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Management of extremity soft tissue sarcoma after unplanned incomplete resection: experience of a regional musculoskeletal tumour centre

未經計劃的非完整切除肢體軟組織肉瘤後的處理：一所肌肉骨骼地區腫瘤中心的經驗

This study reviews the presentation and management of extremity soft tissue sarcoma after unplanned incomplete resection in a musculoskeletal tumour centre in Hong Kong. Medical records of 18 patients who were referred to our centre for further management from January 1995 to May 2001 after inadequate tumour excision were reviewed. Fourteen patients had been referred from private clinics and four from public hospitals. At initial presentation, 10 patients had lesions exceeding 5 cm, nine had a tumour deep in the subfascial plane, and eight had tumours that had recently increased in size. Sixteen had no preoperative radiological assessment or biopsy performed before excision. All except two patients needed additional skin and muscle reconstruction in a subsequent re-resection, and 12 required postoperative radiotherapy. Two patients subsequently developed distant metastases, and one patient died of an unrelated cause. No amputations were required, and no major complications arose from second surgery. Physicians' alertness towards the possible malignancy of soft tissue masses in extremities is important to avoid a potentially mutilating second resection. Well-planned re-resection in a specialised tumour centre can achieve satisfactory local control of disease.

本研究回顧香港一所地區腫瘤中心處理的肢體軟組織腫瘤病人，在未經計劃的非完整切除後的表徵，以及腫瘤中心的處理方法。我們回顧了18名病人的病歷，他們都是在1995年1月至2001年5月期間，在不完整地切除腫瘤後，被轉介到本中心進一步處理。其中14名病人由私家診所轉介，其餘4人由公立醫院轉介。初步徵狀顯示，10名病人的腫瘤超過5厘米，9人筋膜下平深處有腫瘤，8人有近期變大的腫瘤。16人在進行手術前，並未接受放射檢查或活組織檢查。除了其中兩人，所有病人均在其後接受再切除手術，及進行額外皮膚及肌肉重組；另12人在手術後需接受放射性治療。兩名病人其後出現遠處轉移，1名病人死於不相關的原因。並無需要截肢的個案，第二次手術後亦沒有出現嚴重的併發症。醫生如對可能出現的肢體軟組織惡化保持警覺，可避免可能導致傷殘的第二次切除手術。於專科腫瘤中心妥善安排再切除手術，原發地疾病控制亦可達至令人滿意的效果。

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Introduction

Soft tissue sarcomas of the extremity are mesenchymal tumours arising from connective tissue elements; such tumours feature local invasiveness, as well as a high propensity to local recurrence and distant metastasis. Fifty percent of patients with sarcoma eventually die of the disease.[1] However, these tumours are rare and have an average annual incidence of 169 cases, according to the figures reported to the Hong Kong Cancer Registry from 1993 to 2000, with a slight male preponderance.[2] The rarity of such tumours could, in turn, lead to an inadequate awareness of diagnosis and thus improper excision. This 'unplanned incomplete resection', defined as excisional biopsy only or unplanned resection of the lesion without prior information from preoperative imaging and without regard for the

necessity to resect the lesion with a margin of normal tissue,[3] will lead to higher local recurrence[4-6] and may jeopardise overall survival.[7,8] Subsequent 'well-planned resection' with adjuvant radiotherapy is indicated to improve overall local control.[9-11] However, a second operation frequently leads to further extensive and potentially mutilating surgery.[12] This study aims at analysing the initial features of presentation of soft tissue sarcomas and the possible harm incurred by primary unplanned surgery in terms of skin and muscle reconstruction, and the need for additional adjuvant therapy (ie brachytherapy, external beam radiotherapy, or chemotherapy) after surgery.

Methods

From January 1995 to May 2001, 76 patients with soft tissue sarcoma were operated on in the Department of Orthopaedics and Traumatology, Queen Elizabeth Hospital—a designated musculoskeletal tumour centre of the Hospital Authority. Of the patients, 18 had had prior operations and had been referred to our centre for further management because of incomplete primary excision. Case records of these patients, who were followed up for an average of 42 months (range, 23-100 months), were reviewed retrospectively.

All patients had been jointly assessed in a multi-disciplinary sarcoma clinic by dedicated tumour surgeons, clinical oncologists, radiologists, and pathologists to delineate the plan of further management. Our protocol was to perform complete wide resection of the previously operated site if technically feasible, and to add adjuvant radiotherapy in the form of external beam radiotherapy with or without perioperative brachytherapy.[13,14] Before the second operation, all patients underwent chest radiography, computed tomography (CT) of the thorax, and isotope bone scanning to exclude distant metastasis, as well as magnetic resonance imaging (MRI) of the previous primary tumour site for surgical planning. When possible, pathologists specialising in musculoskeletal tumours reviewed slides of the initial specimen. The demographic data, initial presenting features, nature of primary operation, and subsequent treatment were recorded.

Results

Demographic data
Table 1 shows the details of all 18 patients included in this study, of whom 10 were male and eight were female. The mean age was 55 years (range, 17-80 years).

Initial presentation
Tumours were located in an upper limb in nine cases, a lower limb in five, and the trunk in the remaining four. For 17 patients, a mass had been present for more than 4 weeks (mean, 6.6 months). In eight cases, the leading symptom was an enlarging soft tissue mass. Pain was not a significant symptom in any patient. The mass was larger than 5 cm in 10 patients, and nine tumours were located deep in the fascia.

Overall, seven patients had a subfascial mass of larger than 5 cm at presentation, which was commonly regarded as a feature to suggest malignancy. Only one patient underwent preoperative MRI, which revealed a subfascial mass, but not a subsequent biopsy. Sixteen patients had no biopsy before excision; the remaining two patients underwent fine-needle aspiration biopsy, yielding mesenchymal tumour of uncertain nature in one and inadequate tissue for diagnosis in the other.

Primary operation and histology
Two patients underwent marginal excision, whereas 15 had intralesional excision performed and one underwent only piecemeal removal. The surgery in 14 patients was performed in private clinics and that in four were done in public hospitals. Histological studies revealed a diversity of tumours, including dermatofibrosarcoma protuberans (n=5), malignant fibrous histiocytoma (4), undifferentiated sarcoma (2), leiomyosarcoma (1), high-grade myxoid liposarcoma (2), well-differentiated liposarcoma (1), de-differentiated liposarcoma (2), and high-grade myxofibrosarcoma (1).

Deleterious effects of inadequate primary operation
All but two patients required additional skin and muscle reconstruction during a subsequent operation. Reconstruction was necessary because of the deleterious effects caused by primary surgery in 10 patients: three cases for oversized scarring, three for the presence of a distant drain site (Fig 1a), one for broad mattress-stitch scarring (Fig 1b), one for extensive postoperative haematoma (Fig 1c), and two for repeated inadequate excision. In addition, adjuvant radiotherapy was indicated in five patients because of incomplete excision during primary surgery.

As a case example, patient No. 7 presented with a 1-year history of a 3-cm subcutaneous mass over the right upper arm. Initial marginal excision was performed under local anaesthesia, and histological examination revealed myxofibrosarcoma. The second excision, with a 1-cm margin, was performed 4 weeks later by the same surgeon, but remained inadequate because the resection margin was still involved. The patient was then referred to our centre for further management. After discussion in the combined sarcoma clinic, wide excision was performed and a trans-positional parascapular flap was created to cover the large cutaneous defect (Fig 2a, 2b). Brachytherapy catheters were also inserted during the operation (Fig 2c). Perioperative brachytherapy and external beam irradiation were delivered subsequently. The donor wound was closed primarily. All wound healed uneventfully but left prominent scars in the shoulder and back regions (Fig 2d). There was no local recurrence or distant metastasis detected for this patient after 32 months of follow-up.

Subsequent management
The main curative therapy for soft tissue sarcoma is wide excision with 2- to 3-cm margin of grossly normal tissue. In

Table 1. Patients with sarcoma who were referred to the Queen Elizabeth Hospital from January 1995 to May 2001

Patient No.	Sex/age (years)	Initial size (maximum length) [cm]	Site/plan of tumour	Histology	Primary wound closure possible?	Reconstruction done in re-resection	Presence of residual tumour	Adjuvant therapy
1	M/49	4	Buttock/subcutaneous	Undifferentiated sarcoma	No	Myocutaneous TFL* flap	Yes	None
2	M/38	2	Arm/subcutaneous	Dermatofibrosarcoma protuberans	No	Full-thickness skin graft	Yes	EBRT [†]
3	M/80	8	Arm/subfascia	Malignant fibrous histiocytoma	No	Functional muscle transfer + partial-thickness skin graft	Yes	BT [‡] + EBRT
4	M/77	7	Thigh/intramuscular	Malignant fibrous histiocytoma	No	Partial-thickness skin graft	No	None
5	M/70	9	Shoulder/subcutaneous	Dermatofibrosarcoma protuberans	No	L-dorsi flap + partial-thickness skin graft	Yes	None
6	F/72	4.5	Back/intramuscular	Malignant fibrous histiocytoma	No	Reverse flow L-dorsi myocutaneous flap	Yes	EBRT
7	M/74	3	Arm/subcutaneous	High-grade myxofibrosarcoma	No	Transpositional parascapular flap + partial-thickness skin graft	No	BT + EBRT
8	M/76	12	Thigh/intramuscular	Well-differentiated liposarcoma	Yes	Direct wound closure	Yes	EBRT
9	M/56	6	Shoulder/subcutaneous	Dermatofibrosarcoma protuberans	No	L-dorsi myocutaneous flap	No	None
10	F/39	5	Groin/subcutaneous	Dermatofibrosarcoma protuberans	No surgery done	(Surgery not advised)	N/A [§]	EBRT
11	M/61	1.5	Arm/subcutaneous	De-differentiated liposarcoma	Yes	Marginal excision	Yes	BT + EBRT
12	F/21	3	Arm/subcutaneous	Poorly differentiated sarcoma	No	Z-plasty + radial forearm flap + partial-thickness skin graft	No	BT + EBRT
13	F/47	5	Thigh/subfascia	De-differentiated liposarcoma	No	Biceps femoris and sartorius tendon transfer + free microvascular L-dorsi myocutaenous flap	No	BT + EBRT
14	M/46	3	Shoulder/subcutaneous	Dermatofibrosarcoma protuberans	No surgery done	No surgery done	N/A	EBRT only
15	F/68	2	Forearm/subfascia	High-grade myxoid malignant fibrous histiocytoma	No	Radial forearm flap + partial-thickness skin graft	Yes	BT + EBRT
16	F/59	9	Groin/intramuscular	High-grade liposarcoma	No	Pedicled rectus abdominis myocutaneous flap	No	BT + EBRT
17	F/17	10	Groin/intramuscular	Moderate differentiated leiomyosarcoma	No	Recutus abdominis myocutaneous flap	No	BT + EBRT
18	F/37	7.5	Thigh/subfascia	High-grade myxoid liposarcoma	Yes	Wide excision + direct wound closure	Yes	BT + EBRT

* TFL   tensor fascia lata
[†] EBRT   external beam radiotherapy
[‡] BT   brachytherapy
[§] N/A   not applicable

all 18 patients, adequate margins were not achieved. Hence, subsequent well-planned resection with adjuvant radiotherapy was indicated to improve overall local control.

Accordingly, all patients underwent MRI of the previous surgical site to delineate the extent of residual disease. In addition, CT of the thorax and isotope bone scanning were

Table 2. Magnetic resonance imaging (MRI) and histological results after re-resection

MRI	n*	Histological evidence of residual tumour	n
Positive	2	Yes	2
		No	0
Uncertain	4	Yes	1
		No	3
Negative	10	Yes	6
		No	4

* MRI was not done in two cases because surgery was not performed
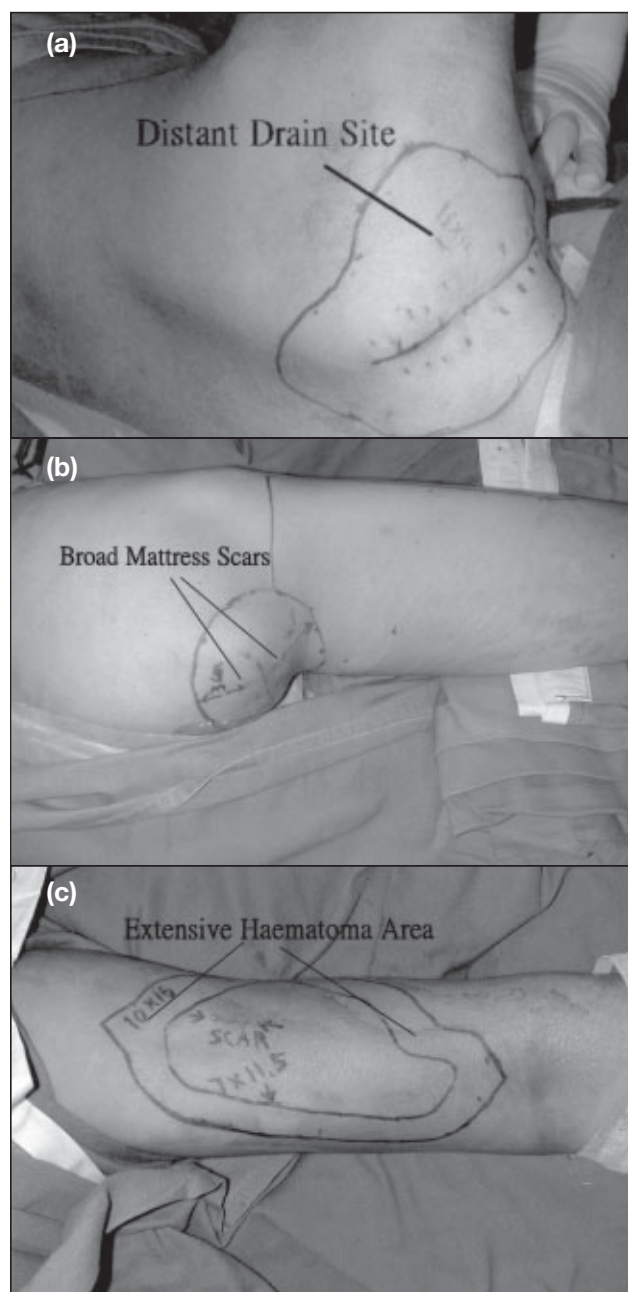
Fig 1. Patient No. 7: (a) distant drain site, (b) broad mattress scars, and (c) extensive haematoma

also performed for tumour staging. Table 2 shows the correlation of the radiological findings of MRI with the final

pathology after repeated resection. Overall, MRI was neither sensitive nor specific enough to accurately detect residual tumour. However, the MRI scan was still necessary in the planning of surgery, because subsequent wide excision needed to include tissue with abnormal signal changes to facilitate complete tumour removal. Tumour staging showed no evidence of distant metastasis in any of the patients at the time of second surgery.

Two patients underwent no further surgery and received radiotherapy alone. In one of these patients (No. 10), remedial wide margin resection would have resulted in major disfiguration of external genitalia, and hence it was recommended against by a gynaecologist. The other patient who had low-grade sarcoma had a clear, although close, margin in the primary operation. Wide-margin excision was achieved in the remaining 16 patients. In two patients, direct wound closure was possible followed by subsequent radiotherapy. Four patients required wide excision with skin grafting and muscle flap creation, whereas a combination of wide excision, skin grafting, muscle flap creation, and radiotherapy was performed in 10 patients. In all patients, the involved limb was preserved after completion of all treatment. All excised tissue was sent for sectioning and histological analysis, which showed that nine of the 18 patients had had residual tumour at the primary surgical site.

Follow-up outcomes were obtained at an average interval of 42 months (range, 23-100 months). Until the last follow-up visit, two patients had distant metastasis: the first, patient No. 1, had metastases in the kidney and left leg diagnosed at 9 months and 28 months after re-resection, respectively. He, however, refused further treatment and was still alive at the last follow-up. The second patient (No. 16) had lung metastasis at 31 months after re-resection, and a further treatment plan was being formulated at the last follow-up. Among the 18 patients, only one (No. 6) died because of an unrelated cause at 19 months after surgery; there was no evidence of local recurrence or distal metastasis. The remaining patients survived without evidence of tumour recurrence, high-grade complications affecting daily life, or any neurovascular deficits or wound complications that needed further flap surgery.

Discussion

Soft tissue "swelling" of an extremity is frequently seen in daily practice, and the majority of them are benign lesions. To diagnose sarcoma among these soft tissue swellings requires a level of clinical suspicion. Clinical features suggestive of malignancy include the following: (1) a mass of larger than 5 cm, (2) pain in a previously painless lump, (3) rapid increase in size,[15] and (4) subfascial location of a mass. These suspicious masses should be subjected to further investigation before definitive excision. Magnetic resonance imaging is the most accurate and valuable imaging technique to visualise the anatomy of the lesion and its relationship with surrounding vital structures, such as the neurovascular

bundle, and to allow detailed preoperative planning of resection margins.[16] Biopsy should be performed only after MRI, because the procedure may alter the appearance of the MRI scan. Image-guided percutaneous tru-cut biopsy is currently our preferred method of obtaining tissue for pathology. One study showed an overall diagnostic accuracy of 96% with such a biopsy method, and other studies have demonstrated variable success rates, ranging from 60% to 100%.[17] Besides the high diagnostic accuracy, image-guided biopsy also has the added advantages of avoiding damage to nearby vital neurovascular structures and tumour contamination by transversing the tissue plane during the procedure. The morbidity and mortality rates were also lower than those associated with open biopsy.[18,19] Communication between the surgeon and radiologist is of utmost importance to ensure a proper biopsy site, so that positions of operative incisions and musculocutaneous flaps are correct. When inadequate tissue is obtained from image-guided needle biopsy, open-biopsy should be performed. Open-biopsy itself is not a minor procedure and should be performed in a specialised centre by a surgeon especially trained in musculoskeletal oncology who will also perform the subsequent resection.[20] Once proper investigations have been completed, limb-sparing surgery consisting of wide excision with a 2- to 3-cm margin of grossly normal tissue is the main curative therapy. Adjuvant radiotherapy, in form of external beam radiotherapy with or without brachytherapy should be considered in cases of high-grade sarcoma, because this treatment is very effective in preventing local recurrence in patients after wide local excision.[21,22]

This study reveals the lack of awareness of potential malignancy in soft tissue swellings despite the presence of one or more clinical clues. The incomplete resection during the primary operation implies that local relapse can be expected in more than 90% of patients without further therapy,[23,24] in contrast to the 10% recurrence rate after a primary well-planned wide excision with or without adjuvant radiotherapy.[23-26]
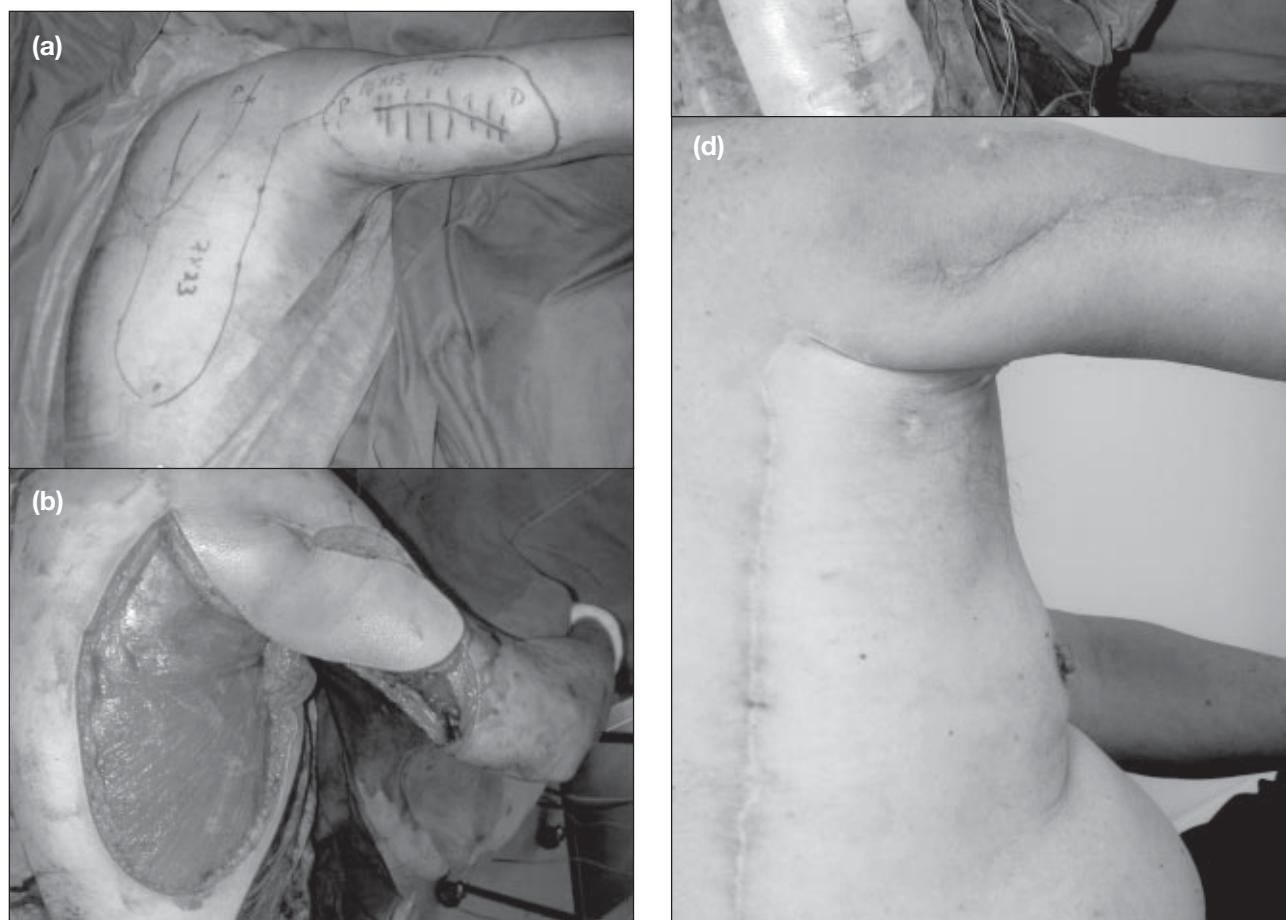
Fig 2. Patient No. 7: (a) planned wide excision and design of parascapular flap; (b) transposition of parascapular flap; (c) insertion of brachytherapy catheters; (d) prominent scarring in shoulder and back

Radiotherapy alone is not advocated as a remedial approach, as demonstrated in a study by Giuliano and Eilber,[11] in which 90 patients were referred after an excisional biopsy of soft tissue sarcoma; all were treated with adriamycin (doxorubicin) and radiation therapy before re-resection. Despite the intensive preoperative treatment in that study, half of the patients still had gross evidence of residual sarcoma in final pathology. The presence of residual tumour in 50% of re-resected specimens in this study again supports the current recommendation of repeated wide-margin resection after incomplete primary surgery, so as to improve the local control of disease.[7,9] These secondary surgeries should be performed in musculoskeletal tumour centres by a multidisciplinary team of dedicated tumour surgeons, clinical oncologists, radiologists, and pathologists, all contributing to optimal tumour control.

As demonstrated in this study, re-resection in the majority of cases necessitates more extensive surgery. If the initial management were planned properly, more than half of the patients (10/18) would have avoided such extensive surgical reconstruction and more than a quarter of them (5/18) additional adjuvant radiotherapy. The loss in functional outcome and the emergence of potential complications due to the additional procedures could therefore be avoided.

Conclusion

A high level of clinical suspicion and proper investigation will avoid incomplete resection. Early referral to a specialised musculoskeletal tumour centre for clinically suspicious masses should be encouraged, because diagnostic errors and treatment complications are far less likely if biopsy is performed properly.[20] Subsequent definitive treatment aiming at complete eradication of tumour while sparing the tumour-bearing limb requires the joint effort of various specialties. Re-resection for patients referred after inadequate primary surgery by surgeons specialised in musculoskeletal oncology can still achieve local tumour-free status, thereby avoiding more extensive and mutilating surgery.[27,28]

References

1. Mann GB, Lewis JJ, Brennan MF. Adult soft tissue sarcoma. Aust NZ J Surg 1999;69:336-43.
2. Hong Kong Cancer Registry, Hospital Authority. Soft tissue sarcoma registered in Hong Kong. Hong Kong: Hospital Authority; 2002.
3. Noria S, Davis A, Kandel R, et al. Residual disease following unplanned excision of a soft-tissue sarcoma of an extremity. J Bone Joint Surg Am 1996;78:650-5.
4. Goodlad JR, Fletcher CD, Smith MA. Surgical resection of primary soft-tissue sarcoma. Incidence of residual tumour in 95 patients needing re-excision after local resection. J Bone Joint Surg Br 1996;78: 658-61.
5. Ueda T, Yoshikawa H, Mori S, et al. Influence of local recurrence on the prognosis of soft-tissue sarcomas. J Bone Joint Surg Br 1997;79:553-7.
6. Davis AM, Kandel RA, Wunder JS, et al. The impact of residual disease on local recurrence in patients treated by initial unplanned resection for soft tissue sarcoma of the extremity. J Surg Oncol 1997;66:81-7.
7. Lewis JJ, Leung D, Espat J, Woodruff JM, Brennan MF. Effect of reresection in extremity soft tissue sarcoma. Ann Surg 2000;231: 655-63.
8. Lewis JJ, Leung D, Heslin M, Woodruff JM, Brennan MF. Association of local recurrence with subsequent survival in extremity soft tissue sarcoma. J Clin Oncol 1997;15:646-52.
9. Zornig C, Peiper M, Schroder S. Re-excision of soft tissue sarcoma after inadequate initial operation. Br J Surg 1995;82:278-9.
10. Schwarzbach M, Attigah N, Willeke F, et al. Results of oncological reoperation in primary oft tissue sarcomas [in German]. Chirurg 2000; 71:1359-64.
11. Giuliano AE, Eilber FR. The rationale for planned reoperation after unplanned total excision of soft-tissue sarcomas. J Clin Oncol 1985; 3:1344-8.
12. Siebenrock KA, Hertel R, Ganz R. Unexpected resection of soft-tissue sarcoma. More mutilating surgery, higher local recurrence rates, and obscure prognosis as consequences of improper surgery. Arch Orthop Trauma Surg 2000;120:65-9.
13. Alekhteyar KM, Leung DH, Brennan MF, Harrison LB. The effect of combined external beam radiotherapy and brachytherapy on local control and wound complications in patients with high-grade soft tissue sarcomas of the extremity with positive microscopic margin. Int J Radiat Oncol Biol Phys 1996;36:321-4.
14. Schwarz R, Krull A, Zornig C, Weh HJ, Alberti W. Radiotherapy of soft tissue sarcomas [in German]. Schweiz Rundsch Med Prax 1998; 87:1072-80.
15. Solomon L. Apley's system of orthopaedics and fractures. 8th ed. New York: Oxford University Press; 2001:195.
16. Dee R, Hurst LC, Gruber MA, Kottmeier SA, editors. Principles of orthopaedic practice. New York: McGraw-Hill; 1997:229.
17. Logan PM, Connell DG, O'Connell JX, Munk PL, Janzen DL. Image-guided percutaneous biopsy of musculoskeletal tumors: an algorithm for selection of specific biopsy techniques. AJR Am J Roentgenol 1996; 166:137-41.
18. Murphy WA, Destouet JM, Gilula LA. Percutaneous skeletal biopsy 1981: a procedure for radiologists—results, review, and recommendations. Radiology 1981;139:545-9.
19. Tehranzadeh J, Freiberger RH, Ghelman B. Closed skeletal needle biopsy: review of 120 cases. AJR Am J Roentgenol 1983;140:113-5.
20. Mankin HJ, Lange TA, Spanier SS. The hazards of biopsy in patients with malignant primary bone and soft-tissue tumors. J Bone Joint Surg Am 1982;64:1121-7.
21. Hilaris BS, Bodner WR, Mastoras CA. Role of brachytherapy in adult soft tissue sarcomas. Semin Surg Oncol 1997;13:196-203.
22. Yang JC, Chang AE, Baker AR, et al. Randomized prospective study of the benefit of adjuvant radiation therapy in the treatment of soft tissue sarcomas of the extremity. J Clin Oncol 1998;16:197-203.
23. Gustafson P. Soft tissue sarcoma. Epidemiology and prognosis in 508 patients. Acta Orthop Scand Suppl 1994;259:1-31.
24. Yang JC, Rosenberg SA. Surgical treatment of soft tissue sarcomas of the extremities. In: Sugarbaker PH, Malawer MM, editors. Musculoskeletal surgery for cancer. Principles and techniques. New York: Thieme Medical Publishers; 1992:1-11.
25. Peabody TD, Monson D, Montag A, Schell MJ, Finn H, Simon MA. A comparison of the prognoses for deep and subcutaneous sarcomas of the extremities. J Bone Joint Surg Am 1994;76:1167-73.
26. Rydholm A, Gustafson P, Rooser B, et al. Limb-sparing surgery without radiotherapy based on anatomic location of soft tissue sarcoma. J Clin Oncol 1991;9:1757-65.
27. Wilson AN, Davis A, Bell RS, et al. Local control of soft tissue sarcoma of the extremity: the experience of a mutlidisciplinary sarcoma group with definitive surgery and radiotherapy. Eur J Cancer 1994;30A:746-51.
28. Clasby R, Tilling K, Smith MA, Fletcher CD. Variable management of soft tissue sarcoma: regional audit with implications for specialist care. Br J Surg 1997;84:1692-6.