Review Article

DIAGNOSIS AND MANAGEMENT OF SOFT-TISSUE SARCOMAS

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ABSTRACT

Soft-tissue sarcomas are locally aggressive tumours with a tendency to spread haematogenously, especially to the lungs. Most patients present without obvious metastases. Their management is dependent on an adequate incisional biopsy to assess the grade of the tumour. The biopsy incision must be carefully placed so as not to compromise subsequent radical excision. Of patients so treated, 20 to 30% experience local recurrence within the first 3 years postoperatively. The use of adjuvant radiotherapy decreases the incidence of local recurrence to about 15%. Patients with retroperitoneal sarcomas have a greater tendency to suffer recurrence, with disseminated disease throughout the abdomen. The overall 5-year survival rate is about 50%. Patients may, however, have persistent disease or develop metastases beyond the 5-year period. The optimal timing of radiation and chemotherapy remains unresolved, but multimodality treatment at least allows the advocacy of limb-sparing procedures for patients with soft-tissue sarcomas.

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Introduction

Soft-tissue sarcomas largely comprise tumours arising from the extraskeletal connective tissues of the body that connect, support and surround other discrete anatomical structures. Most of these structures are derived from the embryonic mesoderm. They include muscles and tendons, fibrous tissue, fat and synovial tissue. These tumours demonstrate similarities in pathological appearance, clinical presentation and biological behaviour. Tumours that arise in Schwann cells are also included in the category of soft-tissue sarcoma.

Similarly, some tumours that arise from the lining of the vascular and lymphatic channels or the lining of the body cavities and visceral organs behave like, and resemble, tumours that develop from connective tissue cells.

Soft-tissue sarcomas comprise 0.7% of all cancers [1]. They comprise 6.5% of all can-

cers in children under the age of 15 years and rank fifth as the cause of cancer death in this age group, behind leukaemias, cancer of the brain and central nervous system, renal cancer and bone cancer. At Tata Memorial Hospital, lower extremity soft tissue sarcoma were commonest (36.0%) while other soft tissue sarcomas included those of trunk including peritonium (30.3%), upper extremity (11.2%) and head and neck (19.5%) [2].

Soft-tissue sarcomas are thought to occur with increased frequency in patients with certain genetically transmitted diseases such as Gardner's syndrome, tuberous sclerosis, familial intestinal polyposis and Von Recklinghausen's disease. Association between wood preservatives (chlorophenols) and certain herbicides (phenoxy acetic acid) and the development of soft-tissue sarcomas has been reported [3]. Soft-tissue sarcomas are likely to occur in areas of the body previously exposed to ionizing radiation, although sarcomas in radiotherapy fields are uncommon [4]. Os-

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teosarcomas appear to be the sarcomas most commonly induced by radiation; their latent period may be more than 20 years.

Soft-tissue sarcomas can arise at any site where connective tissue is found. About 40% of soft-tissue sarcomas arise in the lower part of the body and about 75% of these are at or above the knee [5]. Ten percent of all sarcomas arise in the upper part of the body [6]. Sarcomas of the trunk are divided between the retroperitoneum 10%, and the abdominal or chest wall 20%.

Pathological Classification

Classification of soft-tissue sarcomas is complicated by the large number of different tissues and the variety of histologically distinct but often grossly similar sarcomas. In addition, certain 'benign' soft-tissue tumours are grossly similar to sarcomas and, although rarely metastatic, they are locally invasive and can be aggressive (for example desmoid tumours-infiltrating fibromatosis). Pathological classification based on describing the appearance of the predominant cell in the lesion is unhelpful in the management of these tumours, which depends on their grading and staging. Because of the complex constellation of malignant neoplasms, there is no simple formula for grading. Generally, the following histological parameters are considered: differentiation, cellularity, amount of stroma, vascularity, extent of necrosis and the number of mitoses [7] (Table 1). A grading system of primary soft-tissue sarcomas based on the tumour type is shown in Table 2. The prognosis of a soft-tissue sarcoma is dependant on the size, site and histological grade of the

tumour, and can be staged according to these parameters.

The pathologist may sometimes feel uncomfortable with specific histological designation and describe the sarcoma as 'Unclassified' but this does not necessarily imply a poor prognosis. A knowledge of the histological grading of the tumour is critical to developing the proper management strategy. Histological grading is a powerful indicator of the tumour's biological behaviour and is more valuable to the clinician involved in the management of a sarcoma patient than is the knowledge of the exact histopathological variety of the tumour.

Diagnosis

Soft-tissue sarcomas often present as asymptomatic soft-tissue masses. Generally, they do not cause any symptoms until they are quite large and produce pressure or traction on adjacent nerves or muscles. They do not have to be large, however, to produce symptoms in a digit or toe, where they may be less than 1 cm in diameter on presentation. Soft tissue sarcomas have almost no tendency to develop a scar/skin deposit [8].

As there are no reliable symptoms or signs that distinguish benign tumours from malignant soft-tissue tumours, it is imperative to biopsy all soft-tissue lumps that persist or grow. In performing a biopsy, it is vital that the surgeon places the incision in such a location so as not to compromise subsequent definitive surgical excision [9]. Although it has recently been suggested that a true-cut biopsy is useful in the diagnosis of soft-tissue sarcomas [10], it is generally agreed that a large sample of tissue is necessary to assign the accurate diagnosis and grade of tumour, especially if tissue culture and or electron microscopy is required to obtain the final histopathological diagnosis. The incisional biopsy provides a generous sample of tissue with minimal disturbance of the surrounding tissue planes. Unless a biopsy incision is appropriately sited, proper radical resection of the lesion may be precluded and amputation of an extremity may be the only alternative to

TABLE 1
Guidelines to the Histological Grading of Sarcomas

Feature	Low grade sarcoma	High grade sarcoma
Differentiation	Good	Poor
Cellularity	Hypo	Hyper
Stroma	Much	Minimal
Vascularity	Hypo	Hyper
Necrosis	Minimal	Much
Mitoses	<5/HPF	>5/HPF

TABLE 2

Grading of Primary Soft-tissue Sarcomas

Type of sarcoma	Low grade	Low or High grade	High grade
Malignant fibrous histiocytoma		Fibroblastic Histiocytic Pleomorphic	
Fibrous sarcomas	Desmoid tumour	Fibroblastic fibrosarcoma	Pleomorphic fibrosarcoma.
Tendosynovial sarcomas		Biphasic synovial sarcoma. Choroid sarcoma.	Monophasic synovial sarcoma (spindle cell type) Epitheloid sarcoma Clear cell sarcoma
Sarcomas of adipose tissue	Well-differentiated liposarcoma Myxoid liposarcoma	Fibroblastic liposarcoma	Lipoblastic liposarcoma
Sarcomas of muscles		Leiomyosarcoma Leiomyoblastoma	Pleomorphic liposarcoma Embryonal rhabdomyosarcoma Rhabdomyoblastoma Pleomorphic rhabdomyosarcoma
Sarcomas of vessels	Kaposi's sarcoma Malignant glomus tumour	Haemangiosarcoma Haemangiopericytoma	Angiosarcoma Lymphangiosarcoma
Sarcomas of nerves		Malignant peripheral nerve sheath tumour (PNST)	Primitive neuroectodermal tumour (PNET)
Miscellaneous sarcomas		Chondrosarcoma Malignant granular cell tumour Alveolar soft-part sarcoma Malignant mesenchymoma Undifferentiated soft-tissue sarcoma	Osteosarcoma Ewings sarcoma Angioendotheliomatosis

ensure adequate treatment. Incision over lesions in the extremities should therefore be placed longitudinally in the long axis of the principal underlying muscle.

As these tumours grow in the line of least resistance, the surrounding tissue is compressed to form a pseudocapsule, within which fronds of tumour are found. Any attempt to resect the tumour using this false capsule as a plane of dissection will inevitably result in early local recurrence to the tune of upto 90% within 2 years [11].

Radiography in the Diagnosis

Computed tomography (CT) scanning through the affected region is the most useful radiographic technique in diagnosing soft-tissue sarcomas [12]. Magnetic resonance imaging (MRI) also promises to be helpful [13]. The contrast between tumour and muscle,

and tumour and vessel, is better with MRI than with CT scanning. Arteriography is frequently used to assess the possible involvement and vessel displacement by the tumour [14]. Direct invasion of major vessels by the tumour is uncommon. Bone scans although often used [15], are unreliable for extra osseous sarcomas, as a periosteal reaction from a contiguous tumour will give a false positive result. Soft tissue sarcomas rarely invade bone.

A chest X-ray with tomography is helpful in identifying metastatic disease. Computerized lung tomography is also helpful but has a higher rate of false-positive results than does lung tomography. Apart from childhood embryonal rhabdomyosarcomas, soft-tissue sarcomas rarely metastasize to lymphnodes and lymphangiography is not usually indicated [16].

Staging

Histological grade is the single most important prognostic factor in patients with soft-tissue sarcomas [17]. A simplified method of staging in relation to favourable versus unfavourable prognostic signs is shown in Tables 3 and 4. The tumour node metastasis (TNM) classification is shown in Table 5 [18]. In lesions of the extremities, proximal tumours are generally less curable than are distal tumours. Size is also an important parameter, especially when combined with the site of the tumour, for example in the head and neck or retroperitoneal lesions. The size of the tumour also limits the effectiveness of radiotherapy [5]. Involvement of the lymphatics, although rare, is a poor prognostic factor and occurs with a higher frequency in epithelioid sarcomas [16]. Younger patients with fibrosarcomas and liposarcomas appear to do better than do older patients. While age does not have a significant impact on the natural history of the tumour [19], there does appear to be a direct correlation between increasing age and the risk of local recurrence [5].

The histological grading and prognostic signs of individual histological subtypes of soft-tissue sarcomas are outlined in Table 2

TABLE 3

Factors Influencing the Prognosis of Sarcomas

Factor	Prognostic Sign	
	Favourable	Unfavourable
Size	Small (< 5 Cms)	Big (> 5 Cms)
Site	Superficial	Deep
Histological grade	Low	High

TABLE 4

Correlations between the Prognostic Signs and Stage of Sarcomas

Stage of sarcoma	Number of prognostic signs	
	Favourable	Unfavourable
0	3	0
I	2	1
II	1	2
III	0	3
IV	Evidence of metastases	

TABLE 5

Tumour Node Metastasis (TNM) Staging of Soft-tissue Sarcomas

Stage T Tumours	
T1	: Tumour less than 5 cms in diameter.
T2	: Tumour 5 cms or greater in diameter.
T3	: Tumour grossly invades bone, vessels or nerves.
Stage N Tumours	
N0	: No histologically verified metastasis to lymphnodes.
N1	: Histologically verified regional lymphnode metastasis.
Stage M Tumours	
M0	: No distant metastases.
M1	: Distant metastases.
Stage G Tumours	
G1	: Low
G2	: Intermediate
G3	: High

[7]. Although soft-tissue sarcomas generally have a similar natural history, some of the subtypes possess unique biological behaviour, as described below.

Malignant fibrous histiocytomas : These tumours arise from histiocytes. They comprise the most common histological diagnosis attached to soft-tissue sarcomas and encompass the complete spectrum of histological grade. Prognosis is very variable.

Liposarcomas : These tumours arise from adipose tissue. They tend to be more locally aggressive and metastasize late. The round cell type tends to be the most aggressive and has a poor prognosis.

Synovial Sarcomas : These tumours arise from tendosynovial tissue and are of two pathological subtypes; monophasic, which tend to have a poorer prognosis, and biphasic, which are more likely to be of a lower grade.

Fibrosarcomas : These tumours are derived from fibrocytes. Many soft-tissue sarcomas have, in the past, been designated incorrectly as fibrosarcomas, which has added to the confusion surrounding these tumours.

Rhabdomyosarcomas : These tumours account for 15% of all soft-tissue sarcomas. They are tumours of stratified muscle and are

subdivided into embryonal, pleomorphic and alveolar types. They are the most common soft-tissue sarcomas of childhood. Multidisciplinary management has greatly improved the survival of children with these tumours.

Neurofibrosarcomas : These tumours originate in the neural sheath and can arise anywhere in the body. They are found most commonly in association with Von Recklinghausen's disease, that is multiple neurofibromas and skin pigment lesions (*cafe-au-lait spots*). The proportion of patients with Von Recklinghausen's disease developing neurofibrosarcomas is 10-15%.

Leiomyosarcomas : These tumours arise from smooth muscle. They can arise anywhere in the body and can develop from the walls of blood vessels. They arise in the viscera and in the retroperitoneum, where they are particularly aggressive.

Angiosarcomas : These tumours arise from blood vessels and lymphatic channels and generally carry a poor prognosis. They have been most frequently reported in patients with lymphoedema of the extremities, from whatever cause.

Epithelioid sarcomas : These tumours are of unknown cell origin. They usually occur in the extremities and about 30% metastasize to regional lymphnodes. Wide excision and, often amputation with regional lymph-node dissection is the recommended treatment.

Alveolar soft-part sarcomas : These tumours are also of unknown cell origin. They are uncommon, with a generally protracted course. Recurrence may be very late (more than 5 years), but patients usually die from the disease.

Haemangiopericytomas : These tumours arise from the pericyte cells around smooth muscle. They are very rare and may present as benign or malignant lesions.

Mesotheliomas : These tumours arise from the lining cell of the pleural, pericardial and peritoneal surfaces. Their association with asbestos is well known. There is no satisfactory treatment for these tumours, and most patients die from the disease within 12

months of the diagnosis. Pleuropneumonec-tomy and adriamycin may be helpful to a few patients, and radiation treatment may provide some palliation.

Kaposi's Sarcoma : These tumour presents as a raised pigmented lesion on the skin. Four sub-types are generally recognised. All occur more frequently in males. Kaposi's sarcoma in childhood is extremely rare and is almost invariably fatal. It has been recognized most frequently in Central Africa particularly in eastern Zaire and Uganda. The type of Kaposi's sarcoma seen in elderly Mediterranean males and in people of Jewish extraction is an indolent tumour that is slowly progressive. African Kaposi's sarcoma occurs in adults and is also slowly progressive, occurring mainly in the extremities and following an indolent course. The type of Kaposi's sarcoma seen most frequently at present is in patients with the acquired immune deficiency syndrome (AIDS). It is seen in 34% of all AIDS patients, where it is rapidly progressive and generally fatal. It resembles the type of Kaposi's sarcoma seen in children and young adults. Kaposi's sarcoma is believed to arise from cells of reticuloendothelial origin. It has been suggested that it represents a multicentric proliferative lesion of endothelial origin. Human immune deficiency virus (HIV), either directly or indirectly, may be the underlying aetiological factor in the development of Kaposi's sarcoma. Cytomegalo virus has also been implicated in the promotion of Kaposi's sarcoma.

Management

Although the management of soft-tissue sarcomas of the extremities is controversial, surgery remains the primary treatment. It involves resection of the lesion with adequate margins, excising normal, uninvolved surrounding tissue for at least 2 cms in all directions. It is important to obtain a complete tissue plane free of tumour in order to gain adequate local control [19]. All of the skin and subcutaneous tissue near the tumour, all previous scars and areas of previous biopsies, must be excised. The tumour should not be

seen during the surgical procedure. Metallic clips should be placed to serve as important markers for postoperative external beam radiotherapy.

Increasingly, limb-sparing surgery is being performed in combination with postoperative radiotherapy and some times chemotherapy [5,20]. Postoperative radiotherapy is used to clear the tissue of microscopic disease. The treatment doses are delivered in progressively decreasing fractions as determined by the estimated number of viable tumour cells obtained by radiobiological techniques.

The use of brachytherapy in certain specialized centres allows a greater radiation dose to be administered to the tumour field, thereby decreasing the level of radiation to uninvolved surrounding structures [4]. Brachytherapy involves the use of intraoperative implantation of after loading catheters and subsequent temporary insertion of iridium seeds or wires into the catheters [21]. A dose of 45 Gy (4500 rads) by this method is equivalent to 60 Gy (600 rads) by external beam irradiation. While attempts at limb-sparing surgery using adjuvant therapies may increase the risk of local recurrence, limb-sparing surgery with adjuvant radiation and chemotherapy has proved to be as effective as amputation and chemotherapy in terms of survival [22]. Local recurrence may not necessarily have an adverse effect on overall survival, particularly in low-grade lesions.

All patients with high-grade lesions are recommended to have a chemotherapeutic scheme that includes adriamycin. Patients who require amputation generally have a poorer prognosis, as amputation is determined by the size and position of the tumour. Detailed descriptions of amputation procedures are available elsewhere [23].

For truncal sarcomas, the same general management principles apply. However, because of their anatomical location, the margins of excision are frequently inadequate. Following resection of sarcomas of the thoracic and abdominal wall, prosthetic devices may be required to repair the defect.

This does not preclude subsequent radiotherapy to the area. For all high-grade truncal sarcomas, radiotherapy should be used postoperatively.

The apparent improvement in survival after chemotherapy in patients with sarcomas of the extremities has not been paralleled in patients with truncal sarcomas for whom surgery is still the mainstay of treatment [24]. Aggressive attempts at the resection of pulmonary metastases may be worth while in selected patients. There are reports of multiple pulmonary resections giving upto 20% 5-year survival [25]. The criteria for patient selection have still to be fully established.

REFERENCES

1. De Vita Jr, Hellman S, Rosenberg SA (eds) *Cancer : Principles and Practice of Oncology*. Philadelphia : Lippincott, 1989.
2. Desai PB, Rao DN, Shroff PD. Hospital Based Cancer Register - Annual Report 1988. Tata Memorial Hospital, Bombay - 1990; 98.
3. Ericksson M, Hardell Berg NO, Moller T, Axelsson O. Soft tissue sarcomas and exposure to chemical substances : a case referenced study. *Brit J Indust Med* 1981; 38 : 27-33.
4. Davidson T, West-bury G, Harmer CL. Radiation included soft tissue sarcoma. *Brit J Surg* 1986; 73 : 308-9.
5. Collin C, Hadju SI, Godbold J, Shiu MH, Hilaris BI, Brennan MF. Localised operable soft tissue sarcoma of the lower extremity. *Arch Surg* 1986; 121 : 1425-33.
6. Collin C, Hadju SI, Godbold J, Friedrich C, Brennan MF. Localized soft-tissue sarcoma of the upper extremity : presentation, management and factors affecting local recurrence in 108 patients. *Ann Surg* 1987; 205 : 331-9.
7. Hadju SI (ed). *Differential diagnosis of soft tissue and bone tumours*. Philadelphia : Lea and Febiger, 1984; 964-967.
8. Mc Cormack PM, Martini N. The changing role of surgery for pulmonary metastases. *Ann Thorac Surg* 1979; 28 : 139-45.
9. Brennan MF. The management of soft tissue sarcomas. *Brit J Surg* 1984; 71 : 964-7.
10. Kissin MW, Fisher C, Carter RL, Horton LWL, Westbury G. Value of Tru-cut biopsy in the diagnosis of soft-tissue tumours. *Brit J Surg* 1986; 73 : 742-4.
11. Gerner RE, Moore GE, Pickren JW. Soft tissue sarcomas. *Ann Surg* 1975; 181 : 803-8.
12. Neifeld JP, Walsh JW, Lawrence JW Jr. Computed tomography in the management of soft tissue tumours. *Surg. Gynecol Obstet* 1982; 155 : 535-40.

13. Chang AE, Matory YL, Dwyer AJ *et al.* Magnetic resonance in aging versus computed tomography in the evaluation of soft tissue tumours of the extremities. *Ann Surg* 1987; 205 : 340-8.
14. Hudson TM, Haas G, Enneking WF *et al.* Angiography in the management of musculoskeletal tumours. *Surg Gynecol Obstet* 1975; 141 : 11-21.
15. Simón MA, Enneking WF. The management of soft-tissue sarcomas of the extremities. *J Bone Joint Surg* 1976; 58A; 317 (Abstract).
16. Weingrad DW, Rosenberg SA. Early lymphatic-spread of osteogenic and soft tissue sarcomas. *Surgery* 1978; 84 : 231-40.
17. Trojani M, Contesso G, Coindre JM *et al.* Soft tissue sarcomas of adults. Study of pathological prognostic variables and definition of a histopathological grading system. *Int J Cancer* 1984; 3 : 37-42.
18. Russel WO, Cohen J, Enzinger FM *et al.* A clinical and pathological staging system for soft tissue sarcomas. *Cancer* 1977; 40 : 1562-70.
19. Soule EH, Pritchard DJ. Fibrosarcoma in infants and children : a review of 110 cases. *Cancer* 1977; 40 : 1711-21.
20. Enneking WF, Spanier SS, Malawer MM. The effect of the anatomic setting on the results of surgical procedures for soft parts sarcoma of the thigh. *Cancer* 1981; 47 : 1005-22.
21. Krementz ET, Carter RD, Sutherland CM, Hulton I. Chemotherapy of sarcomas of the limbs by regional perfusion. *Ann Surg* 1977; 185 : 555-64.
22. Shiu MH, Turnbull AD, Nori D, Hadju S, Hilaris B. Control of locally advanced extremity soft tissue sarcomas by function saving resection and brachytherapy. *Cancer* 1984; 53 : 1385-92.
23. Rosenberg SA, Tepper J, Glatstein E *et al.* The treatment of soft tissue sarcomas of the extremities : prospective randomized evaluation of¹ limb sparing surgery plus radiation therapy compared with amputation and the role of adjuvant therapy. *Ann Surg* 1982; 196 : 305-15.
24. Sugarbaker P. *Atlas of Extremity Surgery*. Philadelphia : Lippincott, 1985.
25. Felix EL, Wood DK, Das Gupta TK. Tumours of the retroperitoneum. *Curr Probl Cancer*. 1981; 6 : 3-47.