Bone Tumours - a synopsis

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SpR in Histopathology
QAH 2009
Aims

• General approach to diagnosis
• Common entities….and not so common ones.

• Mini – quiz…
Challenge of bone tumour diagnosis

- Bone tumours are relatively rare
- Precise incidence is not known
- Cause of most tumours is unknown
- Symptoms are most often non-specific

Close interaction needed between surgeon, pathologist and radiologist in diagnosis.
A general approach to diagnosis

- Clinical symptoms
- **Age** of patient
- **Location** of lesion
- Extent of lesion
- Solitary/multiple
- Radiographic appearance
Clinical symptoms

• Most often non-specific
  – Pain
  – Swelling
  – Pathological fracture

• Specific
  – Pain relieved by aspirin – osteoid osteoma

• Misleading
  – Fever and raised ESR – Ewing tumour
Age

- Children
  - High grade sarcomas
eg. Ewing tumour and osteosarcomas

- Adults
  - Low-grade sarcomas
eg. chondrosarcoma
Location, Site, Extent

- Epiphysis
- Metaphysysis
- Diaphysysis

- Axial skeleton, long bones, small bones

- Solitary vs multifocal.
Round cell lesions:
- Ewing sarcoma
- Histiocytic lymphoma
- Myeloma

Diaphysis:
- Adamantinoma
- Osteoid osteoma
- Chondromyxoid fibroma
- Fibrous dysplasia
- Fibrosarcoma
- Fibrous cortical defect
- Bone cyst
- Osteochondroma
- Aneurysmal bone cyst
- GCT

Metaphysis:
- Osteosarcoma
- MFH
- Enchondroma

Epiphysis:
- Chondroblastoma
Radiographic appearance

- **Benign**
  - Well-circumscribed
  - Sclerotic rim
  - Periosteal reaction
    * Thick regular new bone.

- **Malignant**
  - Poorly circumscribed
  - Destructive pattern
    * Geographic
    * Permeative (motheaten)
  - Periosteal reaction
    * Multiple layers of poorly organised new bone
Classification of primary bone tumours


- Haematopoietic (40%)
- Chondrogenic (22%)
- Osteogenic (19%)
- Unknown origin (10%)
- Histiocytic origin
- Fibrogenic
- Notochordal
- Vascular
- Lipogenic
- Neurogenic
## Classification of primary bone tumours


<table>
<thead>
<tr>
<th>Histological Type</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haematopoietic (40%)</strong></td>
<td></td>
<td>Myeloma</td>
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<tr>
<td></td>
<td></td>
<td>Malignant lymphoma</td>
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<tr>
<td><strong>Chondrogenic (22%)</strong></td>
<td>Osteochondroma</td>
<td>Chondrosarcoma</td>
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<tr>
<td></td>
<td>Chondroma</td>
<td>Dedifferentiated chondrosarcoma</td>
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<tr>
<td></td>
<td>Chondroblastoma</td>
<td>Mesenchymal chondrosarcoma</td>
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<tr>
<td></td>
<td>Chondromyxoid fibroma</td>
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<td><strong>Osteogenic (19%)</strong></td>
<td>Osteoid osteoma</td>
<td>Osteosarcoma</td>
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<td></td>
<td>Osteoblastoma</td>
<td>Parosteal osteosarcoma</td>
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<tr>
<td><strong>Unknown origin (10%)</strong></td>
<td>Giant cell tumour</td>
<td>Ewing tumour</td>
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<td>Giant cell tumour</td>
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<td>Adamantinoma</td>
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</table>
### Classification of primary bone tumours


<table>
<thead>
<tr>
<th>Histocytic origin</th>
<th>Fibrous histiocytoma</th>
<th>Malignant fibrous histiocytoma</th>
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</thead>
<tbody>
<tr>
<td>Fibrogenic</td>
<td><em>Metaphyseal Fibrous defect (non-ossifying fibroma)</em></td>
<td>Desmoplastic fibroma Fibrosarcoma</td>
</tr>
<tr>
<td>Notochordal</td>
<td></td>
<td>Chordoma</td>
</tr>
<tr>
<td>Vascular</td>
<td>Haemangioma</td>
<td>Angiosarcoma Haemangiopericytoma</td>
</tr>
<tr>
<td>Lipogenic</td>
<td>Lipoma</td>
<td>Liposarcoma</td>
</tr>
<tr>
<td>Neurogenic</td>
<td>Neurilemmoma</td>
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Most common neoplasm of bone

Lytic lesion composed of plasma cells
Myeloma

- Accounts for almost half of all bone neoplasms.
- Most frequent symptoms: bone pain, weight loss and fatigue.
- May present with pathological # or spinal compression.
- Hypercalcaemia, anaemia, increased ESR
- Monoclonal protein in serum & urine
- Xray: multiple punched-out purely lytic lesions
Differential diagnosis of MM

- Osteomyelitis
- Metastatic carcinoma
- Malignant lymphoma
Lymphoma of bone – permeative destructive process
Rare small blue cell tumour of bone
Ewing Tumour (sarcoma)

- 6% of all malignant bone tumours
- Most cases in 20s
- Slight male predominance
- Usually long bones
- Fever, pain, swelling,
- Anaemia, ESR
>Extensive lesion
>Involving shaft
>Permeative destructive lesion
>Periosteal new bone formation

“onion skin appearance”
Cytogenetic diagnosis of ET

• 90% of Ewing tumour have \( t(11;22)(q24;12) \) translocation

• EWS gene on chromosome 22

• FLI-1 gene on chromosome 11

• 10% have \( t(21;22)(q22;12) \) translocation

• ERG gene on chromosome 21
EWING TUMOUR

PERIPHERAL NEUROECTODERMAL TUMOUR (PNET)

CLINICAL FINDINGS
MORPHOLOGY
IMMUNOPROFILE
CYTOGENETICS
Most common **benign** tumour of bone
Osteochondroma

- Young patients
- Distinct male predominance
- Metaphysis of long bones
- Some develop secondary overlying bursa
• Thickened cartilage cap
• Matures via endochondral ossification

• Solitary exostoses similar –
• Multiple hereditary exostoses result from EXT1 EXT2 mutations
Benign cartilaginous neoplasms of bone

Chondroma

- Enchondroma (intramedullary)

- Enchondroma of small hands and feet

- Periosteal chondroma

- (Soft tissue chondroma)
Enchondroma

Most asymptomatic
True incidence not known
No sex or age predilection

Microscopically hypocellular
Abundant uniform blue matrix
*No cytological atypia*
*No myxoid change*
*No cystification*
Enchondromas of hands and feet

• Radiography shows thinning of cortex – but not sign of malignancy unless soft tissue infiltrated!

• Tumour is hypercellular

• Differentiation of enchondroma from low-grade chondrosarcoma can be difficult.
CHONDROBLASTOMA

- Well circumscribed
- Expansile
- Epicenter in epiphysis
- Extend to metaphysis
- Sclerotic border
- Ends of long bones
• Benign
• Patients in second decade
• Slight male predom.
• May show areas of aneurysmal bone cysts.

Pulmonary metastases occur – rarely.

CHONDROBLASTOMA
Differential diagnosis of chondroblastoma

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<tr>
<th>Chondromyxoid fibroma</th>
<th>Chondrosarcoma</th>
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<tbody>
<tr>
<td>• Occur in metaphysis</td>
<td>• Aggressive x-ray appearance</td>
</tr>
<tr>
<td>• Scalloped rim on xray</td>
<td>• Lobulated appearance</td>
</tr>
<tr>
<td>• Lobulated appearance</td>
<td>• Cytological atypia</td>
</tr>
<tr>
<td>• Rare</td>
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</table>
Chondromyxoid fibroma

- Rare
- Occur in 20s & 30s
- Involve metaphysis of long bones
- Histological similarity to chondroblastoma in some cases
CHONDROSARCOMA

- 3rd most common malignant tumour of bone
- Subtypes:
  - Conventional Chondrosarcoma
  - Chondrosarcoma of small bones
  - Secondary Chondrosarcoma
  - Clear cell chondrosarcoma
  - Dedifferentiated chondrosarcoma
  - Periosteal chondrosarcoma
  - Mesenchymal chondrosarcoma
Conventional chondrosarcoma

- Shoulder and pelvic girdle frequent sites
- Most cases in 40s to 60s
- Symptoms non-specific – usually pain

- Characteristic gross appearance: blue/white myxoid tumour with white gritty areas
- Erodes through cortex and forms soft tissue mass
Grade 1 to grade 3 Chondrosarcoma
Secondary Chondrosarcoma

- Arise in pre-existing conditions;
  - Exostoses (multiple and single)
  - Chondrodysplasias

*Diagnosis can be difficult*

- Radiographic and gross features important
  - Thickness of cartilage cap (>1cm)
  - Myxoid change
  - Permeation into surrounding tissue
Dedifferentiated chondrosarcoma
Osteosarcoma

Malignant tumour in which osteoid or bony matrix is produced by tumour cells

- Osteosarcoma within bone
- Surface osteosarcoma
Osteosarcomas arising within bone

- Conventional osteosarcoma
  - Osteoblastic
  - Chondroblastic
  - Fibroblastic
- Small cell osteosarcoma
- Telangiectatic osteosarcoma
- Low-grade central osteosarcoma
- Osteosarcoma in Paget’s disease
- Post-irradiation osteosarcoma
- Osteosarcoma in other precursors
Surface Osteosarcoma

- Parosteal osteosarcoma (juxtacortical)
- Periosteal osteosarcoma
- High-grade surface osteosarcoma
Conventional Osteosarcoma

Long bones
Predominantly metaphyseal
Mixed lytic and sclerotic appearance
Extensive geographic destruction

High grade malignant tumour of adolescents and young adults
Male predominance
Tumour destroys cortex and lifts up periosteum – results in reactive new bone formation in between –

‘CODMAN’S TRIANGLE’
Soft tissue extension of osteosarcoma
Gross appearance is variable depending on type

Typical 'Fish flesh appearance'

(Heavily mineralised or obviously cartilaginous)
Microscopic appearances of Osteosarcoma

Osteoblastic Osteosarcoma
(50% of conventional osteosarcomas)

Chondroblastic osteosarcoma
(25% of conventional osteosarcomas)
**Sarcoma in Paget’s disease**

Small risk

Usually high grade

Can be:

- osteosarcoma
- fibrosarcoma
- malignant fibrous histiocytoma
osteosarcoma

- metastasise to lungs
- 5yr survival with modern chemo - 50-60%
- Pre-op chemo decreases incidence of amputation
Benign osteogenic tumours

- Osteoid osteoma
  - rare

- Osteoblastoma
  - marked male predominance

- Osteoma
Osteoid osteoma

- Limited growth potential
- Males usually in their second decade of life
- **Pain** – severe, worse at night, dramatically relieved by aspirin.
- Usual site: metaphysis or shaft of long bones
Osteoid osteoma

Typical radiological appearance

- Extremely well circumscribed
- No permeation
- Associated with extensive area of sclerosis
- Nidus radiolucent with sclerotic rim
- Tends to involve cortex not medulla
Typical gross appearance of osteoid osteoma

Nidus composed of irregular thin trabeculae of bone rimmed by numerous osteoblasts
Osteoblastoma

• Histologically *indistinguishable* from Osteoid osteoma…but differs in that:
  
  – One-quarter as common
  – Predilection for spine
  – May be painful
  – Radiographic appearance non-specific
  – May show aggressive features
Tumours of unknown origin

- Benign giant cell tumour
- Malignancy in giant cell tumour
- Adamantinoma of long bones
Giant cell tumour of Bone
Definite female predilection
Adults in 3rd- 4th decade

Majority occur in ends of long bones
In order of frequency:
- Distal femur
- Proximal tibia
- Distal radius
- Sacrum
GCT – purely lytic lesion
Poorly defined extending to the ends of the bone

Malignant tumour cannot be excluded on radiographic appearance
Mimics of bone neoplasms

- Metastatic carcinoma
- Simple cysts
- Aneurysmal bone cysts
- Fibrous dysplasia / osteofibrous dysplasia
- Metaphyseal fibrous defect
- Fracture callus
- Myositis ossificans
- Subungual exostosis
- Bizarre parosteal osteochondromatous proliferation
- Osteomyelitis
- Langerhans cell histiocytosis
- Chest wall hamartoma
- Fibrocartilaginous mesenchymoma
Grading and staging

- The Enneking et al system (1980)
  - Grade (cytological differentiation)
  - Anatomic location (compartments)

- Stage I: Low grade
- Stage II: High grade
- Stage III: Distant metastases evident
  - A: tumour confined to one compartment
  - B: tumour involves more than one compartment
Mini quiz
CASE 1

17 YEAR OLD MALE
INCREASING PAIN OVER LEFT UPPER ARM OF 3 MONTH DURATION
RECENT ONSET LOW GRADE FEVER
O/E – TENDER AND SOFT TISSUE SWELLING OVER LEFT HUMERUS
Ewing tumour
Case 2

- 20 year old male
- Painless hard subcutaneous mass in popliteal fossa
- Present for several years with no change in size.
osteochondroma
Case 3

- 13 year old pain
- Knee pain after rugby tackle
- Pain worse at night and at rest

- o/e tibial mass with soft tissue swelling
CONVENTIONAL OSTEOSARCOMA
Case 4

- 40 year old female
- Increasing pain in wrist
- Normal Ca, Phosphate and Alk phosph
Giant cell tumour of bone
60 YEAR OLD MALE
MULTIPLE SCLEROTIC LESIONS IN SPINE WITH COLLAPSE
The future

• A long way to go…
• Earlier detection
• Molecular and cytogenetics to better classify and understand biological traits.
• Prognostication and response to chemo
• Better and safer adjuvant treatment
• Improved surgical methods and technology
3. Fletcher CDM (ed): Diagnostic Histopathology of Tumors. Third Ed. 2007
Thanks for your attention

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