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Pathology #3

مجموعة التعريف السريع

MSS

Subject: Bone Tumors

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بسم الله الرحمن الرحيم

The doctor started the lecture remembering us that she started in the last lecture talking about the bone tumors and some good diagnosis that we should pay attention about it :

1.good history

2.appearance in x-ray

3. site of tumor (80% OF DIAGNOSIS)

And she mentioned that the tumors could be in different parts of one bone (diaphysis.. metaphysis .. epiphysis .. etc) or in different location of the body (skull bone .. vertebra..long .. etc)

Let's go to today's lecture ☺

Bone tumors

Tumors IN Bone may be :

I- PRIMARY

II- SECONDARY (Metastatic)… which is more common than primary

- Any tumor can metastasize to the bone but **Common sites of <u>primary cancers</u> that metastasize to bone : prostate, breast, thyroid, kidney, lung, GIT**
- **<u>Secondary tumor</u> (metastatic legions) may radiologically be :**
  - **1- Osteoblastic (bone forming) (prostate, breast),**
  - **2- osteolytic (bone distraction) (kidney, lung and melanoma**)
  - **3- Mixed (both Osteoblastic or osteolytic)**

The main tumors that metastasize to bone in children are:

1- **Neuroblastoma, may be diagnosed in the bone before diagnosed as primary tumor**
2- **Nephroblastoma**
3- **Ewing's sarcoma , which in fact a tumor in a bone but can metastasize to another bones ..**

The most common site to find the tumor is :

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

2- proximal femur

3- humerus

❖ Less common to see the metastasis tumor in short bone compration with big bones

I- <u>Primary bone tumors</u>

- **Could be benign or malignant**
- **They classified into :**
  A- **Bone forming**
  B- **Cartilage forming**
  C- **Miscellaneous: large group of tumors sometimes its origin not defind**

- **The most common tumors in <u>middle age</u> is : Multiple myeloma (tumor of plasma cells) .**
- **The most common tumors in <u>children or adolescents</u> is : Osteosarcoma**

The list which you found in the slide is not to memorize so we didn't put it here … ♡

A- **Bone Forming Tumors**

Classified to benign and malignant

Benign :

1- **OSTEOID OSTEOMA/OSTEOBLASTOMA**

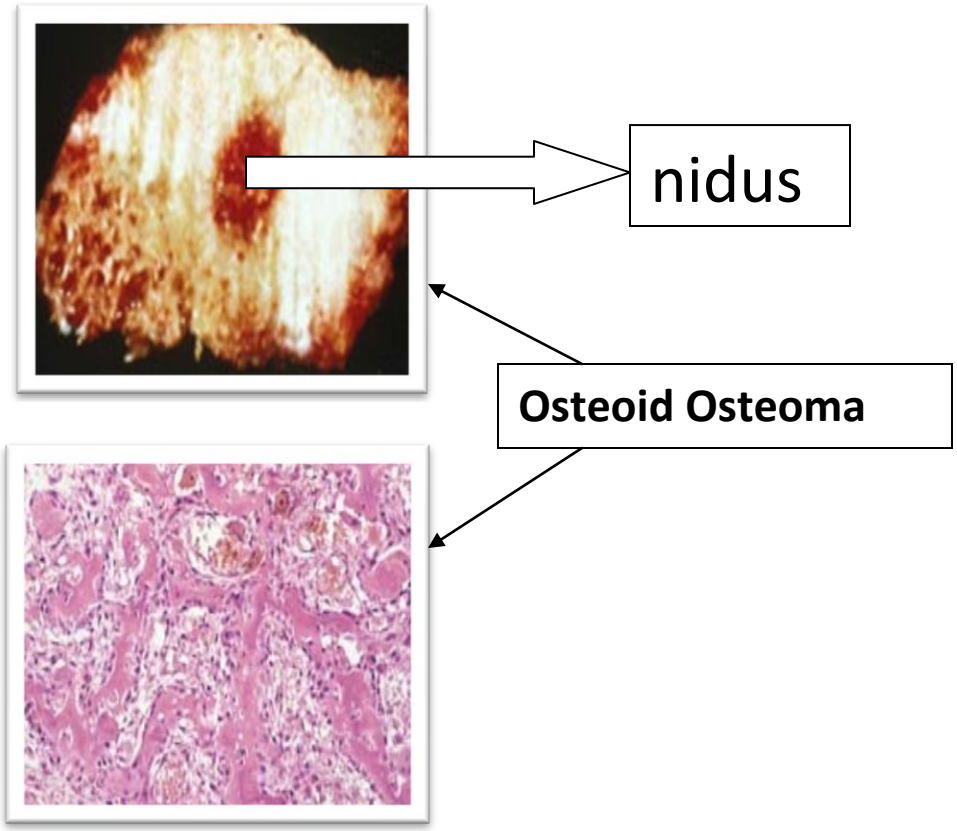
- **O.Osteoma common site proximal femur It's diameter less than 1.5-2cm**
- **It's seen more in teenage & twenties and In male more than female m:f 2:1**
- **Typical symptom :**

❖ **localized pain ..** it's throbbing pain (pain-pulsating).

❖ **worse at night**

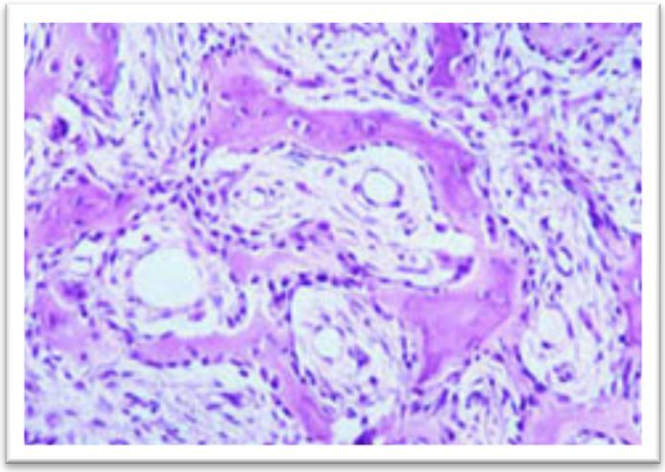
❖ **unrelieved by aspirin**

- **X-ray: well defined cortical tumor with well defined radiolucent central nidus(nodule) مثل الندبة …** The nidus is intramudallary
- **Simple OSTEOMA occurs in bones of skull causing a pain due to the pressure on various nerves.**
- **Histology: Trabeculae of woven bone surrounded by osteoblasts with central vascularized nidus.**

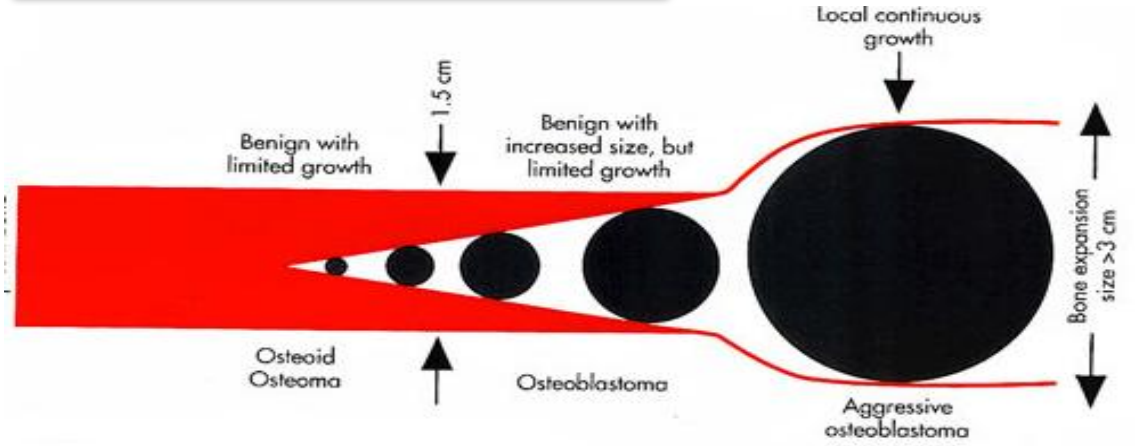


Osteoblastoma

- Histolgically osteo. osteoma and osteoblastoma are similar.
- it's bigger than osteo. osteoma it's size more than 1.5-2 cm. it could be 3 cm in diameter… but in some cases it is more than 3 cm and we call it in this case Aggressive osteoblastoma
- more in axial skeleton.



this is osteoblastoma there's osteoblast … no mitosis .. no vasularity

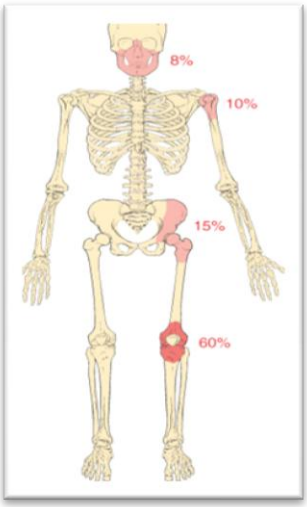


- **We should differentiate between osteoblastoma(aggressive) and osteosarcoma (malignant)**

Malignant :

2- **OSTEOSARCOMA**

- **Malignant mesenchymal neoplasm. The neoplastic cells produce OSTEOID**
- **Most common malignant primary, non hematopoietic, bone tumor**
- **More in male than female**
- **Common in the younger. 75% < 20 years old**
- **Common site is knee bone**
- **Common part is metaphysic**
- **May be multiple in children with p53 mutation**



This pic. shows the common site of the skeleton can involve by osteosarcoma

Primary, arising de novo

- Now basically osteosarcoma is arising by itself without a pre-exposing underlying condition these called **de novo**, however you can get **Secondary to an underlying bone** disease, **Paget's disease** which we toke previously is a rabid turnover of bone and muscularity, and in adults who pre-expose to osteosarcoma these why I said its can occur in other each groups. so it occur especially male who is above 40 we have to exclude the possibility of UNDERLYING BONE disease .
- The other thing that may initiate of sarcoma is : **Radiation** where is **therapeutic or exposure**

- **<u>Most are intramudallary</u> but they extend into cortex and then into periosteum to outside and extend to the soft tissue until very late it may extend into the joints otherwise it does not .**
- **There is variance which are of lower grade and less aggressive which are called <u>Paraosteal (Juxtacortical)</u> and <u>Periosteal</u> (not intramudallary area)**

Pathogenesis :

- **Genetic mutation :**
  - **can be identify first of all retinoblastoma gene mutation chromosome 13 in 60-70% of sporadic cases and also familial cases of retinoblastoma.**
  - **So inherited familial retinoblastoma other mutation p53, cyclins, CDK's…and others**
- **Predisposing conditions…**

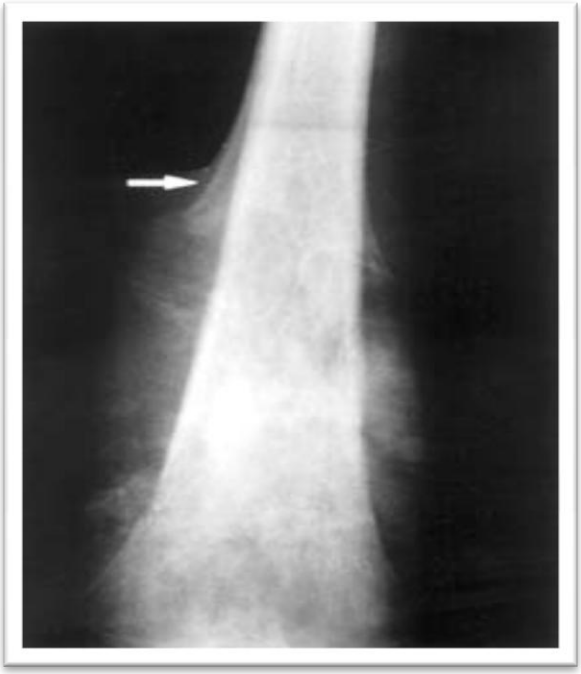
Clinical features

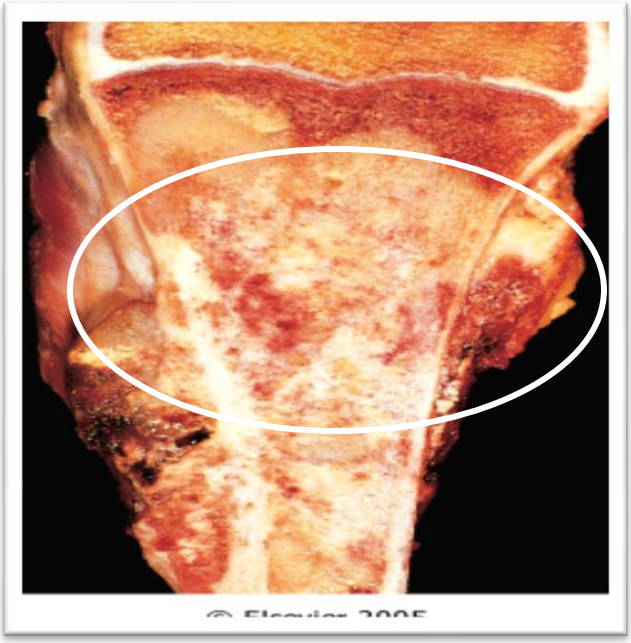
- **very enlarging mass with or without pain but usually with pain because it is large.**
- **At late present with pathological fracture, maybe a problem in the diagnoses which is the tumor bone and which is the repair bone.**
- **Hematogenous metastasis is common, mostly to the lungs in fact in many cases with the patient presents, the first diagnoses if may he already have metastasis to the lung before the treatment is** initiated .
- **Radiologically there is cortical destruction and extension into the marrow or sub-tissue .**
- **There is feature is seen Radiologicaly which is very suggested of ostosarcoma this is the <u>codman's triangle</u> where is periosteal reaction to the tumor with new bon formation its raises perosteum.**

This is Codman's triangle you see the triangle (which pointed by the arrow) and there is extension of the tumor

And you can see the thickened **periosteom** which is raised and there is an angel producing triangle which is called Codman's triangle …

لا تحزن إن الله معنا

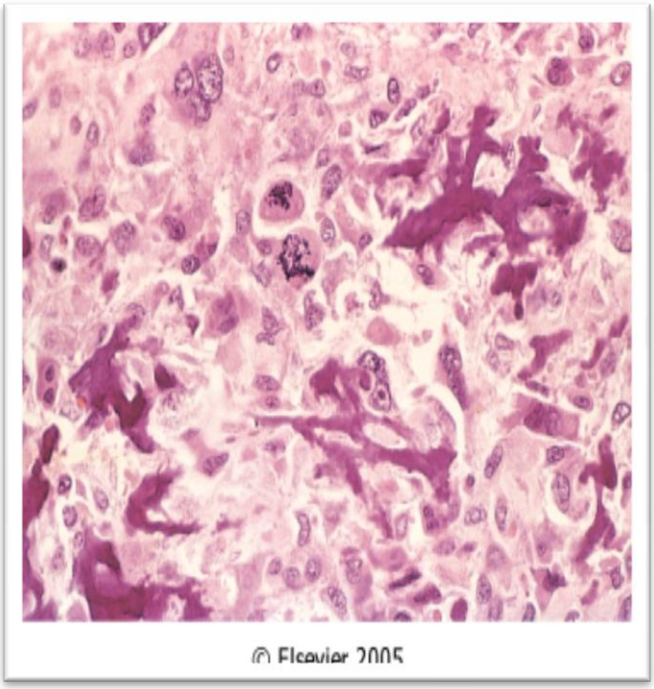




This is a gross appearance you can see the tumor which is extending to the outside .. ☹

Pathology and Treatment

- The pathology is the presence of **large malignant cells, prominent mitoses many of which is abnormal**
- **The osteoid is different from the repair osteoid is very less like irregular it has a proper orientation and form directly by the malignant cell .**
- **it also may have <u>Numerous osteoclasts</u> and this important osteoclastes as well because miss leading and diagnose of something else.**
- **There are variance subtypes (Predominantly osseous… Chondroblastic… Fibroblastic) which they do not affecting the prognosis but (Telengiectatic) affect it.**
- **in general it could be mainly bone it could contain cartilage it could be fibroblastic and it could be a mixture of anything than osteosarcoma… But important significant finding <u>you have to see osteoid</u> (if you didn't see the osteoid you cannot call it osteosarcoma) and sometime osteoid is very little and you have to find it .**



This is type of ostosacroma is lees like .and we see the tumor cells is very huge cells

The treatment nowadays : **give the chemotherapy** a heave coarse induce the necrosis in the tumor cells . the more necrosis in the tumor the better for the patient and actually measured how mach necrosis there is and is link to prognosis and may be flowed by **surgery** and **radiation** …

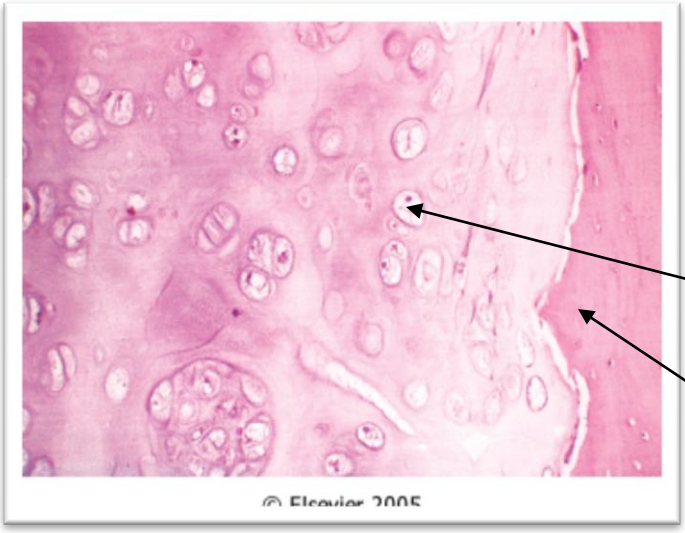
Prognosis :

- **Aggressive tumor**
- **The prognosis depends on the stage & variant of the tumor (conventional or other variants), location……etc**
- **The grade is not as important as stage in osteosarcoma.**

B-Cartilage tumors :

1- Chondroma & Enchodroma

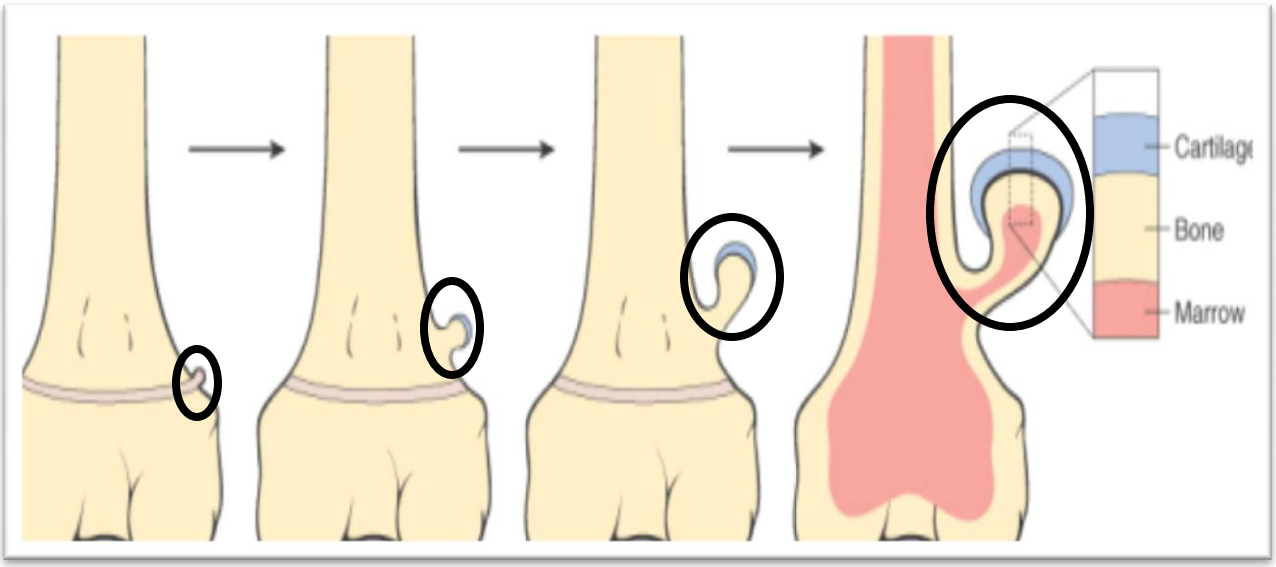
- Usually these are **solitary benign** growths of mature cartilage.
- When it is inside : **intracortical / enchodroma** , inside the bone .
- Or it is in the periphery : **extracortical .**
- **Any age can be affected**.
- In the case of chondromas , they **affect small bones** of the hand and the feet , pelvis , long bones , and so on..
- You can have it **multiple** , usually it is inherited syndromes of multiple cartilage tumors together with other findings , one of them olier's disease . now here the tumors are often larger and the insedience of the malignant transformation to **chondrosarcoma is seen in about 1/3** of the patients .
- Usually the chondrosarcomas occur in the exoskeleton , it is highly unlikely to have in the fingers and toes a chondroma which changes to chondrosarcoma , this is unacceptable .



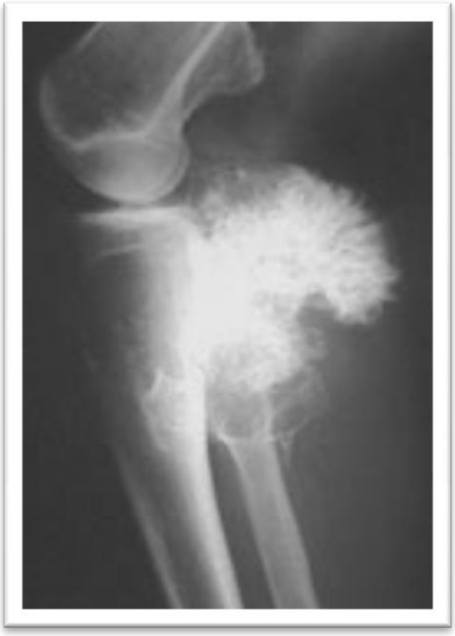
It is usually a worse ……. Of mature cartilage . and this is a mature cartilage and this is the periphery

2- **Osteochondroma (exostosis)**

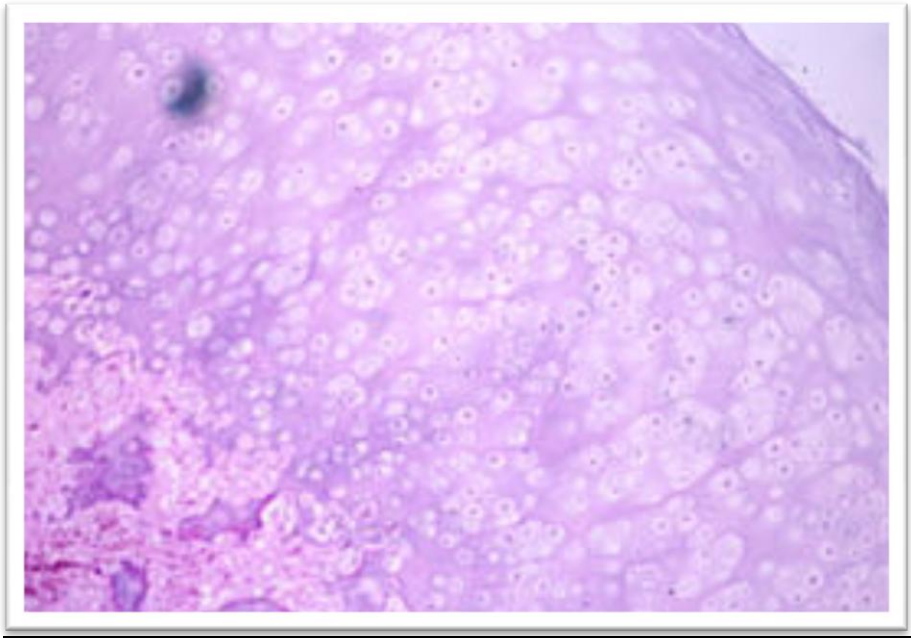
- It is very common , single , anybody can get it , a lot of people get it , or it could be inherited and multiple .
- They arise from the metaphysis near the growth plate of long tubular bones , may reach 1-20 cm in diameter .
- the majority is around the knee .
- composed of outgrowth of cartilage cap overlying bone and bone marrow . and the whole thing.
- may be ossified and very very rarely you may find osteosarcoma arising in Osteochondroma , and the first sign if the change is very thick cartilage cap .



this is the plate , and here there is an outgrowth and it becomes bigger , this is the cartilage , and here it is bigger .



this is the section



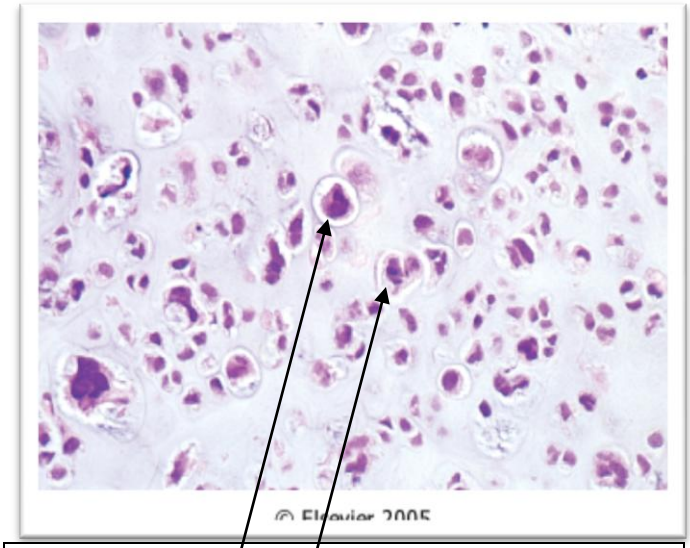
this is very cellular cartilage , so there are cartilage cap on the bone , by time it is not removed , it is very slow symptom , all of this become bony instead of cartilaginous .

3- Chondrosarcoma

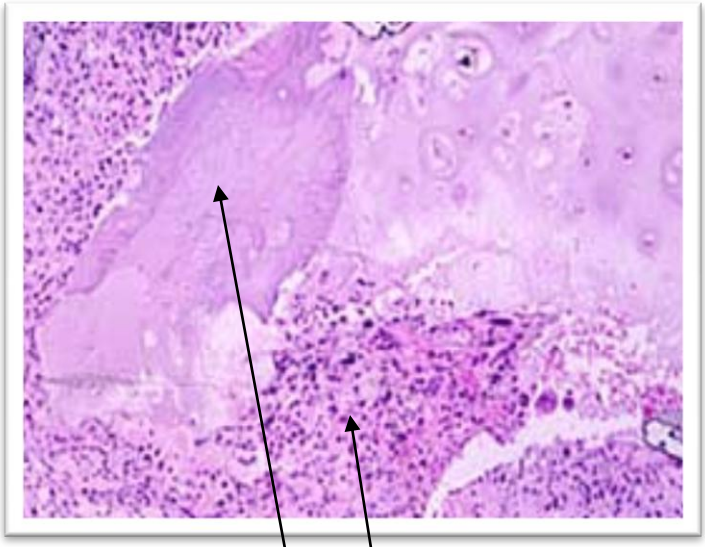
- Is a **malignant tumor** that produces cartilage matrix .
- Usually in **older patients** 40-60 , **more in males** .
- In the **central skeleton** , it is unlikely that the peripheral skeleton will ever get chondrosarcoma >> pelvis , shoulder , ribs are sites that known ,
- The primary (de novo) is the majority . The secondary : multiple enchondromas and rarely osteochondromas .

Morphology :

- **Grossly** : it is glistening mass in the medullary cavity .
- **Histologically** : variable polymorphism , and nucleation and this is very important . **no osteoid formation** in chondrosarcoma . if we find osteoid then this is propably Chondroblastic type of osteosarcoma .
- **Prognosis depend on the grade** , some tumors may be very well differentiated , it will be difficult to differentiate from benign one except for the thick cartilage .
- 10% show dedifferentiation , which means they become much worse and then they metastasize to the lung … etc



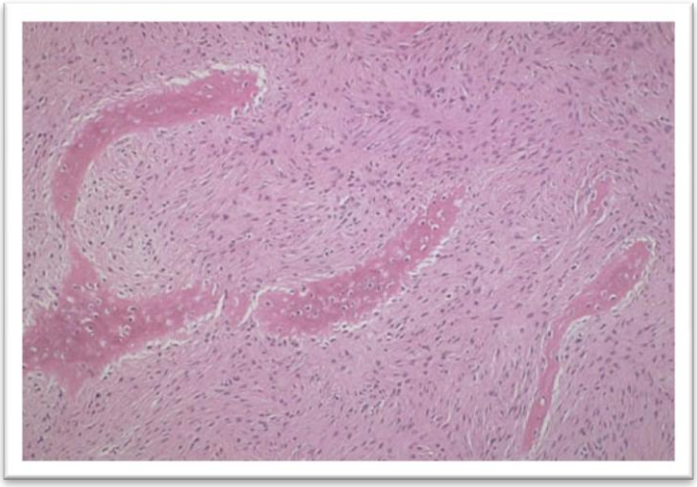
there are some pleomorphic chondrosarcoma , the cells are very pleomorphic , u see 2 or 3 in the same lacunae , and very cellular



this one is a somewhat a low grade cartilaginous tumor , wherease this one here outside is a very cellular differentiated sarcoma … prolofiration . so , this here is a dedifferentiated chondrosarcoma to call it we have to see the better cartilage with the worst like in this picture .

Fibrous Dysplasia :

- It something may be related to growth , or inherited failure of normal bone elements to differentiate into mature bone . so , it could be something in abnormal growth rather in actual tumor .
- Basically it is one of two types , it could be single one and this is called **monostotic** , and It could be **polystotic** where you have more than one lesion , and there name point to it is that it may lead to fracture and it is systic.
- what we get is localized intramudallary fibrous lesion with the bone is very curved and what is called woven bone **'Chinese letters'** .. and there is no osteoblast because there is no proper bone formation .



if you look at this , it looks like an irregular (y) and have many curved areas , and it is usually in young people , and treatment : you just

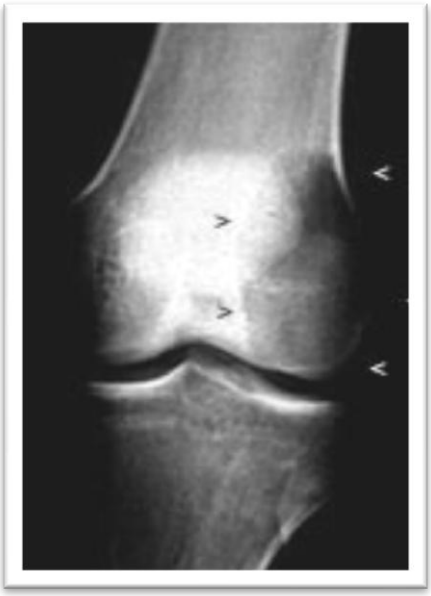
C- Miscellaneous Tumors

1- Giant cell Tumor (osteoclastoma)

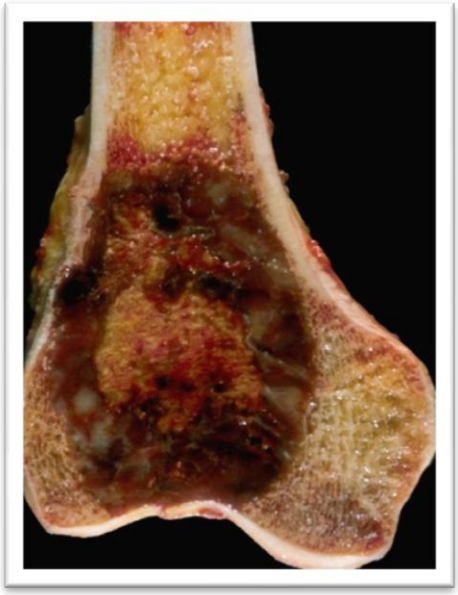
- The origin of this is debatable but this is a very important tumor its fairly common compared to other tumors , its also called osteoclastoma because it contains numerous tumor's osteoclasts .
- It's a **bulky big tumor** at the end of long bones which is the most common site ,mainly in adults (20 - 40) and more in females.
- **Sites** : epiphysis of long bones , tibia , fibula and extends into the joints (important .. when u look at giant cell tumors)
- **The majority are solitary** but u can have more than one lesion but its unlikely as said above its solitary and this is important because when talking about BROWN Tumors (which enter with differential diagnosis) both of them contain giant cells but in brown tumors its more probably that its multiple related to hyperparathyroidism.
- **Histolgically** : there are **two basic populations** of cells :

  1 : Multinucleated large osteoclast : which are very big and they contain Nemours nuclei .. these are mixed with ordinary giant cells like forgein body giant cells but the nuclei here is smaller

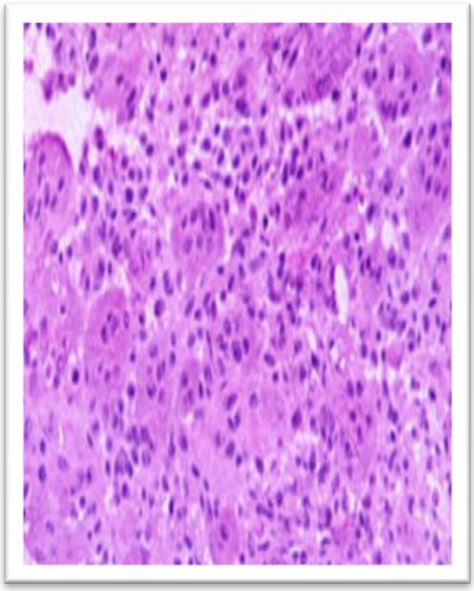
  2 : in the background of mononuclear stroma , the cells are mononuclear and they are the cells that are the neoplastic ones not the osteoclast but in spite the name its osteoclastoma it is the stromal cells which are neoplastic and forming the osteoclast.



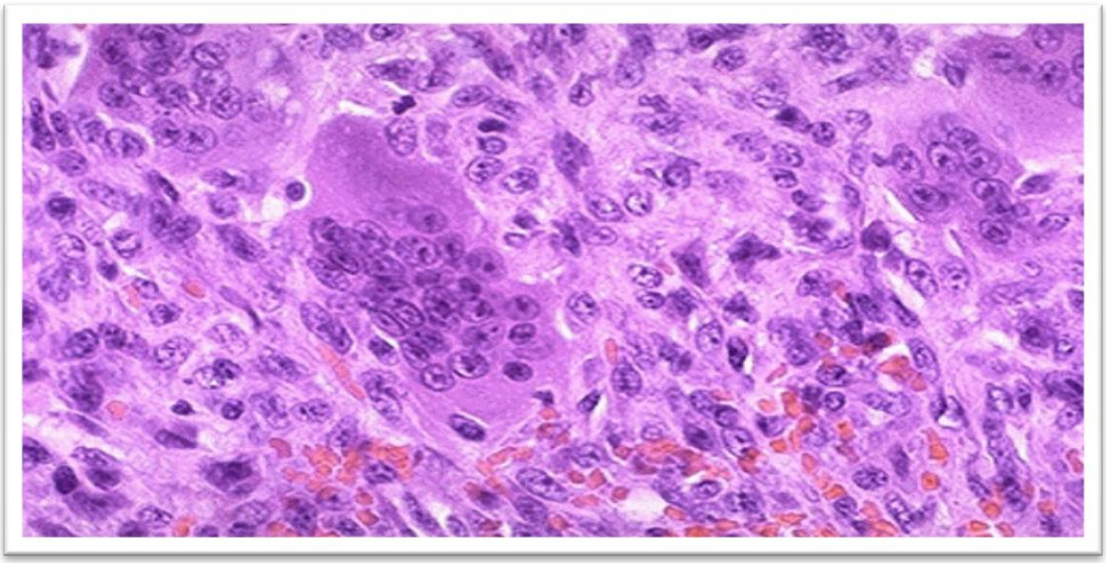
Radiologically figure



this is hemorrhagic big tumor and its extending into the fibrous plate



Numerous osteoclasts



if u notice this osteoclast and look at the nuclei they are exactly similar

to these nuclei which are outside and this is a clue to help in diagnosis

(i.e. the nuclei of osteoclast is similar to stromal ones) in other giant cells are don't look like stromal cells

so this is very important

- **Differential diagnosis:** a similar picture maybe seen in many regions :

  - aneurismal bone cysts
  - Brown tumors of hyperparathyrosidm
  - osteosarcoma of Giant cells
  - Many , many others

- they all contain giant cells so you really have to a good clinical and radiological correlations ,

  if its enter the joint it unlikely to be those
  if it has cheats of osteoclasts its unlikely to be those
  if it's in a child with multiple lesions its unlikely to be those either

Clinical behavior

- The behavior of giant cell tumors is **very unpredictable**

  - The majority are benign , less commonly aggressive or reoccur

  -It has been found that even if they are benign rarely they may metastasize to the lung but not as ordinary metastasis and kill the patient .

  - patient can also have sarcomatous transformations which is common , can metastasize anywhere specially to the lung so its a true sarcoma compared to the previous one (which rarly metastesize to lung) which maybe a true or maybe not

- now when we look at any tumor of this type **we have to check for the mitosis in the stromal cells** not in the osteoclasts because these what form the tumor..

- **treated by : surgical curretage or resection**

2- EWING SARCOMA

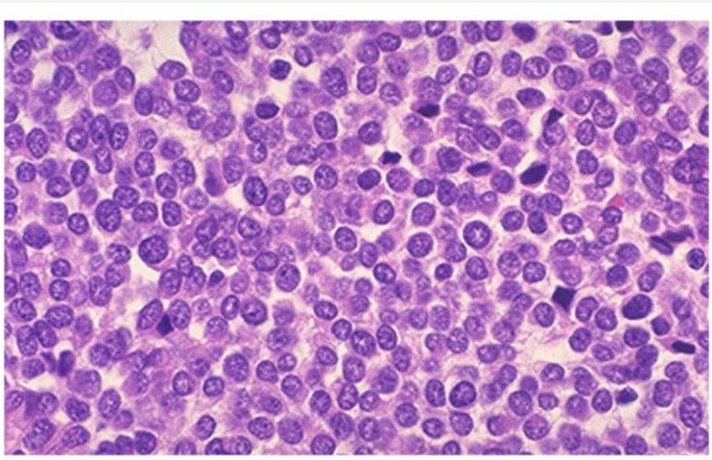
- This is a **Primitive Neuro-Ectodermal Tumor (PNET)**
- it's really composed of cheats of undifferentiated brown cells within the marrow cavity , **SMALL BLUE CELLS TUMORS** , because in many sites EWING Sarcoma is one , Retinoblastoma , and Neuroblastoma is another , and so on .These small blue cells tumors lead a pattern of **immunohistochemical stains** , we'll hear about them in the lab .

- **More in males** , **mostly teenagers**
- There is a **classic translocation t(11:22)**
- **Radiologically** : it's a bone Destroying Lytic medullary lesion and around it the periosteiom is laid down in layers which form what is called **onion skin** ,the timorous cells in the centre and the periosteiom around them…

Morphology

- **Gross** : usually affects the diaphysis of long bones , pelvis , tibia with necrosis and hemorrhages
- **Micro** : cheats of undifferentiated round blue cells , these blue cells are composed of more than 80% from glycogen so they are **Pas Stain Possitive** , if you put diastase on them they will be cleared and this is one of the clues and of course it has to be packed by a number of immunohistological stains
- **Tumor cells destroy the cortex** --> the periosteum --> then invade the surrounding tissues.

this is a huge tumor extending to the outside and this is what it looks like ,



these small blue tumor cells look exactly like lymphocites (lymphoma)

and so , lymphoma is considered in the differntial diagnosis of small blue cells tumor

Clinical Features: Mass, pain with local inflammation

Treatment : chemotherapy, surgery and/ or radiation

Prognosis: 5 year survival rate of 75%

THE END

FORGIVE US FOR ANY MISTAKE

هذا العمل من إعداد "المحاربون القدامى" ☺:

1 حسن نايل الرحابنه
2 عمار السـرحان
3 عمار العناقرة
4 إسماعيل أبو الشعر
5 زيـــــد نخلة