



Musculoskeletal System

Sub-System

Pathology

Lecture Title

Bone tumors (continued)

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BONE TUMORS

CLASSIFIED INTO : (1) primary bone tumors (2) secondary bone tumors

(1) Primary bone tumors

- Bone-forming tumors
 - Osteosarcoma - **Malignant**
- Cartilage-forming tumors
 - Chondrosarcoma - **Malignant**
 - Osteochondroma - **Benign**
 - Chondroma/enchondroma - **Benign**
- Tumor of unknown origin
 - Ewing sarcoma family tumors - **Malignant**
 - Giant cell tumor - **Benign**
 - Aneurysmal bone cyst (ABC) - **Benign**

Chondroma → originates from **bone cortex** (outside)

Enchondroma → originates inside in the **medullary cavity** of bone

Aneurysmal bone cyst :

- ✓ Consists of **multiloculated blood-filled cystic spaces**
- ✓ Can be either :
 - **primary tumor** (as a discrete entity)
 - **morphological appearance** adjacent to another bone tumor (as a **reaction to certain bone tumors**)

(2) Secondary bone tumors

- Metastases → **most common malignant bone tumor**

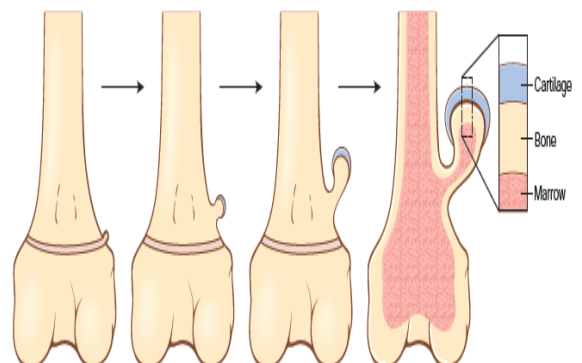
➤ Osteochondroma (Exostosis)

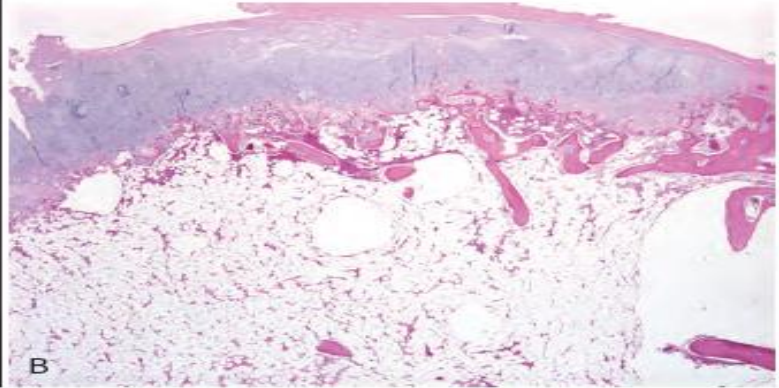
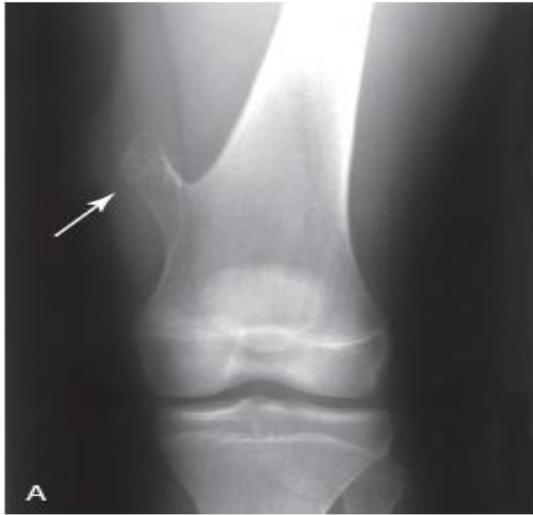
- ✓ The most common benign bone tumor (cartilage-forming tumors)
- ✓ 85% (mostly) → solitary/ acquired (late adolescence and early adulthood)
- ✓ the remainder → multiple hereditary exostosis syndrome : 5-20% progress to chondrosarcoma
- ✓ Most commonly: metaphysis of long bones especially around the knee
- ✓ slow-growing masses
- ✓ can be painful if they impinge on a nerve or if the stalk is fractured
- ✓ can lead to pathologic fracture (any problem in bone can lead to pathological fracture which is a fracture with minor trauma)
- ✓ In many cases they are detected incidentally
- ✓ Osteochondromas usually stop growing at the time of growth plate closure (when bones stop growing)

*osteochondroma is originally a

chondrocyte in growth plate → formed cartilaginous mass → then undergoes endochondral ossification → forming a stalk (continuous with the original bone) with a cavity containing bone marrow (in red) continuous with the original bone's bone marrow

*Cartilage Cap (in blue) → is the remainder cartilaginous part of the stalk





✓ Microscopically :

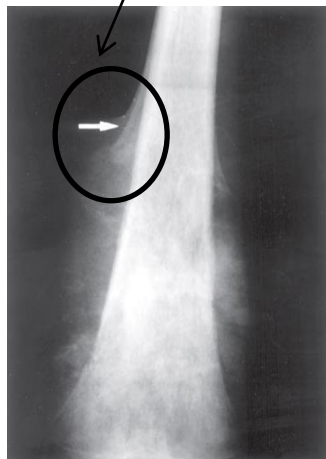
- Benign cartilage on benign bone
- Normal trabeculae
- Unremarkable bone and bone marrow
- Cartilage cap resembles a disorganized growth plate

➤ **Chondroma/Enchondroma**

- ✓ cartilage-forming tumors – benign
- ✓ **Enchondroma** → originates inside in the **medullary cavity** (central) of bone
- ✓ Age: 20s-50s
- ✓ Most cases → solitary
- ✓ Some cases → syndromes = Ollier disease & Maffucci syndrome (non-hereditary syndromes)
 - Multiple enchondromatosis
 - more risk for progressing to chondrosarcoma
- ✓ Hand and foot bones are most common
- ✓ Mainly metaphysis

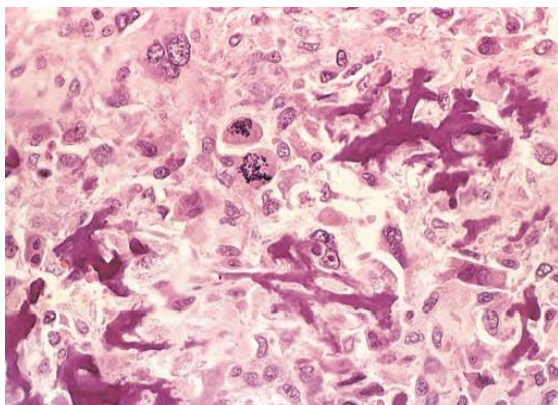
➤ **Osteosarcoma**

- ✓ Bone-forming tumors –malignant
- ✓ Most common primary malignant tumour of bone – exclusive of myeloma and lymphoma
- ✓ Due to breaking through cortex and periosteum lifting, a reactive bone formed a triangle (Codman triangle)



- ✓ Codman triangle (on X-ray)
 - Characteristic
 - Not pathognomonic → because we can see it on osteomyelitis and other benign conditions

- ✓ Grossly :
 - Tumor destroys the medullary cavity inside and expands outward (may reach soft tissue)



- ✓ Microscopically :
 - Malignant cells
 - Pleomorphic cells and abnormal mitoses
 - It may form malignant bone matrix → lace like osteoid (irregular bone) → may be mineralized/calcified later on

- ✓ Most common site → around knee – metaphysis
- ✓ Bimodal age distribution :
 - Mostly : <20 years old
 - Smaller ratio : Older adults 60/70 → secondary commonly due to underlying conditions such as : (paget disease of bone / benign tumors/ bone infarcts/ chronic osteomyelitis / radiation of bone/foreign body in bone)
- ✓ Males > females
- ✓ Typically : painful, progressively/slowly enlarging masses
- ✓ Sometimes → sudden fracture in bone is FIRST SYMPTOM
- ✓ Common genes affected:
 - Retinoblastoma gene (RB) – 70% of sporadic cases (tumor suppressor gene → loss of function mutation)
 - TP53 - (tumor suppressor gene → loss of function mutation)
 - INK4a encodes 2 tumor suppressors → * p16 : inhibitor of cyclin-dependent kinases *p14 : augments p52 function
 - MDM2 (inhibitor of p53) (oncogene → gain of function mutation)
 - CDK4 (inhibitor of RB) (oncogene → gain of function mutation)

Li-fraumeni Syndrome → a synd where TP53 is damaged/suppressed (germline mutation)

Several subtypes of osteosarcoma are recognized and are grouped according to:

- Site of origin (intramedullary, intracortical, or surface)
- Histologic grade (low, high)
- Primary (underlying bone is unremarkable) or secondary to preexisting disorders (benign tumors, Paget disease, bone infarcts, previous radiation)
- Histologic features (osteoblastic, chondroblastic, fibroblastic, telangiectatic, small cell, giant cell)

Not required

The most common subtype arises in the metaphysis of long bones and is primary, intramedullary, osteoblastic, and high grade.

- ✓ Remember that the fracture due to trivial trauma because of bone disease is called: pathological fracture
- ✓ Hematogenous spread → esp. to lung

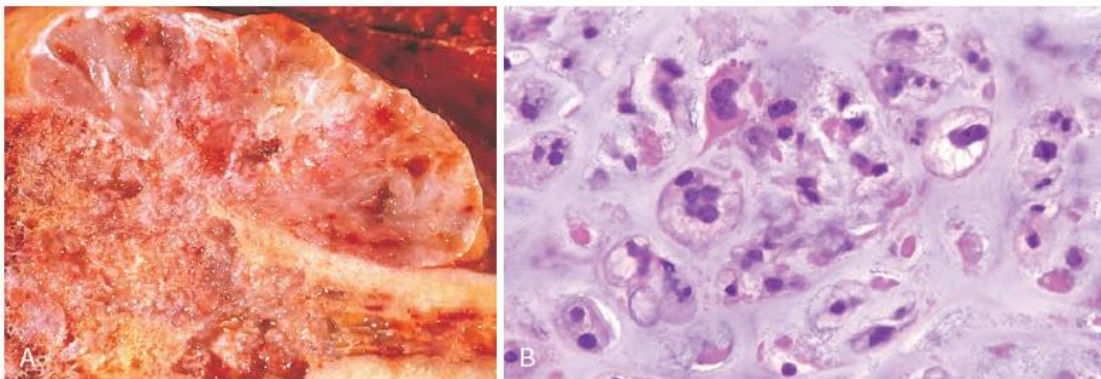
NOTE THAT:

- **Sarcoma → hematogenous spread**
- **Carcinoma → lymphatic spread**
- ** many cases of osteosarcoma are diagnosed as metastasis in LUNG**

- ✓ Recurrent, metastatic and secondary osteosarcomas have worse prognosis
- ✓ Treatment: chemotherapy + surgery

➤ **Chondrosarcoma**

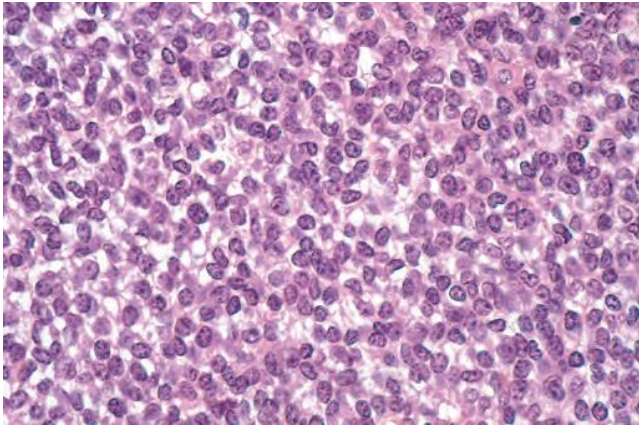
- ✓ Cartilage forming tumor –Malignant
- ✓ 2nd most common malignant matrix forming primary bone tumor
- ✓ Most common subtype → conventional chondrosarcoma (in older ages)
- ✓ Axial skeleton more : esp. Pelvis
- ✓ Mostly central (intramedullary)
- ✓ Painful / progressively enlarging mass
- ✓ Resembles malignant chondrocytes forming cartilage



Chondrosarcoma. **A**, Nodules of hyaline and myxoid cartilage permeating throughout the medullary cavity, growing through the cortex, and forming a relatively well-circumscribed soft tissue mass. **B**, Anaplastic chondrocytes amid hyaline cartilage matrix in a grade 3 chondrosarcoma.

➤ **Ewing sarcoma family tumors**

- ✓ Primary bone tumor of unknown origin malignant
- ✓ Second most common bone sarcoma in children
- ✓ Recently, Ewing sarcoma and primitive neuroectodermal tumor (PNET) have been unified into a single category: the Ewing sarcoma family tumors (ESFT)
- ✓ striking predilection for whites; blacks and Asians are rarely afflicted
- ✓ SITE : mainly diaphysis of long bones , esp. → femur



- ✓ Microscopically :
 - One of the small round blue cell tumors

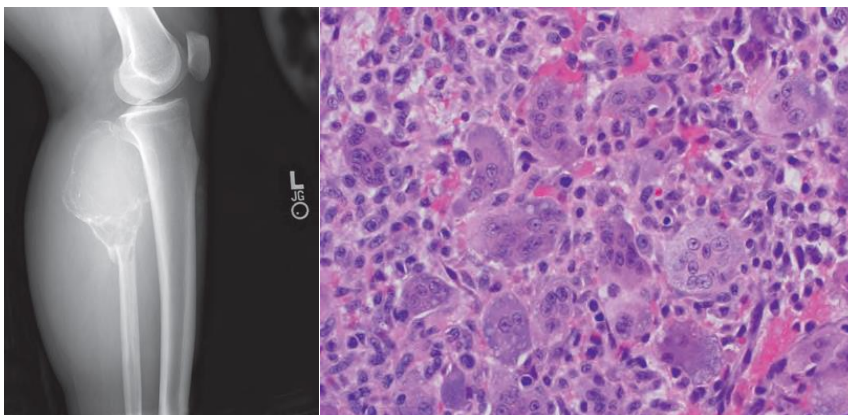
- ✓ EWS gene (on chromosome 22) rearrangement
- ✓ Characteristic periosteal rxn produces layers of reactive bone deposited in an onion skin fashion



Onion- skinning layers

➤ **Giant cell tumors – Osteoclastoma**

- ✓ Primary bone tumor of unknown origin – Benign
- ✓ SITE: epiphysis of long bones
- ✓ Benign but locally aggressive
- ✓ Rare
- ✓ Age : 20-40s



- ✓ Microscopically :
 - Giant cells (not malignant cells) -- they are present as a reaction
 - Single mononuclear cells (b/w giant cells) → they are the neoplastic cells