over several years in 2 general Iraqi hospitals are presented. Relevant literature is reviewed trying to answer this question.

Patients and Methods

Six male patients with STS of the extremities or trunk wall surgically treated at the Departments of Thoracic and Vascular Surgery/ Sulaimaniyah and Basra Teaching Hospitals (STH, BTH) are studied. Patients were clinically assessed by taking a detailed history and performing physical examination. The presenting symptoms and signs were recorded. Investigations included blood tests, plain radiographs and imaging studies (MRI, MRA and/or CT scans with and without contrast). The patients were usually managed by a team of an oncologist, orthopedic and a vascular surgeon. Preoperative tissue diagnoses were made by FNAC and/or an incisional biopsy which was carefully planned so that it would not interfere with the subsequent surgical resection of the tumors. Soft tissue sarcomas of the extremities were usually removed by wide surgical excision (WSE) aiming at limb salvage unless this was not possible due to neurovascular involvement by tumors of proximal extremities in which limb amputation deemed necessary. Biopsy specimens were sent for at least 2 pathologists known to have an interest and expertise in STS. Radiotherapy was given to patients postoperatively if residual tumor tissue was suspected. Chemotherapy was also added for patients with disseminated disease.

Results

The youngest patient was 14-yr old while the oldest was a man of 68 with a mean age of 39 years. One patient (the 4th) was admitted to BTH in 2001 whereas others were admitted to STH over the period 2004-2010. The details of patients are summarized in **Table 1** and **Figures 1-6**.

Five patients had slowly growing painless tumor masses of long durations (3-yr to 18-yr) associated with secondary varicose veins due to mass compression (n=3). All had localized disease except one patient (the 3rd) who presented with bilateral pulmonary metastases and malignant pleural effusion shortly after resection of p PNET from the right thigh. Plain radiographs revealed soft tissue swellings in all cases while MRI and/or CT scan was performed in 4 patients and was very helpful and informative. FNAC was performed in 2 patients and revealed a diagnosis of undifferentiated sarcoma in one patient though it was inconclusive in the second. Biopsies were performed 5 times resulting in 3 accurate diagnoses. Local recurrence was noted once in fibromatosis, twice in extremity liposarcoma and 8 times in trunk wall liposarcoma. Five patients were treated by WSE. Forequarter amputation was necessary in a patient with huge fibrosarcoma of right shoulder girdle involving subclavian vessels and humerus. Radiotherapy was offered for 2 patients with recurrent liposarcoma and was very effective in preventing recurrence after last resection whereas chemotherapy was given postoperatively to the patient with p PNET.

Table 1: Details of Patients

Case No.	Age (yr)	Symptoms & Signs	Investigations	Definite Treatment	Final Diagnosis
1	68	Huge recurrent masses in the thigh-3 yrs.	Blood tests & MRI	WSE	Liposarcoma See Fig. 1a-1e
2	26	R knee mass for 4 yrs+ vv*	Blood tests & plain X-ray.	WSE	ASPS See Fig. 2a-2b
3	14	SOB-2 weeks, R thigh mass recently resected.	CXR & Chest CT scan.	WSE+chemotherapy	pPNET See Fig. 3a-3d
4	55	Huge supraclavicular & axillary mass-3 yrs, shoulder pain, vv	Blood tests, CXR, MRA, MRI, FNAC, Incisional biopsy.	Forequarter amputation	Fibrosarcoma See Fig. 4a-4d
5	47	Recurrent trunk wall masses-18 yrs, lymphoedema of LUL**	Blood tests, CXR, chest CT, CDUS@	WSE	Liposarcoma See Fig. 5a-5d
6	24	Recurrent big mass in R axilla & subscapular region.	CXR, chest CT & FNAC	WSE	Aggressive Fibromatosis See Fig. 6a-6d

@ Color Doppler ultrasonography * varicose veins **Left upper limb.

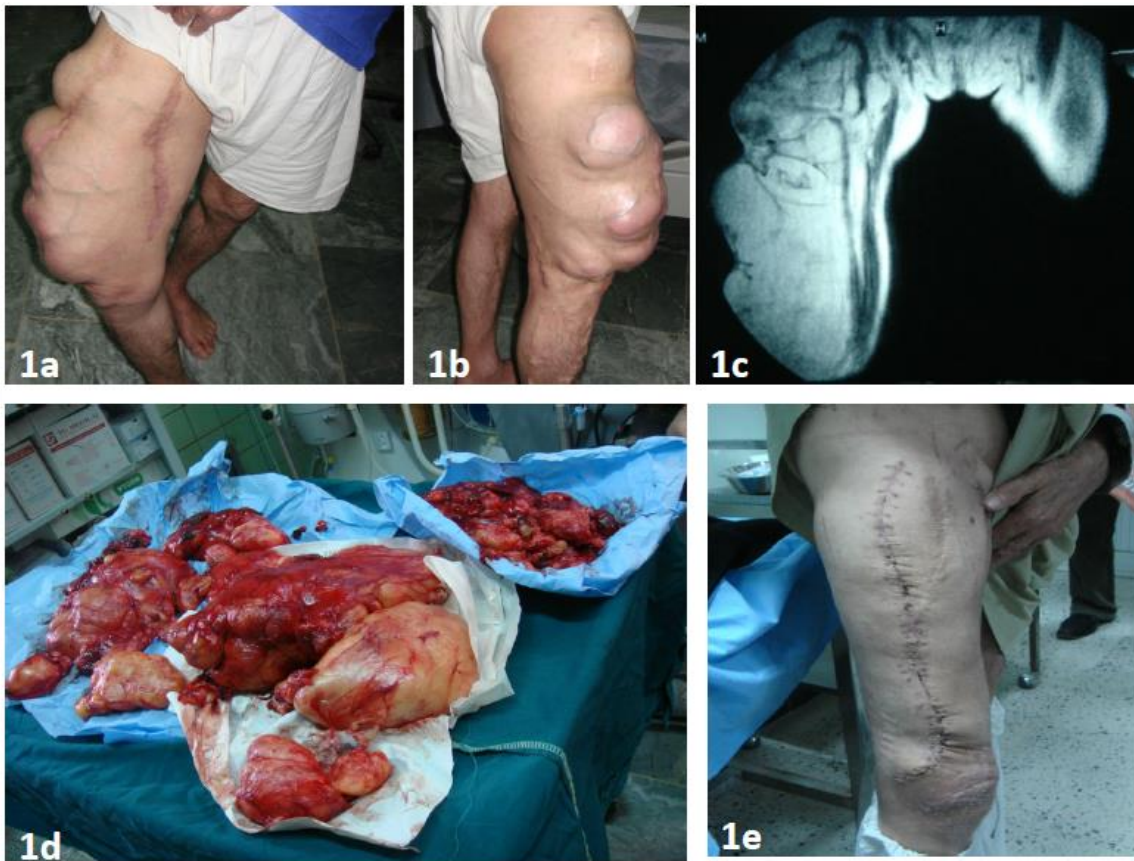


Figure 1a and 1b: Huge lobulated tumor masses of right thigh extending from groin to knee level, soft on palpation, horizontally movable with distended superficial veins and 2 old scars of previous resections 1-yr and 3-yr earlier. **1c:** MRI showing fat-containing masses reaching the cortex of femur and displacing but not involving blood vessels, muscles or bone. **1d:** Huge multiple yellow-brown tissue masses almost filling a trolley! Biopsy result: well-differentiated liposarcoma (mainly mature lipocytes and some cells with deep staining nuclei and some degree of pleomorphism). **1e:** Postoperative appearance of right thigh. The postoperative course was smooth. The patient was referred for radiotherapy.

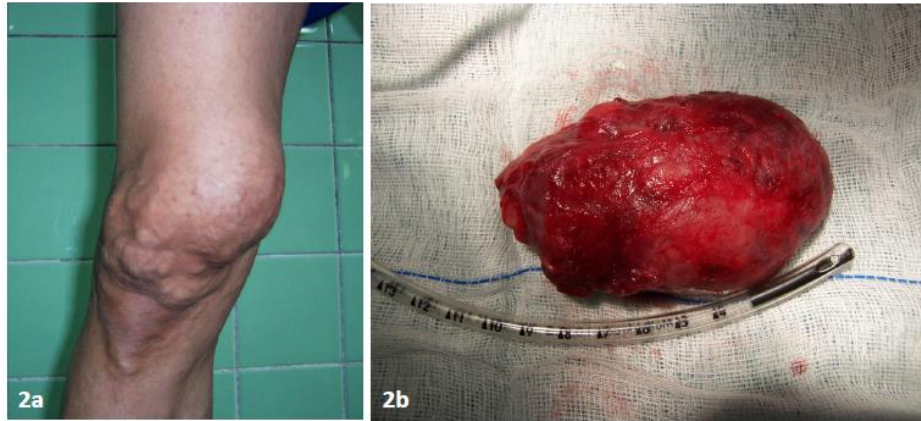


Figure 2a: A mass over right knee of 4-yr duration **2b:** The mass was totally removed; biopsy: ASPS.

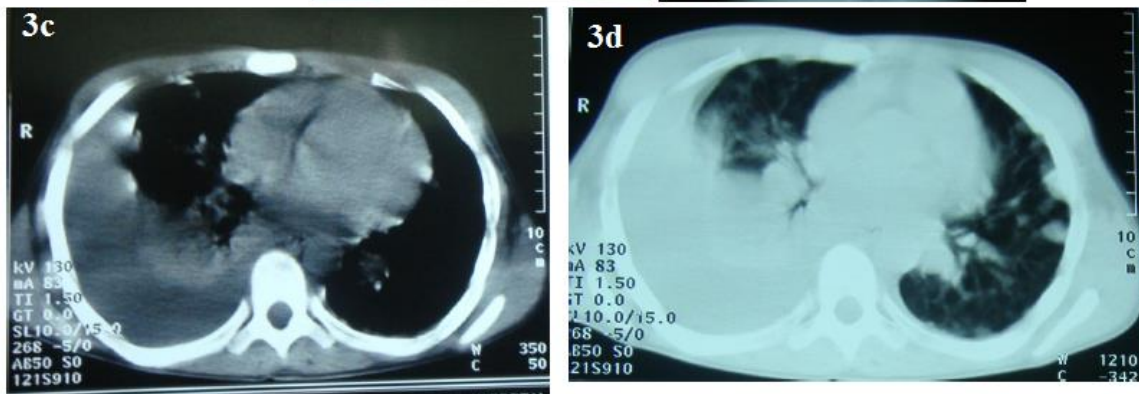
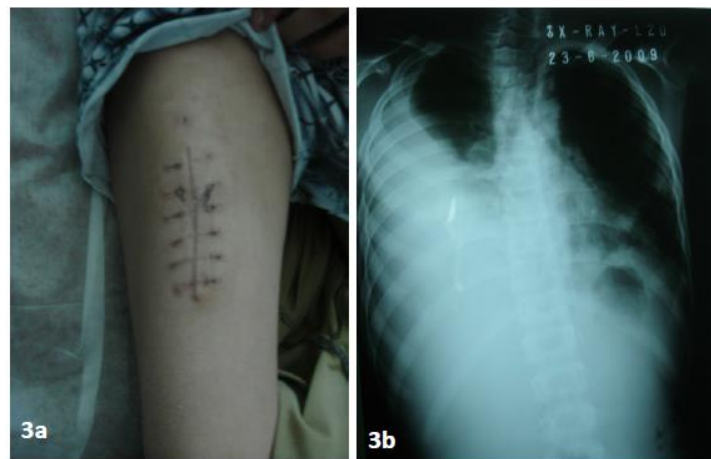


Figure 3a: Recent resection of STS from the right thigh; biopsy: p PNET **3b-3d:** Moderate pleural effusion and bilateral pulmonary metastases. Tube thoracostomy drained 1500 ml of hemorrhagic fluid. The patient received postoperative chemotherapy.

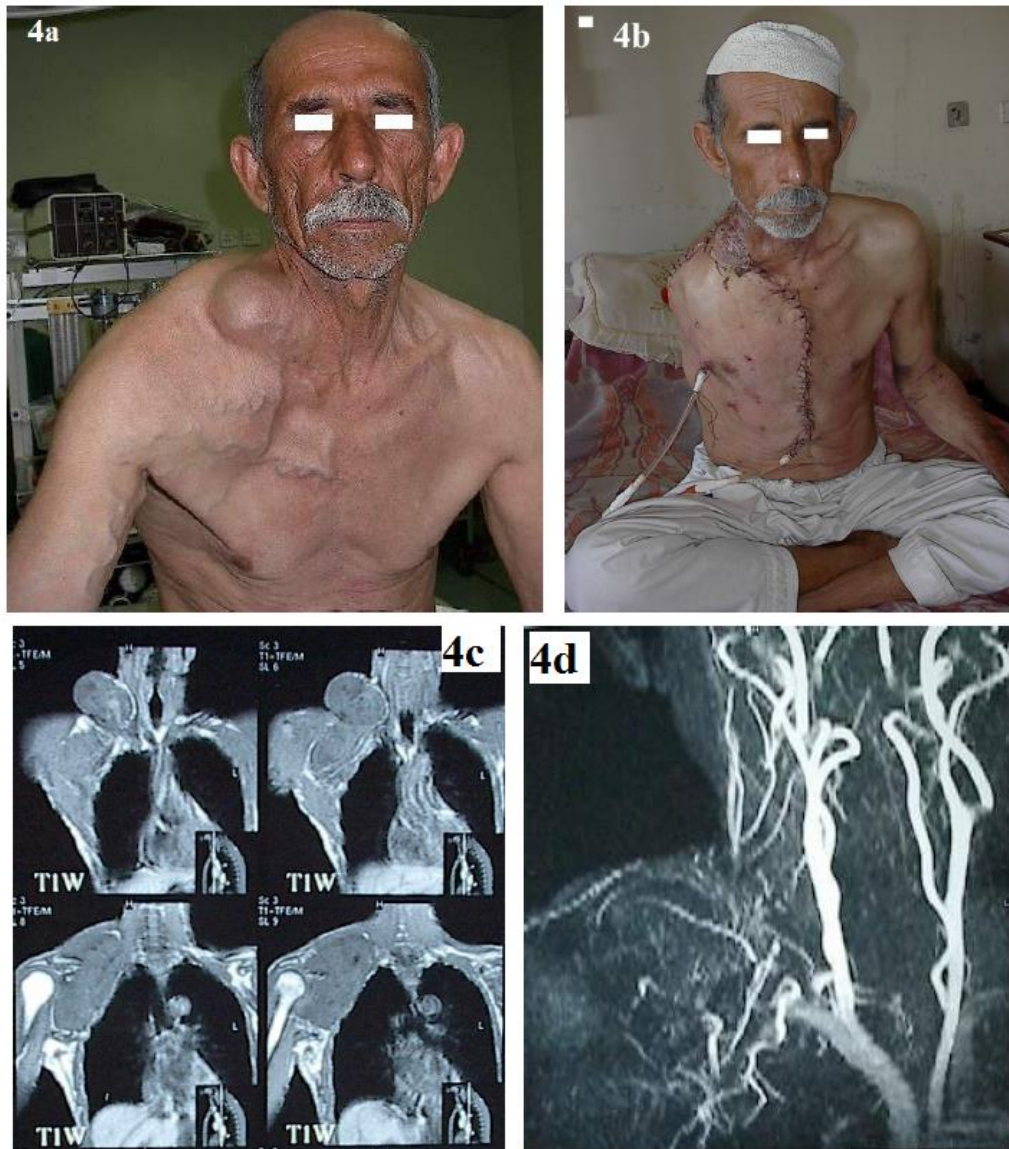


Figure 4a: A solid mass bulging above right clavicle fixed to deep structures, marked varicose superficial veins on anterior chest and right upper arm, palpable right radial pulse and a normal chest examination
4b: Forequarter amputation was necessary for this advanced fibrosarcoma involving subclavian vessels and humerus. Due to close proximity of the tumor to brachiocephalic trunk, proximal vascular control required median sternotomy with supraclavicular extension and resection of clavicle. **4c:** MRI showing big axillary and supraclavicular masses. **4d:** MRA showing highly vascular tumor engulfing subclavian artery. The patient received postoperative radiotherapy.

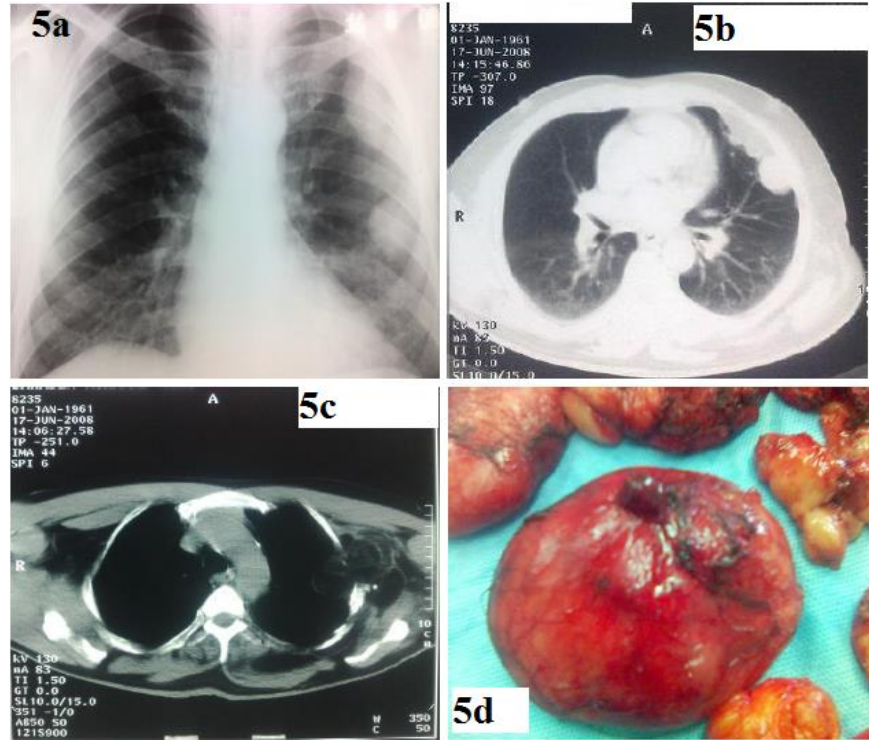


Figure 5a-c: Chest wall masses protruding into the thoracic cavity in a patient with 9 operations for resection of recurrent well-differentiated liposarcoma. The first resection was done in 1994 while the last one was performed in 2012 followed by radiotherapy.

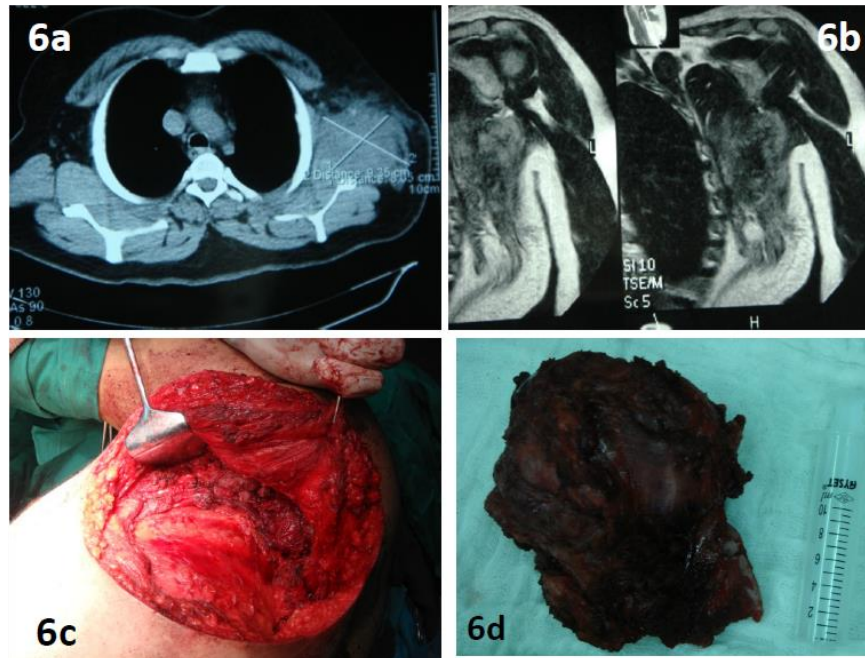


Figure a-b: CT scan of a patient with big solid mass in left axilla and subscapular region fixed to trunk wall of 3-yr duration revealing a well-defined soft tissue mass (9.3 x 8 cm) in size in the left axillary region. A prior FNAC was inconclusive whereas an incisional biopsy 6 months earlier showed features consistent with low grade fibrosarcoma. **6c-d:** The patient was explored via a direct incision over the mass. There was a big hard mass attached to nearby muscles and scapula but not invading the chest wall. It was completely removed. The mass was 15 x 12 x 6 cm in size. Histopathological examination revealed features of aggressive fibromatosis (an opinion shared by 2 consultant pathologists).

Discussion

In the present study, we have found that STS developed in the extremities or trunk wall of predominantly adult patients. All patients were managed by a team of oncologist, vascular and orthopedic surgeons. Wide surgical excision was the main stay of therapy. Limbs were spared in all but one patient.

Maretty-Nielsen K et al [cited in 3] estimated the incidence of STS to be 1.4 per 100,000 populations. Although STS may occur at any age [6], it is mostly a disease of 40-70 years adults [11]. All our patients were adults except one teenager. Two locations were involved (trunk wall and extremities). However, connective tissue anywhere in the body such as pelvis, retro peritoneum, head and neck can be the site of origin of these tumors. Apart from synovial sarcoma, STS usually present as a painless mass [11]. Likewise, 5 of our patients had slowly growing painless masses. Pain, on the other hand, is a common feature of benign soft tissue tumors such as angioliopoma and schwannoma [11].

MRI is the favored imaging technique; other options include computerized tomography or ultrasound depending on local skill [6]. Tissue diagnosis can be obtained by core needle biopsy. However, an incisional biopsy may occasionally be needed and excisional biopsy may be the most sensible option for superficial lesions smaller than 5 cm. The biopsy should be designed in such a way that the tract can be securely removed at the time of definitive surgery. Fine needle aspiration cytology is not suggested as a primary diagnostic modality, although it may be helpful in confirming disease recurrence [6]. In our series, MRI and/or CT scan was performed in 4 patients. Fine needle aspiration cytology was done twice revealing a diagnosis of undifferentiated sarcoma in one patient while it was inconclusive in the second. Five patients had biopsies with 3 accurate diagnoses.

The histological subtype of STS is important in selecting chemotherapeutic agents when needed [12] as well as in predicting the prognosis of patients. Investigators found that the best indicator of a tumor's biological behavior and the strongest predictor of metastasis and fatality from STS is tumor grade [1] [3]. In the present series, half the patients had histologically common sarcomas (liposarcoma and fibrosarcoma) whereas the other half had rare tumors (fibromatosis, ASPS and p PNET).

Well-differentiated LS is the 2nd most common STS [11] mostly occurring in the thigh followed by retro peritoneum and trunk wall [11]. Both of our patients exhibited characteristic findings on MRI (a uniform fat appearance) and typical histopathological criteria (mature fat cells with scattered lipoblasts). In contrast, lipomas consist of ordinary adipose tissue without lipoblasts. Liposarcoma has a known tendency to recur locally. Surgery alone for STS can be followed by LR in 40% of cases. However, 90% local control rate can be achieved if radiotherapy is added [1]. Local recurrence was observed 2-8 times in our patients with liposarcoma. However, addition of radiotherapy prevented LR in both. Liposarcoma has a good prognosis with 100% 5-year survival [11].

Fibrosarcoma is most commonly seen in persons aged 30–55 years. It has no characteristic clinical findings but pathologically consists of elongated fibroblast-like cells arranged in a uniform, fasciculated growth pattern [13]. Our case was a man of 55 with long-standing huge tumor mass at proximal right upper limb involving subclavian vessels and humerus; thus required forequarter amputation.

Desmoids tumors (aggressive fibromatosis) are fibrous neoplasms arising from the musculoaponeurotic structures throughout the body. The term “desmoid” is derived from the Greek word “desmos” meaning

tendon-like. The cell of origin is the fibromyoblast. The synonym aggressive fibromatosis describes the marked cellularity and aggressive local behavior. These tumors account for 0.03% of all neoplasms and are more common in persons aged 10-40 years with a higher rate of female involvement [7] [8]. Our patient (6th in the series) was a man of 24 with a long-standing mass in left axilla and subscapular region. The tumor had recurred after a previous resection. Desmoids tumors tend to infiltrate adjacent muscle bundles [7]. Hence, incomplete resection could explain recurrence in this case.

Alveolar Soft Part Sarcoma is a very rare soft tissue sarcoma which arises primarily in children and young adults [5]. It accounts for 0.5–1% of all soft tissue sarcomas [5]. To date, the definitive origin of this tumor remains unknown [5]. The fact that all tumors were located within or close to muscle may support the thesis that the origin of ASPS is myogenic [4]. The name "alveolar" was derived from its pseudo-alveolar appearance with clustered polygonal cells lacking central cohesion [4]. Disease usually presents as a painless, soft, slow growing lesion that rarely causes functional impairment [5]. It presents at almost every part of the body with a predominance of the trunk and the proximal extremities [4]. Metastases (most often to the lungs and central nervous system) develop in 80% of patients during the course of treatment [5]. Lieberman et al. [cited in 5] provided the first evidence that surgical intervention appears to be the only clinically effective therapy for ASPS. The resistance of ASPS tumors to conventional chemotherapies and radiation makes this type of tumor challenging to treat [5]. Our patient (the 2nd in the series) was a man of 26 with a long-standing slowly-growing painless mass adjacent to the knee managed surgically.

Primitive Neuroectoderm Tumor (PNET) is a rare malignant tumor originating from neuroectoderm accounting for 4% of all soft tissue tumors [9]. It is clinically aggressive tumor with a gloomy prognosis [9]. It consists of primitive undifferentiated small round cells and can be divided into central PNET (c PNET) and peripheral PNET (p PNET) tumors based on the tissue of origin [9]. Peripheral PNET can be found in all age groups, but, is more common in young children [9]. Peripheral PNETs are often associated with distant metastases and local recurrence following treatment [9]. Due to their aggressive nature, distant micro-metastasis must always be assumed to be present and, hence, all patients should receive adjuvant chemotherapy for systemic control [10]. Our case (the 3rd in the series) was a boy of 14 with a rapidly growing thigh mass. Resection of the mass was shortly followed by malignant pleural effusion and bilateral pulmonary metastases; thus, chemotherapy was administered. The prognosis for STS with pulmonary metastasis is poor with a 5-year survival of 15% after resection of metastases as opposed to 65% in patients without metastases [11].

The treatment of STS remains a surgical challenge [11]. The National Comprehensive Cancer Network (NCCN) guidelines recommend that "all patients with STS be evaluated by a multidisciplinary team with experience managing STS. In this setting, experienced surgeons and radiation oncologists can work together to optimize therapy to achieve local control and preserve limb function whenever possible" [1].

Conclusion

Patients with STS out of a sarcoma center can be satisfactorily managed by a surgical team with adequate experience providing that standard guidelines are followed.

Informed Consent Statement

All involved persons gave their verbal and written informed consent.

Conflict of Interests

None declared.

Disclosure

The 4th case in this report was published in a previous article of the author (Taha AY. Forequarter amputation for primary malignant tumors of proximal upper limb: a report of 3 cases. The Journal of Neurological and Orthopedic Medicine and Surgery - April 2016. Available from <http://aanos.org/publications/articles/>). However, it is included in this paper for complete coverage of the subject.

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