* the location and the age are important to help you narrow your diagnosis.

- **Tumors of Unknown Origin:**

Ewing sarcoma: (ES) سرطان الدم والأنسجة الرخوة

- <20 years (between 10 and 20)
- in diaphysis.
- Malignant.

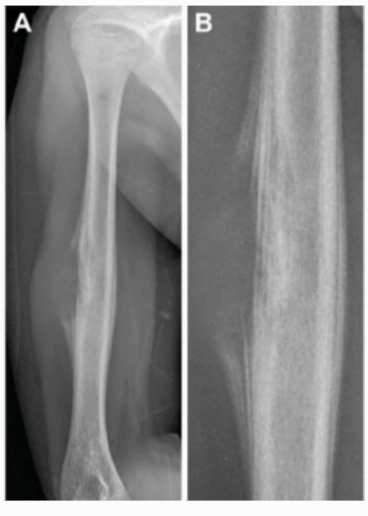
small blue cell tumor (when we stain those tumors by routine H & E stain, they appear blue because of the blue color of the nucleus which occupies 98% of the cell volume (small size tumor cell with large nucleus , little cytoplasm))

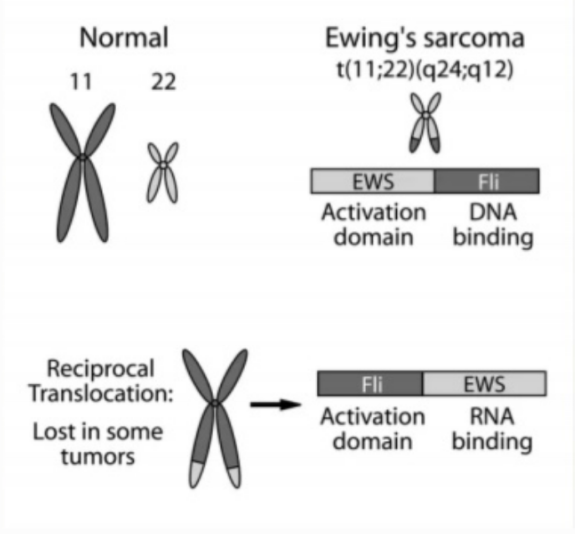
- called primitive neuro ectodermal tumor (PNE); have neuro ectodermal differentiation.
- Histologically: high grade primitive tumor
- **second most common sarcoma of bone** after osteosarcoma.

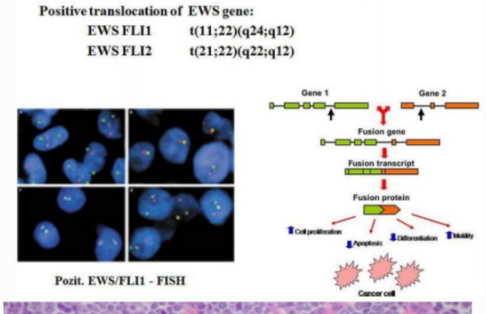
-The most common translocation, which is present in about 90% of Ewing sarcoma cases, is **t(11;22) (q24;q12)**, which generates an aberrant transcription factor through fusion of **EWSR1** gene **with** **FLI1** gene.

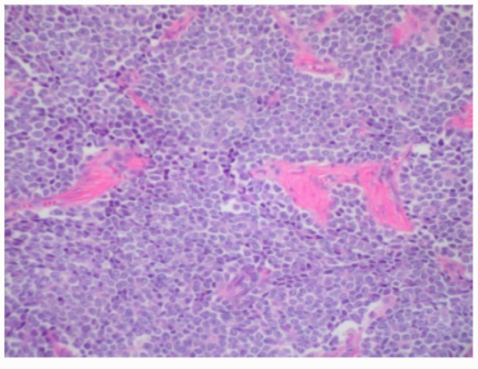
-**Trx**: neoadjuvant **CT** followed by **surgery**; long term survival now reaches 75%.

- this tumor infiltrating the soft tissue and elevating the periosteum causing Codman triangle.
- **fish analysis** is the most sensitive test for Ewing sarcoma using florescent insitu hybridization (FISH).
- **classic cytogenetic analysis method:** shows the fusion protein where the translocation is.
- The chromosome 11 is bigger than chromosome 22.









Giant cell tumor of bone: (osteoclastoma)

*the histology is composed of numerous wall to wall osteoclast-like multi-nucleated giant cells.

- in adults.
- in the epiphses.
- rarely malignant (95% is benign).
- locally aggressive neoplasm.
- Soup-bubble appearance expanding the cortex of bone.

without infiltration to the extracortical space.

- Histologically:

*sheets wall to wall.

*multi-nucleated Giant cells (or osteoclast-like giant cell), -the tumor cells are the giant cells and the one in between are stromal cells (single mononuclear cells)-.

- cells contain high levels of **RANKL** (stimulates the differentiation of osteoclast in the bone)

-**Trx**: curetting or resectionاستئصال جزئي.

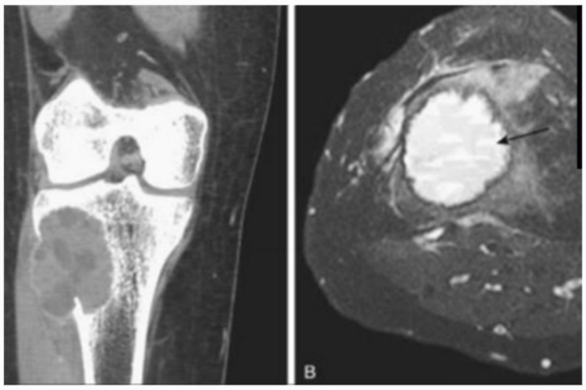
Aneurysmal bone cyst: (ABC of bone) تمدد تكيسات العظام

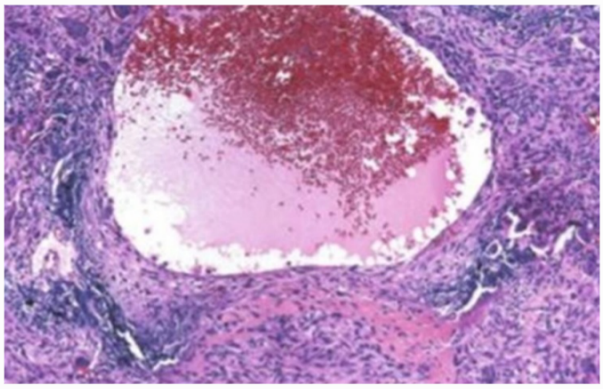
- in adults.
- in the metaphysis.
- benign.
- blood-filled cyst with fibrous reaction around it.

some argue that (ABC) is not a true neoplasm (probably reactive condition caused by previous trauma or infection).

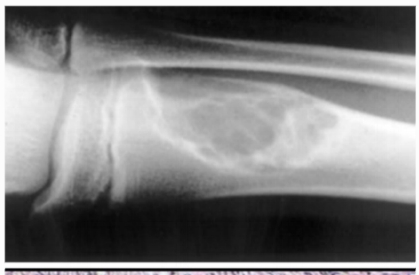
-**Trx**: curetting or resection.

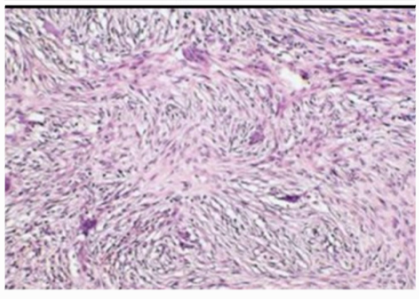
*If it is localized you can remove it without impact the function of the limb.





Non ossifying fibroma: (fibrous cortical defect (FCD) OR metaphyseal fibrous defect (MFD))





- Benign maybe a reactive, not true neoplasm
- in the metaphysis
- a fibroma in the bone.
- not destroying the surrounding structure & not elevating the periosteum
- well circumscribed.
- the biopsy looks like benign fibroma (mostly fibroblast some multinucleated giant cell).
- Histology: bland fibroblastic proliferation.
- May resolve spontaneously.

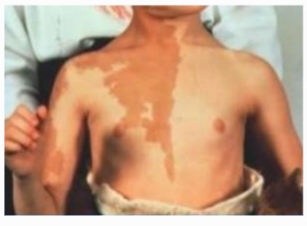
FIBROUS DYSPLASIA: (FD)

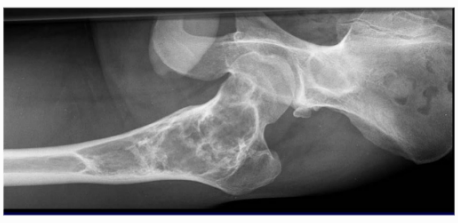
- a group of diseases or syndromes.
- Not a real tumor (a developmental abnormality of bone genesis due to mutations in GNAS1 gene (**cAMP mediated osteoblast differentiation**).
- **maxillary and mandibular bones** in face are more affected, causing cherubism in children.

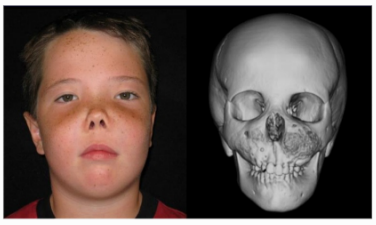
– Mazabraud syndrome: **FD** (monostotic or polystotic) **+ soft tissue myxoma** (not a common tumor of soft tissue).

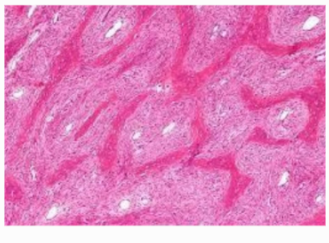
- McCune-Albright syndrome: **polystotic FD + café-au-lait skin pigmentation** (brownish pigmentation of the skin) **+ endocrine abnormalities** (precocious puberty).

- somehow similar to Paget disease, differentiate between them histologically:
McCune-Albright syndrome has a Chinese letters appearance while in Paget disease the bone appears in a mosaic pattern (pathgnomic).







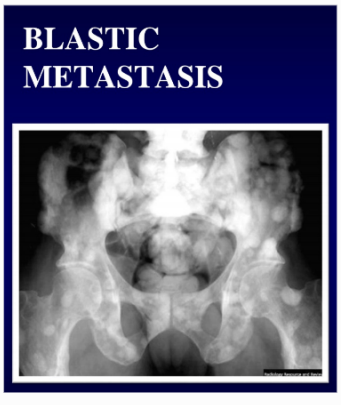


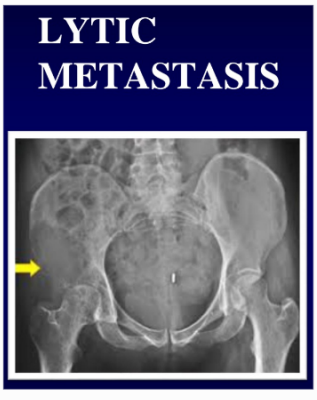
METASTATIC TUMORS TO BONE:

- More common than primary bone tumors (tumors going to the bone from carcinoma or from hematopoietic malignancies is much more common than seeing osteosarcoma, Ewing sarcoma and chondrosarcoma).
- In children: Neuroblastoma, Wilms tumor (kidney) and rhabdomyosarcoma (Usually we don't see carcinoma)
- in adults, the most common is carcinoma (adenocarcinoma) in lung (mostly), prostate, breast, kidney, thyroid & liver.
- **adenocarcinoma = (gland forming carcinoma)**
- Usually multiple and axial (vertebral bodies, shoulders, pelvic): mostly **hematogenous** spread.
- **Types of metastasis:** lytic, blastic or mixed (via mediators secretion), (The radiographic appearance of metastasis may be purely lytic (bone destroying), purely blastic (bone forming), or mixed).
- The presence of **multiple lytic metastatic** is much more common than blastic and mixed metastatic.
-the **prostate** is commonly associated with **blastic** metastatic.

(Prostatic carcinoma ➡️ osteoblastic lesions)

- after stage 4 (bad prognosis) most patients don't survive beyond 6-12 months.





Summary

Bone Tumors and Tumorlike Lesions

Primary bone tumors are classified according to the cell of origin or the matrix that they produce. The remainder is grouped according to clinicopathologic features. Most primary bone tumors are benign. Metastases, especially from lung, prostate, kidneys, and breast, are far more common than primary bone neoplasms.

Major categories of primary bone tumors include

- **Bone forming:** Osteoblastoma and osteoid osteoma consist of benign osteoblasts that synthesize osteoid. Osteosarcoma is an aggressive tumor of malignant osteoblasts, predominantly occurring in adolescents.
- **Cartilage forming:** Osteochondroma is an exostosis with a cartilage cap. Sporadic and syndromic forms arise from mutations in the *EXT* genes. Chondromas are benign tumors producing hyaline cartilage, usually arising in the digits. Chondrosarcomas are malignant tumors of chondroid cells that involve the axial skeleton in adults.
- **Ewing sarcomas** are aggressive, malignant, small round cell tumors most often associated with t(11;22).
- **Fibrous dysplasia** is an example of a disorder caused by gain-of-function mutations that occur during development.

دعواتكم

لو في أخطاء احكولي