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GFFCC Expanded International Cooperation

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Abstract

This is a retrospective study of 57 patients with extremity soft tissue sarcomas treated at Gujarat Cancer Research Institute, Gujarat, India from January 2005 to December 2007. It aims to review the feasibility of limb sparing surgery for extremity soft tissue sarcoma in Indian population. Twenty-eight percent (28%) of tumors were located in the upper limbs and 72% in the lower extremities. The goal of treatment was limb salvage if feasible. The treatment consisted of amputation in 17 (30%) and local wide excision i.e. limb salvage surgery (LSS) in 40 (70%) patients. The most common histology was pleomorphic sarcoma (21%). Sixty-four percent (64%) of the patients were treated with surgery alone, 32% with surgery plus radiation and 4% with surgery plus systemic chemotherapy. Inadequate margins were present in 12% of the patients. All the patients were followed up for at least 2 years. Recurrence in the form of local and distant occurred in 39% of the patients. Local recurrence occurred in 18% of the patients who underwent LSS and in 35% of those who underwent amputation. Pulmonary metastasis was detected in 16% of patients. The 2 year mortality was 10.5% with the most common etiology being lung metastasis and the most common histology being leiomyosarcoma. We concluded that limb salvage surgery for soft tissue sarcoma is feasible in the Indian population (70%) although the rate is lower than that of world literature at 90%.

Keywords

soft tissue sarcoma, wide excision, amputation, limb salvage surgery, Indian population

Introduction

Sarcoma is a Greek term which means “fish flesh”\(^1\). Soft tissue in this context is defined as nonepithelial extraskeletal tissue, including muscle, fat and fibrous supporting structures, arising mainly from embryonic mesoderm, with some neuroectodermal contribution \(^2\). Collectively sarcomas account for approximately 1% of all adult and 15% of pediatric malignancy \(^3\). The extremities are the most common location for a soft tissue sarcoma (STS), accounting for 59% of cases, the trunk for 19%, the retro-peritoneum 15% and the head and neck 9% \(^4\). Accurate pre-treatment evaluation is critical for treating soft-tissue sarcomas. Surgery for localized disease is often curative, alone or in combination with radiotherapy and chemotherapy in selected patients. Function-preserving limb conservation is the goal of treatment for soft-tissue sarcomas of the limbs\(^5\). Integration of multidisciplinary approach has remarkably changed the management of the extremity soft tissue sarcoma in the last two decades from amputation to limb salvage surgical (LSS) technique that are universally applied and has also provided an enhancement of local and systemic control \(^2\). More recently adjuvant radiation preoperatively and/or postoperatively, has been used consistently in all of the series\(^4\). In some series, neoadjuvant radiation and intraarterial chemotherapy have been employed. The implicit suggestion is that adjuvant therapy is obligatory for at least all high-grade sarcomas, and that this is necessary in order to avoid the high local recurrence rates of the past or the need for frequent amputation.
Materials and Methods

This is a retrospective study of 57 patients with extremity soft tissue sarcomas treated at Gujarat Cancer Research Institute, Ahmedabad, Gujarat, India from January 2005 to December 2007. There were 31 men (54%) and 26 women (46%) with median age of 45 years. All the patients underwent an MRI of the local part to identify the extent of the tumor and for surgery planning purposes. All patients underwent either a core biopsy (56%) or if the biopsy was done outside a pathology review by our pathologists. During the core biopsy, care was taken to ensure that the biopsy site was along the proposed incision for surgery as a poorly planned biopsy site can be disastrous. A CAT Scan of the thorax was done to rule out lung metastasis. After complete haematological and radiological investigations, the patients underwent surgery. No patient received neoadjuvant therapy. The goal of surgery was limb preservation whenever feasible with adequate surgical margins (Figures 1 and 2). Patients presenting with very large tumors with the involvement of the neurovascular bundles underwent amputation (Figure 3 and 4). The surgical treatment consisted of amputation in 17 (30%) patients and 40 (70%) LSS (Table 1). A gross intracompartmental margin of at least 2 cm was considered as adequate. The patients who have on pathologic examination an intracompartmental margin of < 2 cm at some point around the tumor circumference and high grade tumors were advised adjuvant radiation. Patients who developed pulmonary metastasis received adjuvant chemotherapy in a nonrandomized fashion based on patient preference and/or recommendation by the medical oncologist. Thus, 37 (64%) patients were treated with surgery alone, 18 (32%) with surgery plus radiation, 2 (4%) with surgery plus systemic chemotherapy. Radiation treatment, when given, was started about 3 weeks after the operation, except in the presence of local complications (12%) where up to a 5-week delay occurred. Four patients received brachytherapy immediately postoperatively following intraoperative placement of ports. The field covered the whole operative area initially, but after 4,500 cGy, it was restricted to a smaller area corresponding to the site of narrow margin. A total tumor dose of 6,000 cGy over 6 weeks was delivered according to a fractionation schedule of 200 cGy/day, 1,000 cGy/week using 4 or 6-MeV X-rays using anteroposterior and posteroanterior parallel-opposed ports. Systemic chemotherapy consisted of adriamycin (doxorubicin) 6 doses repeated every 3 weeks. Functional assessment was done on subjective basis by assessing the functional...
Figure 3. Locally advanced sarcoma of the thigh

Figure 4. MRI images of the above patient

Table 1: Type of surgery

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Type</th>
<th>Number</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amputation</td>
<td>Above Knee</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Below Knee</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Hindquarter</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Forequarter</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Local Wide Excision</td>
<td>With brachytherapy</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>without brachytherapy</td>
<td>37</td>
<td>40</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>57</td>
<td>57</td>
</tr>
</tbody>
</table>

Table 1: Type of surgery

activity of the preserved limb. Survival time was calculated from the date of resection to the date of last follow-up or death. The median follow-up time was 25 months. Disease-free survival was calculated from the date of resection to the date of first recurrence or death, whichever occurred first.

Results

This is a retrospective analysis of patients with soft tissue sarcoma treated in our institution from January 2005 to December 2007. On presentation, 24 patients had recurrent or residual (inadequate previous surgery) disease while 33 patients presented with a primary disease.
Among those with recurrent or residual disease, the median disease free interval (DFI) was 6 months (m) ranging from 1m to 2 years and 5cm. Forty-one patients (72%) had disease in lower limb while 16 (28%) had upper limb disease (Table 2). The thigh was the most common site. Tumor was superficial in 20 cases (35%) and deep in the rest. The surgery consisted of local wide excision with a minimal 2 cm margin (LSS) in 70% or amputation in 30%. The most common histology was Pleomorphic sarcoma (Malignant Fibrous Histiocytoma) in 21% (Figure 5). The size of tumor ranged from 2.5 to 30 cm. The average margin of resection on final histopathology was 2.4 cm ranging from 0.5 cm to 30 cm. The base of resection was involved in one case and the margins were close (< 2 cm) in 6 cases (10.5%). The final TNM Staging is depicted in Table 3. Post operative wound complications consisting of wound infection, wound gape or skin necrosis occurred in 12 patients (21%). After final staging, post-operative radiotherapy (PORT) was advised on 22 patients (39%) however 4 did not comply. All the 4 patients who did not receive PORT developed local recurrence for which an amputation was done in 3 cases and LSS in one. Of the 18 patients who received radiotherapy, 8 (44%) developed local recurrence. Post operative chemotherapy was given to 2 patients with leiomyosarcoma who developed pulmonary metastasis. All patients who underwent limb salvage retained some function of the limb however complete function was attained in only 28 (70%) patients. All the patients were followed up for at least 2 years with a median of 2y 2 month (range 2y – 3y). Recurrence in the form of local and distant occurred in 22 cases (Table 3). The median DFI was 2y 2 month. The 2 year mortality in our study was 10.5%. The most common cause was pulmonary metastasis and the most common histology was leiomyosarcoma.

<table>
<thead>
<tr>
<th>Location</th>
<th>Site</th>
<th>Number</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Upper extremity</td>
<td>Proximal</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Distal</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>At Shoulder joint</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Lower extremity</td>
<td>Proximal</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Distal</td>
<td>12</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>Popiteal fossa</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>57</td>
<td>57</td>
</tr>
</tbody>
</table>

Table 2: Distribution of extremity sarcoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>16</td>
<td>28%</td>
</tr>
<tr>
<td>II</td>
<td>17</td>
<td>30%</td>
</tr>
<tr>
<td>III</td>
<td>24</td>
<td>42%</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Table 3: TNM Stage Group
### Table 4: Histology and recurrence rates.

<table>
<thead>
<tr>
<th>Histology</th>
<th>Number</th>
<th>Local recurrence</th>
<th>Lung metastasis</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant fibrous histiocytoma (MFH)</td>
<td>21</td>
<td>8(38%)</td>
<td>3(14%)</td>
<td>1(5%)</td>
</tr>
<tr>
<td>Synovial sarcoma</td>
<td>8</td>
<td>2(25%)</td>
<td>1(13%)</td>
<td>1(13%)</td>
</tr>
<tr>
<td>Neurofibroma</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Fibromatosis</td>
<td>5</td>
<td>1(25%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>5</td>
<td>2(40%)</td>
<td>2(40%)</td>
<td>2(40%)</td>
</tr>
<tr>
<td>Malignant peripheral nerve sheath tumor (MPNST)</td>
<td>4</td>
<td>1(25%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Liposarcoma</td>
<td>3</td>
<td>-</td>
<td>1(33.3%)</td>
<td>-</td>
</tr>
<tr>
<td>Mesenchymal chondrosarcoma</td>
<td>2</td>
<td>-</td>
<td>1(50%)</td>
<td>1(50%)</td>
</tr>
<tr>
<td>Malignant Pigmented villonodular synovitis (PVNS)</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>1</td>
<td>-</td>
<td>1(100%)</td>
<td>1(100%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>57</strong></td>
<td><strong>14(25%)</strong></td>
<td><strong>9(18%)</strong></td>
<td><strong>8(10.5%)</strong></td>
</tr>
</tbody>
</table>

Table 4: Histology and recurrence rates.

**Figure 5.** Histology of the tumors.
Discussion

The local treatment of a soft-tissue sarcoma in an extremity has progressed from radical operative intervention, including amputation (5), to the use of multidisciplinary treatment and a less extensive resection that emphasizes the preservation of function of the limb as well as control of the disease. The availability of cross-sectional imaging with computerized tomography and magnetic resonance imaging has contributed to the development of better limb-sparing procedures (6). There has been considerable improvement in the last 20 years in achieving limb preservation with adequate local control in extremity soft tissue sarcomas (7). In the past, at a time when surgical treatment was relied upon exclusively, the rate of amputation in cancer centers ranged from 40% to 48% for these tumors (8, 9). At that time, the rate of local recurrence was considerable i.e. 28% to 36% (65% following LSS and 8% following amputation) (10). In one series, the rate of local recurrence after local excision was 90% (11). In this study we have made an effort to analyze the demography of the patients affected by this tumor and evaluated the management and recurrence rate. In our study the median age of diagnosis was 45 years with a greater incidence in males (54%). In the study by Constantine et al of 194 cases of primary extremity soft tissue sarcoma, the median age of diagnosis was 54 years and 50% of the patients were males (12). In another study by Michael et al, males outnumbered females by 1.32 to 1 (13). The reason for this is unknown but may be due to occupational exposure to carcinogens. The lower limb was the most common site i.e. 72% in our study which was at par with the study by Constantine et al at 73% (12). This probably reflects the greater soft tissue bulk of the lower limb. In our series, limb salvage surgery was done in 70% while it was 89% in the series of Constantine et al. In the study by Michael et al, limb salvage rate was 90% (13). When compared with previous studies, the relative incidence of histological types showed some marked disparities. The most common histology was pleomorphic sarcoma i.e. MFH (37%) followed by synovial sarcoma (14%) in our series. In the series by Constantine et al, 30% of the cases were of liposarcoma followed by pleomorphic sarcoma (21%). In the study by Alkis et al, the most common tumor was also liposarcoma (16%) (14). Wound complications in the form of wound infection, gape or seroma formation occurred in 21% which was similar to other series (12, 13). After final staging PORT was advised to 22 patients (39%) of whom 4 did not comply. The patients who did not receive post operative radiotherapy developed local recurrence for which an amputation in three cases and LSS in one case was done. Of the 18 patients who received radiotherapy 8 developed local recurrence (44%) as compared to 24% in the series by Constantine et al. All the patients with local recurrence in our series underwent surgery and are now on regular follow up. In this series the local recurrence rate following LSS was 22.5% and amputation was 17.6%. The reported local failure rate for patients treated by amputation was 15.8% (14). Patients who develop local recurrence are clearly at increased risk of developing distant metastasis and tumor related mortality. Histological type also appears to influence local recurrence. Pleomorphic sarcoma (38%) and synovial sarcoma (25%) have the maximum local recurrence rate in our series. In earlier series pleomorphic sarcoma, rhabdomyosarcoma and synovial sarcoma have high local recurrence rates of 90, 80 and 69.2%, respectively (14). Several analyses of prognostic factors influencing both local recurrence and overall survival in patients with extremity soft tissue sarcomas show that tumor stage, grade, size, depth, and anatomic site are most important for patient survival (15). Cahlon et al have devised a nomogram for extremity STS that includes age, size, margin status, grade of tumor, and histology which predicts the 3- and 5-year risk of local recurrence after limb-sparing surgery in the absence of adjuvant RT (16). The overall mortality in our study was 10.5% with systemic metastasis being the most common cause and leiomyosarcoma as the most common histology. The highest histology specific mortality was in cases of rhabdomyosarcoma (100%) and mesenchymal chondrosarcoma (50%). All the patients in our series who expired had undergone an amputation as the primary
surgery implying that the tumors were locally advanced at presentation. In one series the 5 year survival was 62% \(^{(12)}\) and 45.1% in another series \(^{(17)}\). The 2 year survival in our patients was 89.5%. The drawback of this study is that the functional assessment of the salvaged limb was done through a subjective assessment by the surgeons and objective criteria like MusculoSkeletal Tumor Scale (Enneking’s scale) were not applied. Also a quality of life (QoL) assessment was not done. A recent study has shown similar QoL in patients treated with amputation and LSS, however in contrast to patients with LSS who described QoL in terms of a high physical performance status with sports and recreational activities, amputees’ QoL was strongly associated with their social acceptability \(^{(18)}\).

**Conclusion**

The presence of soft tissue sarcoma is no longer considered an indication for amputation \(^{(19)}\). Management of patients with STS of extremity requires a multidisciplinary approach in which surgery, radiotherapy and chemotherapy are used in complementary with each other. Local wide excision with adequate margin with post operative RT as indicated provides excellent local control with restoration of satisfactory limb function. We have achieved an acceptable limb salvage rate which is less than that of the earlier studies. Thus we conclude that limb salvage surgery for soft tissue sarcoma is feasible in our population (70%) even though the rate is lower than that of world literature (90%) \(^{(20,21)}\).

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1. Frederick R. Eilber. Soft tissue sarcomas of the extremity, Current Problems in Cancer Volume 8, Issue 9, March 1984, Pages 1–41
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