Centre-Based Care for Bone and Soft Tissue Sarcoma

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1.1 Introduction

Bone and soft tissue sarcomas are rare tumours that constitute less than 1% of all cancers in adults [1]. Misrecognition, misdiagnosis and, as a consequence, inexpert attempts at management occur frequently [2]. With rare cancers such as sarcomas, the prognosis is improved when patients are managed at specialist centres with a multidisciplinary team [3]. Such centres are associated with better compliance with clinical practice guidelines, a better quality of diagnosis and management as well as a lower recurrence rate with notably less frequent reoperations compared to non-specialist centres [4]. This review provides the current evidence to support the multidisciplinary team approach to sarcomas and explains the operational structure of the multidisciplinary care at our centre.

1.2 The Rationale for Multidisciplinary Sarcoma Care

Sarcomas are rare tumours that require complex pathological diagnosis [5] and imaging interpretation [6–9]. Careful biopsy technique to ensure tissue extraction without contaminating healthy tissue is essential for optimal management of sarcomas. Surgical treatments of bone and soft tissue sarcomas are sophisticated and frequently require coordinated care from multiple surgical disciplines such as

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orthopaedic oncology, general surgical oncology, thoracic surgery, plastic surgery and other anatomically indicated surgical disciplines. Chemotherapy is routinely used for many high-grade bone and soft tissue sarcomas and often entails multiple agents with significant toxicity. Radiation therapy is given for select tumours as an adjunct to surgery or as a solitary management option. The doses used for sarcomas are far greater than those used for more routine indications such as bone metastasis [10]. Together, the management of sarcomas mandates close cooperation of experts within the multidisciplinary team.

1.3 Diagnosis

Patients suspected of bone and soft tissue tumours should undergo a diagnostic work-up. This consists of clinical evaluation, local and systemic imaging of tumour extent and histological examination of the tumour. Radiographs can be helpful in revealing areas of calcification, soft tissue shadowing and bony destruction [11, 12]. Magnetic resonance imaging (MRI) is the modality of choice to determine the size and location of soft tissue lesion as well as the proximity to adjacent anatomic structures. Functional imaging, such as positron emission tomography (PET) [13] and bone scan [14], is often performed to decide the needle trajectory to target the most metabolically active area [14] within the lesion, to improve the overall diagnostic accuracy [15] and to assess for local recurrence [12].

Systemic staging is critically important for the management of sarcomas. A computed tomography (CT) scan of the chest should be obtained on initial presentation because sarcomas are known to metastasise to the lungs, and the findings of metastatic disease may alter the goals of treatment [12, 16]. In non-specialist centres, only 43% of patients with soft tissue sarcomas underwent radiological examination of the tumour, while 24% of patients were investigated for metastatic disease before treatment. This contrasts with specialist sarcoma centres where 100% of patients underwent local imaging of the tumours and 78% had systemic staging [17].

Biopsies allow for tissue diagnosis. In non-specialist centres, biopsies are often inadequately or inappropriately performed. Biopsies not performed by an expert may lead to delay in treatment from repeating a previously non-diagnostic biopsy, complications from improperly placed incision that confounds future surgeries and healthy tissue contamination [18]. Pre-referral biopsy can lead to increased local relapse and mortality as well as more radical surgery resulting in loss of function and long-term disability [19]. Incorrectly performed biopsy with poor techniques can lead to profound implications such as missing the chance of timely diagnosis of a potentially curable disease and adding morbidity to the definitive surgery.

Unlike many other cancers, in bone and soft tissue tumours, pathological interpretation requires understanding of the clinical presentation and radiological interpretation of aggressiveness due to their heterogeneous morphology [12]. Particularly, in low-grade cartilage bone tumours (Figs. 1.1, 1.2, 1.3, and 1.4), the specimen cannot be interpreted in isolation, but rather in the clinical and imaging context. The diagnosis made by the referring pathologist often exhibits significant discrepancies

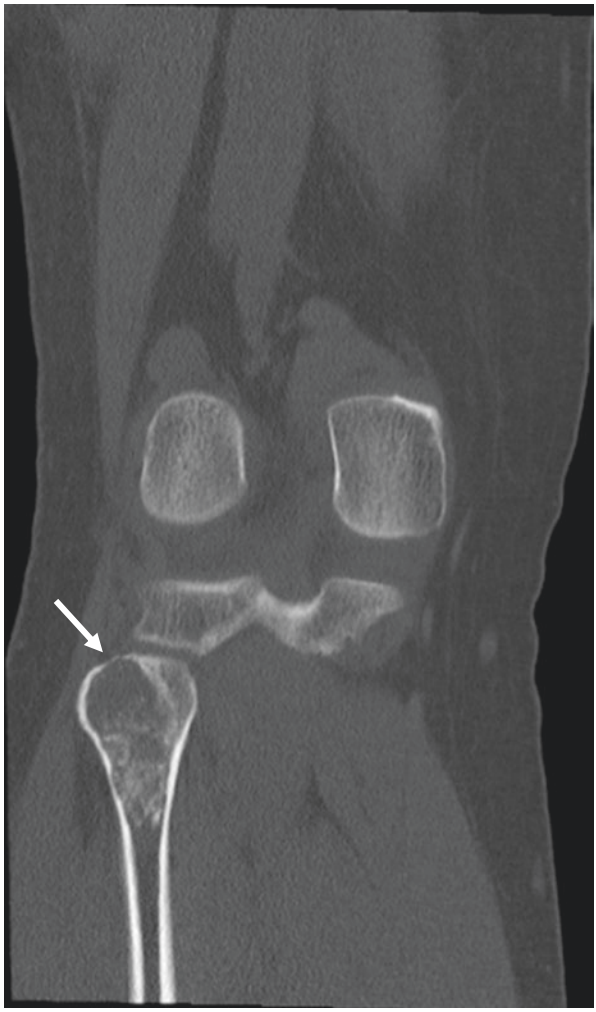

Fig. 1.1 Coronal computed tomography of proximal fibula of a 41-year-old female presenting with 2-week history of pain. Grade 1 chondrosarcoma. Image shows a chondroid lesion involving the proximal fibula. There is thinning of cortex without frank cortical breach (arrow)

from the final diagnosis by a musculoskeletal pathologist. Review of diagnosis by a specialist pathologist improves the accuracy of diagnosis in these rare and heterogeneous tumours [20] and is advised by current clinical practice guidelines [21–23]. The final diagnosis of sarcomas can be made collectively by experts following a discussion of all relevant clinical, imaging and histological findings.

1.4 Treatment of Bone Cancers

Primary bone cancers may be treated with resection, chemotherapy and radiation. Chemotherapy usually extends 10–12 weeks preoperatively, and significant toxicity is often associated. Specialist medical oncologic input is necessary to medically

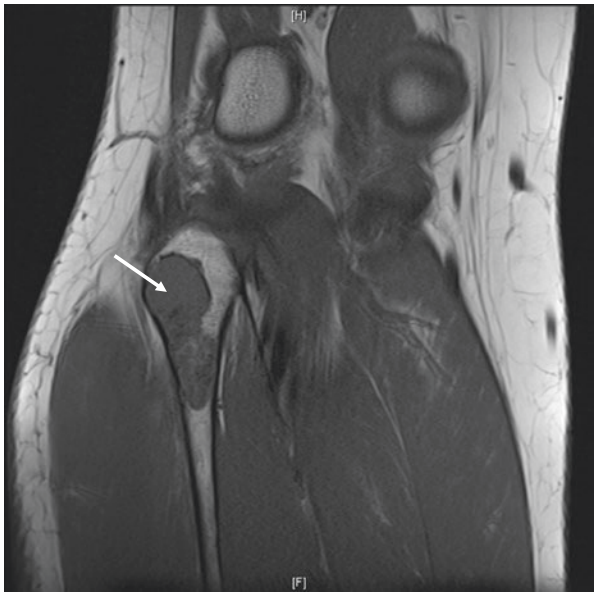

Fig. 1.2 T1 coronal sequence shows lobulated, expansile lesion of the right fibula head and neck (arrow), compatible with low-grade chondroid aetiology

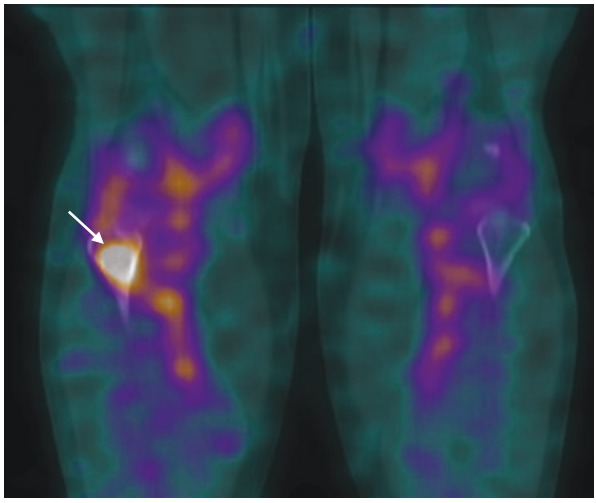

Fig. 1.3 Tc-99m DMSA (V) image demonstrates moderately intense tracer uptake uniformly within the chondroid abnormality of the proximal fibula (arrow). *Tc-99m DMSA (V)* technetium-99m dimercaptosuccinic acid

optimise patients for surgery and deal with any resultant toxicities. The surgical removal of the tumour is often complex and requires multiple surgical disciplines: orthopaedic oncology for resection of bone and skeletal reconstruction and plastic surgery for optimal tissue coverage. Effective communication and coordination between the disciplines prevent delay in providing the necessary care to patients. Pathological interpretation of the surgical specimen by the bone tumour pathologist regarding margins and degree of tissue necrosis is an important predictor of prognosis and guides subsequent management [10].

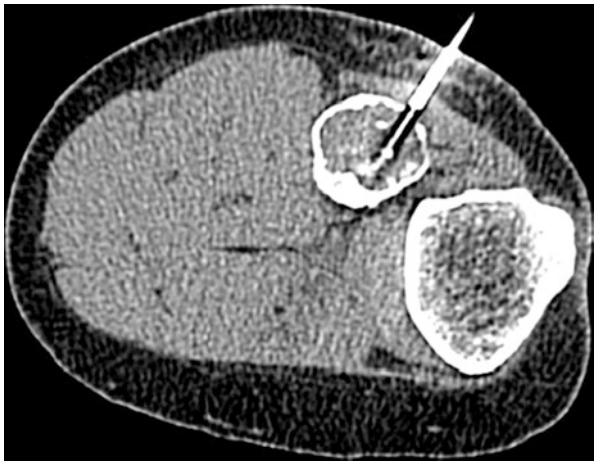

Fig. 1.4 Image-guided biopsy was carried out under computed tomography by a diagnostic radiologist through the shortest path to the tumour to minimise potential contamination. Optimal needle trajectory was determined upon discussion at the multidisciplinary meeting

1.5 Treatment of Soft Tissue Sarcoma

Currently, the mainstay treatment for soft tissue sarcoma is surgical removal of the entire tumour [10]. For localised sarcomas, a complete resection with a margin of several centimetres of healthy tissue to secure a free margin may achieve cure [24]. Unfortunately, unplanned soft tissue sarcoma excision occurs frequently without the utilisation of the multidisciplinary team, execution of necessary surgical margins or appropriate assessments of tumour diagnosis and local and systemic staging [1]. Unplanned surgery without a proper knowledge of the diagnosis is highly associated with residual disease or contamination of surrounding structures [25]. Positive excision margins have been reported to be as prevalent as 67–93% in patients treated outside of specialist centres [26–29]. Local recurrence rates at non-specialist centres are two to four times higher than those achieved in specialist centres [30–33]. Despite the tendency of excising potentially more aggressive and larger tumours [34], specialist hospitals showed better local control than community hospitals [1].

Due to the risks associated with incomplete excision, reoperation occurs frequently for patients initially treated inappropriately at non-sarcoma centres. Reoperation is often more complex and extensive [4]. The rates of plastic reconstruction and amputation were much higher in the re-excision group compared to the rates for patients who had appropriate initial resection. The required size of resection is increased at reoperation, thereby making the nature of reconstruction of defects more complex and increasing the need for tissue coverage [35]. As a result, these patients may experience greater surgical morbidity, potentially worse long-term functional outcomes [34] and significantly worse final results in terms of quality of surgery [4]. Nonetheless, re-excision has not been associated with worse local recurrence, metastasis-free survival nor overall survival [36–38].

With advantages of radiotherapy, the need to resect important neurovascular structures, or musculoskeletal structures, may be reduced, allowing for limb-sparing surgeries [39]. Radiation therapy pre- or post-limb-sparing surgery increases locoregional control in more than 90% of patients compared to conservative surgery without radiation therapy [4]. The role of chemotherapy in soft tissue sarcomas is controversial due to high toxicity and non-significant benefits to long-term survival and prognosis [12, 40]. Some evidence suggests chemotherapy can provide survival benefits in specific subtypes such as synovial sarcomas with metastasis [41, 42]. The decision to chemotherapy should be made on a case-by-case basis by medical oncologist with specific expertise.

1.6 Management of Metastatic Sarcoma

The decision of how to evaluate and treat suspicious nodules in the setting of a diagnosis of sarcoma (non-surgical, surgical or medical treatment with chemotherapy) must be carefully determined in the multidisciplinary setting with the treatment goals, prognosis and functional status of patient in consideration. The differentiation between metastatic nodules and other non-specific lung nodules or infection requires diagnostic radiologist comparing with previous scans. Definitive diagnosis may require biopsy to be taken by an interventional radiologist and interpreted by a pathologist. Patients with bone and soft tissue sarcomas with solitary metastasis to lungs or isolated lesion in the body are now treated more aggressively by thoracic surgeon, orthopaedic surgeon and other anatomically directed surgeons. This is due to the improved the prognosis for the patients [43].

1.7 Multidisciplinary Sarcoma Team and Clinic at St. Vincent's Hospital Melbourne and Peter MacCallum Cancer Centre

1.7.1 Sarcoma Clinic

Each patient referred to our sarcoma centre is triaged and receives scheduled appointments with orthopaedic or general surgical oncologists for initial investigation of bone and soft tissue mass. Concurrent appointments with medical oncologists and radiation oncologist can be organised on the same day and within the same building. This enables coordinated care, particularly for patients who travel a long distance. The services of another discipline are often able to be incorporated because the expectation for multidisciplinary needs for patients is embedded within the centre. Patients post definitive treatment of sarcomas must be followed up closely for early detection of potential recurrence of disease or metastasis. They are reviewed three to four monthly for the first 2 years with clinical examination and appropriate imaging (i.e. plain radiographs and MRI of the surgical site and CT of the chest) and

six monthly for a further 2 years with a plan for yearly review for the following 4 years. Thus, a routine clinical follow-up spans at least 8 years.

1.7.2 Multidisciplinary Meeting

At St. Vincent's Hospital Melbourne, we have a weekly multidisciplinary meeting. Attendees include orthopaedic oncologists, medical oncologists, surgical oncologist, radiation oncologists, thoracic oncologist, plastic surgeon, musculoskeletal diagnostic radiologists, pathologists and administrative personnel (Fig. 1.5). Other disciplines may also bring relevant cases for discussion. Patients are presented with all relevant clinical, radiological and pathological findings. Specific questions are brought up and addressed with the unique input from different specialties. A consistent, comprehensive and institutional approach to manage sarcomas can prevent management instituted by a single provider within their own discipline. This also provides fantastic educational opportunities for specialists of one filed to learn about expertise and current advances that are outside of their field. Trainees are welcome to attend and observe a greater number of sarcoma cases than would otherwise encounter in a single non-sarcoma practice.

Fig. 1.5 St. Vincent's Hospital/Peter Mac Cancer Centre weekly multidisciplinary meeting. Orthopaedic oncologists, medical oncologists, radiation oncologists, thoracic surgeon, plastic surgeon, radiologists, pathologists, orthopaedic trainees and administrative staff are reviewing imaging

1.7.3 Clinical Trials

Clinical trials drive important advancements in the management of uncommon diseases like sarcomas. The multidisciplinary tumour team is often up to date with ongoing or new national and institutional trials and can provide an excellent platform for enrolling patients in appropriate clinical trials and maximising options [44].

1.8 Impact of Delayed Referral on Patient Outcomes

Delayed referral to a sarcoma centre occurs frequently and can be prolonged. Some causes for delayed referral include delayed presentation of patients to primary carer or non-compliance of referring hospitals with clinical practice guidelines [45]. Sixty-three percent of patients with delayed referral had been subjected to extensive imaging studies, and 34% received biopsy or surgery at local hospitals prior to referral [46]. Regardless of the cause of the delay, it has been shown to impact on patient management and prognosis [46, 47]. Only 28% of patients who were referred after undergoing inappropriate excision and developing local recurrences achieved disease-free survival as opposed to 73% of patients who were referred directly to a specialist centre [47]. Delayed referral was further associated with increased total number of operations and local recurrence rate [48]. However, there are conflicting evidence suggesting that the impact of delayed definitive treatment on overall survival or metastasis is not significant [49, 50].

1.9 Recommendation

The general recommendation is to refer patients with a tumour larger than 5 cm in size and lesions deep to or adherent to deep fascia directly to a sarcoma centre to be managed by a specialist sarcoma unit. Diagnostic investigations before referral are not required [51]. Patients treated at sarcoma centres with high patient load had greater survivorship even if they travelled further distances than those who stayed close to home and underwent treatment of sarcoma at a regional centre [4].

1.10 Conclusion

Due to the rarity of bone and soft tissue sarcomas, the likelihood of patients undergoing correct biopsy and imaging tests, initial curative management with wide margin and appropriate medical treatment is significantly higher at specialist centres with multidisciplinary team. Similarly, the rates of incomplete excision, reoperation and local recurrence are lower when patients receive treatments within a specialised sarcoma centre. Timely referral to a specialist centre equipped with a multidisciplinary team of experts before the commencement of any treatment would optimise management and reduce morbidity.

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