Soft Tissue Sarcoma—Review of Experience at a Tertiary Care Cancer Centre

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Abstract This study is a retrospective analysis of prospective data base of soft tissue sarcoma (STS) maintained in the department of Surgical Oncology, Bhim Rao Ambedkar Institute Rotary Cancer Hospital (BRA-IRCH), All India Institute of Medical Sciences, which is a tertiary care cancer centre. A total of 300 patients of STS were treated between 1995 and 2006. The mean age at presentation was 40.6 years and males were more affected than females. Extremity sarcomas were more common than non extremity sarcoma and lower limb dominated upper limb. The median size of tumor was 8 cm (range 1–40 cm). MRI scan was the preferred imaging modality and tissue diagnosis was obtained by core biopsy. Synovial Sarcoma and Malignant Fibrous Histiocytoma were the common histology. Majority (75%) tumors were of high grade. Patients were staged according to MSKCC staging system. Limb Salvage Surgery was offered to all patients where ever feasible. Wide excision with a gross three dimensional tumor free margin of 2 cm was performed. Adjuvant external beam radiotherapy was offered to all high grades, large and recurrent tumors along with perioperative brachytherapy implant for tumor bed. High grade tumors were also offered adjuvant Adriamycin based Chemotherapy. Limb salvage rate was 68% in extremity sarcoma. During follow up 114 (38%) patients had relapse of disease mainly systemic, lungs being the commonest site.

Keywords Soft tissue sarcoma · Malignant mesenchymal tumors · Surgical resection · Adjuvant therapy · Perioperative brachytherapy

Introduction

Soft tissue sarcomas (STS) are a rare and heterogeneous group of solid tumours. These tumours arise from the mesenchymal tissues. Soft tissue sarcomas are a diverse group of tumour with a wide spectrum of histology and varied clinical behaviour. They constitute about 1% of all solid tumours [1]. The management of soft tissue sarcomas has evolved over last two decades with the advances made in the fields of imaging, histopathology, molecular biology, cytogenetic and multimodality management. Due to rarity of the disease entity, there is paucity of literature pertaining to STS especially from developing countries. This study is undertaken to review the clinical profile, treatment pattern and outcome of soft tissue sarcomas treated in a tertiary care cancer centre.

Materials and Methods

In the department of surgical oncology BRA—IRCH, AIIMS a computerized prospective soft tissue sarcoma data base was created and the details of the all patients operated in the department were prospectively entered in to the database. In this study a retrospective analysis of prospective soft tissue sarcoma database was performed. All patients with a proven histological diagnosis of soft tissue sarcoma were included for analysis. At IRCH, AIIMS, sarcoma patients are managed in a dedicated multidisciplinary sarcoma clinic.

Treatment Protocol

Tissue diagnosis A core biopsy is routinely done to establish the diagnosis. In patients presenting with prior surgical

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intervention slides were reviewed. Rarely an incision / excision biopsy was performed for confirmation of diagnosis.

Imaging Imaging of the involved site was done in all patients except in those with small, superficial and mobile tumors and in patients where limb salvage was clearly not an option. CT scan was the main imaging modality in the earlier part of the study period. However, as MRI became more freely available, it became the preferred modality of imaging during the later part. A CT chest was performed in all patients with high grade soft tissue sarcomas to rule out pulmonary metastasis.

Staging All patients were staged based on tumor size (<5 cm, 5–10 cm and >10 cm), depth (superficial or deep) and histological grade (high or low), as per the MSKCC staging proposed by Hadju et al. [3]

Surgical protocol A wide excision with a gross three-dimensional tumor free margin of 2 cm was performed whenever feasible. In patients with extremity sarcomas, limb salvage was offered to all patients except those with neurovascular bundle involvement, pathological fractures and extensive skin and soft tissue involvement. In all patients presenting with prior surgical intervention, a thorough evaluation for adequacy of surgery was performed including clinical assessment, review of operative notes and histopathology and imaging. Re-surgery was performed in patients with unknown margins, and residual or recurrent disease. Regional lymphadenectomy was performed in all patients with clinically positive draining nodes. Soft tissue defects not amenable for primary closure were managed using local and regional flaps and in a select group of patients with limited vascular involvement vascular reconstruction was offered.

Adjuvant treatment Adjuvant external beam radiotherapy (50 Gy/ 25 Fractions/ 5 Weeks) was offered to all patients with high grade, margin positive, large and recurrent sarcomas. Peri-operative brachytherapy implant for tumor bed boost was performed whenever feasible. Patients who underwent amputation were not offered adjuvant radiotherapy. In the later part of the study, majority of high grade sarcoma patients were offered adjuvant Adriamycin based chemotherapy.

Results

A total of 300 cases of STS were treated between 1995 and 2006. The mean age of patients at presentation was 40.6 years (range-10 to 85 years). The disease affected almost equally the

age groups of less than 40 and more than 40 years (51% vs. 49%). As far as sex distribution was concerned there was a male preponderance—M: F=2: 1. Table 1 shows the site distribution. Extremity sarcomas predominated over non-extremity sarcomas (65% vs. 35%). Among the extremities, majority presented with lower limb sarcomas (73% vs. 27%). Chest wall and trunk was the most common non-extremity site with 21% of patients presenting with sarcoma at this site. Swelling was the most common presenting symptom with (96%).

Clinical evaluation revealed skin involvement in 56%, bone involvement in 15% and 12% had neuro and / or vascular involvement. The median size of tumor was 8 cm (range 1–40 cm). Majority of the patients (47%) had MRI as the imaging modality and in 30% of patients CT scan was used. In 11% of patients, both CT scan and MRI were used for assessment of local spread. Table 2 shows the various histopathological types. Synovial sarcoma was the most common histology encountered (15%), closely followed by malignant fibrous histiocytoma (13.9%). Dermato fibrosarcoma protuberance (DFSP), malignant peripheral nerve sheath tumors (MPNST), leiomyosarcoma and liposarcoma were other common histological types found in our series. An overwhelming majority of the tumors 225 (75%) were histological high grade tumors. As far as the stage distribution is concerned 66% had MSKCC stage III disease, 20% had stage II disease and 9% had stage I and 5% had stage 0 disease. Sixty two percent had some kind of surgical intervention at primary care centres prior to referral.

Table 3 shows details of treatment. Out of a total of 300 patients 285(95%) had curative resection and 15(5%) had palliative resections or found inoperable, most of them being advanced retroperitoneal sarcomas. Among extremity sarcoma patient's limb salvage could be performed in 132(68%) patients and rest had amputations (32%). Among the patients with high grade tumors, limb salvage was possible in 65% of patients, whereas it was feasible in 93% of low grade soft tissue sarcoma patients. Finally 180 (60%) of patients received post operative adjuvant radiotherapy and 30(10%) of these patients also received perioperative brachytherapy tumor bed boost. As far as adjuvant chemotherapy is concerned only 90 out of 300 (30%) high grade

Table 1 Showing details of site distribution of STS

Site	Number	(%)
Lower Extremities	144	(48%)
Upper Extremities	52	(17%)
Chest wall & Trunk	63	(21%)
Head & Neck	25	(8.5%)
Retroperitoneum	16	(5.5%)

Table 2 Showing details of Histopathological types of STS

Histopathology Type	Frequency (%)
Synovial sarcoma	15.0%
MFH	13.9%
DFSP	10.4%
MPNST	10.7%
Leiomyosarcoma	8.2%
Liposarcoma	6.5%
RMS	5.7%
Angiosarcoma	5.3%
Fibrosarcoma	4.3%
PNET	3.6%
Extra skeletal Osteosarcoma & Chondrosarcoms	2.8%
Clear cell sarcoma	1.4%
Alveolar soft part sarcoma	0.7%
Poorly differentiated Sarcoma	0.7%
Epitheloid Sarcoma	0.4%
Indeterminate variety	4.0%

MFH Malignant Fibrous histiocyoma, *DFSP* Dermato fibrosarcoma protuberance, *MPNST* Malignant peripheral nerve sheath tumor, *RMS* Rhabdomyosarcoma, *PNET* Primitive neuroectodermal tumor

sarcoma patients received Adriamycin based adjuvant chemotherapy. During follow-up 114 (38%) patients had relapse of disease mainly involving lungs in 84 patients and the remaining had loco regional relapse.

Discussion

Soft tissue sarcomas (STS) constitute a heterogeneous group of rare solid tumors of mesenchymal origin. Although STS can arise anywhere in the body the majority occur in the extremities. Benign soft-tissue tumors, especially lipomas are 100 times as common as sarcomas. STS constitute approximately 1% of all adult malignancies [1]. Despite best efforts more than 50% of patients with STS will

ultimately die a figure that has changed little during the last three decades [2]. Due to this heterogeneity and the fact that these are rare tumors, no clear-cut guidelines for the management of sarcomas were available till the late 1970s. With the advances made in the fields of imaging, surgical, medical and radiation oncology along with better understanding of tumor pathology and biology more effective management protocols are currently available. Soft-tissue sarcomas are best treated in multidisciplinary setup for optimum results.

STS present most commonly as an asymptomatic mass. In our series, swelling was the presenting symptom in 96% patients. Due to lack of initial symptoms and accessible location, chances of mismanagement at primary care centers are very high. Most common types of mismanagements encountered are marginal excision, incomplete excision and inappropriate biopsy jeopardizing limb salvage and survival. In the current study 62% had history of prior surgical intervention. Hence, it is recommended to offer re-surgery routinely to patients treated sub-optimally at primary care centers. Only radiotherapy or chemotherapy should not be used as a substitute for inadequate surgery in STS. As far as site of involvement is concerned lower extremity is the most common site followed by upper extremity, trunk, head and neck, and retroperitoneum [1]. In the current study extremity sarcoma constituted 65% and majority involving lower extremity. MRI is the imaging of choice for extremity sarcoma and CT scan is preferred for retroperitoneal STS and for evaluation of lungs to rule out metastases [3]. Recently FDG—PET scan is being tried for imaging STS, predicting grade and assessment of response to neoadjuvant therapy [4]. A number of histopathological variants have been described in STS and an experienced pathologist is crucial for an accurate diagnosis of STS [5]. Immunohistochemistry plays a vital role in differentiating various types of sarcomas. Grade of STS is more important than histological type because grade predicts prognosis and survival in STS [6]. Synovial sarcoma was the most common variety encountered in the current study followed by MFH. As far as staging of STS is concerned AJCC, MSKCC and Musculoskeletal tumor society staging systems are described in literature [7]. Unlike other solid tumors grade plays a crucial role in STS staging and in the recent AJCC staging regional nodes are no more considered as distant metastases. We follow the MSKCC staging system because of the simplicity. Contrary to the western literature majority of patients in the current study presented with MSKCC stage II and III advanced disease. Fifty six percent had skin involvement in the form of direct infiltration or ulceration, 15% had bone involvement and 12% had neurovascular involvement at presentation. All these factors have contributed to a modest limb salvage rate of 68% in the current series, where as majority of the western series report limb salvage rates of 80 to 90% [8]. Despite majority of STS

Table 3 Showing treatment details

Surgery
Curative Resections – 285 (95%)
Palliative Resections – 15 (5%)
Extremity Sarcoma – Limb salvage Surgery – 132 (68%)
Amputations - 63 (32%)
Vascular and soft tissue reconstruction - 51 (17%)
Adjuvant Radiotherapy & Chemotherapy details
Post op adjuvant Radiotherapy - 180 (60%)
Perioperative brachytherapy tumor bed boost - 30 (10%)
Adjuvant Adriamycin based chemotherapy - 90 (30%)

patients presenting with advanced disease 95% had a potentially curative resection and 5% were found to be inoperable or had palliative resection. Majority of retroperitoneal sarcomas were inoperable because of the major vessel encasement. Availability of soft tissue and vascular reconstructive expertise increases limb salvage rates in STS [9]. Role of radiotherapy is well established and adjuvant post operative radiotherapy is routinely recommended for all high grade sarcomas in the limb salvage setting [10]. Local control rates with brachytherapy are better especially in high grade and recurrent STS [11]. Sixty percent of patients in the current study received adjuvant radiation without major short term or long term side effects.

Role of chemotherapy is still evolving. Various cytotoxic agents like Adriamycin, ifosamide; vincristine, cisplatin and dactinomycin have been tried with variable results. Results of a sarcoma meta-analysis have shown a small but significant survival benefit mainly for recurrence free survival with Adriamycin based chemotherapy in localized extremity sarcoma [12, 13]. Since 50% of high grade STS develop pulmonary metastases we routinely offer adjuvant Adriamycin based chemotherapy for these patients. Targeted therapies have an established role for visceral sarcomas like GIST [14].

Conclusions

Soft tissue sarcoma is a rare but challenging disease entity. Majority of cases are mismanaged at primary care level. STS should be treated in centers with multidisciplinary cancer care facilities for optimal outcomes. Surgery along with adjuvant radiotherapy plays a major role in the management of STS.

References

1. Clark MA, Fisher C, Judson I et al (2005) Soft tissue sarcomas in adults. *N Engl J Med* 353:701–711
2. Wietz J, Antonescu CR, Brennan MF (2003) Localized extremity soft tissue sarcoma: improved knowledge with unchanged survival over time. *J Clin Oncol* 21:2719–2725
3. Demas BE, Heelan RT, Lane J, Marcove R, Hajdu S, Brennan MF (1988) Soft-tissue sarcomas of the extremities: comparison of MR and CT in determining the extent of disease. *AJR Am J Roentgenol* 150:615–620
4. Bastiaannet E, Groen H, Jager PL et al (2004) The value of FDG-PET in the detection, grading and response to therapy of soft tissue and bone sarcomas: a systematic review and meta-analysis. *Cancer Treat Rev* 30:83–101
5. Fletcher CDM, Unni KK, Mertens F, eds. Pathology and genetics of tumours of soft tissue and bone. Vol. 5 of World Health Organization classification of tumours. Lyon, France: IARC Press, 2002.
6. Guillou L, Coindre JM, Bonichon F et al (1997) Comparative study of the National Cancer Institute and French Federation of Cancer Centers Sarcoma Group grading systems in a population of 410 adult patients with soft tissue sarcoma. *J Clin Oncol* 15:350–362
7. Wunder JH, Healy JF, Brennan MF (2000) A comparison of staging systems for localized extremity sarcoma. *Cancer* 88 (12):2721–2730
8. Clark MA, Thomas JM (2003) Amputation for soft-tissue sarcoma. *Lancet Oncol* 4:335–342
9. Langstein HN, Robb GL (1999) Reconstructive approaches in soft tissue sarcoma. *Semin Surg Oncol* 17:52–65
10. McCarter MD, Jaques DP, Brennan MF (2002) Randomized clinical trials in soft tissue sarcoma. *Surg Oncol Clin N Am* 11:11–22
11. Janjan N, Crane C, Delclos M, Ballo M (2002) Brachytherapy for locally recurrent soft-tissue sarcoma. *Am J Clin Oncol* 25:9–15
12. Sarcoma Meta-analysis Collaboration (1997) Adjuvant chemotherapy for localised respectable soft-tissue sarcoma of adults: meta-analysis of individual data. *Lancet* 350:1647–1654
13. O'Connor JM, Chacón M, Petracci FE et al. (2008) Adjuvant chemotherapy in soft tissue sarcoma (STS): A meta-analysis of published data. *J Clin Oncol* 26: suppl; abstr 10526
14. Demetri GD, von Mehren M, Blanke CD et al (2002) Efficacy and safety of imatinib mesylate in advanced gastrointestinal stromal tumors. *N Engl J Med* 347:472–480