Hashemite University
H·U·M
Medical School Committee

Scientific Team
الفريق العلمي

PATHOLOGY

Lecture : 6

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Bone of tumor

الملخص يشمل من سلايد 52 و حتى 75

(1) Fibrous Cortical Defect & Nonossifying Fibroma

It is very common

Fibrous cortical defects : عبارة عن سرطان حميد في العظام

Nonossifying Fibroma :

برضه عبارة عن سرطان حميد و يعتبر حالة متقدمة من Fibrous cortical defects و من اسمه يحوي على Fibrous tissue

Fibrous cortical defects: Occurs 30-50% especially children older than 2y / more to be defect than true neoplasm

الغالبية العظمى بكون حجمها اقل من 0.5 cm وموجودة بمكانين

1-metaphysis of the distal femur 2- proximal tibia

الغالبية الاقل بكون حجمها اكبر شوي 5-6 cm و بتطور الىnonossifying fibromas

50% are bilateral or multiple

كل من Fibrous Cortical Defect & Nonossifying Fibroma بكون شكله :

sharply demarcated radiolucencies surrounded by a thin zone of sclerosis.

بكون لونه بين الرمادي و الاصفر عالبني و على شريحة الهستولوجي بكون شكله

storiform or pinwheel pattern + macrophages +multinucleated cell

غالبا بكون بدون اعراض و بظهر بالصدفة على x-ray

متى بكون بحتاج biopsy و متى ما بحتاج ؟

اذا تحول ل normal cortical bone ما بحتاج biopsy (و غالبا هيك بصير و خلال سنوات قليلة)اما اذا زاد حجمه وصار nonossifying fibromas بالإضافة لوجود fracture هون ضروريbiopsy

(2) Fibrous Dysplasia

it is benign tumor +localized

المشكلة بتكون لما خلايا العظام ما بتقدر differentiated, مع انه باقي المكونات موجودة و بتكون على ثلاث اشكال

(1) 70% are Monostotic, involving single bone,

-It begins in early adolescence, & ceases with epiphyseal closure

موجود بشكل متساوي عند الرجال او النساء

From high frequency to low : ribs /femur /tibia / jawbones /calvaria /humerus

Clinically are :

(1) asymptomatic & discovered incidentally

(2) can cause marked enlargement & distortion of bone, & if the face or skull is involved, disfigurement can occur.

X-ray are :

1- characteristic ground-glass appearance

2- well-defined margins & lesions

It cured by surgical curetting.

(2) 27% are Polyostotic, involving multiple bones

It presents earlier than the monostotic type & can progress into adulthood.

In descending order of frequency, femur, skull, tibia, & humerus are most commonly involved.

Craniofacial involvement is present in 50% of patients with moderate skeletal involvement and 100% of patients with extensive skeletal disease.

Polyostotic disease tends to involve the shoulder & pelvic girdles, resulting in

1- severe deformities 2- spontaneous fractures.

(3) McCune-Albright syndrome,

3% i.e., polyostotic disease, associated with

1- café au lait skin pigmentations

2- endocrine abnormalities, especially precocious puberty.

Include

A- sexual precocity

B-hyperthyroidism

C- GH-secreting pituitary adenomas

D-primary adrenal hyperplasia.

3- The bone lesions are often unilateral

عند النساء اكثر من الرجال

Features of the skin macules are :

1- pigmented 2- large 3- dark to light brown (café au lait) 4- irregular

Clinically, polyostotic involvement (in 2 & 3) is frequently

associated with :

A- progressive disease

B- more severe skeletal complications including

(1) fractures

(2) deformities of long bone, craniofacial distortion.

(3)Rarely, polyostotic disease can transform into osteosarcoma, especially following radiotherapy

fibrous dysplasia characterized by:

1- well-circumscribed,

2- intramedullary tan-white

3- gritty masses.

4-Larger lesions expand & distort the bone

Histology:

1- exhibits curved trabeculae of woven bone (mimicking

Chinese characters)

2-without osteoblastic rimming

3-surrounded by a moderately cellular fibroblastic proliferation.

Ewing sarcoma & primitive neuroectodermal tumors

(PNETs) are primary malignant small round-cell Tumor of bone & soft tissue.

السبب بكون تبديل في الكروموسومات

approximately 95% of patients with Ewing tumor have t(11;22) (q24;q12) or t(21;22) (q22;q12)}, viewed as the same tumor, differing only in degree of differentiation.

بكون ال tumor نفس الاشي بس درجة differentiation مختلفة

طب شو الي بفرق بين Ewing sarcoma & primitive neuroectodermal tumors؟

● PNETs demonstrate neural differentiation / Ewing sarcomas are undifferentiated by traditional marker analysis.

□ These two malignancies account for 6% to 10% of primary malignant bone tumors.

After osteosarcomas, they are the second most common pediatric bone sarcomas.

● 80% of patients are younger than 20 years

الرجال و اصحاب البشرة البيضاء معرضون بشكل اكبرمن النساء و اصحاب البشرة الداكنة

☼ Grossly, Ewing sarcoma & PNETs arise im following area to produce a soft tissue mass :

1- medullary cavity

2- invade the cortex

3- periosteum

The T is tan-white, frequently with hemorrhage & necrosis.

◙ Tumor composed of :

1- sheets of uniform small, round cells that are slightly larger than lymphocytes with few mitoses

2- little intervening stroma

The cells have scant, glycogen-rich cytoplasm ///The presence of Homer-Wright rosettes (tumor cells surrounding central fibrillary space)

► Clinically, Ewing sarcoma & PNETs typically present as :

1- painful enlarging masses in the diaphyses of long tubular bones (especially femur) & the pelvic flat bones.

2- fever,

3-ESR

4-anemia

5- leukocytosis that can mimic infection {OM}.

 X-rays show:

(1) A destructive lytic tumor with infiltrative margins & extension into surrounding soft tissues; &

(2) A characteristic periosteal reactive bone deposition in an

(onionskin fashion).

●Treatment :

1- chemotherapy

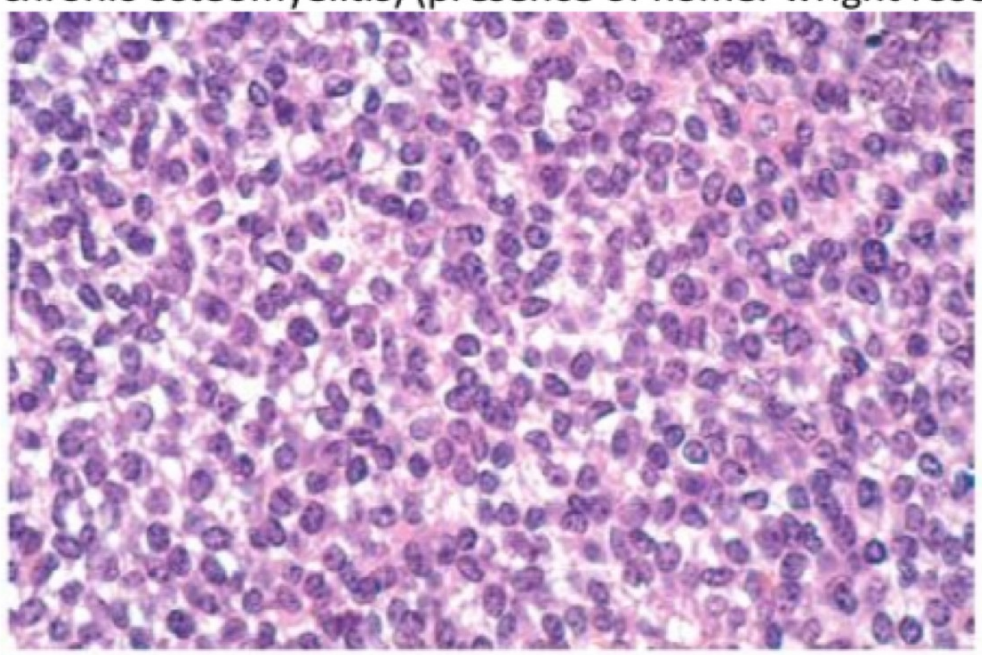
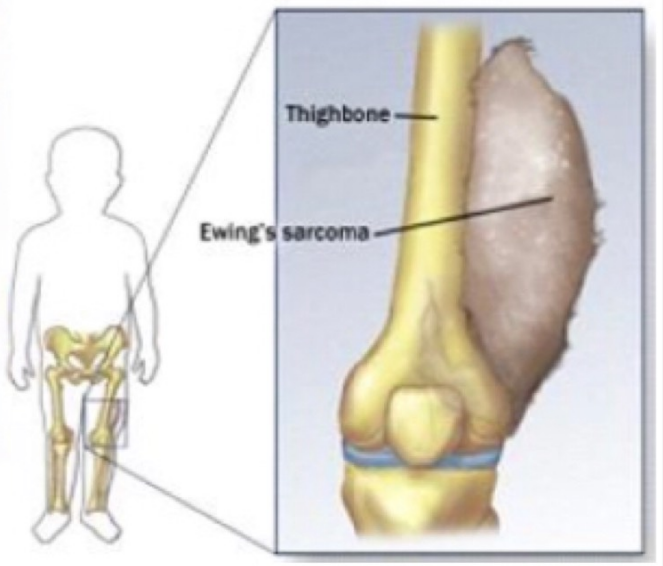
2-surgical excision with or without radiation.

The 5-year survival is currently 75%.

An 11-year-old boy presents to the emergency department complaining of a painful, swollen mass in his right leg. He denies any history of trauma to the leg. Laboratory tests reveal anemia, leukocytosis, and an elevated ESR. An x-ray of the mass demonstrates a lytic tumor with an onion-skin appearance in the medullary cavity of his right femur. You admit this patient to the oncology service and you fear that his prognosis is grim if the mass has metastasized.

Ewing Sarcoma

Etiology and Epidemiology	Associated with chromosomal translocation **t (11;22)** Categorized as a **small round blue cell tumor,** but tumor cell origin is unknown Occurs most frequently in **boys < 15 years old**
Pathology	*Gross:* Arises most often in the medullary cavity of **long bones, pelvis, ribs, and scapula** *Microscopic:* Sheets of small, round, blue, **uniform cells** with little cytoplasm; tumor cells may be arranged in **pseudorosette** fashion; necrosis may be apparent
Clinical Manifestations	**Painful, swollen, enlarging mass;** systemic signs including fever and anemia **(may mimic symptoms of osteomyelitis)** *Imaging:* Lytic tumor with **onion-skin** appearance on radiograph *Lab findings:* Leukocytosis, elevated ESR
Treatment and Prognosis	Surgical resection; chemotherapy; radiation Extremely **aggressive tumor** that is prone to metastasize early; 5-year survival is 70% if localized disease and 30% if metastatic disease

Ewing sarcoma	Defn	- Malignant tumor of poorly differentiated neuroectodermal cells seen most commonly in diaphysis of males <15 years
	Imaging	- Onion skin appearance on X-ray - Tumor arises in medullary cavity and comes outside the cortex to make soft tan-white mass
	Biopsy	- Small round blue cells that resemble lymphocytes (can be confused with lymphoma or chronic osteomyelitis) (presence of homer wright rosettes indicate neural differentiation)  **Figure 20–14** Ewing sarcoma. Sheets of small round cells with scant, clear cytoplasm. 
	Cause	- Often associated with 11;22 translocation (ewing sarcoma gene (EWS) on ch 22 merges with transcripton factor gene; precise pathophys unknown)

	Prognosi	- Often metastasizes but responsive to chemotherapy
	-	
Malignant tumors	- Most common malignant bone tumors - Classic site of origin (lead kettle - PB KTL) - Prostate>breast>kidney>thyroid>lung - Usually causes osteolytic (punched out) lesion except prostate that cause oseoblastic (sclerotic) leison	

Giant-Cell Tumor (GCT) of Bone = osteoclastoma

GCT is dominated by multinucleated osteoclast-type giant cells, hence the synonym osteoclastoma.it is uncommon + it is benign (?)

locally aggressive arising in the 20 to 40 years age group.

giant cell component is :

1- reactive macrophage population

2-the mononuclearcells (which show complex cytogenetic abnormalities) are the neoplastic cells.

Grossly GCT is:

1- solitary 2- large 3-red-yellow-brown (orange), with cystic areas4-necrosis5- hemorrhage

◙ Histology it composes of:

1- uniform oval mononuclear cells with frequent mitoses

2- scattered osteoclast-type giant cells containing up to 100 or more nuclei

►Clinically,

- any bone can be involved

Where is the majority of GCTs?

present an enlarging mass arise in the epiphysis of long bones around the knee (distal femur & proximal tibia)

 On X-ray GCTs are :

1-large, purely lytic, & eccentric

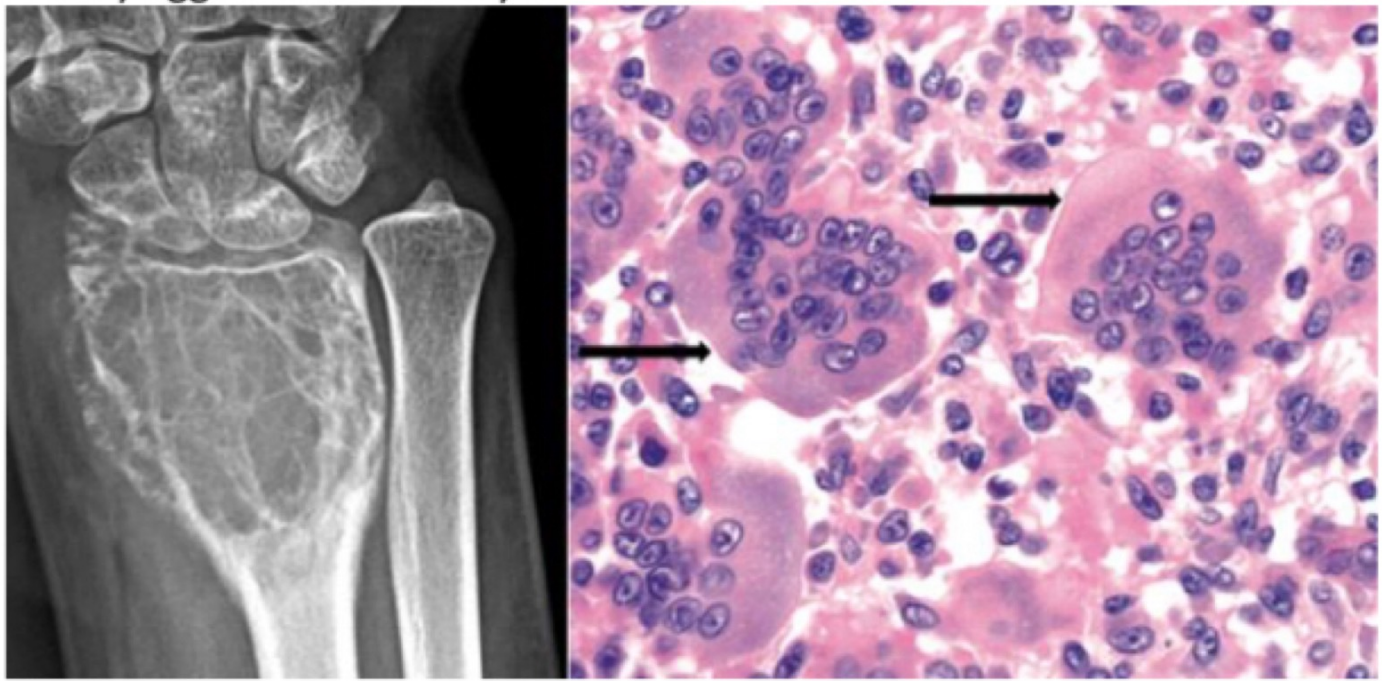
2-the overlying cortex is frequently destroyed, producing a bulging soft tissue mass with a thin shell of reactive bone (Soap bubble appearance).

Although GCTs are histologically benign, half recur after simple curettage & 4% metastasize to the lungs.

A 32-year-old woman presents to your office complaining of pain in her right knee joint. Physical examination does not reveal any evidence of infection. Radiographs of the knee demonstrate a mass with a characteristic soap bubble appearance. You reassure the patient that this mass is probably benign, but you suspect that there is a good chance of recurrence even after surgical excision.

Giant Cell Tumor

Etiology and Epidemiology	Benign tumor derived from monocytes Most commonly affects **women** between the **ages of 20 and 40**
Pathology	*Gross:* Most commonly arises from **epiphyses of long bones especially around the knee (distal femur, proximal tibia);** large and red brown; often see cystic degeneration or necrosis and hemorrhage *Microscopic:* **Uniform oval mononuclear cells** demonstrating many mitoses; spindle-shaped **osteoclast-type giant cells** with up to 100 nuclei; fibrous stroma
Clinical Manifestations	**Joint pain** and other arthritic symptoms; fractures *Imaging:* **Soap bubble or double bubble** appearance on radiograph
Treatment and Prognosis	Surgical excision Very rarely becomes malignant, but is still aggressive and **recurs after treatment 40%–60% of the time**
Notes	**Enchondroma** is a benign cartilaginous neoplasm arising from the intramedullary bone and is most commonly seen in the hands and feet. Enchondromas are often asymptomatic and found incidentally on radiograph (characteristic "*O ring sign*" on x-ray), but they may be painful and cause a fracture.

Giant cell tumor	- Biopsy shows multinucleated giant cells and sromal cells - Soap bubble lesions seen most commonly in epiphysis of long bones - mostly distal femur or proximal tibia - Locally aggressive and may recur 

Metastatic Disease

☼ Metastatic secondaries in bone are the most common malignant tumor of bone.

Pathways of spread include:

(1) Commonly by blood

(2) Direct extension (rarely).

 In adults, more than 75% of skeletal metastases originate from ca of:

Prostate//lung//breast // kidney.

☻ In children, the common sources of bony Metastases:

neuroblastoma /Nephroblastoma (Wilms' tumor)/ osteosarcoma / Ewing sarcoma/ rhabdomyosarcoma .

● Most metastases involve in :

1-the axial skeleton (vertebral column, pelvis, ribs, skull, & sternum)

2-proximal femur

3- humerus, in descending order.

Why?

Because the red marrow in these areas, with its rich capillary network, slow blood flow, & nutrient environment, facilitates tumor cell implantation & growth.

● Bone metastases are usually multiple, & their radiological appearance can be purely lytic, purely blastic, or both.

What is substances that metastatic cells secrete that stimulate osteoclastic bone resorption?

prostaglandins, interleukins, & PTHRp more common type, the lytic lesions

(e.g., from kidney, lung, & melanoma)

(the tumor cells themselves do not directly resorb bone)

●Similarly, metastases that elicit a blastic or sclerotic response (e.g., prostate adenocarcinoma) do so by stimulating osteoblastic bone formation.

Many metastases induce a mixed lytic & blastic reaction.