Pathology

Doctor 2017 | Medicine | JU | MSS

Number >>	6
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1st system - MSS

Table 21.1 Classification of Selected Primary Bone Tumors

Category	Behavior	Tumor Type	Common Locations	Age (yr)	Morphology
Cartilage forming	Benign	Osteochondroma	Metaphysis of long bones	10–30	Bony excrescence with cartilage cap
—	—	Chondroma	Small bones of hands and feet	30–50	Circumscribed hyaline cartilage nodule in medulla
—	Malignant	Chondrosarcoma (conventional)	Pelvis, shoulder	40–60	Extends from medulla through cortex into soft tissue, chondrocytes with increased cellularity and atypia
Bone forming	Benign	Osteoid osteoma	Metaphysis of long bones	10–20	Cortical, interlacing microtrabeculae of woven bone
—	—	Osteoblastoma	Vertebral column	10–20	Posterior elements of vertebra, histology similar to osteoid osteoma
—	Malignant	Osteosarcoma	Metaphysis of distal femur, proximal tibia	10–20	Extends from medulla to lift periosteum, malignant cells producing woven bone
Unknown origin	Benign	Giant cell tumor	Epiphysis of long bones	20–40	Destroys medulla and cortex, sheets of osteoclasts
—	—	Aneurysmal bone cyst	Proximal tibia, distal femur, vertebra	10–20	Vertebral body, hemorrhagic spaces separated by cellular, fibrous septae
—	Malignant	Ewing sarcoma	Diaphysis of long bones	10–20	Sheets of primitive small round cells

Adapted from Unni KK, Inwards CY: *Dahlin's Bone Tumors*, ed 6. Philadelphia, 2010, Lippincott-Williams & Wilkins; by permission of Mayo Foundation.

Neoadjuvant chemotherapy: to administer chemotherapeutic treatment before performing surgery.

Cartilage-Forming Tumors (Hyaline)

Osteochondroma (also named benign exostoses):

- Osteochondroma is **a benign cartilage-capped tumour** that is attached to the underlying skeleton **by a bony stalk**. The cap is composed of benign hyaline cartilage. Histological appearance is that of normal bone, cartilage, and bone marrow.
- The cortex of the stalk merges with the cortex of the host bone resulting in **continuity between the medulla** of the osteochondroma and the host bone.
- About **85% are solitary (only one)**, while **15% are** seen as part of *multiple hereditary exostoses syndrome **(MHE)***.

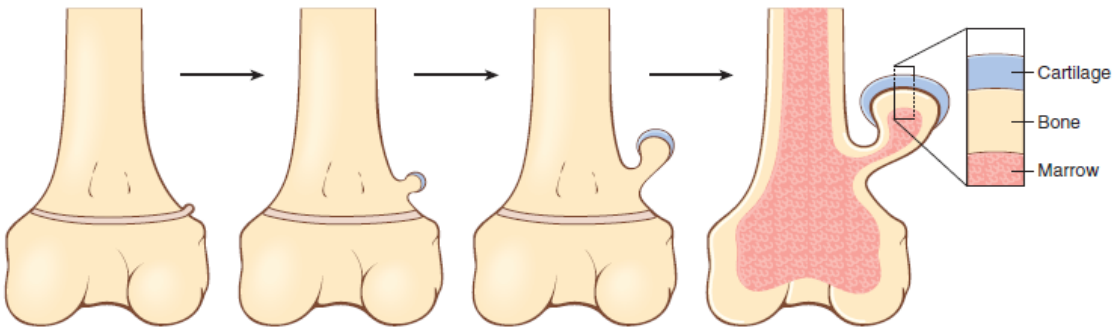
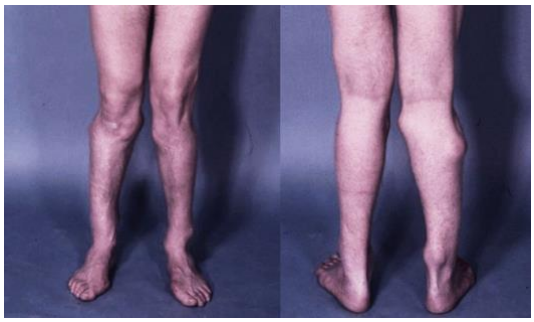


Fig. 21.19 The development of an osteochondroma, beginning with an outgrowth from the epiphyseal cartilage.

- Osteochondromas develop in bones of endochondral origin and **arise from the metaphysis** near the growth plate **of long** tubular **bones**, especially near the knee.
- They present as slow-growing masses, which **can be painful if they impinge on a nerve**. In many cases they are detected incidentally. In multiple hereditary exostoses, the underlying bones may be bowed and shortened, ------→ reflecting an associated disturbance in epiphyseal growth.



- **Pathogenesis**: *EXT1* or the *EXT2*
- **Clinical Course:** Osteochondromas usually stop growing at the time of growth plate closure.

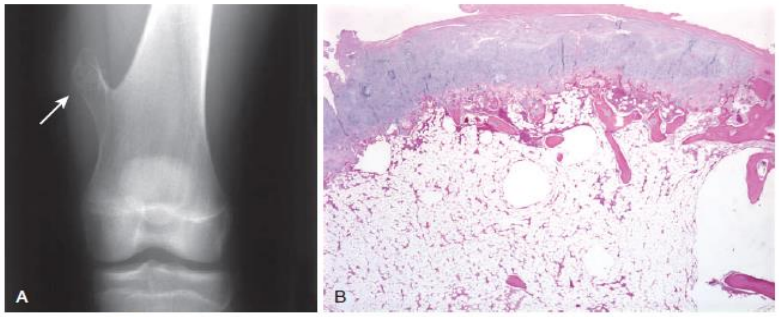


Fig. 21.20 Osteochondroma. (A) Radiograph of an osteochondroma arising from the distal femur *(arrow)*. (B) The cartilage cap has the histologic appearance of disorganized growth plate–like cartilage.

Symptomatic tumours are **cured by simple excision**. Rarely in sporadic cases, but more commonly in those with MHE (**5%**), osteochondromas **progress to chondrosarcoma**.

<u>Enchondroma</u>:

- Chondromas are **benign tumours of hyaline cartilage** that arise **within the medullary cavity** *(enchondroma)* **or on the cortical surface**.
- Are usually diagnosed in individuals **20 to 50** years of age.
- Are typically **solitary** (only one) metaphyseal lesions of the tubular bones of the hands and feet (**digits**). ***Ollier*** *disease* and ***Maffucci*** *syndrome* are disorders characterized by **multiple enchondromas** (enchondromatosis). **Maffucci syndrome also is associated with other rare tumours (hemangiomatosis).**

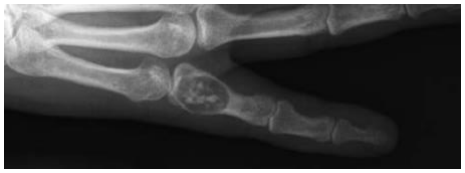
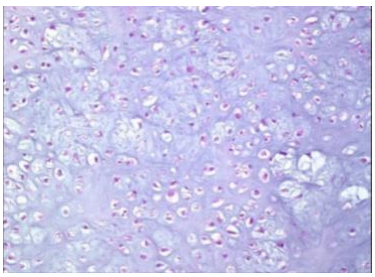


Fig. 21.21 Enchondroma of the proximal phalanx. The radiolucent nodule of cartilage with central calcification thins but does not penetrate the cortex.

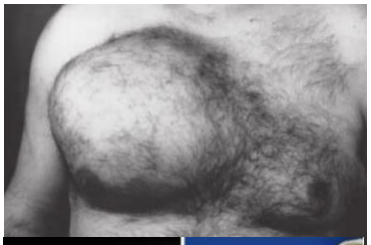


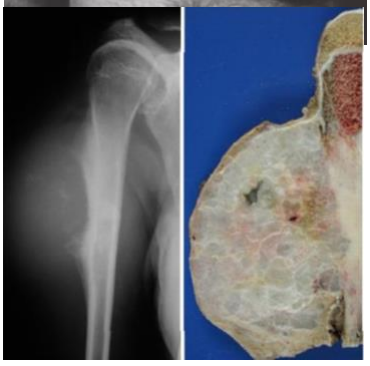
Notice the normal looking cartilage because it is benign.

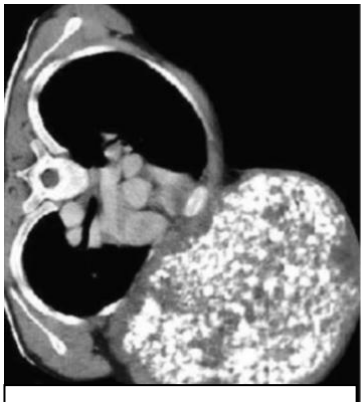
- The radiographic features consist of a circumscribed lucency with central irregular calcifications, a sclerotic rim, and an intact cortex. Most enchondromas of large bones are asymptomatic and are detected incidentally. Occasionally, they are painful and **cause pathologic fracture**. The tumours in enchondromatosis (Ollier/Maffucci) may be numerous and large, producing severe deformities, especially of the digits.
- **Pathogenesis**: mutations in the *IDH1* and *IDH2* genes.

Chondrosarcoma:

- Chondrosarcomas are malignant tumours that **produce cartilage**. Chondrosarcomas **commonly arise in the axial skeleton**, especially the pelvis, shoulder, and ribs. Unlike benign enchondroma, the **distal extremities are rarely involved**.
- Chondrosarcomas present with large masses.
- Chondrosarcomas are half as common as osteosarcomas (Osteosarcoma : Chondrosarcoma = 2:1).
- Patients usually in their **40-50s**.
  Remember: osteosarcomas occur in younger patients while chondrosarcomas in older patients.
- Men : Women = 2:1
- **Pathogenesis**: chondrosarcomas are **almost always genetically heterogeneous**, meaning they need a combination of more than one mutated to gene to develop, involved genes include: *EXT, IDH1, IDH2, COL2A1, CDKN2A.*

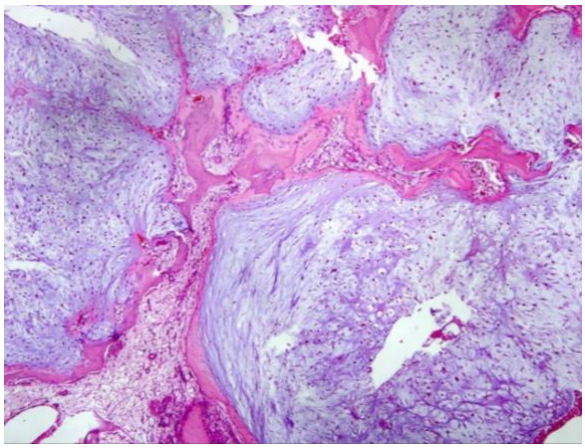






CT scan showing classic chondrosarcoma appearance which is like 'popcorn' or 'bubble soap'.

Notice the low level of differentiation of this cartilage. It is clearly malignant. (Grade 2)

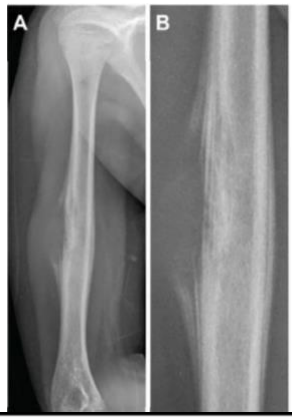


- **Clinical course**: Prognosis of chondrosarcomas heavily depends on the **grade** of the tumour.
  (Grade: level of differentiation. Grade 1 is the most differentiated while grade 4's cell of origin cannot be even recognized from the loss of differentiation.)
  Grade 1 is given the best prognosis and is usually treated with wide surgical excision only. Grade 2 or higher requires chemotherapy.

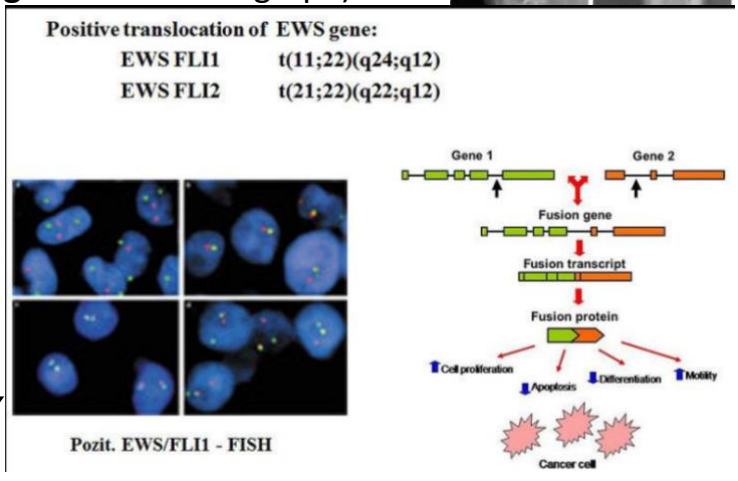
Tumours of Unknown Origin

Ewing sarcoma:

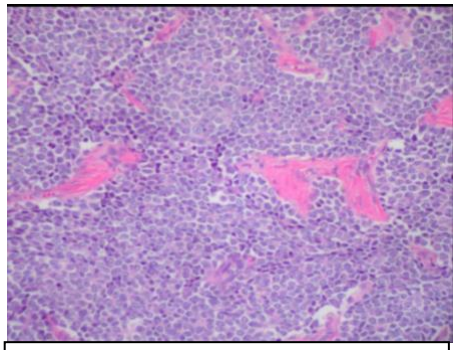
- Ewing sarcoma is a malignant tumour composed of primitive round cells that give the appearance of **small blue cells** under the microscope. Only a few neoplasms present with blue cells and Ewing is one of them. A test specific for Ewing only would be the FLI1 stain, where a positive test gives a brown colour. Ewing sarcoma is also classified as one of the **PNETs** (Primitive NeuroEctodermal Tumour). Metastasis to lungs by blood.
- Ewing sarcoma follows osteosarcoma as the **second most common bone sarcoma in children**. Of all bone sarcomas, Ewing sarcomas have the youngest average age at presentation (**80% are <20 years**).



- The tumours usually arise in the **diaphysis of long** bones. Plain radiographs show a destructive lytic tumour with permeative margins that **extends into the surrounding soft tissues**. Ewing sarcoma usually invades the cortex, periosteum, and soft tissue. The characteristic periosteal reaction produces layers of reactive bone deposited in an *onion-skin* fashion (**Codman triangle** seen in radiograph).
- **Pathogenesis**: The vast majority (**90%**) of Ewing sarcomas contain a balanced **(11;22) (q24;q12)** translocation generating fusion of the *EWSR1* gene on chromosome 22 to the *FLI1* gene on chromosome 11, which results in an aberrant transcription factor. **FISH analysis** shows translocation in the cells.



- **Clinical course**: Ewing sarcomas are aggressive malignancies **treated with neoadjuvant chemotherapy followed by surgical excision** with or without radiation. With chemotherapy, 5-year **survival of 75% of patients** is possible.



Note the blue appearance of cells in Ewing sarcoma.

Giant Cell Tumour (also named Osteoclastoma):

- Giant cell tumours are so named because **multinucleated osteoclast-type giant cells DOMINATE the histology. 90%** of osteoclastomas are benign.
  Many tumours present with what are called reactive osteoclast-like giant cells, like osteosarcomas for example, but osteoclastomas have a LOT more.
- Almost exclusively **affects adults**.
- It is a **locally aggressive** neoplasm that arises in the **epiphyses of long bones**, most commonly the distal femur and proximal tibia.
- **Pathogenesis**: The neoplastic cells express high levels of **RANKL**, which promotes the proliferation and differentiation of normal osteoclast precursors into osteoclasts. The osteoclasts in turn cause localized but highly destructive resorption of bone.

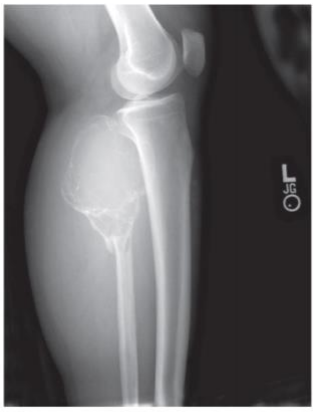


Fig. 21.25 Radiographically, giant cell tumor of the proximal fibula is predominantly lytic, expansile with destruction of the cortex. A pathologic fracture is also present.

- **Clinical Course**: Giant cell tumours are typically **treated with curettage, but many recur locally**.
  Curettage: Removal of tissue with a curette from the wall of a cavity.
  The main reason for recurrence is incomplete removal of the tumour. 5-10% of osteoclastomas metastasize. The RANKL inhibitor, Denosumab, has shown promise in treating giant cell tumour.

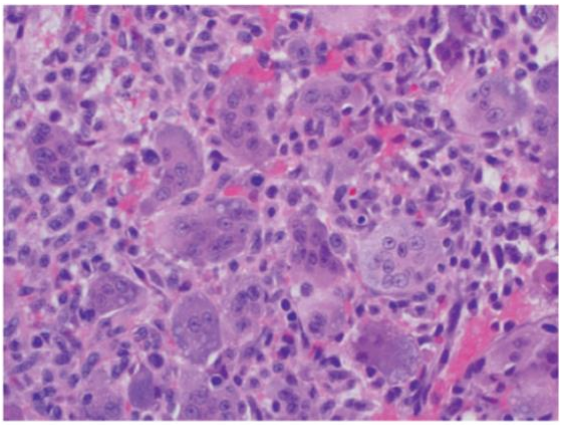
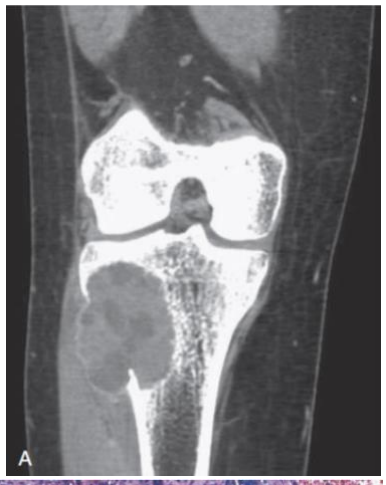


Fig. 21.26 Giant cell tumor illustrating an abundance of multinucleated giant cells with background mononuclear stromal cells.

Aneurysmal Bone Cyst (ABC):



- *Aneurysm: abnormal blood vessel dilation*, therefore ABC means that it is a lesion inside the bone that **contains blood-filled cysts**, it is a benign neoplasm. However, it is argued by some to not be a true neoplasm in the first place but consider ABCs to only be a reactive process from a trauma followed by a long cycle of repair and remodelling leading to blood-filled cysts.
- Occurs in the **metaphysis of long bones and is usually found in adults**.
- Can be confused in radiographs with Giant Cell Tumours but always remember that the distinguishing features of GCTs is the dominance of giant cells in histological pictures.
- **Clinical course**: The treatment of ABC is surgical. Curettage is effective with low risk of recurrence.

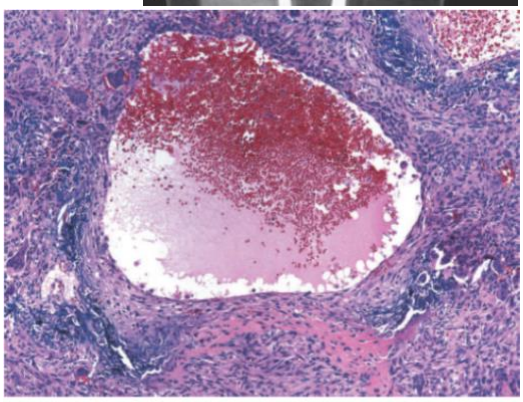
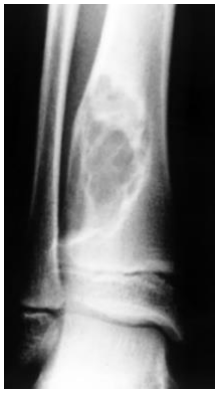


Fig. 21.28 Aneurysmal bone cyst with blood-filled cystic space surrounded by a fibrous wall containing proliferating fibroblasts, reactive woven bone, and osteoclast-type giant cells.

Lesions Simulating Primary Neoplasms

Nonossifying Fibroma:



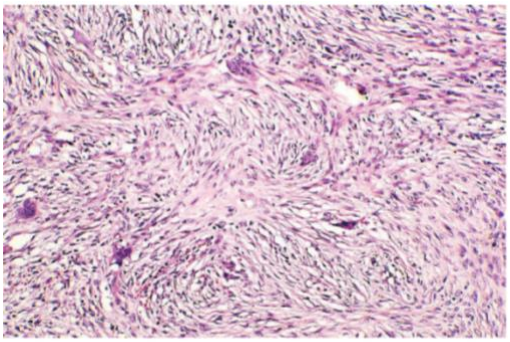


Fig. 21.30 Storiform pattern created by benign spindle cells with scattered osteoclast-type giant cells characteristic of a fibrous cortical defect.

- *Nonossifying* → no bone, *fibroma* → fibroblast proliferation. Meaning it **appears as a lytic lesion with no bone**. It is benign.
- Occurs in the **metaphysis of long bones**.
- Appears like osteosarcoma but that is ruled out because of the absence of Codman's triangle, it is well circumscribed, and no infiltration is observed (these features are named the '**benign features**').
- Also named: FCB or MFD (Fibrous Cortical Defect or Metaphyseal Fibrous Defect).
- **Clinical Course**: It is also argued that it might not be a true neoplasm but only a reactive process since it usually resolves spontaneously (expectant therapy).