■ ASPECTS OF CURRENT MANAGEMENT

Earlier diagnosis of bone and soft-tissue tumours

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Although bone and soft-tissue sarcomas are rare, early diagnosis and prompt referral to a specialised unit offers the best chance of a successful outcome both in terms of survival and surgical resection. This paper highlights the clinical and radiological features that might suggest the possibility of a bone or soft-tissue sarcoma and suggests a succinct management pathway for establishing whether a suspicious bone or soft-tissue lesion could be malignant.

Bone and soft-tissue sarcomas are rare. Their incidence is about 8 to 9 per million population per year for bone sarcomas, and 30 per million population per year for soft-tissue sarcomas.¹ They constitute approximately 1% of all malignant tumours.

There has been marked improvement in the management of both bone and soft-tissue sarcomas over the past three decades as a result of better imaging, effective chemotherapy for osteosarcoma and Ewing's sarcoma, and the increasing use of limb-salvage surgery. Centralising the management of patients in specialist units offers care by experienced multidisciplinary teams and has been advocated by the National Institute for Clinical Excellence (NICE).² Management guidelines for bone and soft-tissue sarcomas have also been produced by a number of national and international organisations, notably the National Cancer Collaborative Network (NCCN) in the United States and the European Society for Medical Oncology (ESMO).³⁻⁵ As a result, there is broad consensus around the world on the preferred management of patients with these conditions. Areas of uncertainty are now being explored by recruiting large numbers of patients into collaborative trials to try and resolve questions that could never be answered by small-scale studies.^{6,7}

Despite these advances, the outcome for many patients is dependent on factors relating to the tumour as much as those relating to the treatment. For soft-tissue sarcomas, the main prognostic factors are grade, size, depth, diagnosis and the age of the patient.⁸ Of these, the only one that can be altered to improve prognosis is the size of the tumour at diagnosis,

which is related to survival, and has also been shown to be strongly correlated with the incidence of detectable metastases at diagnosis.⁹⁻¹¹ For every 1 cm increase in the size of a soft-tissue sarcoma at diagnosis there is a 3% to 5% worsening of the chance of cure,^{11,12} although the effect of size on prognosis is less marked for bone tumours, large studies have confirmed its significance.¹³⁻¹⁶

Data collected at one of our units for the past 20 years has shown that bone and soft-tissue sarcomas have a mean maximum diameter at diagnosis of 10 cm. Although there has been a slight reduction in the size of soft-tissue sarcomas diagnosed in this period, there has been no such improvement for bone sarcomas (unpublished data).¹⁷

The reasons for a delay in diagnosis are numerous and may occur at any stage in the referral pathway. They are usually the result of a lack of awareness of the significance of the clinical presentation by the patient or any of those treating them, including orthopaedic surgeons.^{18,19}

Referral guidelines for cancer patients were published in 2000 and revised in 2005.²⁰⁻²²

These state that: a soft-tissue lump with any of the following characteristics should be considered malignant until proved otherwise: size > 5 cm; increasing in size; deep to the deep fascia; painful; or recurrent after previous excision. They also recommend that any patient with bone pain, particularly non-mechanical pain, should be referred for radiographs, and that the presence of any of the following should lead to further investigation: bone lysis; new bone formation; periosteal elevation; soft-tissue swelling.

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Fig. 1

Algorithm for investigating a soft-tissue mass.

This guide is of equal relevance to hospital clinicians as it is to general practitioners. Unfortunately, there is little evidence that it has yet produced much benefit for patients with a sarcoma.²³ In Scandinavia the simple guidance that ‘any lump bigger than 5 cm should be investigated for possible malignancy’ has led to a gradual reduction in the average size of soft-tissue sarcomas at diagnosis to 7 cm.²⁴

One of the most common causes of delay in hospital practice is a lack of awareness that a lump might be malignant. This may lead to the patient undergoing inappropriate excision of the lump before the diagnosis of malignancy is confirmed. There is then the need for further surgery to excise the surrounding area widely: in over two-thirds of cases this has been shown to harbour tumour cells.²⁵ Any patient with a lump > 5 cm or which is deeply situated should be investigated rather than have the lump simply excised. Imaging (ideally MR) and biopsy should be carried out. This can be performed most expeditiously by referring the patient to the local sarcoma centre. Excision biopsy should only be considered for small subcutaneous lumps of < 5 cm in size, unless there are any of the other worrying features listed above (Fig. 1).

In England and Wales, the 2006 NICE guidance recommended the establishment of diagnostic clinics for patients with suspected soft-tissue sarcomas where a rapid diagnosis could be achieved by clinical assessment, radiological investigation and biopsy.² It also advised that patients with suspected bone tumours should be referred to one of five supraregional centres that deal with these tumours (London, Birmingham, Oxford, Newcastle and Oswestry). Soft-

tissue sarcomas also require treatment at specialist centres, 12 of which are designated in England and Wales.

Earlier diagnosis remains the key to improving outcomes. Orthopaedic surgeons must continue to have a high level of suspicion of any bone lesion that looks abnormal. Radiologically, for patients under the age of 35, the risk of a lytic lesion being a metastasis is low, but above this age it becomes increasingly likely. To assume, however, that a single lytic lesion without an obvious primary is a metastasis is dangerous, it should be treated as a primary bone sarcoma until histologically proven otherwise. The differential diagnosis should include infection, haematological malignancy, benign lesions and normal variants. The investigation of a patient with a suspicious bone lesion or suspected pathological fracture should follow the algorithm shown in Figure 2, and advice should be sought from an appropriate supraregional centre if, at any stage, a primary malignant bone tumour is suspected. In individual cases the suggested pathway may be altered, but only if the consequences of doing so will not affect subsequent management should the lesion prove to be a primary bone tumour.

A common problem at any age is establishing whether a low-velocity fracture is pathological or not, and if so, whether it is due to a primary bone tumour or to a metastasis. The treatment of the two is completely different, and there is clear guidance about how patients should be investigated in this situation.²⁶ Patients with obvious bone metastases will continue to be treated at local centres, adhering to well-established principles.²⁷

Fig. 2

Algorithm for investigating a suspicious bone lesion.

Awareness of the potential for malignancy should be considered in any unusual bone or soft-tissue lesion. To assume that a lesion is benign is not a safe option until malignancy has been excluded. Only by constant vigilance and awareness will we diagnose these lesions earlier and thereby improve the outcome for our patients.

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References

1. No authors listed. SEER Stat Fact Sheet. Cancer: soft tissue. National Cancer Institute. <http://seer.cancer.gov/statfacts/html/soft.html> (date last accessed 9 July 2010).
2. No authors listed. NICE Guidance: improving outcomes for patients with sarcomas. 2006 <http://guidance.nice.org.uk/csgsarcoma/guidance/pdf/English> (date last accessed 9 July 2010).
3. No authors listed. NCCN Clinical Practice Guidelines in Oncology: Soft Tissue Sarcoma. Version 2.2010. http://www.nccn.org/professionals/physician_gls/PDF/sarcoma.pdf (date last accessed 18 July 2010).
4. No authors listed. NCCN Clinical Practice Guidelines in Oncology: Bone Cancer. Version 3.2010. http://www.nccn.org/professionals/physician_gls/PDF/bone.pdf (date last accessed 18 July 2010).
5. Casali PG, Jost L, Sleijfer S, Verweij J, Blay JY; ESMO Guidelines Working Group. Soft tissue sarcomas: ESMO clinical recommendations for diagnosis, treatment and follow-up. *Ann Oncol* 2008;19(Suppl 2):89-93.
6. No authors listed. VORTEX radiotherapy trial. <http://www.vortex.bham.ac.uk/> (date last accessed 9 July 2010).
7. Paulussen M, Craft AW, Lewis I, European Intergroup Cooperative Ewing's Sarcoma Study-92. Results of the EICESS-92 Study: two randomized trials of Ewing's sarcoma treatment: cyclophosphamide compared with ifosfamide in standard-risk patients and assessment of benefit of etoposide added to standard treatment in high-risk patients. *J Clin Oncol* 2008;26:4385-93.
8. Pisters PW, Leung DH, Woodruff J, Shi W, Brennan MF. Analysis of prognostic factors in 1041 patients with localized soft tissue sarcomas of the extremities. *J Clin Oncol* 1996;14:1679-89.
9. Mendenhall WM, Indelicato DJ, Scarborough MT, et al. The management of adult soft tissue sarcomas. *Am J Clin Oncol* 2009;32:436-42.
10. Zagars GK, Ballo MT, Pisters PW, et al. Prognostic factors for patients with localized soft-tissue sarcoma treated with conservation surgery and radiation therapy: an analysis of 1225 patients. *Cancer* 2003;97:2530-43.
11. Grimer R. Size matters for sarcomas! *Ann R Coll Surg Engl* 2006;88:519-24.
12. Kattan MW, Leung DH, Brennan MF. Postoperative nomogram for 12-year sarcoma-specific death. *J Clin Oncol* 2002;20:791-6.
13. Bramer JA, van Linge JH, Grimer RJ, Scholten RJ. Prognostic factors in localized extremity osteosarcoma: a systematic review. *Eur J Surg Oncol* 2009;45:2367-75.
14. Hense HW, Ahrens S, Paulussen M, Lehnert M, Jurgens H. Factors associated with tumor volume and primary metastases in Ewing tumors: results from the (E)ICESS studies. *Ann Oncol* 1999;10:1073-7.

15. **Lee FY, Mankin HJ, Fondren G, et al.** Chondrosarcoma of bone: an assessment of outcome. *J Bone Joint Surg [Am]* 1999;81-A:326-8.
16. **Fiorenza F, Abudu A, Grimer RJ, et al.** Risk factors for survival and local control in chondrosarcoma of bone. *J Bone Joint Surg [Br]* 2002;84-B:93-9.
17. **Grimer RJ, Sneath RS.** Diagnosing malignant bone tumours. *J Bone Joint Surg [Br]* 1990;72-B:754-6.
18. **Johnson GD, Smith G, Dramis A, Grimer RJ.** Delays in referral of soft tissue sarcomas. *Sarcoma* 2008;2008:378574.
19. **Ashwood B, Witt JD, Hallam PJ, Cobb JP.** Analysis of the referral pattern to a supraregional bone and soft tissue tumour service. *Ann R Coll Surg Engl* 2003;85:272-6.
20. **No authors listed.** Referral Guidelines for Suspected Cancer <http://www.dh.gov.uk/assetRoot/04/01/44/21/04014421.pdf> (date last accessed 9 July 2010).
21. **No authors listed.** Referral Guidelines for Suspected Cancer 2005 <http://guidance.nice.org.uk/CG27/Guidance/pdf/English> (date last accessed 9 July 2010).
22. **Mannan K, Briggs TW.** Soft tissue tumours of the extremities. *BMJ* 2005;331:590.
23. **Malik A, Wigney MA, Murray S, Gerrand CH.** The effectiveness of "two week" referrals for suspected bone and soft tissue sarcoma. *Sarcoma* 2007;2007:23870.
24. **Bauer HC, Trovik CS, Alvegård TA, et al.** Monitoring referral and treatment in soft tissue sarcoma: study based on 1,851 patients from the Scandinavian Sarcoma Group Register. *Acta Orthop Scand* 2001;72:150-9.
25. **Chandrasekar CR, Wafa H, Grimer RJ, et al.** The effect of an unplanned excision of a soft-tissue sarcoma on prognosis. *J Bone Joint Surg [Br]* 2008;90-B:203-8.
26. **Tillman RM.** The role of the orthopaedic surgeon in metastatic disease of the appendicular skeleton. *J Bone Joint Surg [Br]* 1999;81-B:1-2.
27. **Al-Hakim WI, Jagiello JM, Briggs TW.** The palliative role of orthopaedics. *BMJ* 2006;332:1227-8.