The Problem of Local Recurrence after Treatment of Soft Tissue Sarcoma

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THE HIGH RATE of recurrence of sarcomas of the soft somatic tissues long ago convinced us that no neoplasms are more indifferently treated in contemporary surgical practice.[1] Our experience is similar to that of Clark, Martin, White and Old[5] who reported that inadequate initial operation is the principal reason for failure of cure, and is the usual history of a patient with sarcoma. Stout[24] in 1947 in a review of 432 primary sarcomas of soft parts occurring between 1906 and 1946, reported local recurrence in 158 (61%) of 259 followed cases. Pack and Ariel[16] in 1958 indicated the magnitude of this problem in their analysis of 717 cases of soft part sarcomas. They reported that 282 patients, or 39.3%, in a series of 528 receiving definitive therapy had recurrent tumors which were operable, and that 91, or 12.7% of 189 patients with inoperable tumors also had local recurrences. Clark *et al.*[5] in 122 patients reported that 55 out of 88 (63.6%), with locally excised sarcomas developed recurrences, as opposed to 7 out of 71 more adequately treated, or an overall recurrence rate of fifty per cent. Later Martin, Butler and Albores-Saavedra[15] reported from the same source 168 patients, or 77.1%, with local recurrences in 218 who had radical surgical excisions out of a total of 449 patients. Krementz and Shaver[13] found approximately 50% recurrences in 41 patients who had restricted excisions and 46 patients who had radical excisions, out of a total of 203. But Shieber and Graham[23] in contrast in an analysis of 103 cases reported that 46 local excisions were followed by 40 recurrences, while only 9 of 23 persisted or recurred after wide local removal.

In detailed reports of histogenetic types of soft part sarcomas, the incidence of local recurrence varies. In fibrosarcoma, Taylor and Nathenson[27] reported a recurrence rate of 56.8%, Stout[25] 60%, Heller and Sieber[10] 52.5%, Phelan and Nigogosyan[21] 56.6%, Seel, Booher and Joel[22] 50.6%, and VanDerWerf-Messing and Unnick[28] 56%.

For liposarcoma local recurrence rates have been reported by Pack and Pierson[18] as 33.3%, 48% by Enterline, Culbertson, Rochlin and Brady,[8] 61% by Kimbrough and Soule,[12] and between 53 and 85% depending on histological types in the series of Enzinger and Winslow.[9]

Rhabdomyosarcomas are also prone to recurrence. Stout[26] reported 61%, Pack and Eberhart[19] about 50%, and Horn and Enterline[11] 51%. Martin *et al.*[15] found persistence of tumor varying from 47.9% to 79.5%, depending on the operative procedure. In large groups of tumors in which specific histogenetic origin cannot be de-

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TABLE 1. *Sarcomas of the Soft Somatic Tissues of the Trunk and Extremities (1935–1959)*

	Patients
Unclassified sarcoma	200
Liposarcoma	135
Rhabdomyosarcoma	133
Fibrosarcoma	110
Synovioma	104
Neurosarcoma	47
Embryonal rhabdomyosarcoma	28
Hemangiopericytoma	11
Angiosarcoma	7
Extra osseous osteogenic sarcoma	5
Leiomyosarcoma	2
Alveolar soft parts sarcoma	2
Total	784

TABLE 2. *Local Recurrence Rate of All Patients with Sarcomas of the Soft Somatic Tissues*

	Patients	Recurrences
Unclassified sarcoma	200	120 (60%)
Liposarcoma	135	85 (63%)
Rhabdomyosarcoma	133	77 (58%)
Fibrosarcoma	110	75 (68%)
Synovioma	104	61 (59%)
Neurosarcoma	47	19 (40%)
Embryonal rhabdomyosarcoma	28	15 (54%)
Others	27	13 (48%)
Total	784	465 (59%)

fined, that is, sarcoma of undetermined histogenesis, Pack and Ariel[20] found 62 out of 147 patients with recurrent operable tumors, 42%.

Synovioma has one of the highest rates of recurrence. Cadmen, Soule and Kelly[3] reported that of 59 synoviomas originally treated by local excision, 54 or 91.5% recurred. MacKenzie[14] recorded recurrences in 28% of patients, Vieta and Pack[29] recurrences in 13 of 28 patients or 46.4%. D'Agostino, Soule, and Miller[6] reported 13 recurrences in 24 patients with primary malignant tumors of nerves and in 7 of 9 patients operated upon from amongst 21 patients with malignant lesions associated with multiple neurofibromatosis.[7]

The effect of local recurrence on prognosis has not been fully investigated. Experience with these lesions at Memorial Cancer Center is reviewed.

TABLE 3. *Local Recurrence Rate after Primary Treatment at Memorial Cancer Center*

	Patients	Recurrences
Unclassified sarcoma	163	42 (26%)
Liposarcoma	116	30 (26%)
Rhabdomyosarcoma	109	29 (27%)
Fibrosarcoma	97	35 (36%)
Synovioma	81	24 (30%)
Neurosarcoma	43	15 (35%)
Embryonal rhabdomyosarcoma	23	6 (26%)
Others	21	6 (29%)
Total	653	187 (29%)

Material and Methods

The study comprises records of 784 patients with malignant tumors of the soft somatic parts of the trunk and extremities observed in the Memorial Cancer Center from 1935 to 1959. A 5-year followup is available on all patients. Not included were tumors primary in the retroperitoneal region or the head and neck areas; the nature and surgical problems of these tumors are different.

The incidence of local recurrence in all 784 patients and in 653 to whom curative treatment could be offered was determined.

The term "local recurrence" refers to recurrence within the confines of the previous surgical dissection or in tissue immediately adjacent to it. Histological confirmation is not available in every instance of imputed recurrence: however, in cases not verified by biopsy or excision it was evident from clinical context. Table 1 presents the distribution of the cases amongst histological varieties of sarcoma. As in previous publications from this hospital, sarcoma of undetermined histogenesis was the most frequently made diagnosis.

Local Recurrence Rate. In the entire group of 784 patients, local recurrence occurred in 465 (59%) (Table 2). The magnitude of the problem is best illustrated by the fact that these patients had a total of 916 recurrences, an average of nearly 2 per

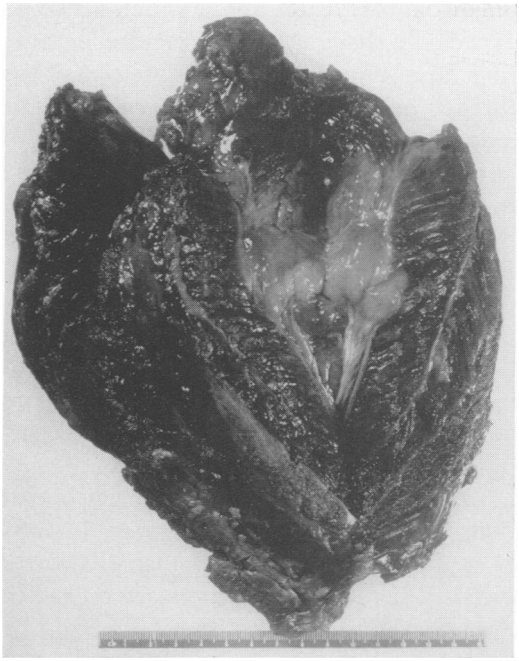


FIG. 1A. Photograph of a failure of wide excision. The specimen an extensive soft tissue resection for fibrosarcoma arising in muscles of the posterior calf. Six months previously a multilobulated tumor of the leg was locally excised, at which time the patient refused a secondary operation.

patient and there were as many as 7 recurrences in some patients. Fibrosarcomas had the highest rate of persistence of tumor (68%) although this rate was only slightly higher than in other major groups, amongst which there is little variation.

Because it is a cancer center, it is probable that Memorial Hospital's patient population is, at least in part, selected. Recurrence rates following treatment at Memorial is probably a more valid estimation of the "recurrence" potential of soft tissue sarcomas. As shown in Table 3 recurrence followed in 187 or 29% of 653 patients treated. Such a high rate after treatment by surgeons experienced in the management of soft tissue sarcomas, is evidence of the difficulty of controlling these tumors.

Influence of Local Recurrence on Clinical Course. Does recurrence modify the eventual prognosis of soft tissue sarcomas? Three facts demonstrate a deleterious effect.

1. As shown in Table 4, distant metastases were present on admission in 11% of previously untreated patients, and in 22% of patients who had recurrent tumors.

2. As stated, there were recurrences in 187 of the 653 patients treated with the objective of cure at Memorial Hospital. 115 or 61%, of the 187 patients died of sarcoma. Of 466 patients without local recurrence, 138, or 30%, died of sarcoma (Table 5).

3. Finally, the pattern of distant metastases was analyzed. At the time of the study 382 had died of sarcoma. Forty-one (11%) already had distant metastases on first consultation; 91 (24%) developed metastases

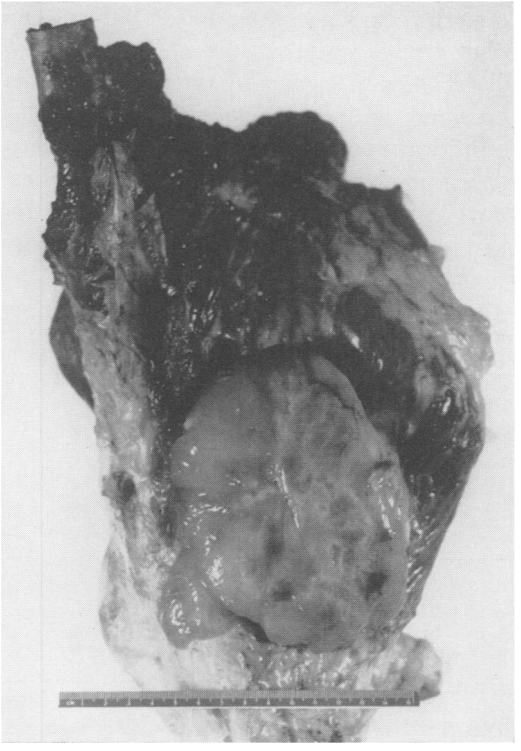


FIG. 1B. Photograph of a high thigh palliative amputation 1 year later. This was done for recurrent fibrosarcoma two months after a left upper lobectomy had been performed for an apparently solitary metastases. The recurrence is at the upper margin of the previous dissection of the posterior muscular compartment of the calf.

directly without local recurrence, but 249 (65%) had distant dissemination only after one or more local recurrences (Table 6).

While sarcomas are described as possessing marked angioinvasive potential, it appears that this event follows inadequate control of the primary sarcoma and a reduction in the incidence of local recurrences would increase the cure rate of soft tissue sarcoma.

A more detailed study of the clinicopathologic factors influencing local recurrence was made in patients treated with the objective of cure. Except for histologic varieties, all cases have been grouped together. The trends in the whole series were similar to those in each histological category.

Influence of Histologic Features. As shown on Table 3, fibrosarcomas had the highest recurrence rate, but differences in other groups is not significant. It seems that all varieties of sarcoma have approximately the same tendency to recur locally.

Influence of Prior Recurrence. Recurrence predisposes to further recurrence. Previously untreated cases had a local recurrence rate of 23%, while cases already recurrent had a recurrence rate of 34%.

Influence of the Size of the Tumor. The influence of size is related to the extent of the surgical excision performed. Small tumors treated by amputation would expectedly have a lower recurrence rate than large tumors treated by excision. Thus three types of operation are categorized: amputation, wide excision with a margin of normal tissue around the periphery of the tumor; and excision without such a margin.

While probably smaller than the actual size, the size is as measured by the pathology department. Table 8 shows the expected: within each type of operation there is an increase in recurrence rate with increasing size of the tumor, and the more radical the operation, the lower the recurrence rate. Some facts emerge:

1. Amputation is the most efficient operation. The overall recurrence rate is 18% after these procedures, less than that after excision. If the largest tumors are excluded, the recurrence rate is 13%.

2. A recurrence rate of 30% following wide excision is indication that excision was not wide enough. Bowden and Booher [1] demonstrated that for selected cases wide excision adequately controls the tumors and there were only 6 recurrences (16%) in the 37 patients operated upon (Fig. 1).

The recurrence rate of 42% after excision only is a clinical confirmation of well-

TABLE 4. *Frequency of Metastases of Sarcomas of the Soft Somatic Tissues at Time of Hospital Admission*

	Patients	Metastases
Primary cases	364	40 (11%)
Recurrent cases	420	91 (22%)
Total	784	131 (17%)

TABLE 5. *The Influence of Local Recurrence of Sarcomas of Soft Somatic Tissues on Prognosis*

	Patients	Deaths
No local recurrence	466	138 (30%)
Local recurrence	187	115 (61%)

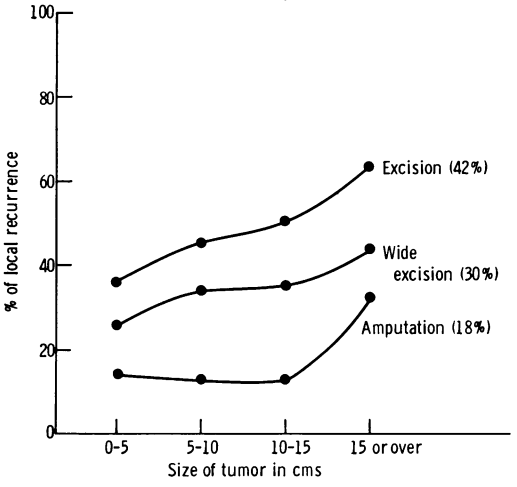
TABLE 6. *Pattern of Distant Metastases of Sarcomas of the Soft Somatic Parts*

	Patients
Present on 1st consultation	41 (11%)
Without local recurrence	91 (24%)
Following local recurrence	249 (65%)
Total	382 (100%)

TABLE 7. *Local Recurrence Rate of Sarcomas of Soft Somatic Tissues According to Status on Admission*

	Patients	Recurrences
Primary cases	324	74 (23%)
Recurrent cases	329	113 (34%)
Total	653	187 (29%)

TABLE. 8. *Local Recurrence of Sarcomas of Soft Somatic Tissues According to Size of Tumor and Operation*



known pathologic features of soft tissue sarcomas: No encapsulation, spread is along fascial planes and nerve trunks, occasional multifocal origin. "Pseudoencapsulation" observed during operation is an indication that the dissection is too close to the tumor for a successful operation.

Influence of the Site of the Tumor. Local recurrence rates for tumors of each extremity and tumors of the trunk are remarkably similar (Table 9). In each extremity, lesions situated distal to each major joint (elbow and knee) recurred slightly more frequently than lesions situated proximal to these joints. On the trunk, abdominal wall tumors were controlled less frequently than those of the thoracic wall, although the reverse might be expected. The highest recurrence rates were in tumors located near joints (knee—33%, elbow—40%, groin—36%).

Gross Pathology. As expected infiltrating tumors recurred more frequently than localized tumors. There is a high rate of recurrence in multinodular lesions, of plurifocal origin (Table 10).

Adjunctive Radiation Therapy. Experience at the Memorial Center with pre and postoperative radiation therapy in the management of soft tissue sarcomas [4] is being

TABLE 9. *Local Recurrence Rate of Sarcomas of the Soft Somatic Tissues According to Site*

Lower extremity	Below knee	31%	29%
	Above knee	27%	
Upper extremity	Below elbow	31%	28%
	Above elbow	27%	
Trunk	Abdominal wall	35%	30%
	Thoracic wall	29%	

reported elsewhere. Results are difficult to interpret with respect to local recurrences: patients receiving adjunctive radiation had higher local recurrence rates than patients treated exclusively by operation. However, patients receiving adjunctive radiation usually had a less favorable prognosis. Yet, in spite of higher recurrence rates, survival rates were good.

Fate of Patients with Recurrences. In Table 5, the deleterious effect on prognosis that recurrence entails is shown. This is particularly evident for two histological categories: embryonal rhabdomyosarcomas and synoviomas. There were six recurrences of embryonal rhabdomyosarcomas and 5 patients died, and 25 of 26 patients with recurrent synoviomas have died.

Timing of Recurrences. Most recurrences occur early. More than half (56%) within one year and 85% within 2 years of treatment. As in other forms of cancer, however, prolonged follow-up study is important, since recurrences have been observed as late as 12 years following treatment (Table 11).

There seems to be a relationship between timing of the recurrence and prognosis. Sixty-nine per cent of patients having recurrences within the first 2 years have died, while 31% of patients with later recurrences have died.

Treatment of Recurrences. Forty-eight (26%) of 187 patients with recurrences

TABLE 10. *Local Recurrence Rate According to Gross Pathology of Soft Tissue Sarcoma*

	Patients	Recurrences
Circumscribed	230	56 (24%)
Infiltrating	218	81 (37%)
Unknown	140	20 (14%)
Multinodular	65	30 (46%)
Total	653	187 (29%)

could not be treated because of distant metastases. Amputation was followed by a higher survival rate than was excision, although the difference is not significant (Table 12).

Discussion

Soft tissue sarcomas are among the most difficult tumors to control at their primary sites. The recurrence rate of 29%, while improved over that of 39% reported by Pack and Ariel [20] some years ago, is evidence of this fact. Of more importance, the prognosis for the majority of patients is conditioned on whether or not there is local recurrence. Two-thirds of patients who developed distant metastases did so only concommitantly with or following local recurrences. In patients treated at Memorial Hospital the presence of local recurrences more than doubled the probability that the patient would die of sarcoma. An attitude for conservative operation based on the premise that prognosis depends on whether or not venous dissemination has occurred seems to be unjustified. Performance of less than a radical operation in the hope of avoiding mutilation or loss of limb, accepts a high local recurrence rate and great risk that distant metastases will follow.

The problem in the treatment of soft tissue sarcomas arising on the extremities is when to amputate. The need for adequate resection is balanced against unnecessary sacrifice of limbs. In this retrospective study in which the histological degree of malignancy has not been evaluated, strict criteria for amputation cannot be derived.

An important factor which was not analyzed, is reported by Shieber and Graham [23]: that the location of the primary sarcoma and not its histologic type is more important prognostically during the first postoperative year. Only after one year did histologic pattern become important in prognosis.

Circumstances where local recurrence is either more apt to occur, or is of particularly grave prognosis have been identified. Under these circumstances amputation should be more seriously considered as the best method of treatment. No single factor is an indication to amputate: however, several factors in the same patient indicates that any operation less than an amputation is likely to result in local recurrence.

Conclusion

Amputation is indicated for a soft tissue sarcoma for which wide excision is not possible: the prohibitive recurrence rate following excision indicates that this procedure is acceptable in only the rarest of circumstances. Size *per se* is not the major factor. As Bowden and Booher [1] commented, the most important factor in choice of therapy is the anatomical setting of the tumor. A 5-cm. tumor in the popliteal fossa obviously is not the same problem as a 5-cm. tumor in the muscles of the thigh.

TABLE 11. *The Time of Local Recurrence of Sarcoma of the Soft Somatic Tissues*

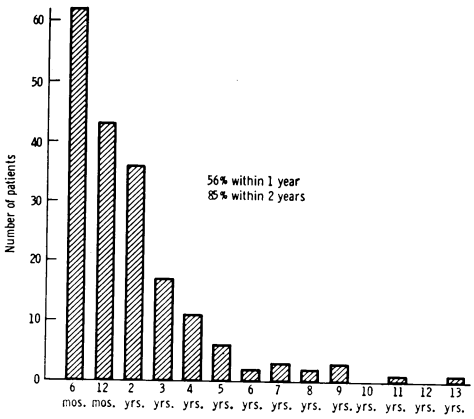


TABLE 12. *Treatment of Local Recurrence of Sarcomas of the Soft Tissues*

	Patients	Died
Untreated	48 (26%)	47
Excision	81	43 (53%)
Amputation	57	25 (44%)
Radiation therapy	1	0
Total	187	115 (61%)

Amputation is probably indicated for recurrent tumors, particularly those which are multinodular. Early recurrences, especially after what was considered adequate operation, probably should be strongly considered for amputation.

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