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SOFT TISSUE SARCOMA RETROSPECTIVE ANALYSIS

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Abstract : Introduction - Soft Tissue Sarcomas (STS) represent a group of rare tumors, histopathologically diverse group of neoplasm arising from mesenchymal cells including adipose, muscle, and connective tissues. The standard treatment of sarcomas in the localized stage is local excision and radiotherapy. Radiotherapy may be delivered either preoperatively, by brachytherapy after intra-operative placement of needles and post-operatively. Results - From August 2012 and December 2013, 85 patients with primary soft tissue sarcoma were seen in Radiotherapy Unit 1. Majority of our patients were above the age of 30 years. The incidence among males was 70. STS predominantly was found in lower extremities (51.1 in lower limb, 16.4 in upper limb). Among the patients treated with surgery most of them had wide local excision. Adjuvant radiotherapy was received by 61 patients. Palliative radiotherapy was received by 2 patients for brain and vertebral metastasis. The follow up period ranged from 6- 24 months. Out of 64 patients, no evidence of disease was seen in 34 patients, local recurrence in 1 patient who was treated with surgery alone and distant metastases in 9 patients. Twenty patients were lost to follow up.

Conclusion - Multimodality local therapy in the form of surgery and radiation is often necessary to local control, limb preservation, and functional outcome in these patients. In select circumstances, adjuvant chemotherapy may augment disease control.

Keyword : Soft Tissue Sarcoma Adjuvant Radiotherapy Chemotherapy

INTRODUCTION

Sarcomas represent a group of rare tumors, accounting for2% of all adult malignancies and 10%–15% of malignancies in children [1]. They are a relatively rare, histopathologically diverse group of neoplasms arising from mesenchymalcells including adipose, muscle, and connective tissues. The natural history of STS typically involves growth and compression of surrounding structures, rather than direct invasion of surrounding tissues. The distant spread of sarcoma is characteristically via early haematogenous spread, most often to the lungs [1]. Lymphatic spread of sarcoma is rare but may occur with certain histologic subtypes such as Rhabdomyosarcoma, Angiosarcoma, Epitheloid sarcoma and clear cell sarcoma [2]. The Centers for Disease Control (CDC) estimated that 10,660 new cases of STS would occur in 2009, with approximately 3,820 deaths as a result. The standard treatment of sarcomas in the localized stage is local excision and radiotherapy. Surgical resection involves conservative resection whenever feasible and in agreement with clinical practice guidelines, i.e., en bloc, macro- and microscopically complete surgical excision of the gross tumor encompassing the biopsy scar (R0 resection). Radiation can be given before or after surgery. Postoperative radiotherapy is recommended following surgical resection of the primary tumour with high-grade tumours, and for selected patients with large or marginally excised, low-grade tumours and also in lesions with microscopically positive margins or residual disease (R1 resection) where secondary resection is not feasible. Several randomized trials have shown that radiation therapy, either brachytherapy or external-beam radiotherapy, improves local tumor control [3, 4]. The recommended dose for postoperative radiotherapy is 60–66Gy in 30-33 fractions. Pre-operative radiotherapy is advantageous in terms of long-term functional outcome with equivalent rates of disease control when compared with postoperative radiotherapy. There is however an increased risk of postoperative wound complications. The recommended dose for pre-operative radiotherapy is 45 to 50.4Gy in 25-28 fractions. Adjuvant chemotherapy has shown benefit in certain histologies Rhabdomyosarcoma, synovial sarcoma and myxoid – round cell liposarcoma. Chemotherapy with Doxorubicin -based regimen remains the treatment of choice for most histological subtypes, with response rates of 25%–35% [5]. In advanced stages, Doxorubicin and Ifosfamide combination has shown a median progression-free survival (PFS) and overall survival (OS) of 6 and 12 months, respectively [6].

MATERIALS AND METHODS

Study Population Retrospective study of patients diagnosed to have Soft tissue sarcoma (STS) between August 2012 and December 2013, treated in the Department of Radiotherapy Unit 1.Data Collection

The data includes details of age, sex, location of the tumour, type of tumour, type of surgery, margin status after surgery, adjuvant radiotherapy or chemotherapy, recurrence if any, treatment at recurrence and patient's condition at last follow up. Analysis The percentage of patients who had limb salvage surgery along with adjuvant radiotherapy and chemotherapy was calculated. Disease status of the patients at last follow up was documented. Locoregional recurrence and metastases at last follow up was compared between the groups which received combined modality and single modality. We analysed 85 patients with STS retrospectively in this current study

RESULTS

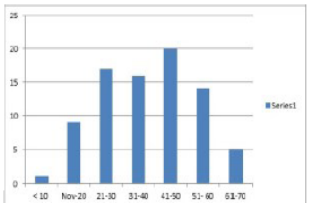
Patient Characteristics

During the study period 85 patients with primary soft tissue sarcoma were seen in Radiotherapy Unit

1.Majority of our patients were above the age of 30 years.

Age Distribution (Table:1)

Age (years)	No	%
< 10	1	1.1%
10- 20	10	11.8%
21-30	18	21.2%
31-40	16	18.8%
41-50	20	23.6%
51- 60	15	17.7%
61-70	5	5.8%
Total	85	100%



(Figure .1)

SEX DISTRIBUTION : (Table: 2)

SEX	No	%
Male	59	69.4
Female	26	30.5

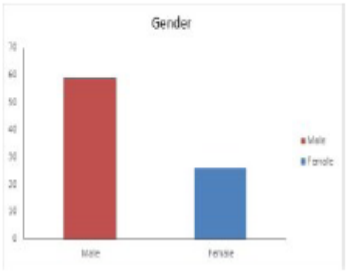


Fig.2 Sex Distribution

Site of Tumor (Table :3)

Site	No	%
Abdomen	6	7.1
Head and Neck	5	5.9
Lower Extremity	43	51.1
Retroperitoneum	4	4.7
Thorax	13	15.4
Upper Extremity	14	16.4

The sites of disease werelower extremity (51.1%), upper extremity (16.4%), thorax (15.4%), head-neck (6.2%), abdomen and pelvis (7.1%) and retroperitoneum (4.7%). STS predominantly was found in extremities (51.1% in lower, 16.4% in upper), maximum occurrence in lower extremities.

Histology of Tumor: (Table:4)

Histology	No	%
Synovial sarcoma	22	25.8
Epitheloid sarcoma	9	10.5
Spindle cell tumour	7	8.2
Liposarcoma	13	15.2
Leiomyosarcoma	4	4.7
High grade sarcoma	3	3.5
Pleomorphic sarcoma	7	8.2
Alveolar soft part sarcoma	2	2.3
Myxofibrosaroma	4	4.7
Malignant fibrous histiocytoma	3	3.5
Chondrosaroma	3	3.5
Haemangiopericytoma	2	2.3
Malignant solitary fibrous tumour	1	1.1
Rhabdomyosarcoma	5	5.8

The most commonly seen adult sarcomas were synovial sarcoma (25.8%) followed by Liposarcoma (15.2%). The incidence of rest of the histologic subtypes were Epitheloid sarcoma (10.5%), Myxofibrosarcoma (4.7%), Leiomyosarcom a (4.7%), Chondrosarcoma (3.5%), Malignant fibrous Histiocytoma (3.5%), Haemangiopericytoma (2.3%), Rhabdomyosarcoma (5.8%) , Alveolar soft part sarcoma (2.3%) and Solitary fibrous tumour (1.1%) .

Treatment Modality: (Table : 5)

Treatment	No. of patients (%)
Surgery with radiotherapy	38 (44%)
Surgery with radiotherapy and chemotherapy	23 (27%)
Surgery alone	3 (3.5%)
Palliative RT	2 (2.3%)
Palliative chemotherapy	5(5.8%)
Didn't receive treatment/supportive care	10(11.7%)
Neoadjuvant chemotherapy followed by surgery and RT	4(4.7%)

Among the patients treated with surgery (75 patients), wide local excision was done in most of the patients 73/75and 2 patients underwent amputation. Adjuvant radiotherapy was received by 61 patients. Radiotherapy dose varied from 60-66Gy in 30-33 fractions for extremities, 45-50.4Gy in 25- 28 fractions for abdominal and retroperitoneal disease. Palliative Radiotherapy was received by 3 patients for brain and vertebral metastasis.

Some patients received only single modality treatment.

Three patients had undergone only surgery and 4 patients received only local palliative radiotherapy. Six patients received palliative chemotherapy upfront due to metastatic disease at presentation. Chemotherapy was either single agent Adriamycin or in combination with Ifosphamide and Mesna. Four patients with Rhabdomyosarcoma had neoadjuvant chemotherapy followed by surgery and radiotherapy.

Disease condition at last follow up (Table : 6)

Condition on follow up	Surgery alone (3)	Surgery and RT (38)	Surgery RT and chemotherapy (23)
No evidence of disease	-	23	11
Local recurrence	1	-	-
Distant metastases	-	6	3
Lost to follow up	2	9	9

The follow up period ranged from 6- 24 months. Out of 64 patients, no evidence of disease was seen in 34 patients, local recurrence in 1 patient who was treated with surgery alone and distant metastases in 9 patients. Twenty patients were lost to follow up.

LITERATURE REVIEW

As classified by the World Health Organization (WHO), the group of soft tissue sarcomas includes more than 50 different histologic subtypes. The most common subtypes that arise in adults are outlined in the Fletcher (2002). The most common STS subtypes and their incidence was

leiomyosarcoma 23%, malignant fibrous histiocytoma 17.1%, liposarcomas 11.5%, dermatofibrosarcomas 10.5% rhabdomyosarcomas 4.6%, angiosarcomas 4.1% in a Surveillance, Epidemiology and End Results program retrospective review of patients diagnosed between 1997 and 2001, using 2002 World Health Organization classification criteria[7]. The most recent analysis from the Sarcoma Meta-Analysis Collaboration (SMAC) suggests 11 percent improvement in survival for Doxorubicin and Ifosfamide based adjuvant chemotherapy compared to resection(8). Neoadjuvant chemotherapy followed by surgery and RT 4(4.7%) Condition on follow up Surgery alone (3) Surgery and RT (38) Surgery RT and chemotherapy (23) No evidence of disease - 23 11 Local recurrence 1 - -
Distant metastases - 6 3 Lost to follow up 2 9 9

CONCLUSION

The proximal lower extremity is the most common site for STS. Multimodality treatment in the form of surgery and radiation is often necessary to local control following limb preservation with good functional outcome in these patients. In select circumstances, adjuvant chemotherapy may augment disease control. Advances in surgery and radiotherapy hold promise both in the primary setting and in managing the difficult scenarios of reirradiation and unresectable tumors.

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