BONE TUMOUR PATHOLOGY
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BONE TUMOUR PATHOLOGY

Introduction

Information required for optimal interpretation of bone biopsies:

- Age of patient
- Which bone (and where in the bone)
- Radiological features
Malignant bone tumours according to age:

**<40 years**
- Osteosarcoma
- Ewing sarcoma

**>40 years**
- Metastasis
- Metastasis
- Metastasis
- Myeloma
- Lymphoma
- Chondrosarcoma
BONE TUMOUR PATHOLOGY

Introduction

• Location, location, location !!!
BONE TUMOUR PATHOLOGY

Introduction

• Which bone?
  – Long bone (humerus, femur, tibia, fibula, radius, ulna)
  – Small bones of hand and feet
  – Pelvis
  – Spine (vertebral body or neural arch)
  – Craniofacial

• Which part of the bone?
  – Epiphysis, metaphysis, diaphysis
  – Medulla, cortex, surface (periosteal, parosteal)
Epiphysis
End of a long bone

- Chondroblastoma
  - Skeletally immature

- Giant cell tumour
  - Skeletally mature
Metaphysis
Region of bone adjacent to the physis (growth plate)

- Chondromyxoid fibroma
- Osteosarcoma
- ABC
- Metaphyseal fibrous defect
Diaphysis
Shaft of a long bone

- Ewing sarcoma
- Myeloma
- Enchondroma
**BONE TUMOUR PATHOLOGY**

**Introduction**

**Radiological findings:**

<table>
<thead>
<tr>
<th>Non aggressive</th>
<th>Aggressive</th>
</tr>
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<tbody>
<tr>
<td>• Narrow zone of transition</td>
<td>• Broad zone of transition</td>
</tr>
<tr>
<td>• Smooth periosteal reaction</td>
<td>• Aggressive periosteal reaction (sunray spiculation, hair on end, onion skinning)</td>
</tr>
<tr>
<td>• No cortical breakthrough or soft tissue mass</td>
<td>• Endosteal scalloping</td>
</tr>
<tr>
<td>• Circumscription</td>
<td>• Cortical breakthrough</td>
</tr>
<tr>
<td>• Sclerotic margin</td>
<td>• Soft tissue mass</td>
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BONE TUMOUR PATHOLOGY

Introduction

• Read the radiology report
• Discuss with radiologist
• Correlate at multidisciplinary meeting

Comment in report:
• Radiological correlation is recommended

Important for most bone biopsies but critical for biopsies of chondroid lesions

• Radiological correlation is required for final diagnosis in biopsies of chondroid lesions of bone
BONE TUMOUR PATHOLOGY CASES
BONE TUMOUR PATHOLOGY
Case 1               M15   Knee pain
Fibrochondroid matrix
Pericellular calcification
(“chickenwire” calcification)
Osteoclast-type giant cells
Mononuclear cells have well defined cell membranes and nuclear grooves.
H3F3 K36M immunostain

- Positive staining in mononuclear cells (chondroblasts)
- Absence of staining in osteoclast type giant cells
BONE TUMOUR PATHOLOGY
Case 1

CHONDROBLASTOMA
BONE TUMOUR PATHOLOGY

Case 1: Chondroblastoma

- Skeletally immature
- Epiphyseal
Case 1: Chondroblastoma

- Fibrochondroid matrix
- Pericellular calcification
- Osteoclast-type giant cells
- Chondroblasts – mononuclear cells with well defined cell membranes, nuclear grooves
- Often have secondary aneurysmal bone cyst

- Positive staining in H3F3 K36M immunostain
Case 1: Chondroblastoma

DIFFERENTIAL DIAGNOSIS:

Giant cell tumour (GCT) of bone

- **Similarities**
  - Epiphyseal location
  - Osteoclast-type giant cells with background of mononuclear cells

- **Differences**
  - GCT skeletally mature (older age)
  - GCT does not contain matrix (fibrochondroid matrix in CB)
  - Mononuclear cells have syncytial appearance in GCT
  - Different histone mutation (H3F3 G34W in GCT; H3F3 K36M in CB)
BONE TUMOUR PATHOLOGY

Case 1: Chondroblastoma

• Common to have secondary aneurysmal bone cyst with chondroblastoma

• May largely obscure the diagnostic features of CB or may be the only component sampled

• Think of chondroblastoma for ABC occurring at typical locations of chondroblastoma (epiphysis, small bones of hands and feet)
BONE TUMOUR PATHOLOGY

Case 4   M15 Lump and pain, lower leg
Septa and blood filled spaces

Some solid areas
Linear osteoid
Osteoclast type giant cells
No anaplasia
No atypical mitotic figures
BONE TUMOUR PATHOLOGY
Case 4

ANEURYSMAL BONE CYST
Primary or secondary
FISH for *USP6*
POSITIVE for rearrangement
BONE TUMOUR PATHOLOGY
Case 4

PRIMARY ANEURYSMAL BONE CYST
Primary ABC

- Young age
- Metaphyseal
- No associated lesion
- Solid, cystic or solid and cystic
- USP6 rearrangement in approximately 70%

Secondary ABC

- Seen with an associated/underlying lesion
- For example: chondroblastoma, giant cell tumour, osteoblastoma
- Sample the entire lesion
- Clinical and radiological correlation
- Consider immunostains for GCT and chondroblastoma (if epiphyseal) and USP6 FISH
BONE TUMOUR PATHOLOGY

Case 4: Aneurysmal bone cyst

Differential diagnosis:

• Primary vs secondary ABC

• Giant cell tumour of bone
  – H3F3 G34W immunostain

• Chondroblastoma
  – H3F3 K36M immunostain

• Telangiectatic osteosarcoma (also radiological DDx)
  – Anaplasia, atypical mitotic figures
BONE TUMOUR PATHOLOGY
Case 5                  M38 Knee pain
BONE TUMOUR PATHOLOGY
Case 5                  M38 Knee pain

- Epiphyseal and metaphyseal
- Extends to subchondral bone
- Narrow zone of transition
- Non-sclerotic margin
- No matrix
Giant cell rich lesion

No matrix
Mononuclear cells form a syncytium
No anaplasia or atypical mitotic figures
Case 5

Giant cell rich lesion

Differential diagnosis:

- Giant cell tumour of bone (favoured at this age and location)
- Brown tumour of hyperparathyroidism
- Solid aneurysmal bone cyst
- Chondroblastoma (but no matrix, no nuclear grooves)
- Giant cell rich sarcoma (but no anaplasia or atypical mitotic figures)
BONE TUMOUR PATHOLOGY

Case 5

Prior to ancillary investigations/radiological correlation
Giant cell rich lesion (descriptive diagnosis)

Differential diagnosis:
• Giant cell tumour of bone (favoured at this age & location)
• Brown tumour of hyperparathyroidism
• Solid aneurysmal bone cyst

• Chondroblastoma (but no matrix, no nuclear grooves)
• Giant cell rich sarcoma (but no anaplasia or atypical mitotic figures)
BONE TUMOUR PATHOLOGY
Case 5

Giant cell rich lesion (descriptive diagnosis)

Differential diagnosis:
• Giant cell tumour of bone
  — H3F3 G34W immunostain
• Brown tumour of hyperparathyroidism
  — serum parathyroid hormone levels
• Solid aneurysmal bone cyst
  — USP6 FISH

• Chondroblastoma (but no matrix, no nuclear grooves)
  — H3F3 K36M immunostain

Radiological correlation
H3F3 G34W immunostain

- Positive staining in mononuclear cells and spindle shaped cells
- Absence of staining in osteoclast type giant cells
BONE TUMOUR PATHOLOGY
Case 5

GIANT CELL TUMOUR OF BONE
BONE TUMOUR PATHOLOGY

Giant cell rich lesions

• Not every giant cell-containing lesion in bone is a giant cell tumour of bone.
BONE TUMOUR PATHOLOGY

Giant cell rich lesions

• Giant cell tumour of bone
• Chondroblastoma
• Brown tumour of hyperparathyroidism
• ABC (aneurysmal bone cyst) primary or secondary
• Giant cell reparative granuloma
• Giant cell rich osteosarcoma
• And others…..

If not told that the lesion is in bone consider also synovial and soft tissue giant cell rich lesions:

➤ Tenosynovial giant cell tumour

➤ Giant cell tumour of soft tissue (rare)
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Giant cell rich lesions

• Age
• Radiology /location
• Osteoclasts
• Stromal/mononuclear cells
• Matrix
• Immunohistochemical or molecular tests
BONE TUMOUR PATHOLOGY

Giant cell rich lesions

• **Age**  
  – Chondroblastoma skeletally immature; GCT skeletally mature

• **Radiology /location**  
  – CB and GCT epiphyseal  
  – CB also in small bones hands and feet; GCRG in jaw

• **Osteoclasts**  
  – GC with >50-100 nuclei are suggestive of GCT of bone (but not required for GCT)

• **Stromal/mononuclear cells**  
  – Syncytial in GCT; distinct and nuclear grooves in CB; anaplasia and atypical mitotic figures in sarcoma

• **Matrix**  
  – Nil in GCT; fibrochondroid in CB; linear osteoid in ABC; osteoid produced by malignant cells in giant cell rich osteosarcoma

• **Immunohistochemical or molecular tests**  
  – H3F3 G34W in GCT; H3F3 K36M in chondroblastoma; USP6 rearrangement (FISH) in primary ABC
BONE TUMOUR PATHOLOGY

Case 10

F14 Leg pain
BONE TUMOUR PATHOLOGY

Case 10                     F14 Leg pain

• Well defined, sclerotic margin
• Lobulated
• Metaphyseal
• Cortical

“leave alone lesion” (LAL)
Giant cells in a storiform spindle cell background
Giant cells in a storiform spindle cell background
No anaplasia, no atypical mitotic figures, no matrix
Case 10
Differential diagnosis

Giant cell containing lesion with spindle cell shaped cells in a storiform pattern (descriptive)

- Non ossifying fibroma (NOF)
- Benign fibrous histiocytoma (BFH)
- BFH-like giant cell tumour
- Solid aneurysmal bone cyst
Case 10
Differential diagnosis

Giant cell rich lesion with storiform background (descriptive)
14 year old, metaphysis

• Non ossifying fibroma (NOF)
  – Age (young); radiology
• Benign fibrous histiocytoma (BFH)
  – Age (skeletally mature); radiology
• BFH-like giant cell tumour
  – Age (skeletally mature); location (epiphyseal, subchondral); radiology
• Solid aneurysmal bone cyst
  – Age, location, radiology, USP6
BONE TUMOUR PATHOLOGY
Case 10

NON OSSIFYING FIBROMA
(fibrous cortical defect/metaphyseal fibrous defect)

Activating mutations in the MAP-kinase pathway define non-ossifying fibroma of bone
Bamhoer D et al J Pathol 2018
BONE TUMOUR PATHOLOGY

Case 13

F13 Leg pain
BONE TUMOUR PATHOLOGY

Case 13                              F13 Leg pain

- Lucent lesion
- Well defined (narrow zone of transition)
- No wider than physis
- Fluid signal on MRI (not shown)
“Cyst” lining

Linear osteoid

Reactive woven bone
Osteoclast type giant cells
Haemosiderin pigment
Reactive woven bone

Non-specific features
Common in cystic lesions
Linear osteoid

Non-specific feature
Common in cystic lesions
Fibrinous cementum-like material
Fibrinous cementum-like material
Fibrinous cementum-like material
BONE TUMOUR PATHOLOGY
Case 13

SIMPLE BONE CYST
(Unicameral bone cyst)
Cystic lesions in bone

• Simple (unicameral) bone cyst
• Aneurysmal bone cyst (primary or secondary)
  • Post traumatic bone cyst

• Cystic change in other bone lesions
  – Cystic fibrous dysplasia
Cystic lesions in bone

• Simple (unicameral) bone cyst
  – Young person; metaphyseal lesion
  – Radiology – lesion not wider than physis (growth plate)
  – Pathology – fibrinous/cementum like material

• Aneurysmal bone cyst
  – Bone more expanded than simple bone cyst; often eccentric location
  – Multiple fluid fluid levels on MRI
  – More cellular (but can see secondary ABC type changes in simple bone cyst)
  – Primary ABC does not have fibrinous/cementum like material
BONE TUMOUR PATHOLOGY

Case 14

F49 Finger pain
BONE TUMOUR PATHOLOGY

Case 14  F49 Finger pain

- Lucent lesion in phalanx
- Contains matrix-type calcification
- MRI – T2 hyperintense, lobulated, peripheral enhancement
Chondroid lesion
Bone encasement pattern
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Case 14

• In isolation (without radiology but with history of age and location)

• Low grade chondroid lesion, no overt features of malignancy in this sample, possible enchondroma but radiological correlation required for final diagnosis
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Case 14

Following radiological correlation:

- Chondroid lesion with radiological and pathological features consistent with an enchondroma
Chondroid matrix

Hyaline cartilage
Encasement pattern
Encasement pattern

embrace
Permeation pattern

Feature of malignancy in a chondroid neoplasm (chondrosarcoma)
Word of caution:

- Prior fracture can result in spicules of bone within chondroid tissue (esp. fingers and toes)
- Disconcerting – mimic of bone permeation
- **Clinical and radiological correlation**

Presence of granulation tissue may be a clue to prior fracture
Low grade chondroid tumour

- Used to encompass enchondroma and grade 1 chondrosarcoma

- Can be used if either the radiology or pathology shows some atypical features that fall short of malignancy

- Management for low grade chondroid tumour is generally curettage with follow-up
BONE TUMOUR PATHOLOGY

Case 9

M35 Leg pain and lump
BONE TUMOUR PATHOLOGY

Case 9                M35 Leg pain and lump

- Lucent lesion
- Metaphyseal location, eccentric
- Cortical loss
- Well defined, scalloped interface with bone
- Sclerotic margin
Lobulated architecture
Lobulated architecture
Accentuation of cellularity at periphery of lobules
Chondromyxoid matrix

Hyaline cartilage present in approx. 20%
(not present in this case)
Accentuation of cellularity at periphery of lobules
Prominent blood vessels
Thin-walled, branching vessels
Haemangiopericytomatous vascular pattern can be seen
Osteoclast type giant cells often present at periphery of lobules
Stellate or spindle shaped cells
Degenerative-type atypia can be present

Different case
BONE TUMOUR PATHOLOGY
Case 9

CHONDROMYXOID FIBROMA
Chondromyxoid fibroma (CMF)
Differential diagnosis:

• Chondroblastoma
  – Epiphyseal location; H3F3 K36M immunostain, radiology

• Enchondroma
  – Hyaline cartilage uncommon in CMF; present in 20% (partic.
in lesions from hands and feet) but other features of CMF should be present; radiology

• Chondrosarcoma
  – Bone permeation by hyaline cartilage (not seen in CMF)
  – Lacks vascularity of CMF
  – Radiology (critical in difficult cases)
  – IDH mutations in chondrosarcoma (GRM mutations in CMF)
BONE TUMOUR PATHOLOGY
Case 7                  F68 Lower back pain
Case 7 F68 Lower back pain

- Lucent/lytic lesion in sacrum
- Bone destruction and cortical breach with soft tissue mass
- T2 hyperintense on MRI
Brachyury
BONE TUMOUR PATHOLOGY
Case 7

CHORDOMA
Lobulated architecture

Different example (not the case provided)
Cords and nests of epithelioid cells in myxoid matrix
Some tumour cells have abundant, vacuolated, “bubbly’ cytoplasm.

**Physaliferous cells**
Chordoma
Differential diagnosis:

- **Benign notochordal cell tumour (BNCT)**
  - Confined to bone (no soft tissue extension)
  - Sclerotic on imaging (no lucency)
  - No myxoid material between cells (alcian blue stain)
  - Same immunoprofile as chordoma

- **Chondrosarcoma**
  - Cytokeratin and brachyury negative

- **Metastatic carcinoma**
  - Clinical history; Brachyury negative

- **Myoepithelial carcinoma**
  - Brachyury negative
BONE TUMOUR PATHOLOGY

Case 2  M18 Knee pain
BONE TUMOUR PATHOLOGY

Case 2  M18 Knee pain

- Metaphyseal location
- Broad zone of transition (ill defined margin)
- Sclerosis suggestive of matrix production
- Aggressive periosteal reaction
What type of matrix?
Chondroid matrix
Aggressive lesion of metaphysis in young person
Atypical chondroid matrix on biopsy (but no bone permeation)

What is the likely diagnosis?
Aggressive lesion of metaphysis in young person
Atypical chondroid matrix on biopsy (but no bone permeation)

What is the likely diagnosis?

Chondroblastic osteosarcoma
(Chondrosarcoma is rare in young people)
Osteoid produced by malignant cells
Osteoclast type giant cells
Necrosis
BONE TUMOUR PATHOLOGY

Case 2

OSTEOSARCOMA
(High grade; chondroblastic and osteoblastic)
Clinical context and radiology

• Chondrosarcoma is a disease of adults

• Osteosarcoma is usually a disease of children/young adults
Malignant osteoid on biopsy in an older person (>50 years) consider the following:

- Dedifferentiated chondrosarcoma (radiological correlation; IDH mutation analysis)
- Paget’s sarcoma (sarcoma arising in Paget’s disease; radiology)
- Malignant transformation of fibrous dysplasia (imaging; GNAS mutation analysis)
- Malignant transformation of bone infarct (imaging)
- Radiation-associated sarcoma (history of prior radiotherapy)
BONE TUMOUR PATHOLOGY
Case 8               M18 Leg pain
BONE TUMOUR PATHOLOGY

Case 8  M18 Leg pain

Mixed lucent/lytic and sclerotic lesion
Metaphysis (and diaphysis)
Codman’s triangle
Cortical breach and soft tissue extension
Severe pleomorphism
Filigree and lace-like osteoid
Anaplasia and severe pleomorphism
BONE TUMOUR PATHOLOGY
Case 8

OSTEOSARCOMA
(High grade osteoblastic)
Conventional osteosarcoma

- High grade, intra-osseous, malignant bone-producing neoplasm
- Osteoblastic
- Chondroblastic
- Fibroblastic
Conventional osteosarcoma

• Most common primary high grade sarcoma of the skeleton

• Bimodal age distribution
  – Majority 10-14yrs
  – Smaller peak in older adults
  • Paget’s disease, radiation-induced, bone infarct, infection, malignant transformation of fibrous dysplasia
Conventional osteosarcoma
Treatment

• Chemotherapy

• Surgery

• Chemotherapy
Osteosarcoma
Resection: response to chemotherapy

- Evaluate 1-2 slabs of tumour in greatest 2 dimensions
- Estimate percentage necrosis
BONE TUMOUR PATHOLOGY

Case 15  F30 Pain for several months then lump
Case 15  F30 Pain for several months then lump

- Ossified lesion arising from posterior surface of distal femur (surface lesion)
- No corticomedullary continuity
Fibro-osseous (matrix-producing) component
Cytological atypia in spindle cell component (nuclear hyperchromasiasia, nuclear pleomorphism)
Cytological atypia in spindle cell component (nuclear hyperchromasia, nuclear pleomorphism)
Peripheral component consists of spindle cells only (no matrix)

Radiological correlation critical
Peripheral component consists of spindle cells only (no matrix)

Radiological correlation critical
Cytological atypia in spindle cell component
Focal chondroid matrix

Not from this case
“Cartilage cap” can be present (mimic of osteochondroma on radiology and pathology)
BONE TUMOUR PATHOLOGY
Case 15

LOW GRADE OSTEOSARCOMA
(Parosteal osteosarcoma)
Parosteal (low grade) osteosarcoma
Differential diagnosis

• Low grade central osteosarcoma

• Fibrous dysplasia (for intraosseous tumour)

• Osteochondroma (for surface lesion/pOS)

• Spindle cell neoplasm (e.g. desmoid-type fibromatosis) if only spindle cell component sampled
Parosteal (low grade) osteosarcoma
Differential diagnosis

**Low grade central osteosarcoma**

- Both are low grade osteosarcomas

- Same pathology, molecular biology (MDM2 amplification) and treatment (complete local excision if no high grade component; chemotherapy and surgery if high grade transformation has occurred)

- Radiology (central lesion vs surface lesion)
Parosteal (low grade) osteosarcoma
Differential diagnosis

Fibrous dysplasia (FD)

- More difficult for intra-osseous lesions (i.e. differential of low grade central osteosarcoma)
- Subtle radiological differences (including change on follow-up for LGCOS vs stable in FD)
- Presence of cytological atypia in osteosarcoma (in spindle cell component)
- GNAS mutations in fibrous dysplasia
- MDM2 amplification in low grade osteosarcoma
  - > importance of no decalcification or gentle decalcification (EDTA) for at least part of the sample in bone biopsies
Parosteal (low grade) osteosarcoma
Differential diagnosis

Osteochondroma

- Both can have overlying cartilage cap
- **Radiology is critical** - parosteal osteosarcoma is a **surface** lesion (underlying cortex is intact) while osteochondroma shows corticomedullary continuity
- Cytological atypia in spindle cells of parosteal osteosarcoma
- MDM2 amplification in parosteal osteosarcoma
FISH for MDM2

• POSITIVE for MDM2 amplification

NB: FISH image in this case is from a well differentiated liposarcoma
BONE TUMOUR PATHOLOGY

Case 11                      F20 Vague leg pain

• Lucent lesion with a well defined sclerotic margin on x-ray
Fibro-osseous lesion
Curvilinear spicules of woven bone in a mildly to moderately cellular fibrous background
Spicules of bone are devoid of rimming osteoblasts
Woven bone
Woven bone (polarised)
Woven bone
(polarised)
Spindle cells in fibrous stroma lack cytological atypia
BONE TUMOUR PATHOLOGY
Case 11

Prior to radiological correlation

FIBRO-OSSEOUS LESION CONSISTENT WITH FIBROUS DYSPLASIA
Fibrous dysplasia
Differential diagnosis:

• Osteofibrous dysplasia

• Low grade central osteosarcoma

• Reactive bone / fracture callus

Fibrous dysplasia is common
Osteofibrous dysplasia and low grade central osteosarcoma are rare
Fibrous dysplasia
Differential diagnosis:

- Osteofibrous dysplasia
  - Almost exclusively located in cortex of anterior tibia (radiological correlation)
  - Osteoblastic rimming
  - Cytokeratin positive cells (not visible on H&E)
  - Lack GNAS mutation
Fibrous dysplasia
Differential diagnosis:

• Low grade central osteosarcoma
  – Radiology important but can be subtle
  – Cytological atypia in spindle cells (can be patchy and subtle)
  – MDM2 amplification (absence of GNAS mutation) ***importance of appropriate decalcification****
Fibrous dysplasia
Differential diagnosis:

• Reactive bone / fracture callus
  – Zonation,
  – Prominent rimming osteoblasts
  – Clinical history and radiology
Case 11

FIBROUS DYSPLASIA

Common locations:
Rib
Skull/craniofacial
Long bones (femur, humerus, tibia)
BONE TUMOUR PATHOLOGY
Case 3      M15 Night pain, relieved by NSAIDS
BONE TUMOUR PATHOLOGY

Case 3  M15 Night pain, relieved by NSAIDS

- Central lucent nidus (showing central calcification)
- Surrounding dense cortical sclerosis
- <2cm
Lesion appears well defined in relation to adjacent bone (no bone permeation)
Bone-forming lesion
Interconnected trabeculae of woven bone
Intervening vascular stroma
Bone formed/lined by plump osteoblasts
Bone-forming neoplasm consistent with osteoid osteoma or osteoblastoma (radiological correlation pending)
OSTEOID OSTEOMA
Osteoid osteoma (OO)
Differential diagnosis

• Osteoblastoma (OB)
  – Size >2cm (radiology)

• Osteosarcoma
  – Atypia can be present in OO/OB but no anaplasia or atypical mitotic figures
  – No bone permeation in OO/OB
  – FOS/FOSB in OO and OB (IHC/FISH)
  – Radiology !!!!!!!!!!!!!!!!!!!!!

• Reactive bone/fracture callus
  – Zonation; clinical and radiological correlation
BONE TUMOUR PATHOLOGY
Case 6 M4 Pain and limp 1 month
Mixture of inflammatory-type cells and osteoclast-type giant cells
Abundant eosinophils
Histiocytes with nuclear grooves/folded nuclei
BONE TUMOUR PATHOLOGY
Case 6

LANGERHANS’ CELL HISTIOCYTOSIS
(eosinophilic granuloma)

BRAF V600E mutations in 50%
Langerhans’ cell histiocytosis (LCH)
Differential diagnosis

• Infection (acute or chronic)
  – Occasionally LCH is neutrophilic
  – Immunohistochemistry

• Other histiocytoses
  – Rosai Dorfman Disease
    • Rare in bone (LCH much more common)
    • Large cells, emperiploesis; positive for S-100 but negative for langerin and CD1a
  – Erdheim Chester disease
    • Negative for S-100, CD1a, Langerin
    • Radiology
BONE TUMOUR PATHOLOGY
Case 12                     M24 Leg pain
Case 12  M24 Leg pain

- Diaphyseal lesion
- Aggressive periosteal reaction
- Centred in bone with big soft tissue mass
Small round blue cell tumour
No matrix, no pleomorphism
Small round blue cell tumour of bone with large soft tissue mass

Main differential diagnoses:

Adolescent/young adult  Older person

1. Ewing sarcoma  1. Lymphoma
2. Lymphoma  2. Ewing sarcoma
CD99

FLI-1

CD45, CD20, CD3 negative
Ewing sarcoma

CD99

Must show membranous staining (Olympic rings)
Does that exclude lymphoma?
Always include TdT to **exclude lymphoblastic lymphoma** (which can be CD99, FLI-1 positive and CD45, CD20, CD3 negative)

And consider **flow cytometry** as part of triage in small round blue cell tumour diagnosis.
Any other ancillary tests?
FISH for EWSR-1 (or EWSR1-FLI-1)
BONE TUMOUR PATHOLOGY

Case 12

Prior to ancillary investigations and radiological correlation:

MALIGNANT SMALL ROUND BLUE CELL TUMOUR

Main differential diagnosis includes Ewing sarcoma (most likely at this age and location) and lymphoma
BONE TUMOUR PATHOLOGY

Case 12

Following ancillary investigations and radiological correlation:

EWING SARCOMA
Diagnoses (on morphology and history alone)

1. Chondroblastoma

2. Favour chondroblastic osteosarcoma (radiological correlation recommended)

3. Bone producing neoplasm, favour osteoid osteoma or osteoblastoma

4. Aneurysmal bone cyst (primary or secondary)

5. Giant cell rich lesion, favour giant cell tumour of bone but hyperparathyroidism should be excluded and radiological correlation is required
Diagnoses (on morphology and history alone)

6. Favour Langerhans’ cell histiocytosis (eosinophilic granuloma)

7. Notochordal tumour, consistent with chordoma, pending immunohistochemistry and radiological correlation

8. Favour high grade osteoblastic osteosarcoma, radiological correlation recommended for final diagnosis

9. Chondromyxoid fibroma (radiological correlation recommended)

10. Storiform spindle cell lesion with giant cells, favour non-ossifiying fibroma but radiological correlation required

11. Fibro-osseous lesion consistent with fibrous dysplasia; radiological correlation recommended
Diagnoses (on morphology and history alone)

11. Fibro-osseous lesion consistent with fibrous dysplasia; radiological correlation recommended for final diagnosis

12. Malignant small round blue cell tumour, main differential diagnoses in this context include Ewing sarcoma (most likely at this age) and lymphoma

13. Simple (unicameral) bone cyst

14. Low grade chondroid tumour with no overt features of malignancy but radiological correlation is required for final diagnosis

15. Favour parosteal (low grade) osteosarcoma, radiological correlation required for final diagnosis
Final diagnoses
After ancillary studies and radiological correlation

1. Chondroblastoma
2. Osteosarcoma (chondroblastic and osteoblastic)
3. Osteoid osteoma
4. Primary aneurysmal bone cyst
5. Giant cell tumour of bone
6. Langerhans’ cell histiocytosis (eosinophilic granuloma)
7. Chordoma
8. Osteosarcoma (osteoblastic)
9. Chondromyxoid fibroma
Final diagnoses
After ancillary studies and radiological correlation

10. Non-ossifying fibromia
11. Fibrous dysplasia
12. Ewing sarcoma
13. Simple bone cyst
14. Enchondroma
15. Parosteal osteosarcoma
Take home points

• Importance of age and location
• Radiological correlation (particularly critical in chondroid lesions)
• Consider appropriate (gentle) decalcification and avoid prolonged formalin fixation
Decalcification

- Should be performed if the lesion is gritty/hard/bony (and consider for any specimen originating from bone)

- The tissue should have formalin fixation prior to decalcification (but avoid prolonged formalin fixation)

- If a primary or metastatic neoplasm is a consideration at least part of the specimen should have no decalcification or gentle decalcification (EDTA, “Osteosoft”) in case molecular tests such as FISH are required

- Routine decalcification, prolonged gentle decalcification and prolonged formalin fixation can preclude molecular testing (FISH, mutation analysis) due to DNA degradation

- Prolonged decalcification affects morphology and can limit interpretation (e.g. evaluation of necrosis). Larger pieces should be sectioned prior to decalcification for this reason.
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  – Dr Judy Soper, Dr Julie Schatz, Dr Wendy Brown

• FISH:
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