MSS

Sheet no.

# Pathology

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# BONE TUMORS AND TUMOR LIKE CONDITIONS:

**Some concepts before we start:**

- **Primary bone tumors are rare: That is, secondary bone tumors arising from metastasis are much common than those originating primarily from bone.**
- **Benign is much more common than malignant tumors (10:1).**
- **Most tumors in the First 3 decades (benign); adults more to be malignant.**
- **Treatment: aims to optimize survival while maintaining function. (Survival rate after the treatment has improved dramatically in the last 25-30 years).**
- **Age & location help narrow diagnosis.**
- **Sign and symptoms: most of them asymptomatic because most of them benign, sometimes they present with pain or pathological fracture.**

| 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 |

- Notice each tumor type with its common location & age.
- Common location doesn't mean that the tumor can't be in a different bone, but we should memorize the common location & age to aid us in the diagnosis.

# BONE-FORMING TUMORS

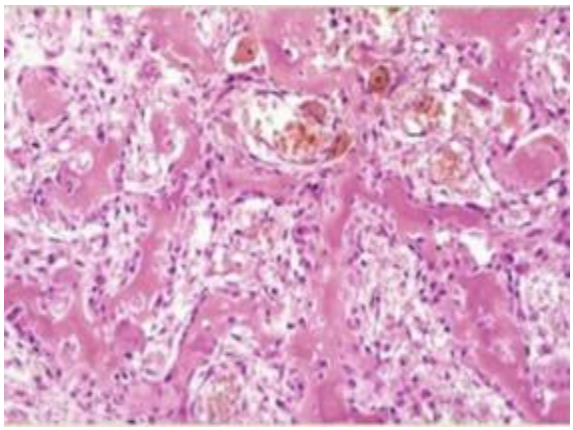
## 1-OSTEOID OSTEOMA

- Less than 2 cm
- Young men
- Metaphysis of long bones: Femur & tibia; nidus with surrounding bone reaction
- Severe nocturnal (night) pain (mediated by **PGE2**), relieved by aspirin & NSAIDS (non-steroid anti-inflammatory drugs).
- Treated by radiofrequency ablation (Removal of tumor by using strong radiation) or surgery.

## 2-OSTEOBLASTOMA

- More than :2 cm
- Posterior vertebrae; no rim of bone reaction by radiology
- Pain unresponsive to aspirin
- Treated by curetting (clean or scrape)

- **Histologically, both** look like reactive bone with some hemorrhage and reactive giant cells, **you don't see atypia**. At our level, they look the same histologically



- **Osteoid osteoma and osteoblastoma are benign tumors.**

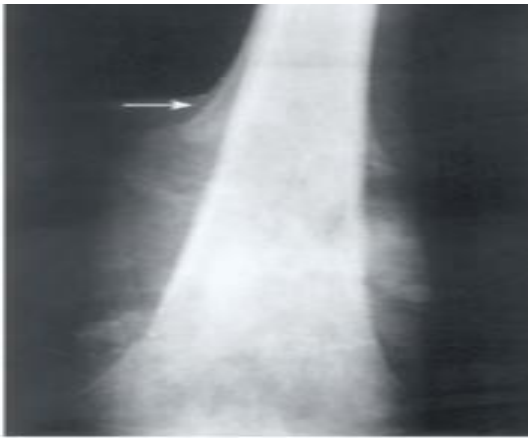
## 3- OSTEOSARCOMA:

- **Malignant osteogenic tumor** (Malignant osteoblast forming abnormal bone- woven bone).
- Excluding hematopoietic malignancies; **it is the most common primary malignant tumor of bone**
- **75% adolescents between (10-20); another peak in older (55-65)** (due to secondary osteosarcomas, they occur on top of a predisposing condition like **Puget disease or Chronic osteomyelitis**).
- **Males > female**s (1.6:1.0).
- **Metaphysis of long bones (distal femur & proximal tibia).**
- Patients present with **Progressive pain or pathologic fracture.**
- **X-ray Imaging**: large destructive and infiltrative lesions with characteristic Codman triangle, these start in the bone, and they go deep into the medulla and outside into the periosteum followed by infiltration of the periosteum and the surrounding soft tissue, they elevate the periosteum, and they start producing abnormal woven bone leading to the appearance of an angle known as **Codman triangle**.

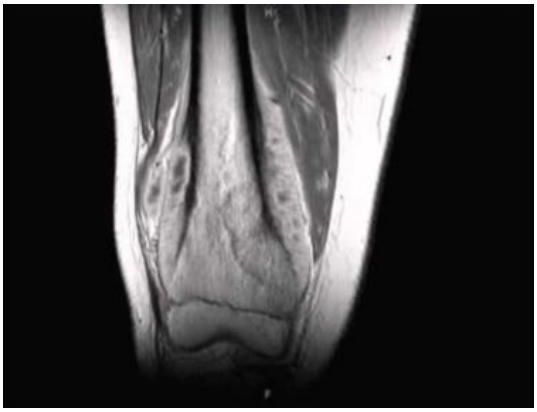
➢ Note: **Codman triangle is not specific for osteosarcomas**; It can be seen in any infiltrative bone lesions whether infectious or other tumors like **Ewing sarcoma.**

- Genetic abnormalities: **mutations in RB gene, TP53 gene, CDKN2A (p16 & p14), MDM2 & CDK2**

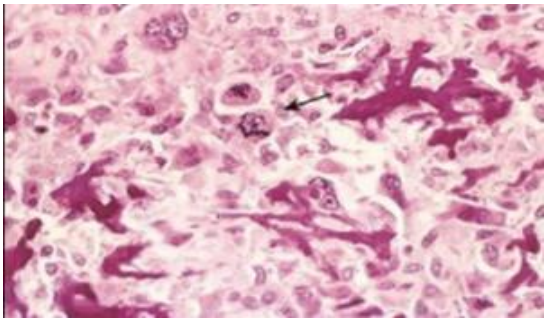
- **simple x-ray**, distal femur showing a process which started in medulla of the bone and infiltrate the surrounding tissue elevating the periosteum (→) and the angle between actual bone and the periosteum is called **Codman's triangle.**



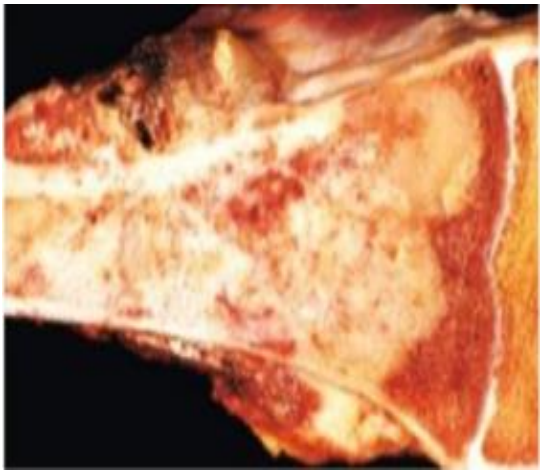
- **MRI** shows the processes, tumor arises at the metaphysis and extends to the soft tissue, the skeletal muscle infiltrated by this tumor, and the **periosteal elevation causing Codman triangle**.



- **histologically**: we saw malignant osteoid with haphazard patterns of frequent abnormal mitosis, **atypia of the osteoblast**.



- **the gross specimen**, we cut it longitudinally and articular cartilage of the distal femur and below it a tumor area



In the past the treatment was amputation, nowadays surgeries do **limb salvage resection** where they remove the affected part of the bone and replace it by artificial part (**Prosthesis**) without needing to amputate the whole limb and thereby affecting the patient activity.

## OSTEOSARCOMA TREATMENT:

**Multimodality approach (MDTeam)**

• **1. Neoadjuvant chemotherapy** (using chemotherapy before the main treatment which is surgery**) 2. Surgery 3. Chemotherapy and radiation**

**Chemotherapy** → to prevent or to kill any metastatic possibility

**Radiation** → to control the local diseases

**Surgery** → to bulk or remove the tumor

• **Hematogenous spread to lungs**: through bloodstream, and the most common location is to the lungs. There's some exception, they don't usually go to the lymph nodes.

• **5-year survival reaches 60-70%**: probably, it's improving now 75-80%.

• **Presence of metastasis at diagnosis is a bad prognostic factor.**

# CARTILAGE-FORMING TUMORS

## 1- Osteochondroma (benign exostoses)

- Its **benign tumor composed of benign bone and cartilage** (very common) and it's exophytic from long bones, **solitary (85%)** or sometimes part of **multiple hereditary exostoses (MHE): characterized by EXT1, EXT2 gene mutations**
- **Rare (<3-5%) transformation to chondrosarcoma**, if they do, usually they do in cases when they are MHE.

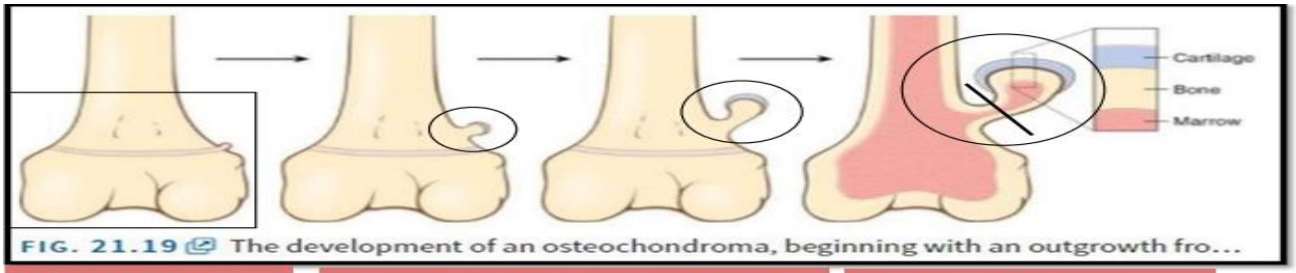


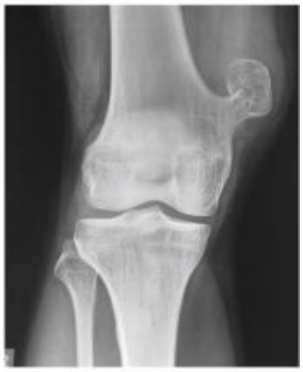

FIG. 21.19 The development of an osteochondroma, beginning with an outgrowth fro...

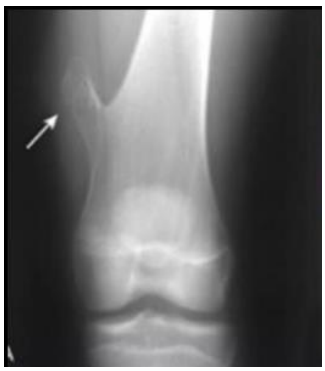
Most common location, around the cartilaginous plate

Extension of this bone and bone marrow goes out

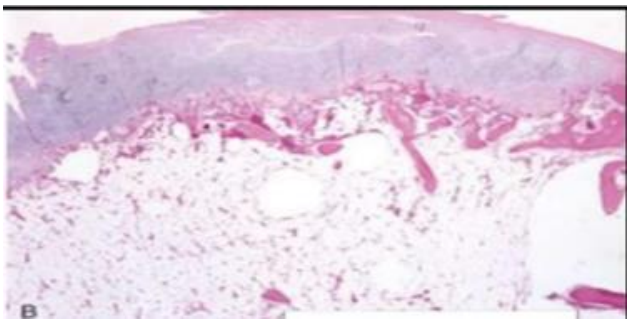
Covering by benign cartilage, so if you cut there, what you will see, normal cartilage, normal periosteum, normal marrow

- **X-ray**: osteochondroma, notice the tumor with normal bone and cartilage. The appearance of an Exophatic peduncaltated mass with a cartiliganinous cap



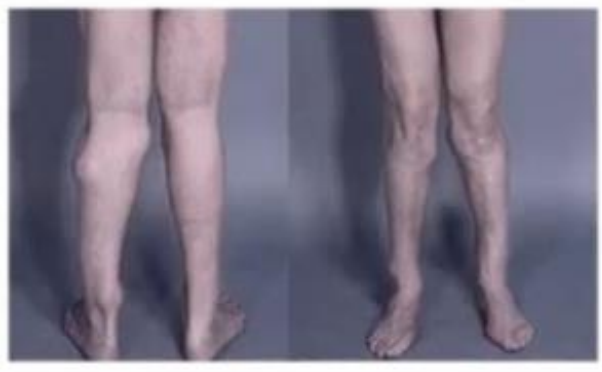


- **Microscopic histology**: normal cartilage, normal subchondral bone and bone marrow.



- **(Multiple hereditary exostoses) MHE case.**

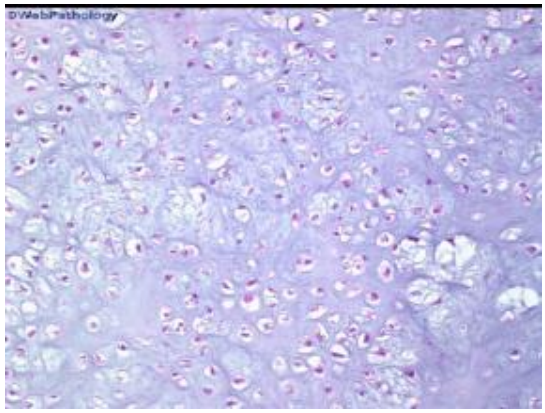
Upon diagnosing a patient with MHE, it is important follow up closely to watch those osteochondromas to avoid transforming to malignant chondrosarcoma



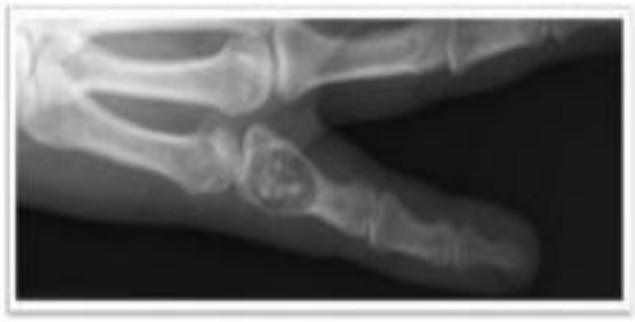
## 2- CHONDROMA(ENCHONDROMA)

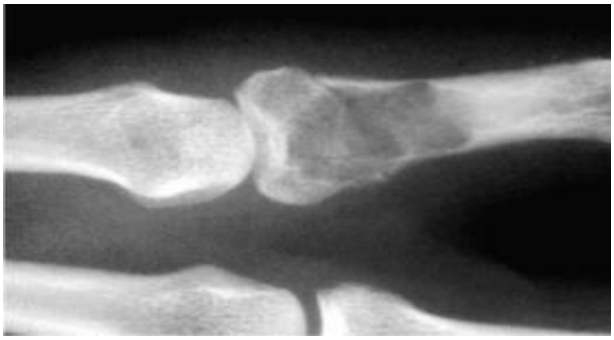
- **Benign hyaline cartilage tumors in bones with endochondral origin**; **medullary enchondroma or cortical chondroma**
- **Most time it's solitary, occurring in the metaphyseal lesions**, most common location: **the hands and the feet; 20-50 years**
- **Ollier disease**: Multiple enchondromas.
- **Maffucci syndrome**: multiple enchondromas + skin hemangiomatosis (red nevi)
- **IDH1 & IDH2 gene mutations**

- **Microscopic histology: normal benign cartilage No atypia**



- **X-ray Radiology**: Cartilaginous appearance on x-ray, no destruction, no elevation in the periosteum, and it's in the medulla.

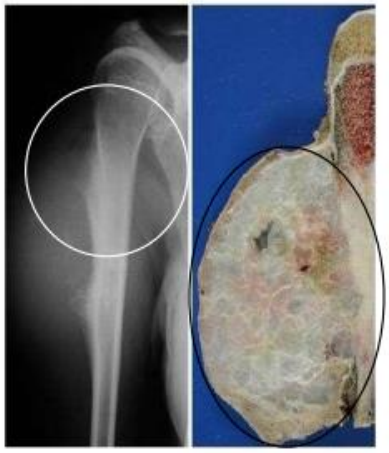




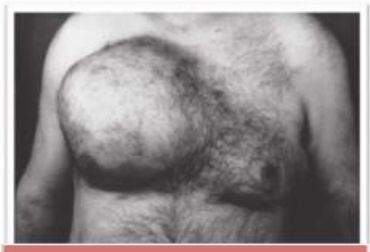
## 3- CHONDROSARCOMA

- **Malignant tumors producing malignant cartilage**
- **50% incidence of osteosarcoma**, chondrosarcoma is less common, if you treat 20 cases of osteosarcoma, you will maybe treat 10 in chondrosarcoma.
- **40-50 years of age; Male: Female (2:1).**
- Characterized with**:**
    1- **large masses around the shoulder, the pelvis, the ribs**.
    2- **Bubble soap appearance seen on CT-scan.**
- Genes**: EXT, IDH1, IDH2, COL2A1, CDKN2A**.
- **Prognosis depends on grade (grade 1 excellent px)**.
- **Treatment: surgical +/- chemotherapy**: Surgery is effective while chemotherapy isn't.

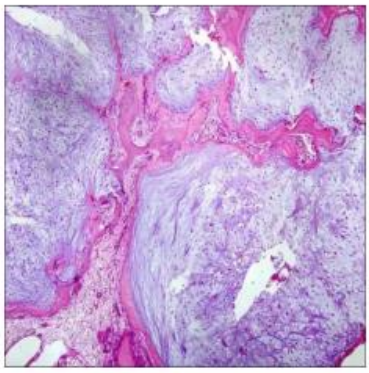
Huge chondrosarcoma in the diaphysis of the humerus, there's Codman triangle, the tumor is infiltrating into the bone marrow and outside of the soft tissue elevating the periosteum.



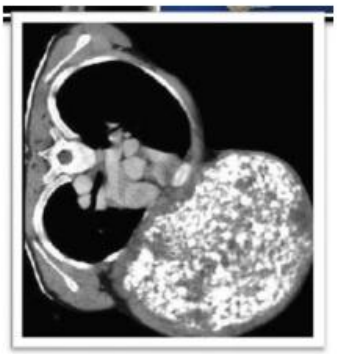
The second half of the pic, the gross specimen which when it was removed, characteristic cut surface of cartilaginous, it's large and infiltrating the soft tissue and the medulla bone.



Large huge chondrosarcoma of the ribs.



Histologically, it's malignant lobulated cartilage, this is probably grade 1 to 2, because I can still see the cartilaginous differentiation is obvious → low grade tumor.



Probably CT scan, where huge mass with a cartilaginous morphology on imaging, this is called bubble soap appearance.

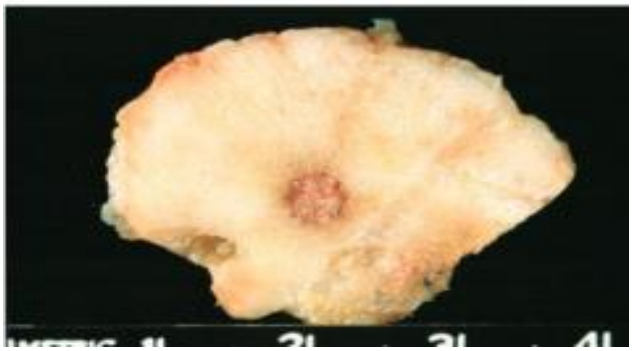
**The End**

## Practice problems:

***1-*** Secondary malignant chondrosarcoma is a possible complication for people who have which of the following benign bone tumors?

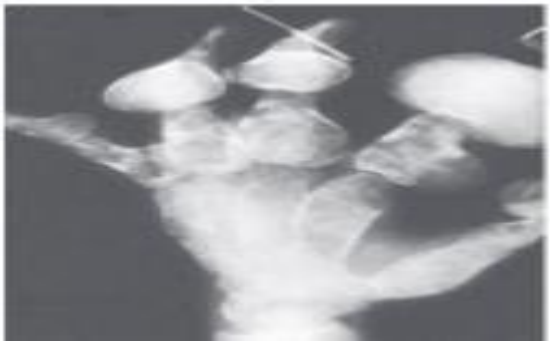
A. Non-ossifying fibroma
B. Enchondroma
C. Multiple osteochondromas
D. Osteoid osteoma

***2-*** A 16-year-old boy presents with a 2-week history of pain in his right leg. He says that he has been taking aspirin to relieve the pain. An X-ray of the leg shows a 1-cm sharply demarcated, radiolucent lesion in the diaphysis of the tibia surrounded by dense, sclerotic bone. The lesion is surgically removed, and the gross specimen is shown in the image. Microscopically, the tumor shows irregular trabeculae of woven bone surrounded by osteoblasts, osteoclasts, and fibrovascular marrow. What is the appropriate diagnosis?



A. Chondroblastoma
B. Giant cell tumor of bone
C. Osteoblastoma
D. Solitary chondroma
E. Osteoid osteoma

***3-*** A 35-year-old woman has multiple cartilaginous lesions in her long and short bones. A radiograph of the hand (shown in the image) reveals bulbous swellings. A biopsy shows abnormally arranged hyaline cartilage, with scattered zones of proliferation. This patient is at risk for which of the following bone diseases?



A. Chondrosarcoma
B. Giant cell tumor of bone
C. Osteosarcoma
D. Histiocytic lymphoma
E. Synovial sarcoma

## Answers: 1- C, 2- E, 3- A