Bone Tumours

Bone tumours include both benign and malignant lesions:

- Benign lesions may cause pain, expansion into local structures, joint dysfunction and predispose to pathological fractures.
- Secondary malignant tumours are much more common than primary malignant bone tumours.

Classification

Benign

- Bone: osteoid osteoma.
- Cartilage: chondroma, osteochondroma.
- Fibrous tissue: fibroma.
- Bone marrow: eosinophilic granuloma (see separate article Langerhans' Cell Histiocytosis).
- Vascular: haemangioma.
- Uncertain: giant cell tumour.

Malignant

- Bone: osteosarcoma.
- Cartilage: chondrosarcoma.
- Fibrous tissue: fibrosarcoma.
- Bone marrow: Ewing's sarcoma\(^1\), myeloma.
- Vascular: angiosarcoma.
- Uncertain: malignant giant cell tumour.

Benign bone tumours

Osteoid osteoma

- Usually less than 1 cm in diameter and surrounded by dense osteoid.
- Often occurs in young adults.
- Most common sites are the tibia, femur and vertebrae.
- Presents with pain, which is often worse at night and relieved by non-steroidal anti-inflammatory drugs.
- X-ray has the characteristic appearance of a radiolucency surrounded by dense bone.
- Local excision is curative.

Osteochondroma

- One of the most common benign bone tumours.
- Sessile or pedunculated lesions arising from the cortex of a long bone adjacent to the epiphyseal plate.
- Lesions can be single or multiple.
- Often presents in adolescence as cartilaginous overgrowth at epiphyseal plate.
- Grows with the underlying bone.
- Presents as a painless lump or occasionally joint pain.
- Excision should be considered if it is causing significant symptoms.
- Problems include nerve compression (especially peroneal nerve), ankle diastasis and angular deformities. Malignant transformation to low-grade chondrosarcoma is more common with multiple osteochondromas and more proximal lesions.
Multiple hereditary exostosis is an autosomal-dominant disorder with a mild decrease in stature, normal intelligence and multiple osteochondromas. It is commonly accompanied by leg length discrepancy, knee and elbow angular deformities and other skeletal abnormalities.

**Chondroma**
- Lesions may be single or multiple (*Ollier's disease*).
- Appears in tubular bones of the hands and feet.
- X-ray shows a well-defined osteopenic area in the medulla.
- Lesion should be excised and bone grafted.

**Giant-cell tumour (osteoclastoma)**
- Represents about 20% of primary bone tumours.
- Aggressive, locally recurrent tumour with a low metastatic potential.
- Found in the sub-articular cancellous region of long bones. Most lesions occur in closed epiphyses around the knee joint and distal radius.
- Only occurs after closure of epiphyses.
- Patients are usually aged between 20 and 40 years. It is more common in females.
- X-ray shows an asymmetric rarefied area at the end of a long bone.
- Cortex is thinned or even perforated.
- Treatment is by local excision and grafting often leads to recurrence.
- The treatment of choice is wide excision and joint replacement.
- Amputation if there is malignant or recurrent tumour.

**Chondroblastoma**
- Rare, normally in epiphysis of long bones - eg, the hip, shoulder and knee.
- Usually presents at age 10-19 years with pain in the joint, muscle atrophy and tenderness.
- Treatment is with curettage and bone grafting.

**Osteoblastoma**
- Locally destructive progressive lesion commonly found in vertebrae.
- Usually presents with dull aching pain.
- Frequently needs biopsy to exclude malignancy.
- Treatment is with curettage/bone grafting or en bloc excision.

**Fibromas**
- These occur in 40% of children aged >2 years.
- Usually asymptomatic.
- Usually no treatment is required, except when it occupies >50% bone diameter when there is a need for curettage/bone grafting to avoid pathological fracture.

**Unicameral bone cysts**
- Fluid-filled lesion. It is rare before the age of 3 years and after skeletal maturity.
- They usually present as pathological fractures (asymptomatic before then) following relatively minor trauma, normally involving the proximal humerus or femur.
- Treatment is to allow a fracture to heal and then aspirate and inject with either methylprednisolone or bone marrow.

**Aneurysmal cyst**
- Usually present before the age of 20, with pain and swelling.
- They are cavernous spaces filled with blood and solid lumps of tissue.
- They mainly affect the femur, tibia and spine, which may lead to cord or nerve root compression resulting in neurological symptoms.
- They grow rapidly and may be confused with malignancy.
- Treated with curettage/bone grafting or excision.
- There is recurrence in 20-30%, usually in the first 1-2 years after treatment and mainly in younger children.
Fibrous dysplasia
- Fibrous replacement of cancellous bone - may be multiple or solitary, stable or progressive.
- Usually asymptomatic but, if involving the skull, may cause swelling or exophthalmos.
- Femoral involvement causes pain and a limp. May also cause limb length discrepancy, bowing and pathological fractures.

Osteofibrous dysplasia
- Presents in children aged 1-10 years.
- Usually involves the tibia with anterior swelling or enlargement of the leg. Usually painless.
- Treatment is with excision and bone grafting, delayed until after the age of 10 years because of the high risk of recurrence if younger.

Eosinophilic granuloma
- Most common in boys aged 5-10 years; usually occurs before the age of 30.
- Most often affects the skull with local pain and swelling, marked tenderness and warmth in the area.
- Treatment is with curettage/bone grafting, low-dose radiotherapy or steroid injection.

Malignant bone tumours

Osteosarcoma
- The most common primary bone malignancy in children.\(^2\) The incidence is highest in 15-19 year olds - 0.8-1.1/100,000/year.\(^3\)
- The male:female ratio is 1.4:1.
- In later life, it is seen associated with Paget's disease of bone.
- Occurs in the metaphyses of long bones. The most common sites are around the knee (75%) or proximal humerus.
- Often presents as a relatively painless tumour.
- Destroys bone and spreads into the surrounding tissue. Rapidly metastasises to the lung.
- X-ray shows combination of bone destruction and formation. Soft tissue calcification produces a 'sunburst' appearance.
- Disease-free survival has increased to 55-75% with surgery and effective chemotherapy.\(^4\) Chemotherapy alone is not as effective.
- Pulmonary metastases are particularly problematic and are associated with a poorer prognosis.

Ewing's sarcoma
- This is a primitive neuroectodermal tumour (PNET) thought to arise from mesenchymal stem cells. Ewing's sarcoma is rare, affecting around 30 children per year in the UK.\(^3\) It is diagnosed in white Caucasians under the age of 25 at an incidence of 0.3/100,000 per year.\(^3\) It is very uncommon in the African and Asian population. The median age at diagnosis is 15 years and there is a male predilection of 1.5:1. The condition is extremely rare over the age of 40.\(^5\)
- It usually presents as a mass or swelling - most commonly in the long bones of the arms and legs, pelvis or chest but also in the skull and flat bones of the trunk. Other symptoms and signs include pain in the area of the tumour, redness in the area surrounding the tumour, malaise, anorexia, weight loss, fever (a poor prognostic sign), paralysis and/or incontinence if affecting the spine, and numbness or tingling as a result of nerve compression by the tumour.
- Investigations:
  - X-ray of the affected bone shows bone destruction with overlying onion-skin layers of periosteal bone formation.\(^6\)
  - Biopsy of the tumour site is used for diagnosis.
  - Molecular pathology techniques can be used on fresh, frozen formalin-fixed paraffin-embedded tissues.\(^7\)
  - FBC and lactic dehydrogenase (LDH) measurement - anaemia and raised LDH levels at diagnosis suggest the presence of metastases and are an indication of a poor prognostic outcome.\(^8\)
  - CT/MRI scanning is used to assess the extent of disease and the local structures involved.
  - Bone scintigraphy is useful in identifying metastases and assessing response to treatment.
Staging of the tumour is undertaken to determine the treatment and also give some indication of the likely prognosis. 

- **Stage IA** - low-grade tumour found only within the hard coating of the bone.
- **Stage IB** - low-grade tumour extending locally into the soft tissues.
- **Stage IIA** - high-grade tumour found only within the hard coating of the bone.
- **Stage IIB** - high-grade tumour extending locally to the soft tissues.
- **Stage III** - low- or high-grade tumour which has metastasised.

The family of a child with Ewing's sarcoma will require long-term support from a number of professionals in both primary care and the hospital setting. It is important that all members of the family know where to access information, support and practical help when required and it is vital that there is good communication between all professionals involved in the care of the child.

Chemotherapy is usually the first line of treatment and is currently initiated using a combination of vincristine, ifosfamide, doxorubicin and etoposide (VIDE). The treatment usually takes the form of six courses of treatment at intervals of three weeks, following which further management decisions will be based partly on the response to treatment. Further courses of chemotherapy using different combinations of drugs are generally used following surgery or radiotherapy.

Radiotherapy may be used in conjunction with surgery and/or chemotherapy. Radiotherapy may occasionally be used in place of surgery where removal of the bone is not possible - eg, in the spine. Some patients are treated with radiotherapy alone but one trial suggests that there is a higher rate of treatment failure and relapse compared to surgery.

Peripheral blood stem cell harvest may be undertaken midway through chemotherapy. The recovered cells are stored in case of future need following further courses of chemotherapy. Allogenic stem cell transplantation may offer a way forward in refractory metastatic patients.

Surgery is often required to remove the tumour. Limb-sparing surgery, where only a part of the bone is removed and replaced if necessary with a segment of prosthetic bone, is increasingly carried out, although amputation of the limb may be required if the tumour is affecting one of the long bones of the arm or leg. Physiotherapy ± prosthetic limb fitting may be required following surgery.

The overall five-year survival rate for Ewing's sarcoma is 50%. When chemotherapy, radiotherapy and surgery are combined, survival is approximately 60-70% for localised tumours and around 20-40% for disease that has metastasised.

**Chondrosarcoma**

- Chondrosarcoma is one of the most frequently occurring bone sarcomas of adulthood. The incidence is about 0.1/100,000 per year. They most commonly present at between 30 and 60 years of age. Males and females are equally affected.
- They may arise from pre-existing lesions (osteochondromas, chondromas) or they can be primary.
- They are usually associated with dull, deep pain.
- Radiographs may show invasiveness and soft tissue extension.
- Occurs in two forms:
  - Central: tumour in the pelvis or proximal long bones.
  - Peripheral: tumour in the cartilaginous cap of an osteochondroma.
- They tend to metastasise late.
- Wide local excision is often possible.

**Spindle cell sarcomas**

- These are a mixed group of malignant tumours including fibrosarcoma, malignant fibrous histiocytoma (MFH), leiomyosarcoma and undifferentiated sarcoma.
- They present between 30-60 years of age and men are more frequently affected than women.
- They are usually found in the metaphysis of long bones, present with pain and have a high incidence of fracture at presentation.

**Metastatic tumours**

- The most common bone malignancies are metastatic carcinomas.
- They are usually multiple but may be solitary.
- The most common primaries are breast, prostate, lung, kidney and thyroid.
- Wilms' tumour and neuroblastoma are the most common metastatic lesions in childhood.
Epidemiology

- Primary malignant bone tumours are rare.
- Secondary tumours are more common, especially in the elderly.

Presentation

- Most present with pain, swelling and localised tenderness.
- Rapid growth and erythema are suggestive of malignancy.
- They may cause pathological fractures.

Investigations

- Plain X-ray.
- MRI and CT scan.
- Bone scan.
- Biopsy.
- Investigation of any occult primary lesion, especially breast, prostate, lung, kidney and thyroid.

Management

- There may be considerable difficulty recognising tumours as malignant in non-specialised centres; therefore, all patients with a suspected primary malignant bone tumour should be referred to a bone sarcoma reference centre or an institution belonging to a specialised bone sarcoma network before biopsy.\[3\]
- As malignant primary bone tumours are rare and management is complex, the accepted standard is treatment either in reference centres or within networks able to provide access to the full spectrum of care or shared with such centres within reference networks.

Pathological fractures

- If there is an existing pathological fracture in a possible primary malignant bone tumour, there is potential for dissemination of tumour cells into surrounding tissues which may increase the risk of local recurrence. In these patients there may be a strong case for immobilising the part following the biopsy, usually by application of an external splint.
- Internal fixation is contra-indicated, as it disseminates tumour further into both bone and soft tissues and also increases the risk of local recurrence. External splintage is recommended, along with appropriate pain control.

Follow-up

The purpose of follow-up is to detect either local recurrence or metastatic disease early enough that treatment is still possible and might be effective. It should include physical examination, imaging of the site and CXR or CT scan.

After completion of chemotherapy, patients should be seen every 6 weeks to 3 months for the first 2 years, every 2-4 months for years 3 and 4, every 6 months for years 5-10 and thereafter every 6-12 months according to local practice.\[3\]

Further reading & references

- Bone health in cancer patients - ESMO clinical practice guidelines; European Society for Medical Oncology (2014)
- Sarcoma; NICE Quality Standard, January 2015
- Denosumab for the prevention of skeletal-related events in adults with bone metastases from solid tumours; NICE Technology/Appraisal Guidance, October 2012
3. Bone sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up; European Society for Medical Oncology (2010)
9. The stages of bone cancer; Cancer Research UK
10. Ewing's sarcoma in children; Macmillan Cancer Support

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