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The Burden of Unplanned Excision of Soft Tissue Tumours in Developing Countries: A 10-Years' Experience at a Regional Cancer Centre

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Abstract

Background: Local recurrence in soft tissue sarcomas is the major onus of the disease which could result in non-functioning extremities. The local recurrence of soft tissue tumours is the major morbidity and cause for this is the unplanned surgery at inexperienced peripheral centers. We noticed that a major proportion approximate one fourth patient with soft tissue tumours presented in outdoor, were with residual or recurrent lesion.

Aim: The aim was to examine the clinical and pathological profile of soft tissue tumours that had undergone unplanned excision in aspect to the natural event of recurrence in respect to surgery which has been performed.

Materials and methods: In total, 126 patients who had undergone prior surgery of the tumour without oncological planning presented to our institute with residual or recurrent soft tissue tumours between January 2005 to December 2014 were analyzed in a retrospective study.

Results: There were a total of 126 patients analyzed. The mean age was 44.3 ± 16.9 years. Average duration from previous unplanned excision to presentation was 5.3 months (1-57months). 29 patients were presented immediately after the first surgery with clinical residual lesion with a diagnosis of soft tissue sarcoma, while 97 patients presented after apparent local recurrence. Most of the tumours were almost evenly distributed among low and high grade (40.5% vs. 59.5%), superficial and deep seated (48.4% vs. 51.6%), and <5 cm in size (62.9%). 99 (78.6%) patients presented within 24 months after unplanned excision. 22 (17.4%) patients were presented with distant metastasis also with local recurrence.

Conclusion: The appropriate planning regarding as diagnosis as treatment purpose for the soft tissue sarcoma without assuming the soft tissue mass as benign lesion. It helps to reduce the morbidity due to recurrence after inadequate surgical excision.

Keywords: Soft tissue tumours; Unplanned excision; Local recurrence

Introduction

Soft tissue tumours (STTs) are a heterogeneous group of malignant tumour originating from connective tissue, fat, muscle or blood and lymph vessels within virtually any location in the body. They make up close to 1% of all malignancies in adults [1,2]. As per WHO, the incidence rate of STTs worldwide is 1.8 to 5 cases/ 100,000/year [3-8].

The painstaking diagnostic and staging work-up in terms of radiological and histopathological evaluation is vital to the management of a soft tissue tumor. The current standard treatment protocol is a multimodality approach, which comprises wide surgical resection along with neoadjuvant or adjuvant radiotherapy and/or chemotherapy [9]. Patients with soft tissue swellings pursue treatment very late, and often the specialists are their last choice due to the undeveloped health care system in a developing country. Most of these patients land up with general surgeons who may not have expertise about the oncological clearance of malignant STS and excise without adequate margins [10]. Local recurrence in soft tissue sarcomas is the major onus of the disease which could result in non-functioning extremities. Soft tissue tumour has the peculiar feature of having a slow but persistent growth [11].

Local control of the disease in STTs can be improved up to 95% with proper clinical assessment of the extent of the lesion by the physician with the additional help of imaging [12,13]. The most common reason of the high incidence of local recurrence seen in these tumours is, inadequate initial surgical excision [14,15]. Although, the individual specific types of soft tissue tumours have their own different prognostic factors for recurrence, but the adequate surgical treatment remains common to all types [16,17]. The burden of STTs undergoing unplanned treatment is still at a higher level, certainly due to inadvertent and inappropriate excision without proper planning and incorrect preoperative assumption as a benign tumor. We hypothesized that the inadequate excision of soft tissue tumours at the time of first surgery is as significant as other clinical and histological risk factors for local recurrence.

Materials

This is a retrospective preclinical study of patients with STS's limited to the extremities and trunk (chest wall, back and anterior abdominal wall) who presented to the Department of Surgical Oncology over a period of a decade. The demographic data and clinical characteristics of the study population were picked up from the clinical records, physician records, and patient correspondence. Patients with incomplete or missing medical records were excluded. A total of 126 patients were included in the study (**Table 1**). All cases were reviewed by an expert onco-pathologist and appropriate imaging by onco-radiologists at our Institute. Diagnosis was confirmed in every case and graded according to the FNCLCC (French Federation Nationale des Centres de Lutte Contre le Cancer) system [18]. For analyses, FNCLCC grade 2 and 3 tumours were defined as high-grade, and grade 1 as low grade [19]. Tumour size was classified into <5 cm or ≥ 5 cm. Tumours were characterized as superficial or deep according to the involvement of the investing fascia [20]. Margins were evaluated by reviewing the paraffin blocks by a committed pathologist. The margin was microscopically categorized as positive (tumour within 1 mm) or negative (absence of tumour within 10 mm), and tumour identified within 10 mm defined as close margin.

Table 1 Trends of patients with soft tissue tumours after unplanned excision

Year	Total number of patients			Recurrent/Residual disease after unplanned excision
	Male	Female	Total	
2005	10	24	34	10(29.4%)
2006	12	17	29	9(31%)
2007	27	23	50	13(26%)
2008	31	39	70	18(25.7%)
2009	40	25	65	14(21.5%)
2010	30	22	52	9(17.3%)
2011	23	28	51	12(23.5%)
2012	35	25	60	14(23.3%)
2013	36	25	61	12(19.6%)
2014	26	22	48	15(31.25%)
TOTAL	270(51.92%)	250(48.08%)	520(100%)	126(24.23%)

All variables noted as percentages of study patients and single sample student t-test performed with two tailed probability calculated, which was <0.05 was considered as significant.

Results

The total number of patients who presented with soft tissue tumours was 520 during the study period. The mean

proportion of the patients who had undergone unplanned excision and referred to our Institute with residual or recurrent disease was 24%, with the range of 17.30% to 31.25% in each year. Collectively 126 (24.23%) were included in our study, out of all 520 cases of soft tissue tumours (**Table 1**).

The female preponderance in this study was seen, with a ratio of 3: 2 ($p=0.03$). The mean age of the study population was 44.3 ± 16.9 years. Three fourth (76%) of tumours were arising from extremities with a higher proportion in lower extremities ($t=6.906$; $p=0.001$). Fifty-one patients (40.5%) had low-grade lesions. The number of small lesions defined as T1 (size <5 cm in the greatest diameter), was very high in comparison with large T2 lesions, and was 79 (62.7%) and 47 (37.3%) cases, respectively ($t=2.172$; $p=0.031$).

The depth of the lesion was almost equally distributed among the superficial and deep seated lesions, 61 (48.4%) and 65 (51.6%) cases, respectively ($t=0.359$; $p=0.71$). The status of resection margin after index surgery was commented upon by reviewing the paraffin blocks in 90 patients. Forty-nine (54.4%) patients had close margin, and negative margin was reported in 24 cases (26.6%). Twenty-eight patients (22.2%) underwent unplanned excision more than one time. The median interval of the time period between the first excision and recurrence was 5.3 months, with a range of 1 to 57 months. Twenty-one patients (16.7%) presented within 6 months, and 78 patients (61.9%) within 6-24 months of first excision ($t=6.652$; $p=0.001$). Delayed presentation (after 24 months) was seen in 27 patients (21.4%). Out of 126 patients, 22 (17.4%) had evidence of systemic metastasis at presentation, and lung ($n=12$) was the most common site in them, followed by liver (5), bone (3), and brain (2) (**Table 2**).

Table 2 Descriptive statistics

Characteristics		N	%	Statistics
Gender	Male	51	40.5	$t= 2.172$; $p=0.03$
	Female	75	59.5	
Mean Age (Years)		44.3 ± 16.9		
Site	Extremity	96	76.2	$t= 6.906$; $p=0.0001$
	Trunk	30	23.8	
Histological Grade	Low	51	40.5	$t= 2.172$; $p=0.03$
	High	75	59.5	
Size	<5cm	79	62.7	$t= 2.948$; $p=0.003$
	≥ 5 cm	47	37.3	
Depth	Superficial	61	48.4	$t= 0.359$; $p=0.71$
	Deep	65	51.6	
Surgical margins*(N=90)	Negative (≥ 10 mm)	24	26.6	$t=5.367$, $p=.0001$
	Negative (<10mm)	39	43.4	

	Positive (<1mm)	27	30	
Residual disease		29	23	
Local recurrence		97	77	
Recurrence	Single	98	77.8	t=7.509, p=.0001
	>1 recurrence	28	22.2	
Time interval between 1st surgery to recurrence/residual	Mean (in months)	5.3 (1 - 57)		
<6 months		21	16.7	t=6.652, p=.0001
6-24 months		78	61.9	
> 24 months		27	21.4	
Distant metastasis		22	17.4	

Discussion

Soft tissue tumors are rare, predominantly asymptomatic and has, moreover, benign pathology, which results in a significant number of unplanned excisions. It is predictable that some soft-tissue sarcomas are unintentionally and improperly excised, before the correct diagnosis is made histologically in an unorganized health care system, as seen in the developing world [21]. The rates of referral after unplanned excision have been reported between 19% and 53% of the new patients with soft tissue tumours seen in cancer centres [1,5,8,22-27]. In our Institute, which is a Regional Cancer Centre located in South India has a number of patients referred after improper excision with a rate of 24% (range 17.30% to 31.25%). The etiology of STSs is yet to be clearly defined and only various predisposing factors have been identified, such as genetic mutations in pluripotent mesenchymal stem cells, exposure to radiation and certain herbicides, including chlorophenol and phenoxy acids [2,3].

Giuliano and Eilber initially demarcated the term "unplanned total excision" [28]. With respect to STSs, the "unplanned resection", without any assistance of preoperative imaging and diagnostic modalities and without an intention to attain tumour-free margins, was described by Noria et al. [22]

The lack of awareness among general surgeons, working at peripheral centres in developing world, about the forthcoming problems after such an excision of soft tissue tumours results in an increase in the rate of local recurrence also. The initial surgical excision with good wide margins after an appropriate planning in soft tissue tumours has a pivotal role to play in avoiding the future adverse events. Certainly, asymptomatic soft tissue lesions are not considered to have malignant potential, which makes it difficult to achieve the tumour-free margin resection at the time of re-excision, due to violation of the soft tissue planes [9,29].

A first operative procedure by a non-expert surgeon without an adequate planning based on relevant clinical or radiological features, compromises the local control of the disease.

The female preponderance in our study denotes the social discrimination between the two genders, which causes a higher rate of local recurrence and poor outcome in females. Soft tissue sarcoma commonly occurs in young age and not significant for the treatment or outcome in a different group except pediatric sarcomas.

Soft tissue sarcoma can arise in any part of the body, and usually presents with an asymptomatic soft tissue mass. The extremity and trunk sarcoma itself and operative scar usually covered with clothes causes higher chances of ignorance. This may lead inexperienced surgeons to operate with an inappropriate oncological method such as transverse skin incision, inadequate haemostasis, violation of nearby joint, unnecessary placement of drainage tubes, and wider skin sutures [9,29]. Although, a few signs in the literature suggest malignancy includes lesion size >5 cm, rapidly enlarging, deep-seated mass, new onset of pain and recurrent swelling. Still, in a significant number of patients are not approaching to the cancer centres. The size of the lesion at the initial occurrence of the disease was impossible to know in our study. Although, soft tissue sarcoma is a slow-growing tumour, our study showed the mean interval between index surgery to presentation with residual or recurrent lesion at 5.3 months (range of 1 to 57 months), which is much less than reported in literature at 15 months to 24 months [14,15,30]. The margin of resection has great significance regarding local control of disease, and affects the further treatment plan and prognosis also. The higher rates of positive and close margin after unplanned excision increases the risk of local recurrence as well as residual disease. Our study showed that only 24% cases had undergone prior unplanned excision with a negative margin. Re-excision after an unintentional violation of the tissue becomes very difficult because of poor surgical differentiation of the residual or recurrent disease from scar tissue. Altered anatomical location of neurovascular bundles in relation to the residual or recurrent lesion hinders a tumour-free margin resection at the time of re-excision [24]. The rate of local recurrence in patients who undergo unintentional excision of STSs is reported at 5% to 34%, in comparison to those with planned excision, at 3% to 16% [1,8,23]. In contrast to most of the reported studies, Lewis et al. showed a poorer 5-year survival in patients undergoing planned excision than that in those with re-excision after unplanned excision. This suggested that re-excision and margin augmentation, is a predictor of better survival and lower distant metastasis [22]. He explained this with a few hypotheses. First, re-excision removes residual margins outside the primary tumour and pseudo-capsule. Second, complete excision of a tumour site during index surgery removes the inhibition of satellite lesions, which subsequently appear as distant metastasis. Third, an unplanned excision switches on the immunity by activation of dendritic cells, which identify antigens in the residual tumour and promote an immune response with memory cells and prevent future local recurrence and distant metastasis [23].

Venkatesan et al. concluded that the presence of pathological residual tumour in re-excised tissue after an unplanned excision has a higher risk of local recurrence and distant metastasis [9]. The imaging including CT/MRI usually

shows a wider lesion after first surgery due to post-operative inflammation and fibrosis. Furthermore, the second surgery of the contaminated tissue needs a larger excision to improve the local control which leads to more compromised limb function as compared to a first planned surgery [9,31]. Almanda et al. suggested that the tumour cells get deposited locally after an unintentional surgery, which makes it very challenging to remove completely at the time of re-excision. The delaying of re-excision, either due to delayed presentation or neo-adjuvant treatment also plays an important role in local control of disease. However, the re-resection of the residual or recurrent disease after prior surgery should be contemplated as early as possible in every case [32].

Moreover, all soft tissue tumours should be undergone a thorough clinical examination, suitable imaging and percutaneous core biopsy, to distinguish potential soft-tissue sarcomas from non-malignant soft tissue masses. The histological subtype and grade of differentiation are also important to decide the required treatment modality [33,34]. This will reduce the number of unplanned excisions for extremity sarcomas and hence improve local control.

Our aim of this report is to provide robust evidence, that the local recurrence of soft tissue tumours is the major morbidity in this disease, and a very common reason for this is an inadequate surgery done at inexperienced peripheral centres. This data is borne witness by the cancer registries mandating the reports. The prevalence of these soft tissue tumours, either benign or malignant, is increasing over the last few decades, which represent a substantial burden in hospitals.

Now-a-days, the current concept of multimodality approach for soft tissue tumours yields the lowest local failure rate of up to 10% at experienced cancer centers [35]. The limb function preservation is very much possible at the time of first planned surgery, but becomes a difficult task at re-excisions.

As anticipated, size, depth, histological grade, and histological type are associated with risk of tumour recurrence, and thus, with disease-specific mortality. Local recurrence is also a poor prognostic indicator for the metastasis-free survival and disease specific mortality. The risk of local recurrence is higher with the re-excision after unplanned excision of soft tissue tumours [15,36].

In the lancet oncology, Thomas DM commented on the growing problem of the benign connective tissue tumours earlier [37]. MSKCC reported that local recurrence in soft tissue tumors would appear prudent to count being at high risk for systemic disease and thus eligible for the multimodality treatment approach at specialized centres [38].

Conclusion

However, this report is essentially annoying to put attention towards the stubborn problem of the local recurrent lesion in soft-tissue tumours, who took treatment at the peripheral centers with unplanned excision, either diagnostic or therapeutic. The unplanned excision is more likely to be performed in small size, superficial, lower grade soft tissue

tumours with inadequate margin, and hence it is a major prognostic factor of local and systemic recurrence free survival. The issue of an appropriate planning regarding as diagnosis as treatment purpose for the soft tissue sarcoma without assuming the soft-tissue mass as a benign lesion. It helps to reduce the morbidity due to recurrence after inadequate surgical excision.

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