Basic science of musculoskeletal tumours

Kenneth S Rankin

Abstract

The basic science of musculoskeletal tumours is a complex subject and has been historically related to pathological descriptions of the lesions. Our understanding of these conditions has increased rapidly with the advent of genetic sequencing and molecular diagnostic techniques. This article covers the main topics and touches on the relevant research strategies which seek to open up further management options, particularly for the sarcomas.

Keywords basic science; musculoskeletal tumours; sarcoma

Introduction

Musculoskeletal tumours encompass a wide variety of entities, and our understanding of them has been historically based on the traditional pathological descriptions of the lesions. These descriptions have evolved into a classification system, of which the World Health Organization (WHO) classification of bone and soft tissue tumours is the essential cornerstone.[1] The histological features of the tumours are now complemented by an array of cytogenetic and molecular diagnostic assays which are increasingly useful for those cases which are equivocal and for further confirmation of a diagnosis. An example of this is cytogenetics to confirm presence of the EWS/FLI1 fusion product in a suspected Ewing's sarcoma with a histological description of small round blue cells along with immunohistochemical staining that demonstrates high expression of CD99. Another example would be an equivocal case of an active lytic bone lesion that is likely to be benign but with persistent concern that it may actually be a telangiectatic osteosarcoma. The presence of a USP6 rearrangement on cytogenetic testing in such a case would be reassuring that it is an aneurysmal bone cyst, which of course has major implications on the treatment strategy. Therefore it is the progressive understanding of the basic science of these lesions which allows us to improve upon diagnosis and management of this diverse group of musculoskeletal tumours. This section will cover the important basic science features of musculoskeletal tumours including tissue of origin, whether the lesion is benign or malignant, common features and pathophysiology. There will also be a discussion of research strategies in the basic science arena which serves to improve our understanding of these conditions and ultimately leads to advances in diagnosis and management.

Kenneth S Rankin *MBChB MD FRCS Honorary Consultant in Orthopaedic Oncology, Northern Institute for Cancer Research, Newcastle University, UK; North of England Bone and Soft Tissue Tumour Service, Freeman Hospital, Newcastle upon Tyne, UK.*
Conflicts of interest: none declared.

Tissues of origin

Musculoskeletal tumours can arise from several main tissue sources. The majority of primary lesions originate from mesenchymal tissue which is analogous to the mesoderm in embryological terms. Neuroectodermal tissue can give rise to primary nerve sheath tumours in the musculoskeletal system and some primary lesions develop from primitive neuroectodermal tissue which is a remnant of embryological neuron precursors. Tumours may be secondary due to spread from carcinomas, with bone being the most common site. These metastatic lesions are therefore of epithelial origin, but have a complex interaction with their host site. Haematological conditions can manifest as musculoskeletal tumours, the main ones encountered by the orthopaedic surgeon being myeloma and lymphoma. Finally, syndromic conditions may give rise to widespread musculoskeletal tumours which are often benign but need to be closely observed for malignant transformation.

Tumours of mesenchymal origin

There is a vast array of primary benign and malignant tumours which arise in the musculoskeletal system. Benign tumours consist of dozens of subtypes based upon histological description. Malignant tumours are mainly the sarcomas of which more than 50 types are described and again, histological description is the mainstay of classification.[1] Broadly, benign tumours are defined by their inability to metastasize but can be locally aggressive and therefore pose significant management problems, as exemplified by fibromatosis. Malignant tumours have the potential to metastasize and cause death and therefore management is complex and multi-modal to optimize outcomes. There are some intermediate tumours which are often locally aggressive but very rarely metastasize such as giant cell tumour of bone. It is important to consider that some benign tumours have the potential to undergo malignant transformation, such as the large atypical lipomas.

Benign versus malignant tumours

The large number of musculoskeletal tumours is too extensive to list but they can be placed into groups to make initial management decisions easier. Figures 1 and 2 show flow diagrams for benign and malignant tissue tumours respectively.

The diagnosis of benign lesions may be achieved with clinical examination and imaging only, but if there is doubt a biopsy, usually in the clinic may be required for confirmation. Management is then dependent on whether the patient is symptomatic or if the lesion has a risk of malignant transformation then excision may be advised.

The largest group of patients with malignant lesions in the musculoskeletal system consists of those suffering from metastatic carcinoma or myeloma affecting bone. Many of these patients require surgical intervention to prevent an impending pathological fracture or to treat a fracture that has already occurred. It is important to remember that melanoma can metastasize to bone and therefore if there is doubt about the origin of a lesion a biopsy should be performed. The management of bone and soft tissue sarcomas (STS) and metastatic disease has been dealt with in chapters 4 and 5.

Please cite this article in press as: Rankin KS, Basic science of musculoskeletal tumours, Orthopaedics and Trauma (2017), http://dx.doi.org/10.1016/j.mporth.2017.03.009

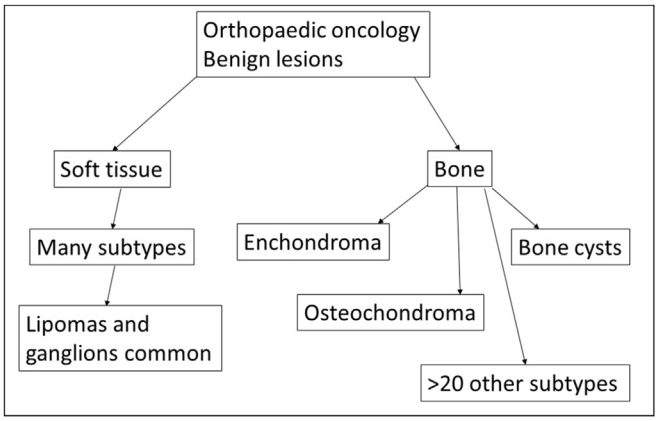

Figure 1 A basic flow chart of benign orthopaedic oncology lesions.

Finally, there are some locally aggressive bone lesions with a low risk of metastasizing. These are listed in Table 1. These lesions should be managed by a bone sarcoma centre.

Benign bone tumours

These lesions will be seen by orthopaedic surgeons in a diverse range of subspecialties and can often be dealt with minimal input from an orthopaedic oncology centre. If there is any concern regarding the diagnosis, it is important that the lesion is discussed with the local oncology team and investigations with the appropriate imaging and biopsy performed. Some benign lesions may require excision by an orthopaedic oncologist if the anatomical location would require an extensive approach with mobilization of neurovascular structures (Figure 3). A detailed review of benign bone tumours is provided in the article on Management of benign bone tumours in this issue (http://dx.doi.org/10.1016/j.mporth.2017.03.008).

It is also important to consider that a benign bone lesion may be related to a syndrome, for example multiple hereditary exostosis (EXT gene mutations) or multiple enchondromatosis, the underlying pathophysiology of which is unclear. Such patients need to be monitored closely for malignant transformation in one of their lesions, particularly if it increases in size or becomes painful.

Enchondromas are commonly referred for further evaluation when they are noted incidentally on an MRI scan for joint pain, typically in the distal femur. It is important to re-scan these lesions to assess for change and in some centres dynamic contrast MRI is used to distinguish between enchondroma and grade 1 chondrosarcoma.[2]

Intermediate bone tumours which rarely metastasize

- Giant cell tumour of bone
- Chordoma
- Epithelioid haemangioma
- Epithelioid haemangioendothelioma
- Adamantinoma

Table 1

Benign soft tissue tumours

There are a huge range of benign soft tissue lesions encountered by the orthopaedic surgeon. Lipomas and ganglia are the most common. Diagnosis should be confirmed by ultrasound and management is based on symptoms. Deep lipomas (subfascial/intramuscular) may reach impressive sizes. MRI is required to exclude areas of dedifferentiation prior to marginal excision. Many of these large deep lipomas will be given a diagnosis of atypical lipomatous tumour (ALT) by the pathologist based on cellular atypia and positive p16 (tumour suppressor protein), MDM2 (tumour promotor protein) and CDK4 (cell cycle regulator) immunostaining.[3] Loss of p16 activity and MDM2 amplification are postulated to be potential events that may lead to the transformation of ALT into liposarcoma.[4]

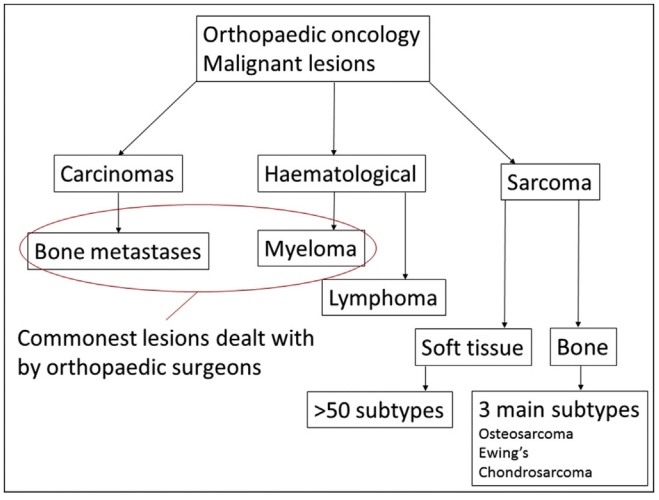

Figure 2 Flow chart depicting the main three groups of orthopaedic oncology malignant lesions.

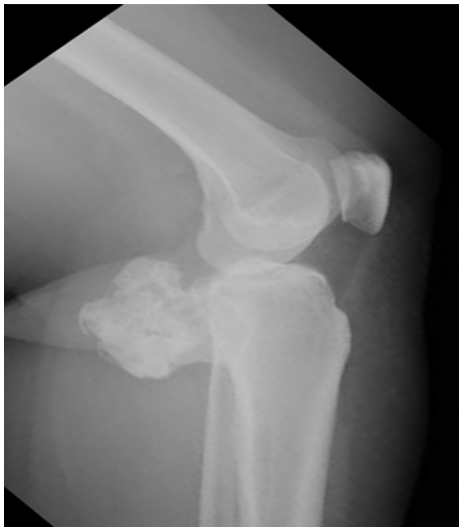

Figure 3 A large sessile osteochondroma arising from the posterior aspect of the proximal tibia. An MRI to check the size of the cartilage cap and position of the critical structures is important pre-operatively. A formal posterior approach to the knee is required with mobilization of the neurovasular bundle to safely excise the lesion.

Please cite this article in press as: Rankin KS, Basic science of musculoskeletal tumours, Orthopaedics and Trauma (2017), http://dx.doi.org/10.1016/j.mporth.2017.03.009