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REVIEW ARTICLE

Benign tumours and tumour like lesions of bone

Muhammad Atif, Obada Hussein Ali Hasan, Umair Ashraf, Mohammad Mustafa, Masood Umer

Abstract

Over the last century, there has been a remarkable development in the study of benign bone tumours. This is primarily due to the improved knowledge of the nature of these lesions and improved imaging technology. They present as a diverse group of clinical and pathological entities, which vary in their clinical behaviour and aggressiveness and, hence, multidisciplinary approach is necessary in their management. Combined opinion from an orthopaedic surgeon, radiologist and a pathologist is therefore required. Incidence of these tumours is debatable because they are often asymptomatic. Many protocols have been reported in studies with respect to the management of these tumours based on the experience of different centres and different surgeons with no set guidelines. English-language studies, including case reports, case series and systemic reviews, from PubMed, ERIC, MEDLINE, EMBASE and Cochrane Reviews databases from 2002 to 2016 were included in the current. Articles reporting all levels of evidence — Level I to V — were included.

Keywords: Benign tumours, Tumour like lesions, Bone tumours, Benign tumours of bone.

Introduction

Benign tumours present as diverse groups of clinical and pathological entities. They vary in their clinical behaviour and aggressiveness and, hence, multidisciplinary approach is required in their diagnosis and treatment. This approach consists of a combined opinion from an orthopaedic surgeon, radiologist, pathologist and an oncologist. Mostly these tumours are asymptomatic and hardly impose a difficulty in treating and therefore their incidence is debatable.

World Health Organisation (WHO) has described a nomenclature for tumours and classifies them into seven different categories.³ Group I comprises bone-forming tumours such as osteoma, osteoid osteoma, and osteoblastoma. Group II includes cartilage-forming

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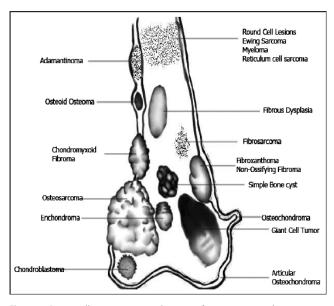


Figure-1: Diagram illustrating common locations of common primary bone tumours. (Redrawn from Radiol Clin North Am 1981; 19 [5].

tumours such as chondroma, osteochondroma, chondroblastoma, and chondromyxoid fibroma. Group III includes giant-cell tumours. Group IV includes marrow tumours. Group V includes vascular tumours such as haemangioma, lymphangioma, and glomus tumour. Group VI includes other connective-tissue tumours such as desmoplastic fibroma, lipoma, and benign fibrous histiocytoma. Group VII includes other tumours such as neunilemmoma and neurofibroma. In addition to these tumours that are classified by the WHO, there are several tumour-like lesions that are similar to these benian tumours. These lesions include solitary bone cyst, aneurysmal bone cysts, osteofibrous dysplasia, myositis ossificans, brown tumour of hyperparathyroidism, and giant-cell granuloma. Enneking classified benign tumours in three stages as follows: stage1, latent; stage 2, active; and stage 3, aggressive.4 We will discuss common tumours (Figure-1).

Bone Forming Tumours

Osteoid Osteoma: It is commonly found in young men in their 2nd or 3rd decades of life but is rarely seen in older patients.⁵ It can be present in any bone (cortical or cancellous) but commonly involves lower extremity with

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Figure-2: Radiograph of osteoid osteoma manifesting as a solitary, well circumscribed tumour associated with sclerotic margin.

femur and tibia. It does not transform into malignancy. High levels of prostaglandins and cyclooxygenase have been reported. Patient presents with pain which is worse at night and relieved by aspirin or non-steriodal anti-inflammatory drugs (NSAIDs). Lesion is located near a joint swelling; stiffness and contracture can occur. Vertebral involvement can result in scoliosis. Plain radiograph is usually diagnostic which shows a lesion (<1.5) with central nidus surrounded by bony sclerosis (Figure-2). Computed tomography (CT) scan is the best diagnostic modality to identify nidus. Technetium shows increased uptake. Magnetic resonance imaging (MRI) is usually not needed, but it reveals surrounding oedema.⁶

Histopathology demonstrates a fibrovascular tissue with immature bone trabeculae surrounded by osteoblast.8 There is no nuclear atypia. Osteoclast and giant cells may be present in the lesion. Treatment options included medical therapy with long-term use of anti-inflammatory medications (spontaneous recovery within 3 to 4 years), percutaneous radiofrequency ablation and open surgical option.⁷

Surgical treatment involved removal of entire nidus by curettage or en-bloc resection (burr down technique is usually preferred). Recurrence rate is less than 10% with power burr.⁸ A new non-invasive radiation-free method is under observation — magnetic resonance guided focussed ultrasound ablation technique — which focuses ultrasound waves on osteoid osteoma.

a. Osteoblastoma: It constitutes less than 1% of bone tumours and occurs in patients between 10 and 30 years of age with male predominance. It mostly involves spine (40-50%).⁹ Pain is the most common complaint having similar behaviour as with osteoid osteoma. In the spine, patient may develop scoliosis or neurological symptoms.

Radiograph shows lesion in posterior element of spine with differential diagnosis including aneurysmal bone cyst and osteoid osteoma.¹⁰ Classically, it represents central nidus with a surrounding radiolucency and reactive sclerosis. Soft tissue extension is found in spinal lesion.

Treatment includes extended curettage or resection. Spinal fusion may be needed in case of instability.¹¹ Radiation therapy can be used in recurrent spinal lesion.¹¹ Some cases of low-grade osteosarcoma are initially misdiagnosed as osteoblastoma. Later on, these lesions develop aggressively and may lead to the death of the patient. Therefore, the patient should be carefully followed up with radiographs of primary site and of chest.

Cartilage-forming tumours

a. Chondroma: They are benign lesions of hyaline cartilage, which is present in all age groups. They can involve any bone but phalanges of hands are the most common sites. 12 Other sites include proximal humerus, distal femur and proximal tibia. Chondroma, which arises from medullary canal, is called enchondroma and if it develops from bone surface, it is referred to as periosteal or juxtacortical chondroma.

Multiple endochondromatosis (Ollier disease) involve large and small tubular and flat bones and are found in epiphysis, metaphysis and shaft. It has a tendency to become malignant. ¹³ By the age of 40 years, 25% patients develop sarcomas. Deformities include shortening (caused by failure of epiphyseal growth), broadening of metaphysis and bowing of long bone. When the disease is associated with haemangiomas of overlying soft tissue, it is called Maffucci syndrome. ¹⁴

Radiograph shows benign nature of disease with irregular intralesional calcification which are referred to as stippled, punctuated or popcorn lesion. There is no associated soft tissue mass but, when present, it is always suggestive of chondrosarcoma. Juxtacortical chondroma are small lesions of less than 3cm in size and well-defined saucer shaped defect with underlying sclerotic cortex. Plain radiograph is usually diagnostic but CT scan reveals endosteal erosions indicative of chondrosarcoma.

Microscopic examination shows mature hyaline cartilage. Enchondroma of hand, juxtacortical lesion and multiple enchondromatosis may present with atypia and hypercellularity which are commonly found in malignant lesions. Hence on microscopic examination it is difficult to distinguish between benign and malignant cartilage lesions. ¹⁵ Mostly these tumours are diagnosed by clinical and radiological examination rather than microscopic

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features.

Treatment of asymptomatic patients having a solitary lesion is observation and follow-up with radiographs. If the patient develops symptoms or tumour grows, then extended curettage is recommended. In case of multiple enchondromas, patients should be monitored for malignancy and deformities should be corrected by appropriate osteotomies.

b. Chondroblastoma: It is a rare lesion comprising 1% of all primary bone tumours, commonly occurring at epiphyses or apophyses of long tubular bones (distal femur, proximal humerus and tibia). ¹⁶ Typically it presents in patients 10-25 years old with male predominance (2:1). ¹⁶ Patient frequently complains of progressive pain at the site of the lesion.

Radiograph (Figure-3) represents well circumscribed centrally located lesion in epiphyses or apophyses with matrix calcification (30-50%) and surrounding reactive bone.¹⁷ CT scan shows areas of calcification which are not



Figure-3: Radiograph demonstrating a well circumscribed solitary lytic lesion on the epiphysis of distal femur.

detectable on plain radiograph. Biopsy reveals sheets of chondroblast with background of chondroid matrix. Cells are round to polygonal with prominent cytoplasmic architecture.¹⁷ Dystrophic calcification is present in the form of chicken wire appearance.

Treatment includes extended curettage and bone grafting or cement placement. Recurrence rate is 10-20% with the same treatment as primary lesion. Resection is recommended for benign pulmonary metastasis which occurs in 1% of cases. 18



Figure-4: Radiograph displaying irregular lesion appearing as an irregular cartilaginous cap in distal femur.

c. Osteochondroma: It is typically found as a mass projecting as a stalk out of underlying bone. It is developed within periosteum as a cartilaginous nodule (producing cartilaginous cap) which is responsible for the lesion. Their growth usually stops with skeletal maturity. It commonly arises from metaphysis near physis and involves distal femur, proximal tibia and proximal humerus. It remained asymptomatic or presented with symptoms due to pressure on surrounding tissue. Intraarticular epiphyseal osteochondroma with multiple joints involvement is called Trevor disease.¹⁹

Osteochondroma is usually asymptomatic but can produce mechanical symptoms, neuropathies due to pressure affect and clinically as a mass. It can present as a painful lesion due to fracture. Multiple hereditary exostoses are autosomal dominant disorders with exostosin (EXT1 and EXT2) gene mutations.²⁰ Many exostoses were found in this condition resulting in growth disturbance in the form of abnormal tabulation of bones, blunting of metaphysis, radius bowing, shortening of ulna with ulnar deviation of hand. About 5-10% of osteochondromas occur as solitary lesions commonly involving men.

Plain radiograph is sufficient to make diagnosis which shows irregular cartilaginous cap with irregular calcification which can be as thick as 2cm in children (Figure-4) Sometimes CT scan and MRI are helpful for diagnosis. Sometimes biopsy is needed for diagnosis. Malignant change occurs in 1% of solitary tumours.

Surgical treatment is indicated when there is recent increase in size, while pressure symptoms are suspicious

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of malignancy. It includes en-bloc resection with removal of cartilaginous cap.

Giant Cell Tumour (GCT)

It is an aggressive lesion and presents as 5% of all bone tumours with slight female predominance in ages between 20 and 40 years old.²² Common location is distal femur proximal tibia and distal radius. Spinal and pelvis involvement is rare. It is usually found as solitary lesion but can be presented with synchronous or metasynchronous lesion in 1-2% of cases. About 3% of diagnosed cases of GCT have pulmonary metastasis with mortality rate of 15%.²²

Malignant GCTs comprise less than 5% of bulk of disease and can be primary or secondary. Secondary GCTs are sarcoma resulting from radiation of primary site. Patient usually presents with pain or pathological fracture (10-30% cases).²²

Radiograph is diagnostic with presence of eccentrically located lytic epiphyseal lesion abutting subchondral bone. MRI is helpful in determining the extent of lesion within bone and involvement of soft tissues. It represents dark on T1-weighted images and bright on T2-weighted images. Aneurysmal bone cyst is present in 20% of GCTs and is easily picked up by identification of fluid filled levels.

Histology reveals many multinucleated giant cells (40 to 60 nuclei per cell) in areas of mononuclear stroma.²³ Nuclei of giant cells and mononuclear cells are identical. Some areas of reactive bone formation, foamy macrophages and spindle cells formation are present.

Treatment consists of extended curettage with recurrence of 5-15%.²⁴ Adjuvant treatment with liquid nitrogen, phenol, bone cement, electrocautery, an argon beam coagulation and bisphosphonate can be used to prevent recurrence.^{25,26} Various treatment modalities are helpful to deal with defects, including autografts, allograft, artificial bone graft substitute or bone cement (methyl methacrylate cement). En-bloc wide resection may be needed in some stage 3 tumours and those with local recurrence.²⁴ For inoperable spine or pelvis tumours, embolisation or irradiation can be used. Recently denosumab is used to treat unresectable disease. Patient should be followed for recurrence.

Tumour-like Lesions Fibrous Lesions

Nonossifying Fibroma: Nonossifying fibroma commonly involves metaphysis of long bones and consists of 40% in distal femur, 40% in tibia with 10% in fibula.²⁷ It is usually found in children as incidental finding between 02-20



Figure-5: Eccentric geographic lesion with a sclerotic margin; a healing nonossifying fibroma is present in proximal tibia.

years of age. Mostly it is asymptomatic and disappears in childhood. Well-defined lobulated lesion with ridges in bony wall and cortical erosions appear on radiograph (Figure-5) which is eccentrically located at metaphysis.²⁷

Microscopic examination reveals spindle shaped cells arranged in whorled shaped manner with fibroblastic proliferation and increased cellularity. Curettage is advised of lesion when it involves greater than 50% diameter on the diseased bone.

Fibrous Dysplasia: In fibrous dysplasia, normal bone and marrow is replaced by fibrous tissue and woven bone in the form of spicules. It is a developmental anomaly which may occur in a monostotic or polyostotic form.^{28,29} It can involve any part of bone, including epiphysis, metaphysis or diaphysis, and may present associated with other abnormalities like intramuscular myxoma, skin pigmentation, sexual precocity and thyroid abnormalities.

Different syndromes are associated with fibrous dysplasia. McCune-Albright syndrome consists of polyostotic fibrous dysplasia, cutaneous pigmentation and endocrine abnormalities. Mazabraud syndrome involves polyostotic fibrous dysplasia and intramuscular myxomas.²⁸

Radiograph shows a lucent area with ground glass appearance surrounded by sclerotic rim.²⁹ Sometimes biopsy is recommended for diagnosis. On microscopy, it appears as spicules of irregular woven bone having fibrous stroma with some cartilaginous metaplasia and cystic benign changes.

Surgical treatment is needed in case of significant pain, deformity and pathological fracture. Recurrence rate is

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higher. Recent studies show bisphosphonate therapy is beneficial for these patients.²⁸

Cystic Lesions

Unicameral Bone Cyst: It is commonly seen in children; 85% in the first two decades of life. It starts in metaphysis and mostly present proximal humerus and femur but in adults ileum and calcaneum are common sites.³⁰ It is asymptomatic but can present with a fracture. It heals spontaneously at maturity.

Plain radiograph shows a multiloculated lytic, centrally located lesion with proper margins but it never penetrates the cortex.^{31,32} Fallen fragment sign with a fracture is a pathogonomic of unicameral bone cyst. Pathogenesis revealed a metaphyseal remodelling defect inhibits drainage of interstitial fluid which increases pressure causing bone necrosis and cyst formation. Cyst filled with yellow serous fluid and containing many mediators, like cytokines, interleukins, prostaglandins and metalloproteinase, enhances bone resorption. Histology reveals cyst wall is formed by fibrous membrane consisting of fibroblast with underlying fibrovascular tissues, fragments of immature bone mesenchymal cells and sometimes lymphocytes.³²

Treatment options vary, depending upon disease presentation, including observation, curettage (with or with bone grafting and fixation), aspiration and injection (corticosteroids, bone marrow aspiration, dematerialised bone matrix).

Aneurysmal Bone Cyst: It is commonly found in proximal humerus, distal femur and proximal tibia and posterior element of spine but any bone could be affected by the disease up to 20 years of life with female predominance.³³ Patient presents with mild to moderate pain at the site of the lesion. Spinal lesions can appear as a cause of neurological deficit or radicular pain.

Radiograph shows expansile lytic lesion with well-defined margins and eccentrically located at metaphysis surrounding by a thin cortical layer.³³ Sometimes it represents a permeative lesion mimicking a malignancy. Diffused or peripheral tracer uptake is seen with a central area of decreased uptake and usual finding on bone scan. CT scan is helpful in localising lesion in area of complex anatomy like pelvis and spine.³² MRI shows multiluculated cavities and fluid levels. Presence of double density fluid level and intralesional septations differentiate it from unicameral bone cyst.

Histopathology is demonstrated by the presence of haemorrhagic tissues and cavernous spaces separated by cellular stroma. Cavity is lined by fibroblasts and histiocytes with presence of haemosiderin laden macrophages, inflammatory cells and multinucleate giant cells.³⁴

Treatment consists of extended curettage and bone grafting with a bone graft substitute or cementing. Lowdose irradiation (slight risk of malignant transformation) and arterial embolisation can be considered a definitive treatment in inaccessible areas like pelvis and spine. Recurrence rate is 10-20% and treatment is the same as for primary lesion.^{33,35}

Bone Island: It is a lesion of cancellous bone, also called enostois. It is usually asymptomatic and is found incidentally. It can be present in any bone, but pelvis and femur are common sites. Plain radiograph is sufficient to make diagnosis. It appears as a small round or oval area of increased homogenous density in cancellous bone with no periosteal reaction and bony destruction. CT scan represents thickened trabeculae which merge with normal bone. MRI presents an isointense lesion to cortical bone with no surrounding oedema and shows low signal on T1 and T2-weighted image.

Histopathology reveals mature bone with thickened trabeculae which merge with normal bone at periphery. Conservative treatment is recommended with observation with serial radiographs. In case of static lesion, no further intervention is needed. If the lesion increases in size or the patient develops pain, biopsy is needed to rule out aggressive lesions like blastic metastasis, sclerotic myeloma or sclerosing osteosarcoma.

Conclusion

Benign tumours are frequently occurring neoplastic conditions which are present in all age groups but commonly affect young population. Most are asymptomatic but can present with pain or pathological fracture. These lesions are commonly diagnosed with plain radiographs. CT scan and MRI may be used to delineate anatomy and extent of soft tissue involvement. Treatment ranges from conservative to en-bloc resection, including extended curettage. Aggressive tumours like GCT should be closely followed up for recurrence and metastasis.

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