Pathology of paediatric bone tumours

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Abstract

Primary bone tumours account for less than 0.2% of all neoplasms but malignant bone tumours represent the third most common cause of cancer deaths in children and adolescents. The rarity of bone tumours in itself is a diagnostic challenge but is compounded by the number of tumour subtypes on top of which the imaging and histological features of degenerative and reactive processes, and benign bone tumours can simulate bone sarcomas. Furthermore, even in children bone lesions may represent metastatic disease. Hence the assessment of a bone tumour in a child or adolescent should be performed in a specialist referral bone tumour centre which has access to a multidisciplinary team and molecular diagnostic tests: the latter provides greater diagnostic accuracy. It is now appreciated that germline alterations occur more commonly than previously recognised in children and young adults presenting with osteosarcoma and Ewing sarcoma. Awareness of this is important as genetic counselling and screening may be appropriate. In this article epidemiology, radiology, pathology, genetics, treatment and prognosis of most commonly encountered bone tumours among the paediatric population are reviewed.

Keywords Bone tumour; children; chondrosarcoma; chordoma; Ewing sarcoma; genetics; mosaic disorder; mutation; osteosarcoma; paediatric; sarcoma

Introduction

Primary bone tumours represent between 4.6% and 7.6% of all cancers in patients under 20 years of age.[1,2] Most paediatric primary bone tumours are benign, however malignant bone tumours account for significant morbidity and mortality in this population. A recent publication reports that the prevalence of germline mutations in sarcoma in patients presenting under 20 years of age comes to about 8% but occurs in closer to 20% and 10% of patients in this age group with osteosarcoma and Ewing sarcoma respectively.[2] Pathological assessment of a bone tumour in a child or adolescent should be performed by histopathologists in a specialist bone tumour referral centre.

In this review we will focus on primary bone tumours that are most frequently encountered in the paediatric population. A classification of these tumours is shown in Table 1.

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Benign bone tumours

Bone-forming tumours

1. **Osteoma and enostosis**

Definition, epidemiology and incidence

Osteoma is a benign tumour occurring on the bone surface, and is referred to as enostosis (bone island) when in the medullary cavity. The sporadic incidence is 0.4% although in patients with Gardner syndrome the incidence is approximately 24%. There is a male predominance (male to female ratio 2:1). Typically arising on the surface of craniofacial bones (jaws, frontal, nasal sinuses) it may block nasal ducts causing headache pain, or exophthalmos.[3]

Pathology

Histology: a thick mass of mature compact bone with decreased marrow space.

Differential diagnosis

Periosteal osteoblastoma, sessile osteochondroma and parosteal osteosarcoma.

Genetics

Multiple osteomas are characteristic of Gardner syndrome: this autosomal dominant (AD) disorder should also be considered when an osteoma presents in the long bones. Gardner syndrome is a variant of familial adenomatous polyposis.

Prognosis

No reports of malignant transformation. Most osteomas require no treatment and do not recur if excised.

2. **Osteoid osteoma**

Definition, epidemiology and incidence

A benign intracortical bone-forming tumour with a male predilection (3:1) accounting for 10–15% of all primary osseous tumours. Characteristically it presents with night pain, effectively relieved with non-steroidal anti-inflammatory drugs (NSAIDs). The signs vary depending on the site: scoliosis in the spine, limping and joint swelling resembling arthritis when at the end of long bones, and loss of function in the small bones of the hands.

Radiology and pathology

Radiology shows a small lucent nidus, less than 2 cm, with a peripheral area of sclerosis.

Microscopic features are shown in Figure 1. The differential diagnoses include stress fracture, a bone island and osteoblastoma.

Treatment and prognosis

No risk of malignant transformation. Surgical removal, or now more commonly minimally invasive procedures, to ablate the nidus is curative, and results in immediate pain relief.

3. **Osteoblastoma**

Definition, epidemiology and incidence

A benign bone-forming intramedullary tumour although rarely periosteal-based accounting for 1% of all primary osseous tumours. There is a male predilection (2.5:1) and presents most commonly in a child or young adult and less commonly later in life. Pain is localized but in contrast to osteoid osteoma it is not characteristically nocturnal nor does it responds consistently to NSAIDs. Most commonly seen in the axial skeleton, 40% arise in the posterior elements of the spine and sacrum but they can also occur in the metaphysis of long bones most commonly femur and tibia.

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Classification of primary bone tumours

Main groups	Benign	Malignant
Bone-forming tumours	Osteoma	**Central**
	Osteoid osteoma	High-grade central
	Osteoblastoma	• Osteoblastic
		• Chondroblastic
		• Fibroblastic/pleomorphic
		• Telangiectatic
		• Giant cell-rich
		• Small cell
		Low-grade central
		Surface
		• Parosteal
		• Periosteal
		High-grade surface
Cartilage-forming tumours	Enchondroma	Mesenchymal chondrosarcoma
	Osteochondroma	
	BPOP	
	Subungual exostosis	
	Chondroblastoma	
	Chondromyxoid fibroma	
Fibrous/osteofibrous tumours	Non-ossifying fibroma	
	Fibrous dysplasia	
	Osteofibrous dysplasia	
Osteoclast-rich tumours	Aneurysmal bone cyst	Malignant giant cell tumour of bone
	Giant cell tumour of bone	
'Small round blue cell tumours' (non-matrix producing)		Ewing sarcoma
		Lymphoma
Miscellaneous origin	Langerhans cell histiocytosis	Adamantinoma (*transformation of osteofibrous dysplasia*)
		Chordoma (notochordal differentiation)

BPOP, bizarre parosteal osteochondromatous proliferation.

Table 1

Radiology and pathology

Radiographically: an irregular, radiolucent lesion with variable patchy intra-tumoural mineralization. The oedema

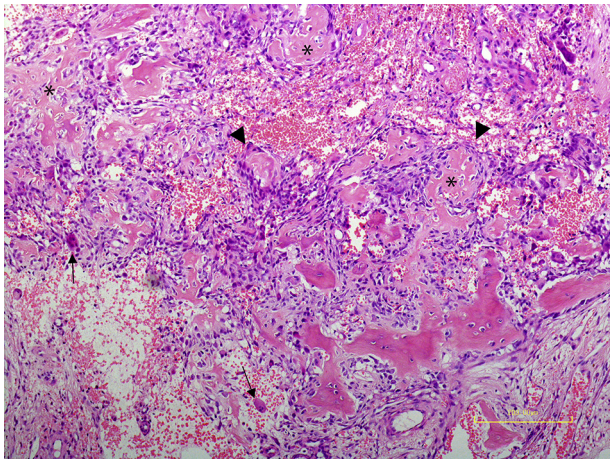

Figure 1 Osteoid osteoma characteristically has a central nidus with anastomosing trabeculae of osteoid (*) and woven bone with prominent osteoblastic rimming (arrow head), set in a loose vascular fibrous background with occasional osteoclasts (arrow).

characteristic on imaging can also be seen associated with Ewing sarcoma, infection. Tumour size varies from 2 to greater than 10 cm. Histologically osteoblastomas are not dissimilar to osteoid osteoma but can generally be distinguished by their size (>2 cm) and their medullary site. Rarely the tumour cells are very atypical when referred to as 'epithelioid', 'bizarre' and 'aggressive' osteoblastomas but the behaviour of such lesions is not different from those with more conventional histology.[3]

Differential diagnosis

Osteoid osteoma, high-grade osteosarcoma, haemangioma.

Treatment and prognosis

No risk of malignant transformation. Complete excision is curative and surgical removal by curettage is the treatment of choice for lesions of the long bone but *en bloc* resection may be required for lesions of the vertebra.

Cartilage-forming tumours

1. **Osteochondroma**

Definition, epidemiology and incidence

Osteochondroma is a benign cartilage-capped bony exostosis with a male predominance (2:1). The marrow in the underlying bone continues directly into the stalk of the exostosis. It is one of

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