GIANT CELL LESIONS OF BONE

PRESENTER-DR. Dhairyasheel Salunkhe

What is a Giant Cell?

- A giant cell is a cell that is larger in dimension than the cells routinely encountered in histology
- A giant cell (multinucleate giant cell) is a mass formed by the union of several distinct cells (usually histiocytes)
- They are usually of monocyte-macrophage lineage
- In chronic inflammation,when macrophage fail to deal with particles that has to be removed;fuse and form multinucleate giant cells
- The size of giant cells vary greatly but is usually between 40µm and 120µm.

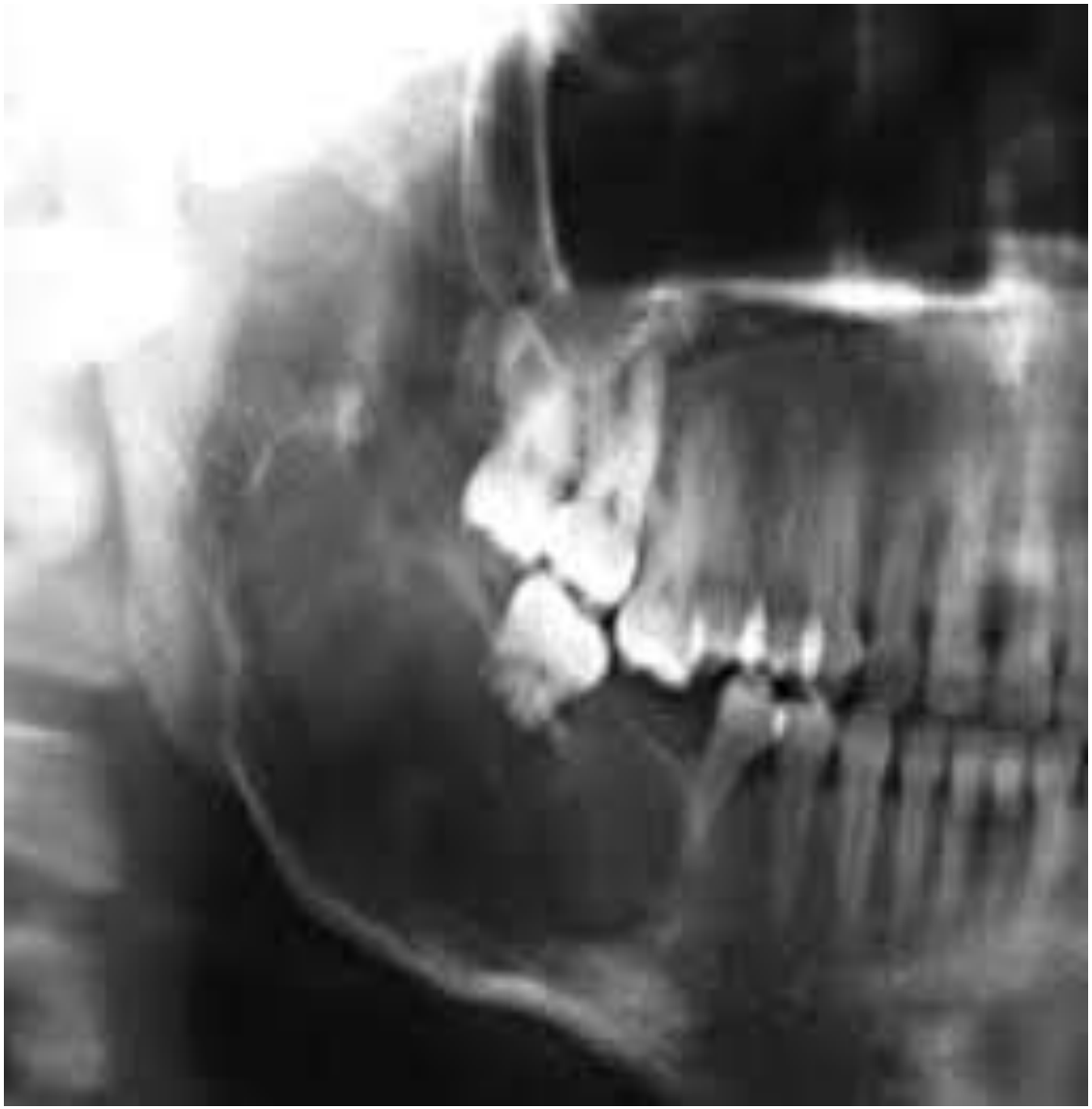
REACTIVE	BENIGN	MALIGNANT
Brown tumor of Hyperparathyroidism	Giant cell tumor	Osteosarcoma-giant cell rich
Giant cell reparative granuloma	Aneurysmal bone cyst	Chondrosarcoma-dedifferentiated
Pseudomalignant myositis ossificans	Chondroblastoma	
	Chondromyxoid fibroma	
	Non ossifying fibroma	
	Langerhans cell histiocytosis	

REACTIVE GIANT CELL LESIONS

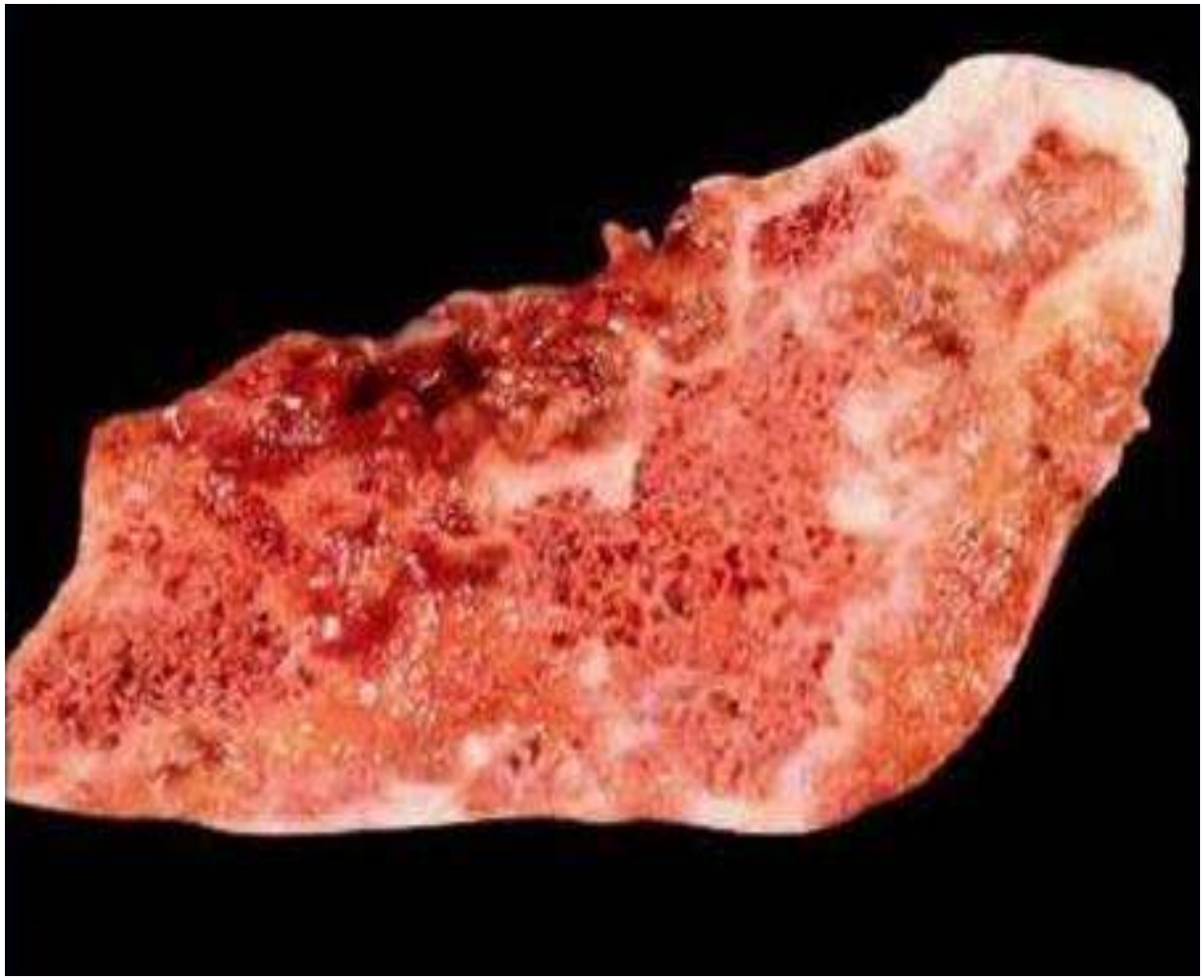
GIANT CELL REPARATIVE GRANULOMA

- A reactive intraosseous proliferation characterized by aggregates of giant cell in a fibrovascular stroma
- Giant cell lesion primarily of jaw, also other craniofacial bones and short tubular bones of hands and feet
- May be response to injury

Radiograph-
Well defined, multilocular, Radiolucent image causing second left molar tooth resorption



Gross-
Unencapsulated, brittle, brown purple, granulation tissue mass



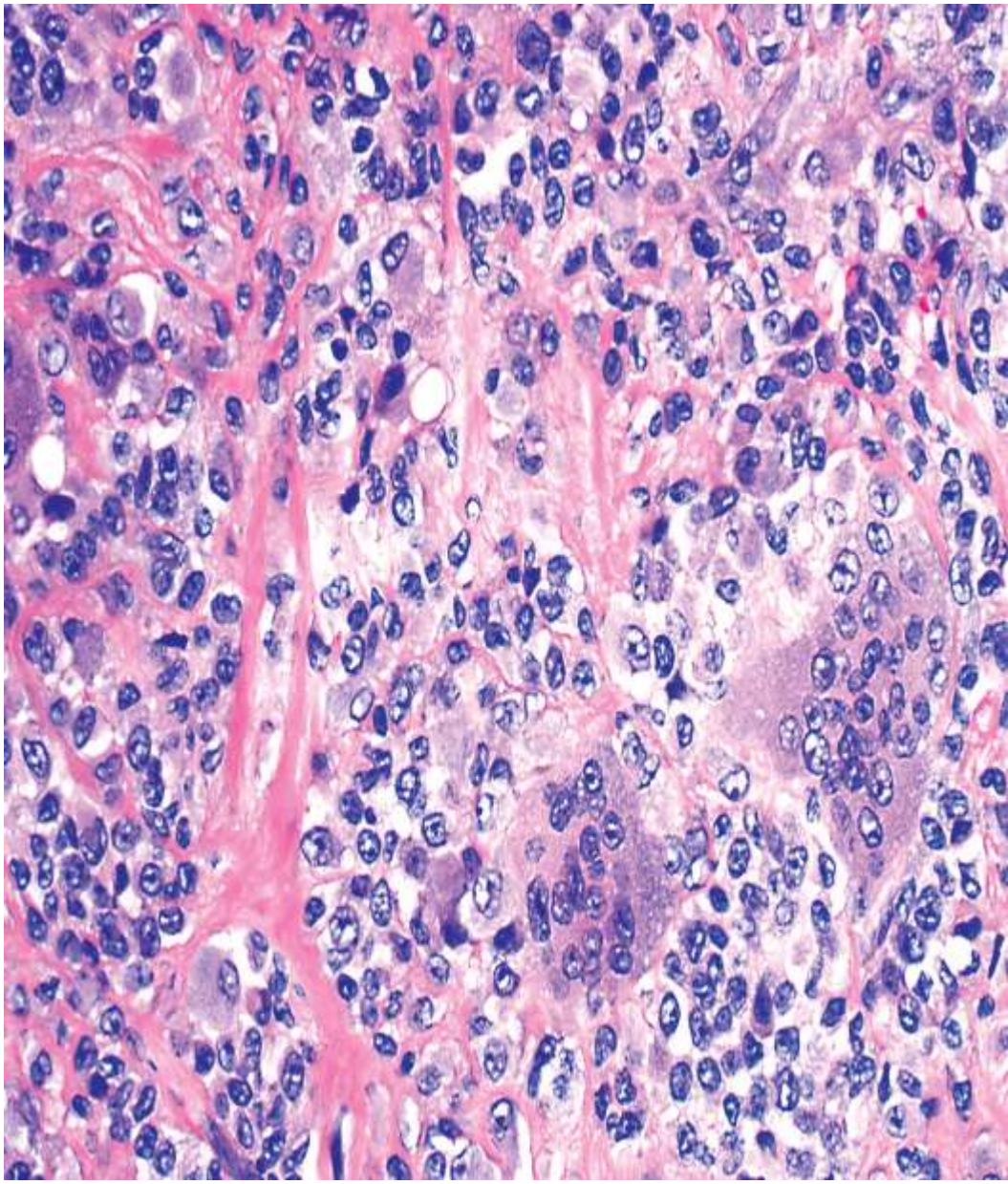
Large,red brown lesion,friable,gritty

Microscopy-

Fibrillar connective tissue stroma with small oval and spindly mononuclear cells mixed with uneven clusters of multinuclear (5 - 40) giant cells

Small capillaries, hemorrhage,

No pleomorphism, no / rare mitotic figures



- D/Ds

✓Brown tumor

✓GCT

✓ABC

✓Non ossifying fibroma

✓Ossifying fibroma

PSEUDOMALIGNANT MYOSITIS OSSIFICANS

- Circumscribed heterotopic new bone formation without a history of trauma is termed pseudomalignant myositis ossificans
- Reactive,often self healing lesion
- In adolescents,young adults

Radiologically-
a circumscribed, radiopaque lesion with a central lucent zone that is separated from the underlying cortex by a radiolucent line

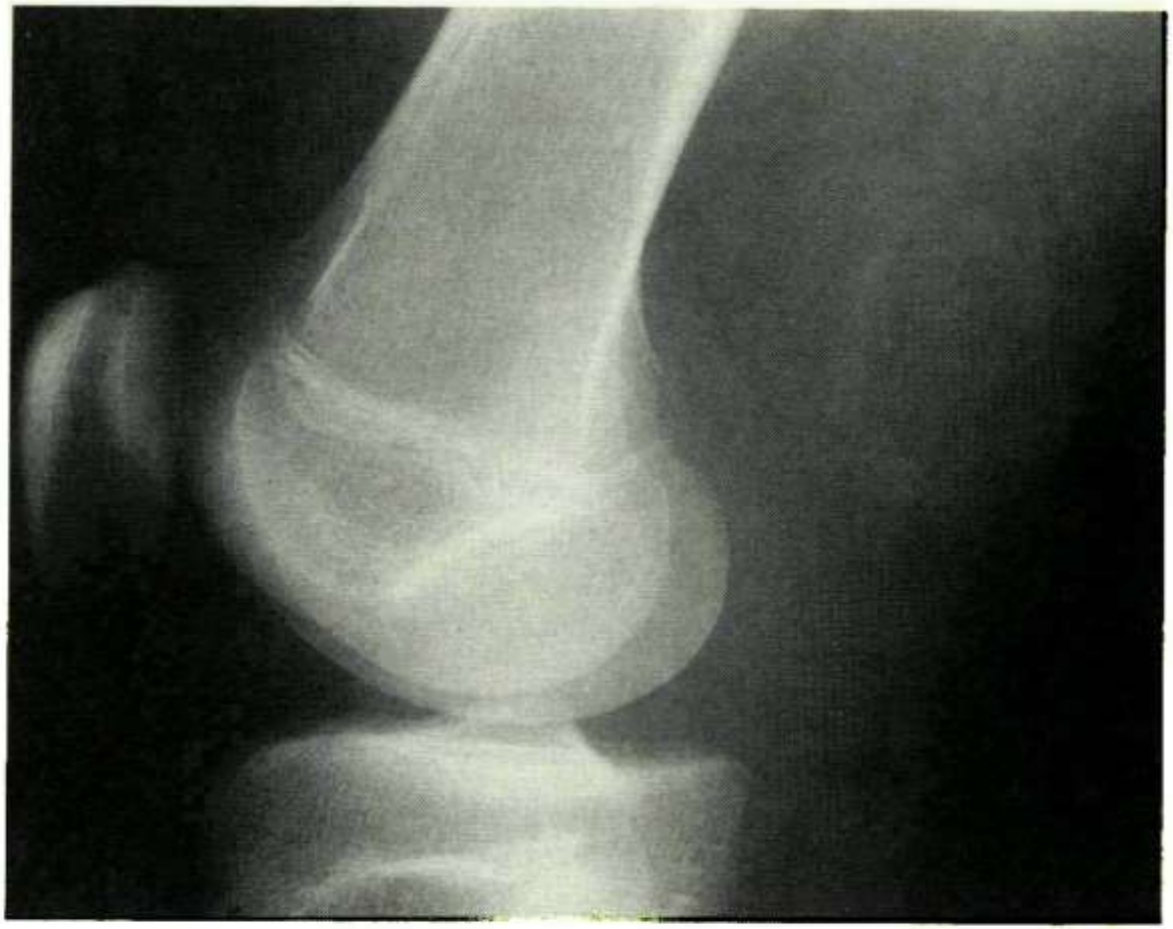
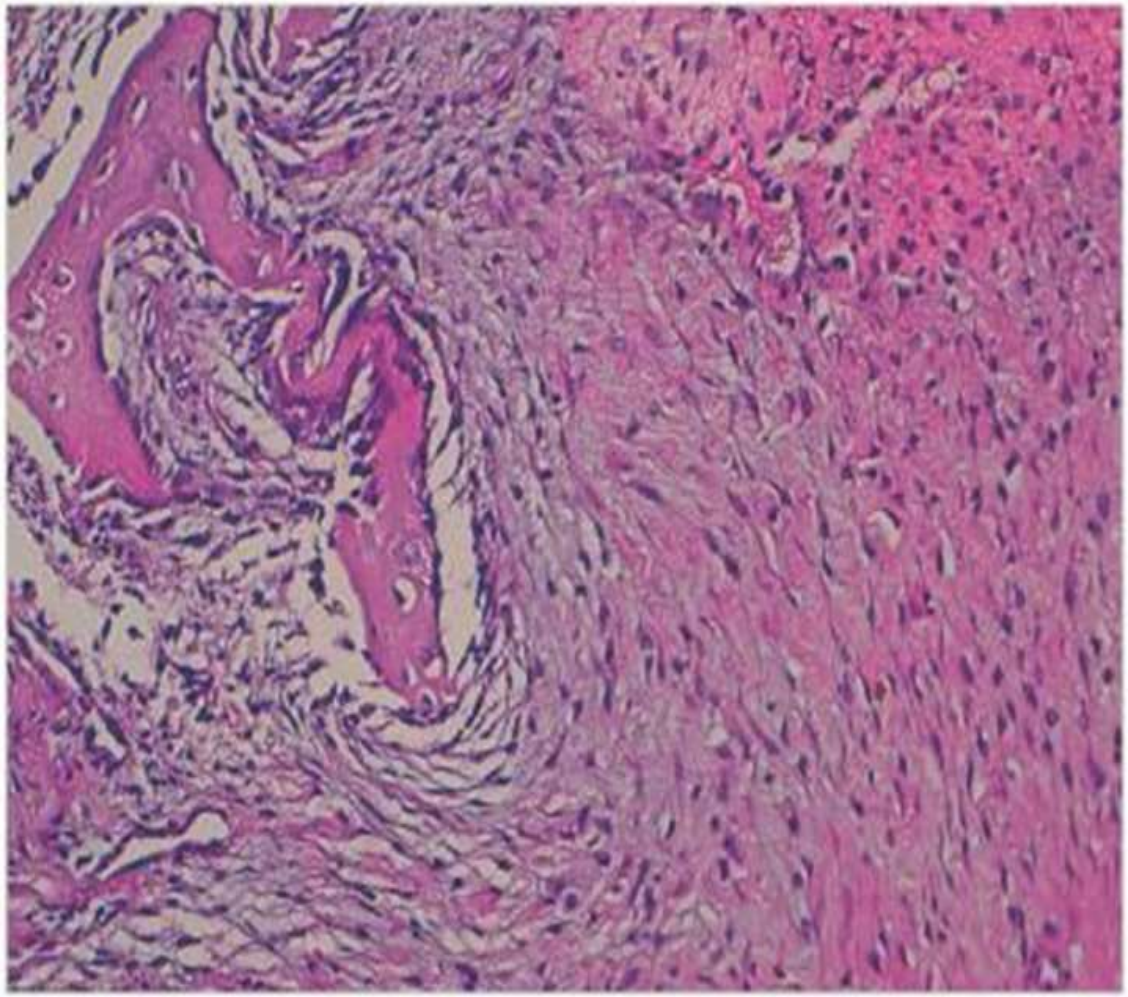


Fig. 1: Radiograph of the left knee reveals soft tissue calcification in a pattern suggestive of pseudomalignant myositis ossificans (fibrodysplasia ossificans circumscripta).

- Microscopy- characteristic zoning pattern of peripheral maturation is present, (the central proliferating zone usually causing the diagnostic problems)



Low power showing zonation with myxoid change(centre) & bone formation (periphery)

BROWN TUMOR OF HYPERPARATHYROIDISM

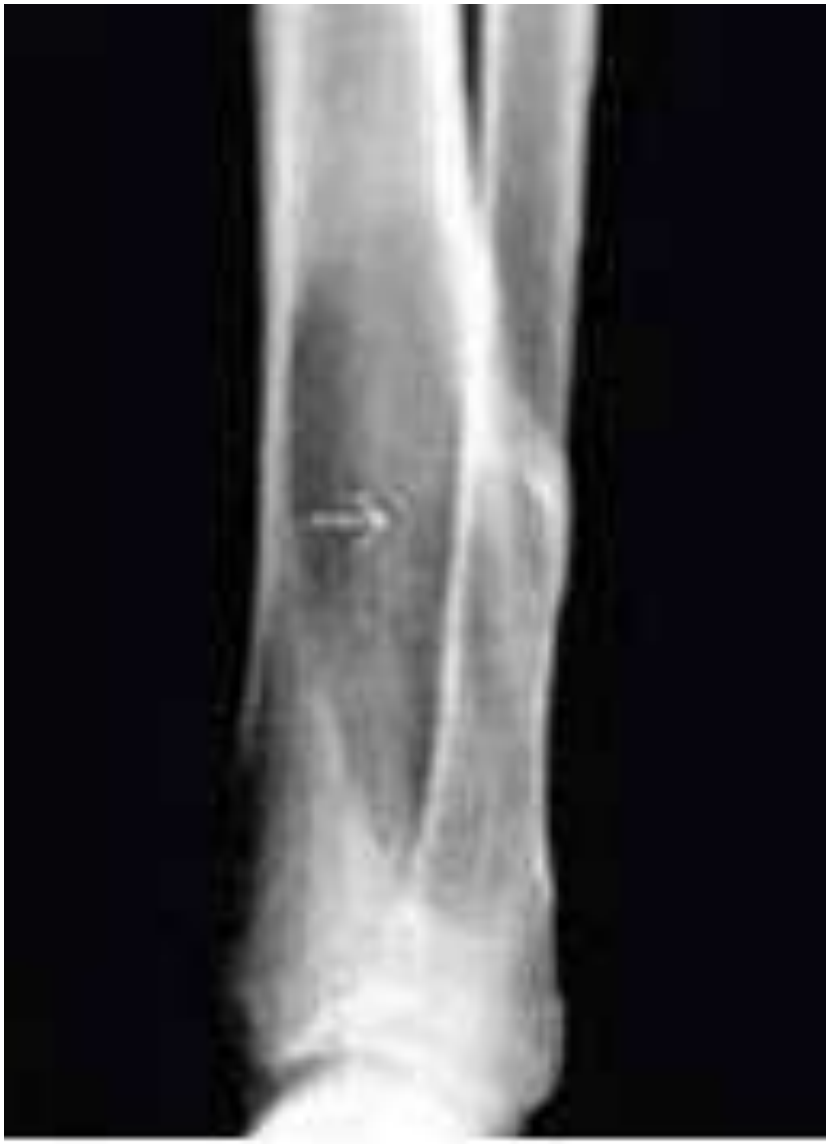
- The brown tumor is a bone lesion that arises in settings of excess osteoclast activity, such as hyperparathyroidism.
- They are a form of osteitis fibrosa cystica.
- Not a neoplasm, simply a mass.
- Most commonly affects the maxilla and mandible, though any bone may be affected.

Biochemically-

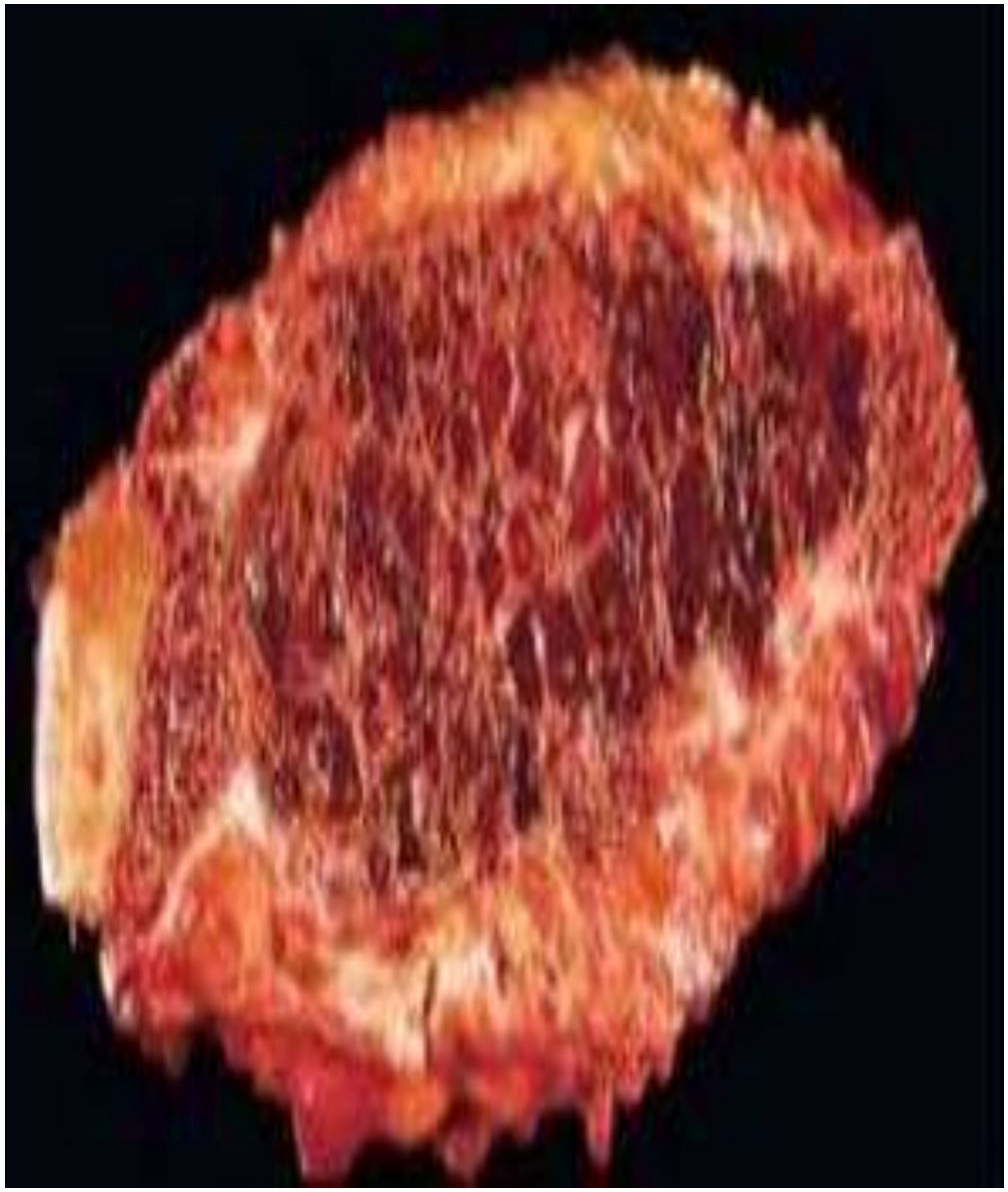
- Hypercalcmia
- Hypophosphatemia
- Hypercalciuria
- Lowering of renal phosphate threshold
- Elevated PTH
- Elevated Vit D
- Enhanced excretion of nephrogenous cAMP
- Elevated serum ALP

Radiograph-

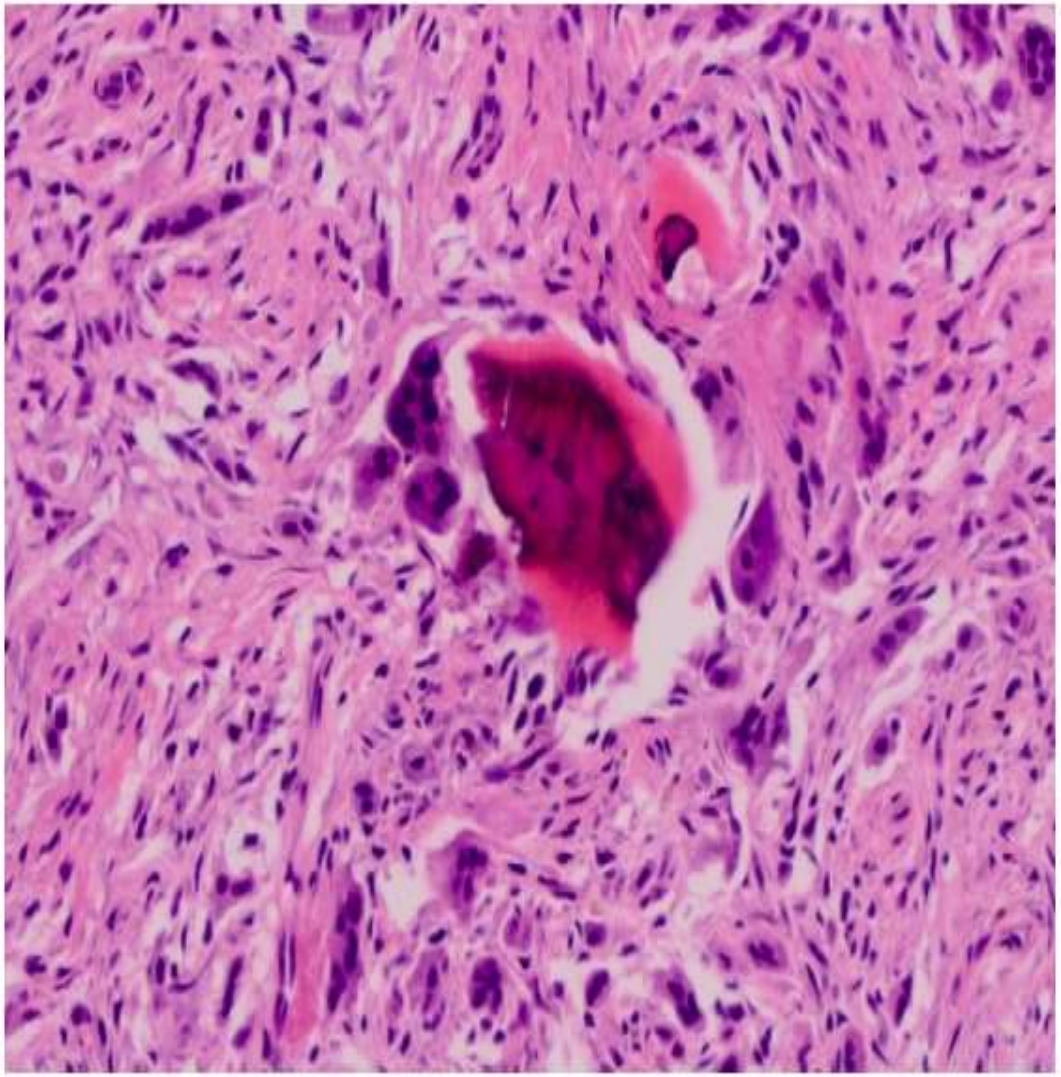
Brown tumor of tibia showing-Expansile,well circumscribed,lytic and thin with subtle osteopenia



Gross- Well circumscribed,reddish brown hemmorhagic mass with lobular architecture
Thin and expanded cortex
Large blood filled cysts may develop(OFC)
Peripheral shell of reactive bone may be present



Microscopy-
Numerous giant cells with interstitial hemorrhage, ingrowth of vascularized fibrous tissue with fibroblasts



Multinucleated giant cells around a spicule of bone amidst a proliferative fibroblastic stroma (H&E, magnification ×400).

D/D-

- Giant cell granuloma: different clinical history and laboratory findings
- Giant cell tumor: more uniformly distributed giant cells, no interstitial hemorrhage, no fibroblastic stromal cells

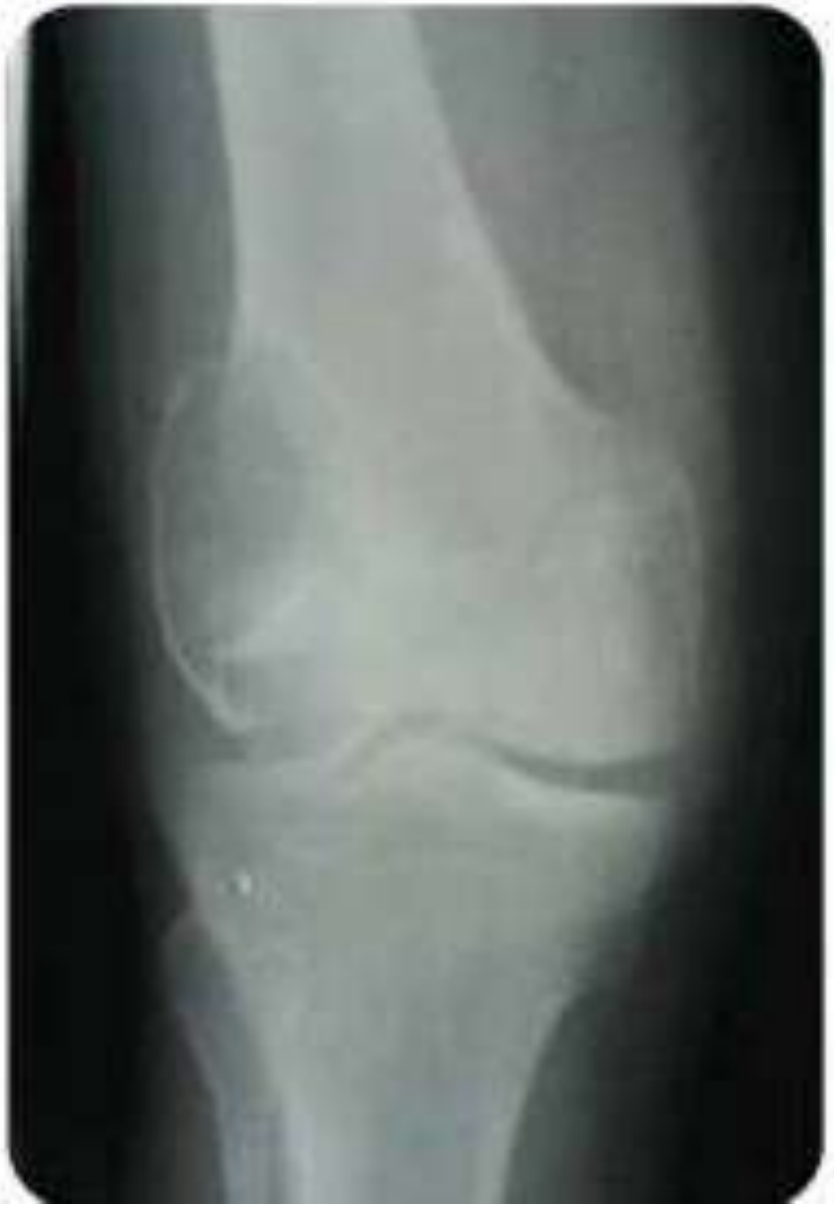
BENIGN GIANT CELL LESIONS

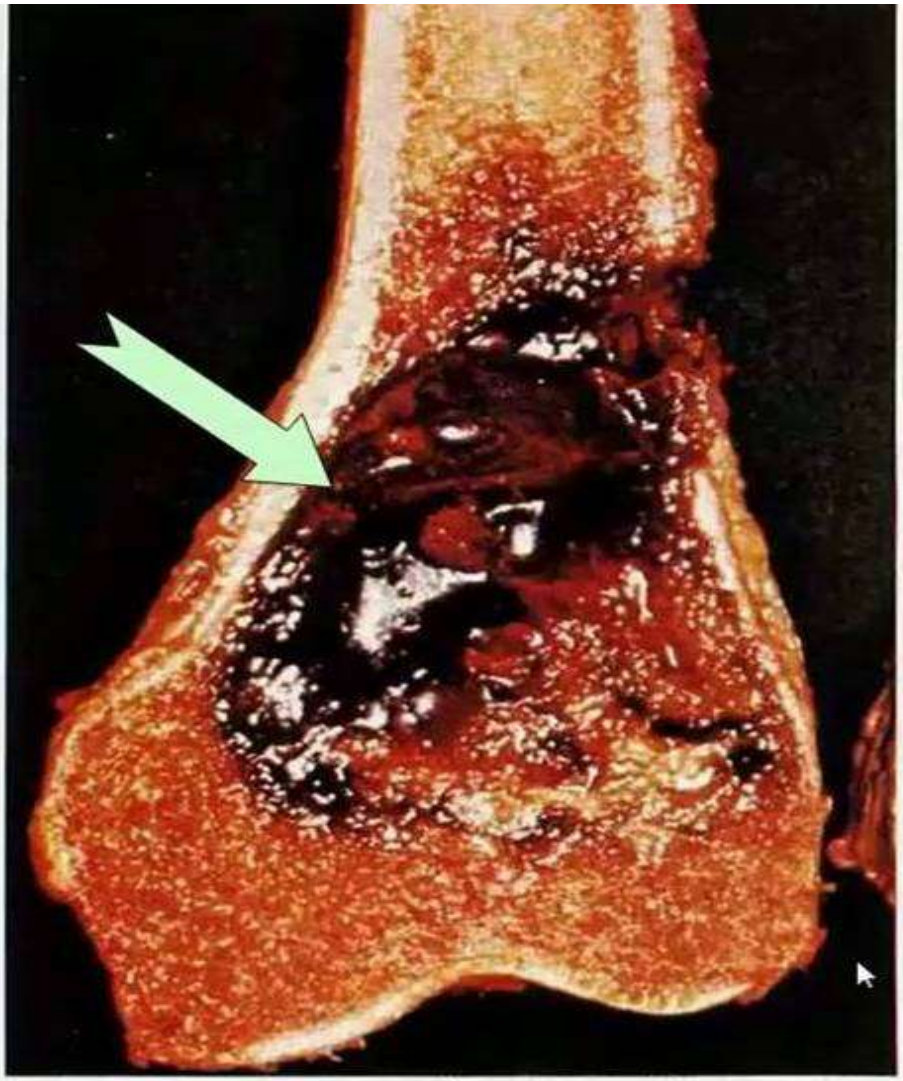
GIANT CELL TUMOR

- Also called as Osteoclastoma
- Usually benign but locally aggressive
- Malignancy in giant cell tumor is rare (< 2% of cases) and is more common at older ages (30 - 50 years)
- Site-End of long bones,
  most common:
  lower end of the femur
  upper end of the tibia
- Young adults, more common in females.

- Malignancy in Giant cell tumor-
- Primary malignant giant cell tumor of bone: a high grade sarcoma arising in a giant cell tumor of bone at initial diagnosis (uncommon)
- Secondary malignant giant cell tumor of bone: a high grade sarcoma arising at the site of a treated giant cell tumor of bone after surgery or low dose radiation therapy (more common than primary malignant giant cell tumor of bone)

Radiograph-
Eccentric lytic epiphyseal/metaphyseal lesion that often extends into the distal epiphysis and borders subchondral bone ,
no e/o periosteal lifting
no sclerotic rim





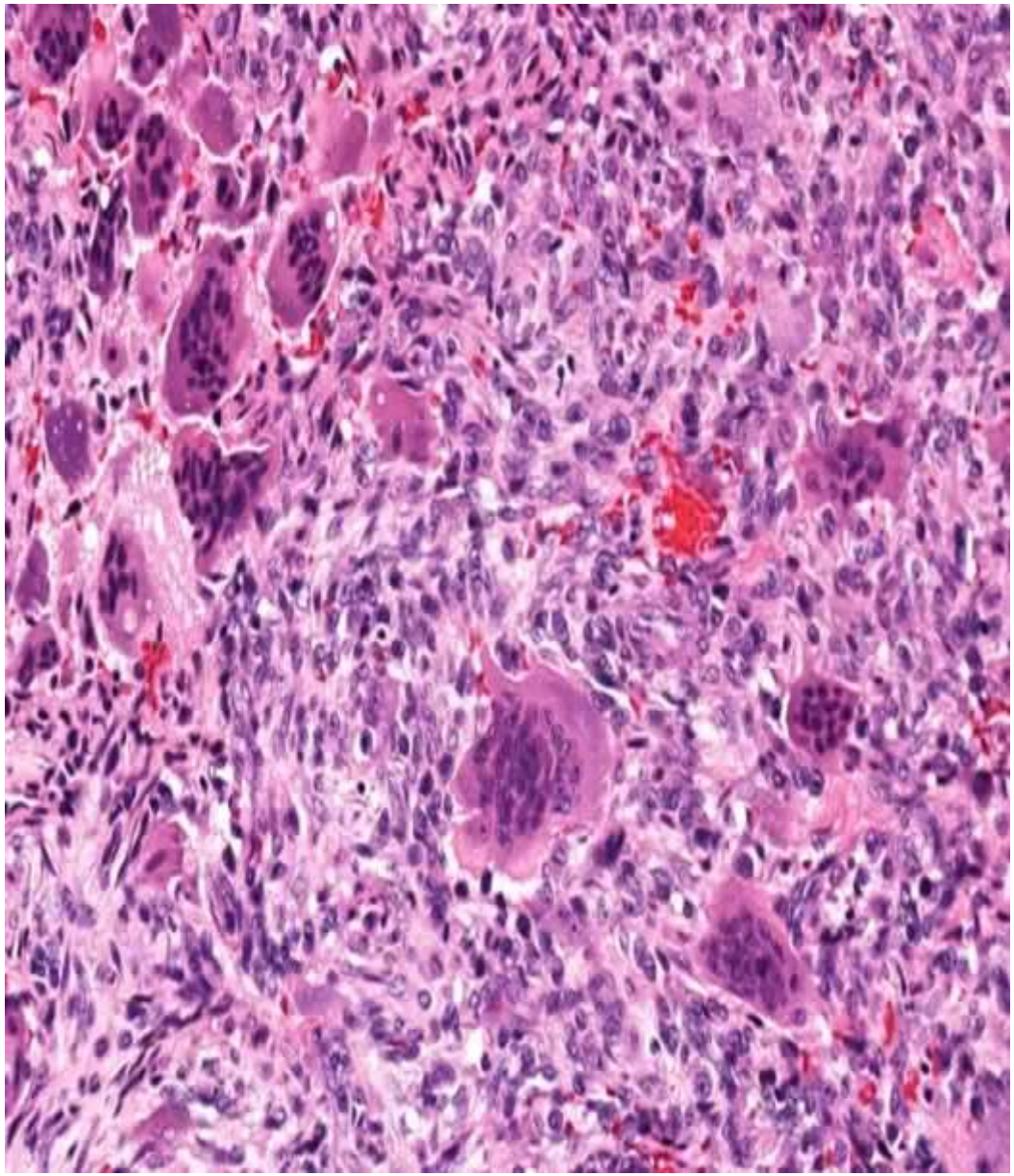
13.64 Giant-cell tumour: femur

F13-64: **Giant-cell tumor (GCT) of bone: femur.**

☻ Hemorrhagic tumor of the lower femur.

Although the overlying cortex is thinned, the bone contour is not expanded.

Microscopy-
Spindle to round mononuclear cells
Multinucleate osteoclast like giant cells.



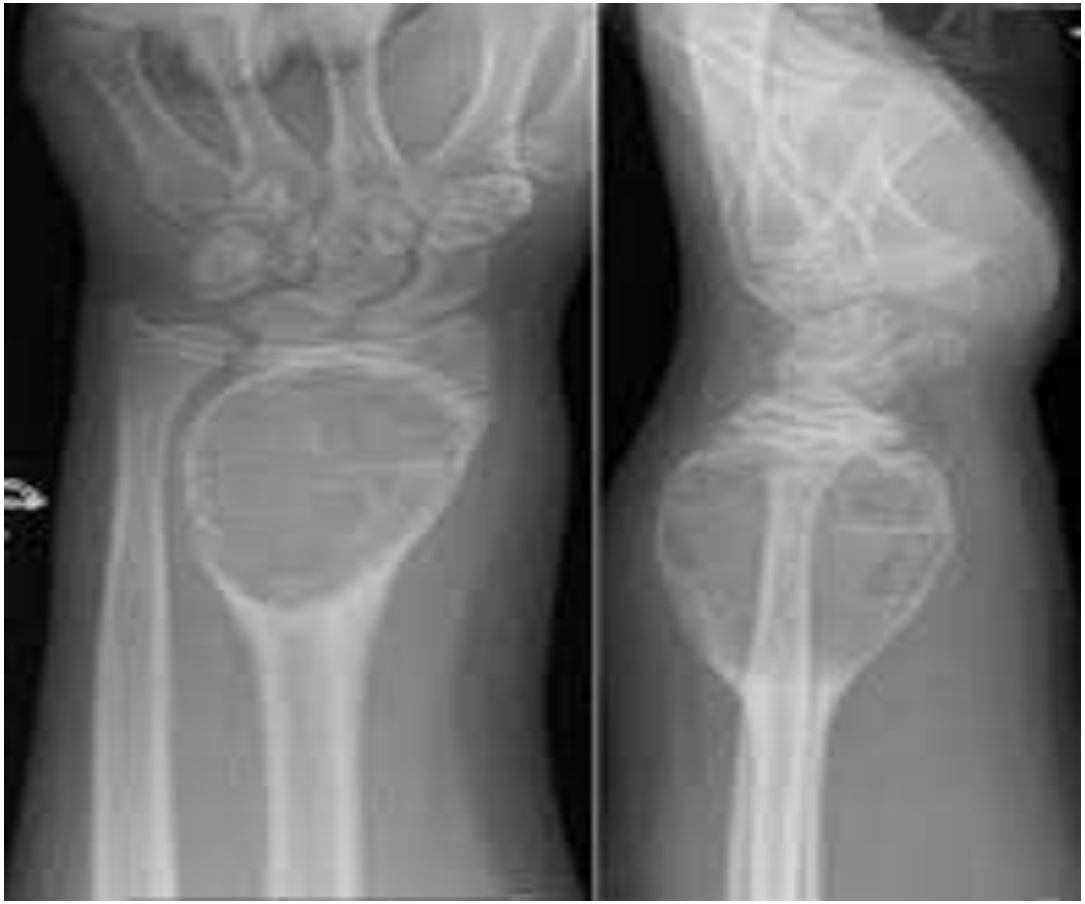
D/D-

- Giant cell reparative granuloma
- Brown tumor of hyperparathyroidism
- Aneurysmal bone cyst,esp. Solid variant
- Osteosarcoma with giant cells
- Metaphyseal fibrous defect

ANEURYSMAL BONE CYST

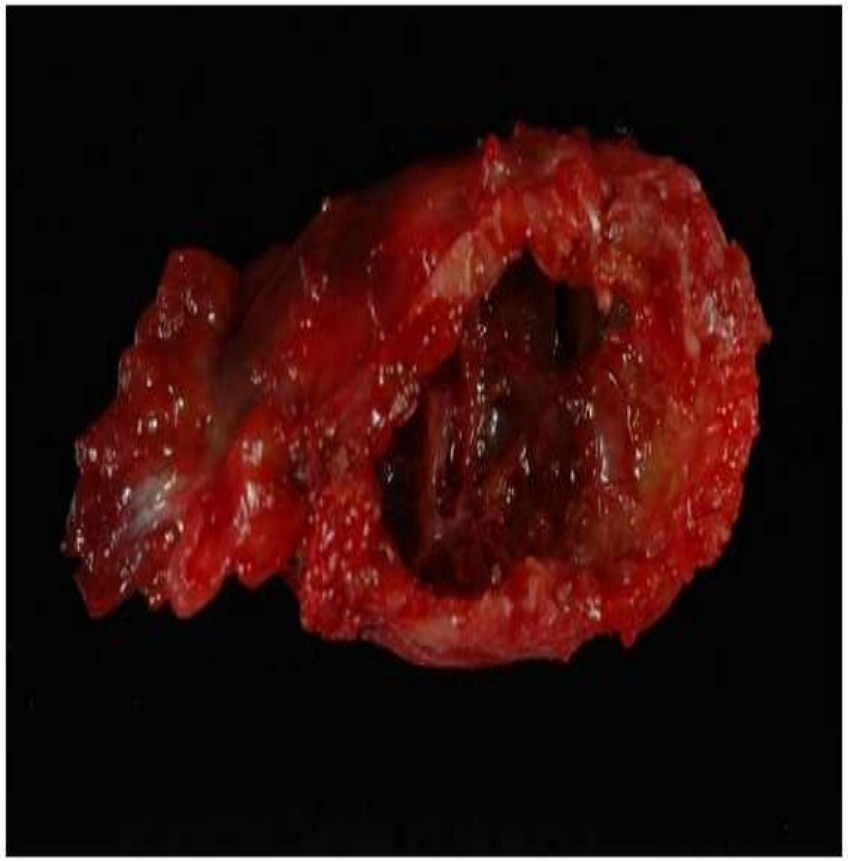
- Expanding osteolytic lesion of blood filled spaces of variable size ,separated by connective tissue septa with osteoclast giant cells and variable reactive bone
- Usual age 1 - 20 years, no gender preference
- Benign but grows rapidly

- Radiograph- Eccentric expansion of bone, cortical erosion and destruction, small peripheral area of periosteal bone formation
- Shown here-aneurysmal bone cyst of distal radius



Gross-

- Spongy, hemorrhagic mass covered by thin shell of reactive bone
- Small amount of tissue compared to large size of lesion on Xray

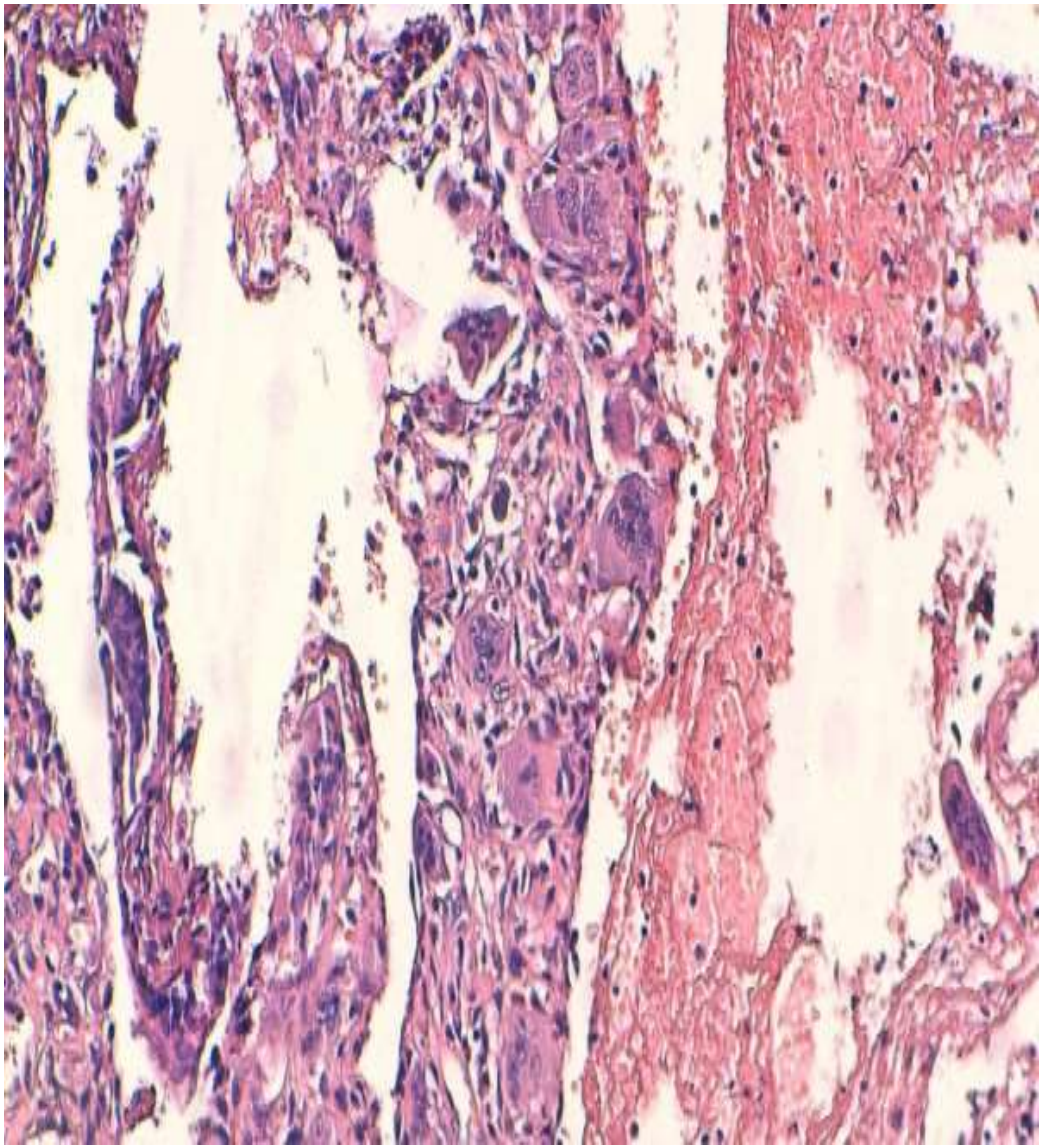


Photograph of the gross specimen shows the cystic space within the cortex of the bone

Microscopy-

- Large cystic spaces filled with blood and separated by fibrous septa, alternating with solid areas
- Cysts and septa lined by fibroblasts, myofibroblasts and histiocytes but not endothelium
- Clusters of osteoclast-like multinucleated giant cells with loose spindly stroma to cellular stroma, reactive woven bone, degenerated calcifying fibromyxoid tissue

(hematoxylin-eosin stain, × 200).



IHC-

- No specific marker
- P63-can stain some tumor cells
- CD 68-osteoclast

D/D-

- GCT
- Solitary bone cyst
- Hemangioma
- Telengiectatic OS

FIBROUS CORTICAL DEFECT AND NON OSSIFYING FIBROMA

- The fibrous cortical defect and the non-ossifying fibroma are benign fibrous tumours occurring, in the cortex of the metaphysis, in the long bones of children and young adolescents.
- The fibrous cortical defect occurs in children usually under ten years of age
- Occasionally it develops into the more extensive lesion found in young adolescents and known as a non-ossifying fibroma.
- Despite the superficial dissimilarities the one most probably gives rise to the other.

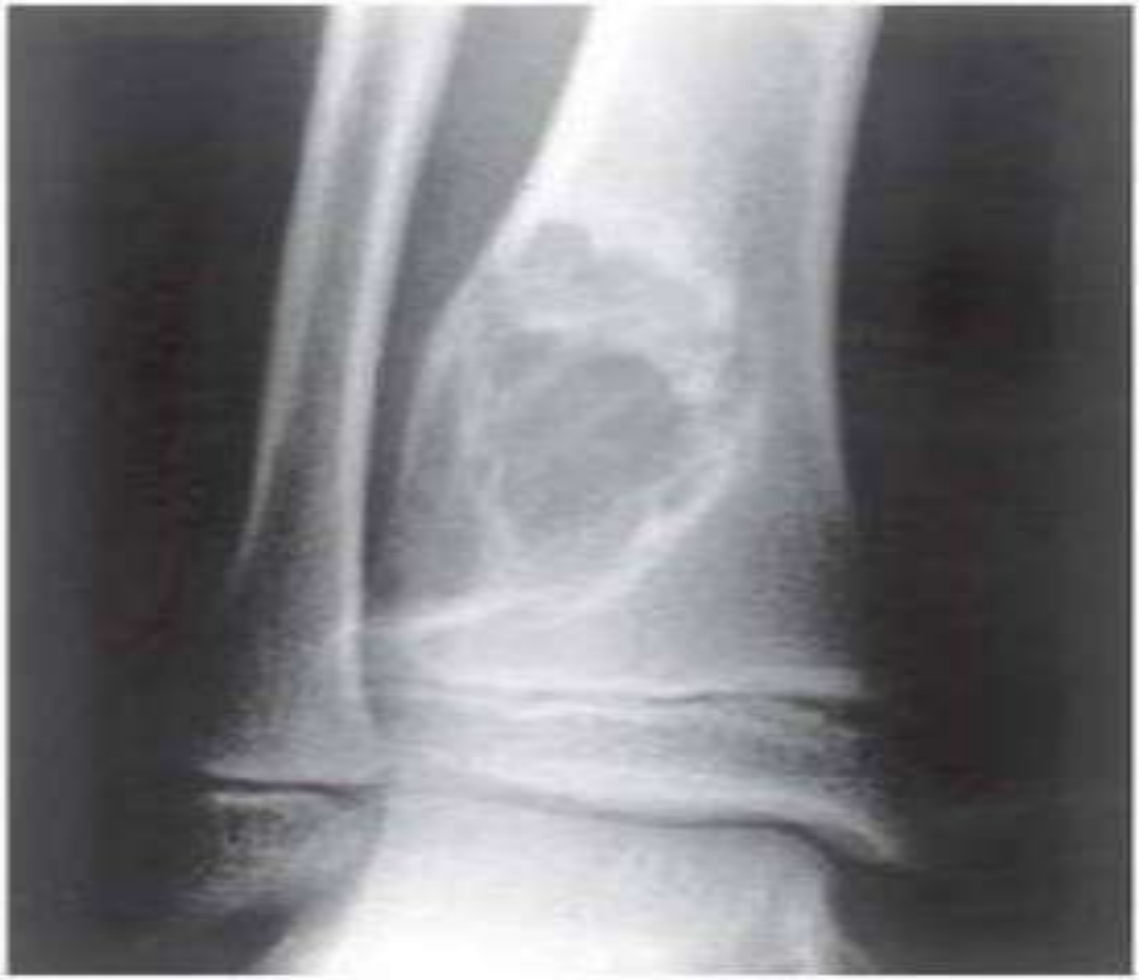
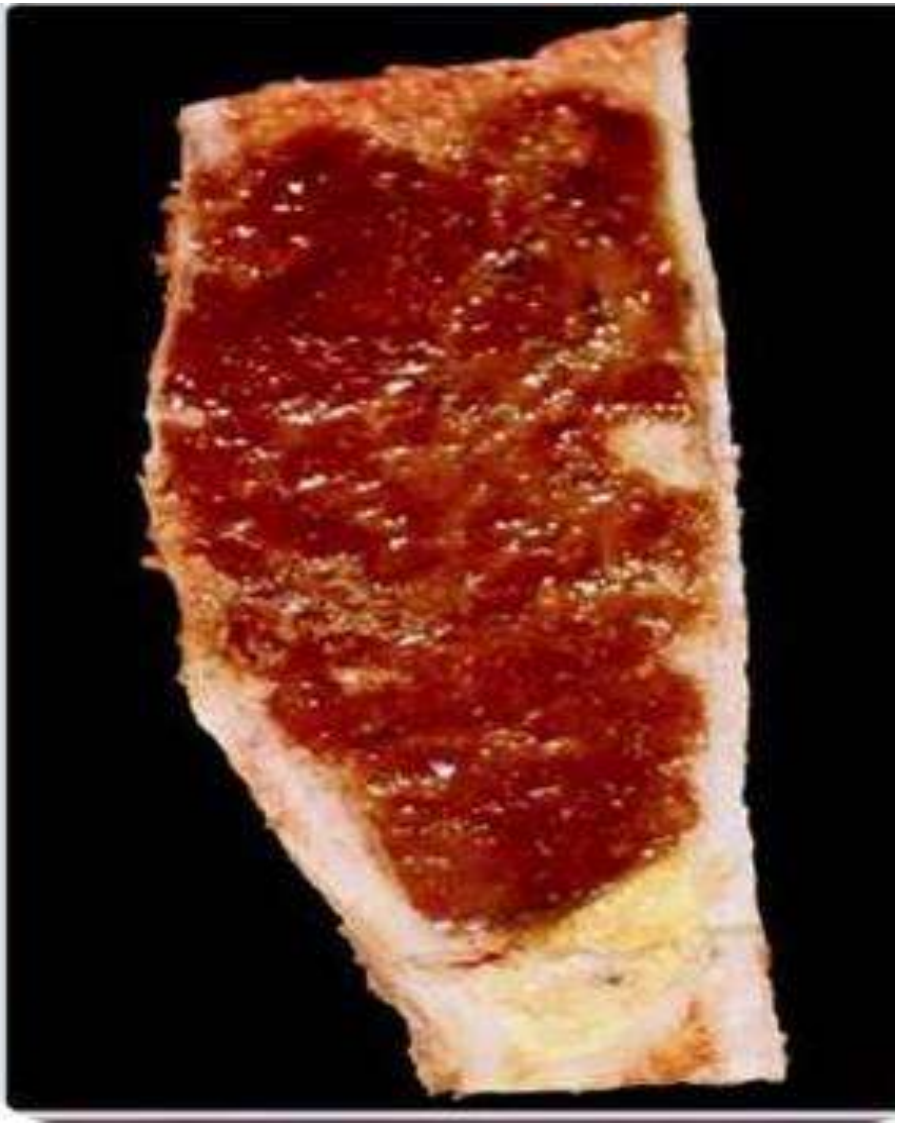


Figure 26-36 Nonossifying fibroma of the distal tibial metaphysis producing an eccentric lobulated radiolucency surrounded by a sclerotic margin.

Both NOF and FCD produce sharply demarcated radiolucencies,surrounded by a thin rim of sclerosis

The solid red-brown tumor has resulted in expansion of the bone and thinning of the cortex.



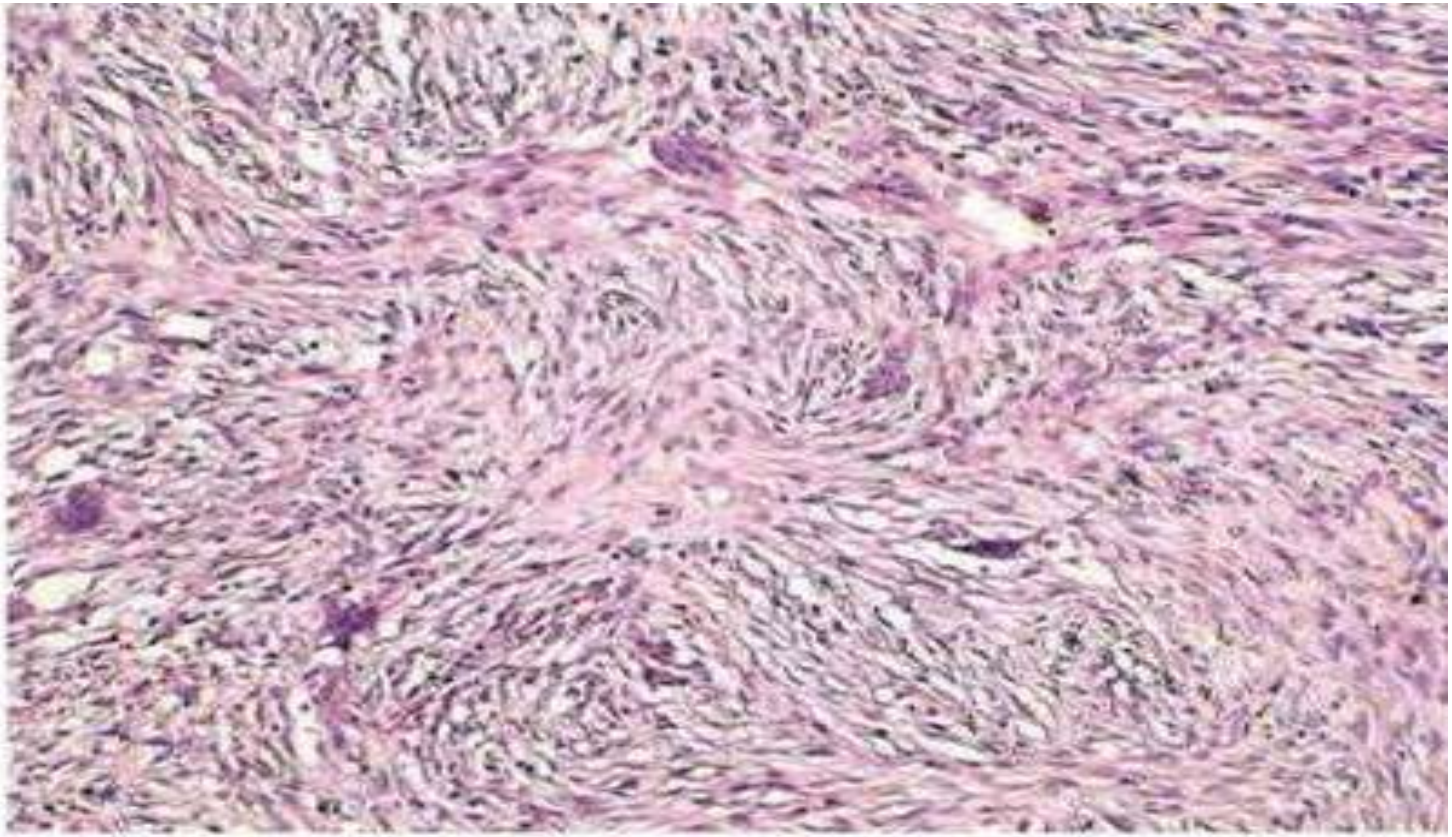


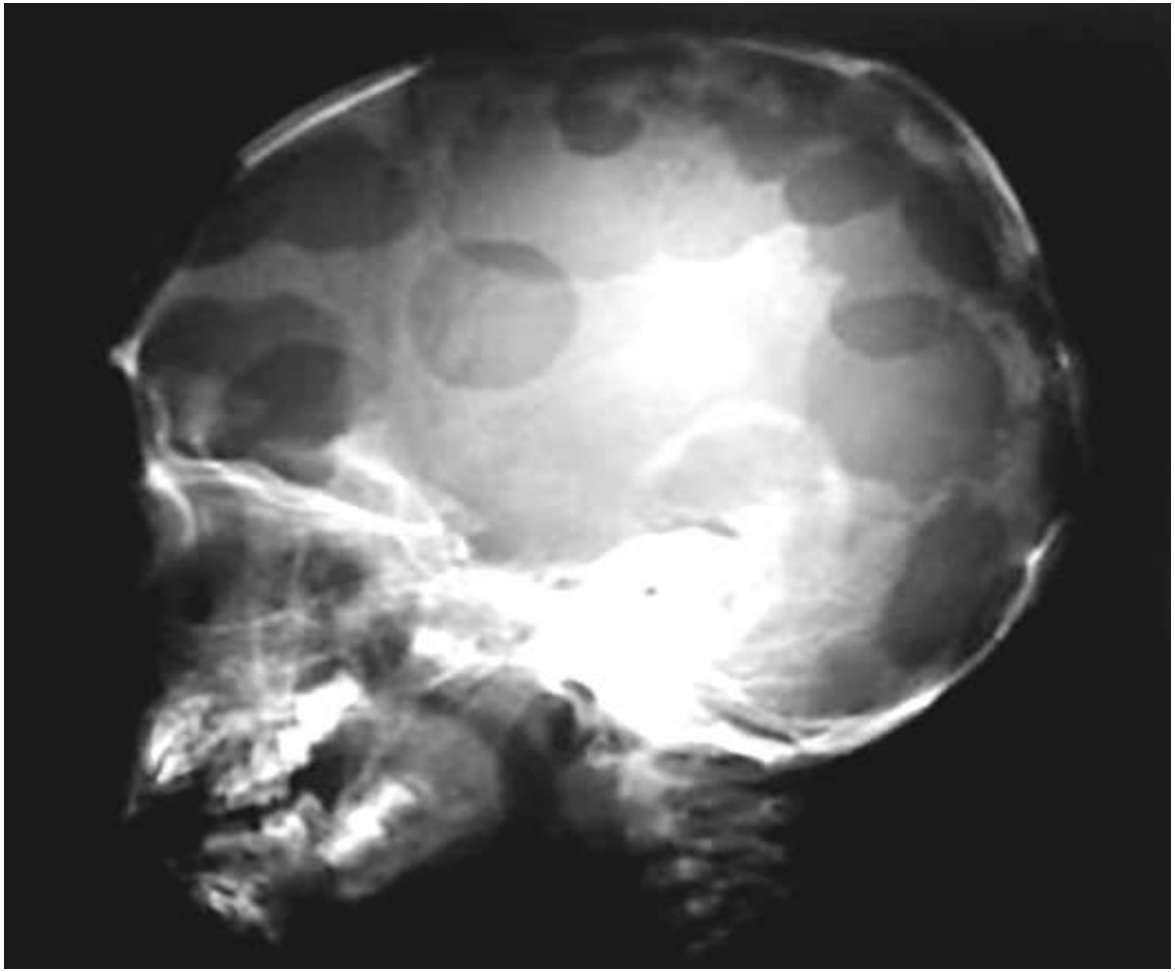
Figure 26-37 Storiform pattern created by benign spindle cells with scattered osteoclast-type giant cells characteristic of a fibrous cortical defect and nonossifying fibroma.

- D/D
- GCT
- Solid ABC

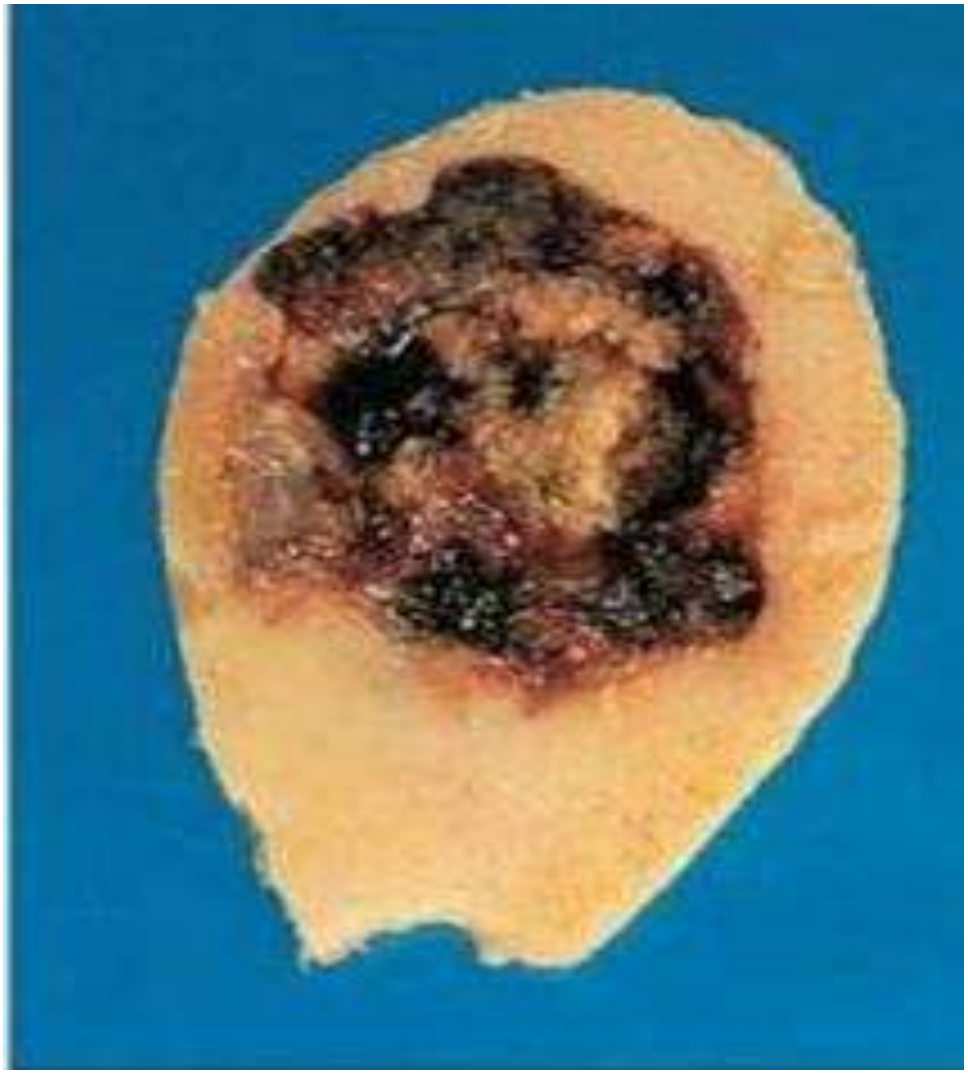
LANGERHANS CELL HISTIOCYTOSIS

- Formerly called Histiocytosis X
- Either solitary bone involvement, multiple bone involvement (variable skin involvement) or multiple organ involvement (bone, liver, spleen, other sites)
- Ages 5 - 15 years, 60% male
- Neoplastic, although cause unknown
- **Sites**: skull, jaw, humerus, rib, femur; metaphysis or diaphysis

Radiograph-
Lytic masses that may extend into soft tissue



Gross-
Appearance of skullbone, sharply circumscribed,dark brown lesion



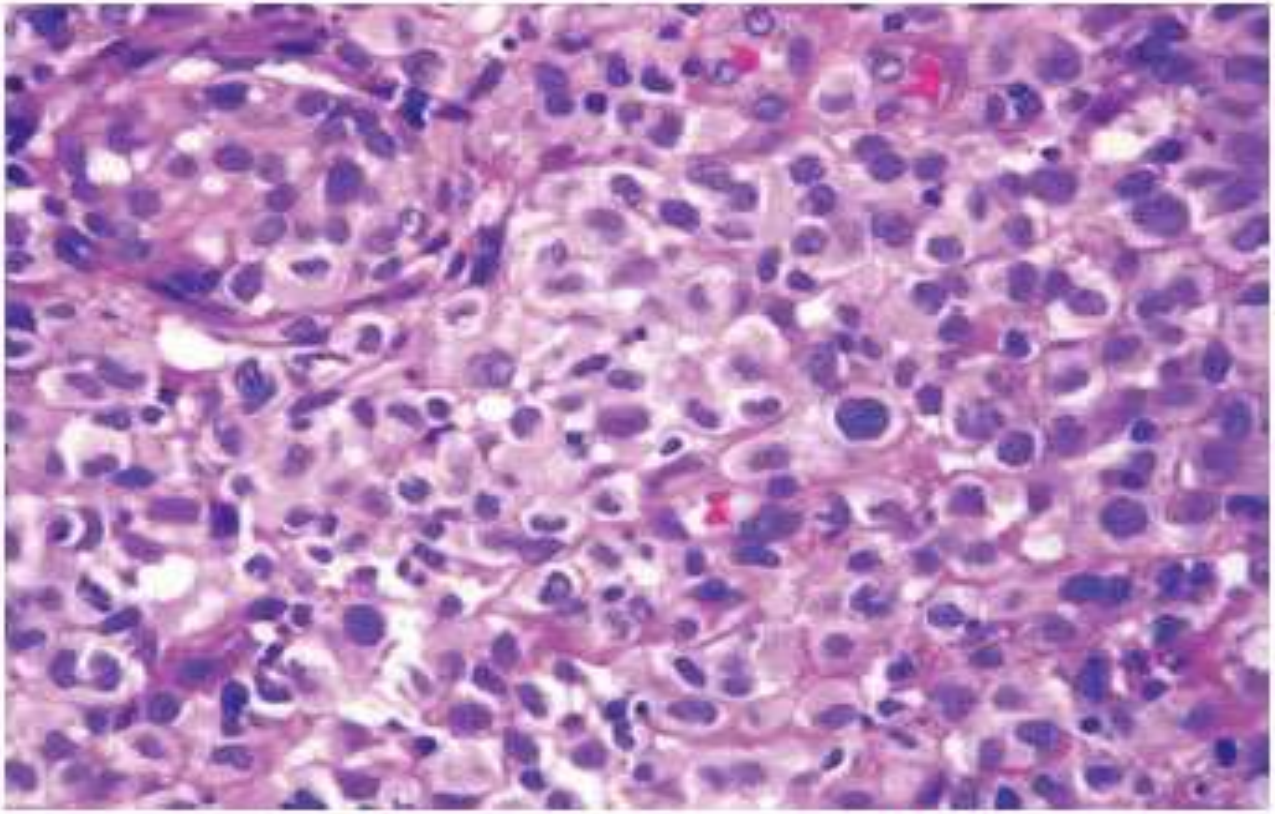


FIGURE 4: Diffuse infiltrate by the Langerhans cells (large cells with eosinophilic cytoplasm, reniform nucleus and evident nucleoli), permeated by lymphocytes, neutrophils and eosinophils (HE - 400X)

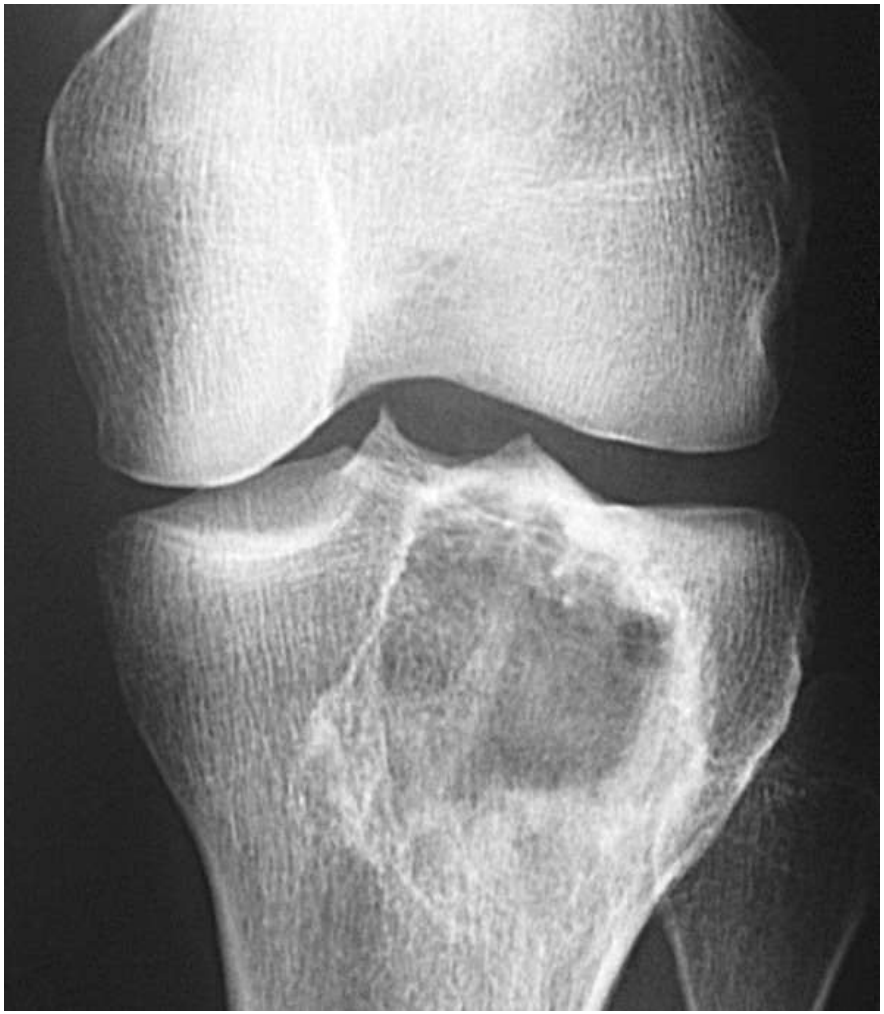
D/D-

- Granulomatous inflammation
- Osteomyelitis
- Hodgkins lymphoma
- Osseous manifestations of Rosai dorfman disease

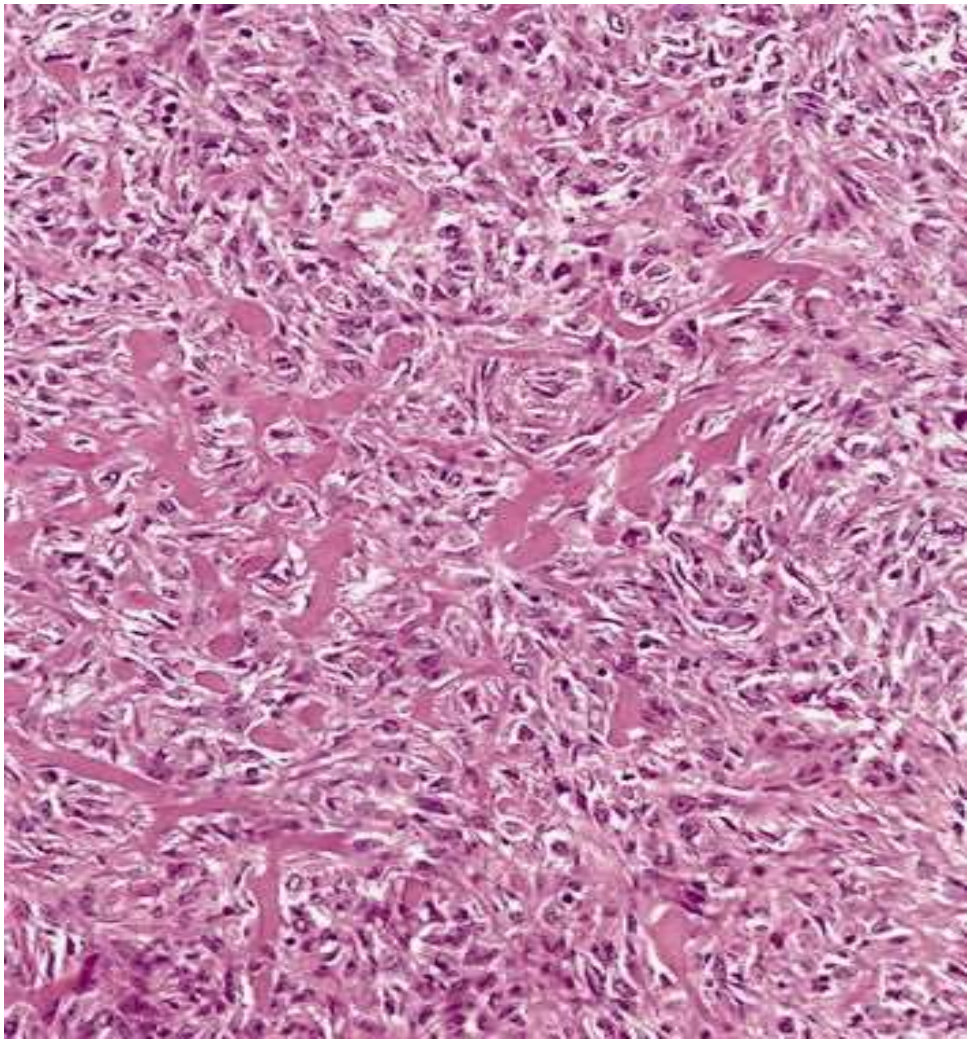
BENIGN FIBROUS HISTIOCYTOMA OF BONE

- Benign primary bone neoplasia
- Female>male,3rd -4th decade
- Site-Spine and long bones,non metaphyseal locations
- Asymptomatic,local pain
- Excellent prognosis,curretage,local excision

- Radiograph-
  Well defined, lytic, expanding lesion



- Microscopy-
  Storiform pattern of spindled cells with occasional foam cells and variable benign multinucleated giant cells



D/D-

- NOF
- GCT
- Malignant fibrous histiocytoma

CHONDROBLASTOMA

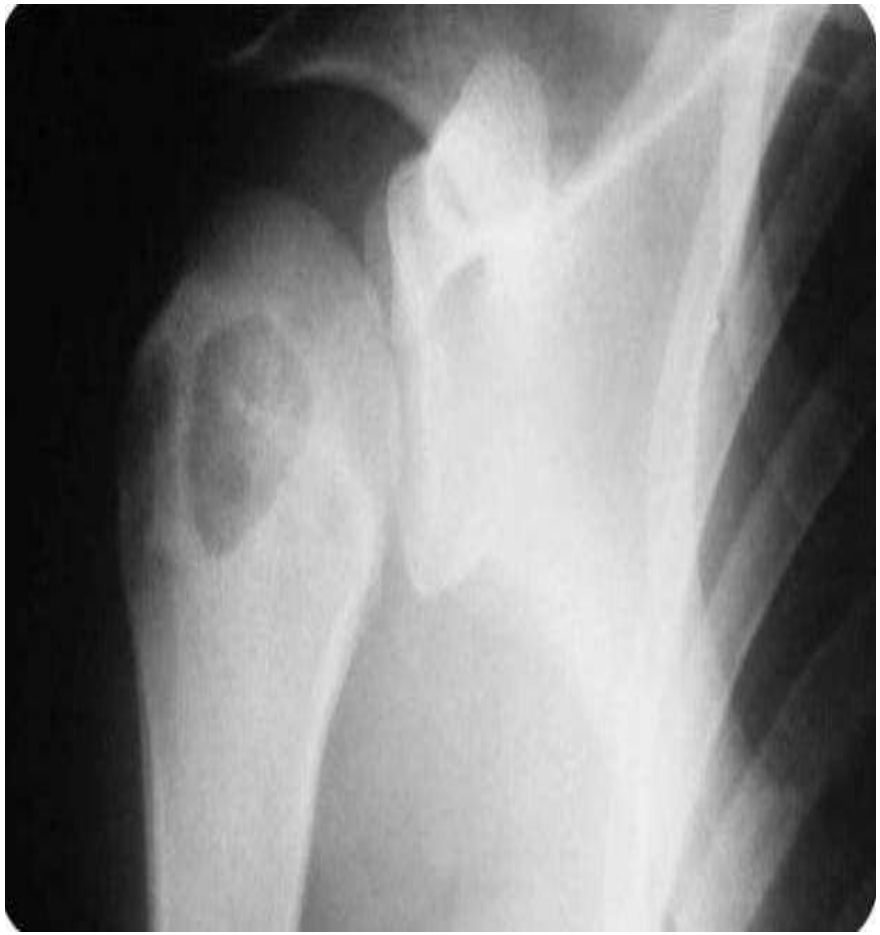
- Benign neoplasm,rare<1%
- Skeletally immature individuals
- Arises in epiphyseal end of long bones before epiphyseal cartilage has disappeared.
- Site-

Distal end of femur

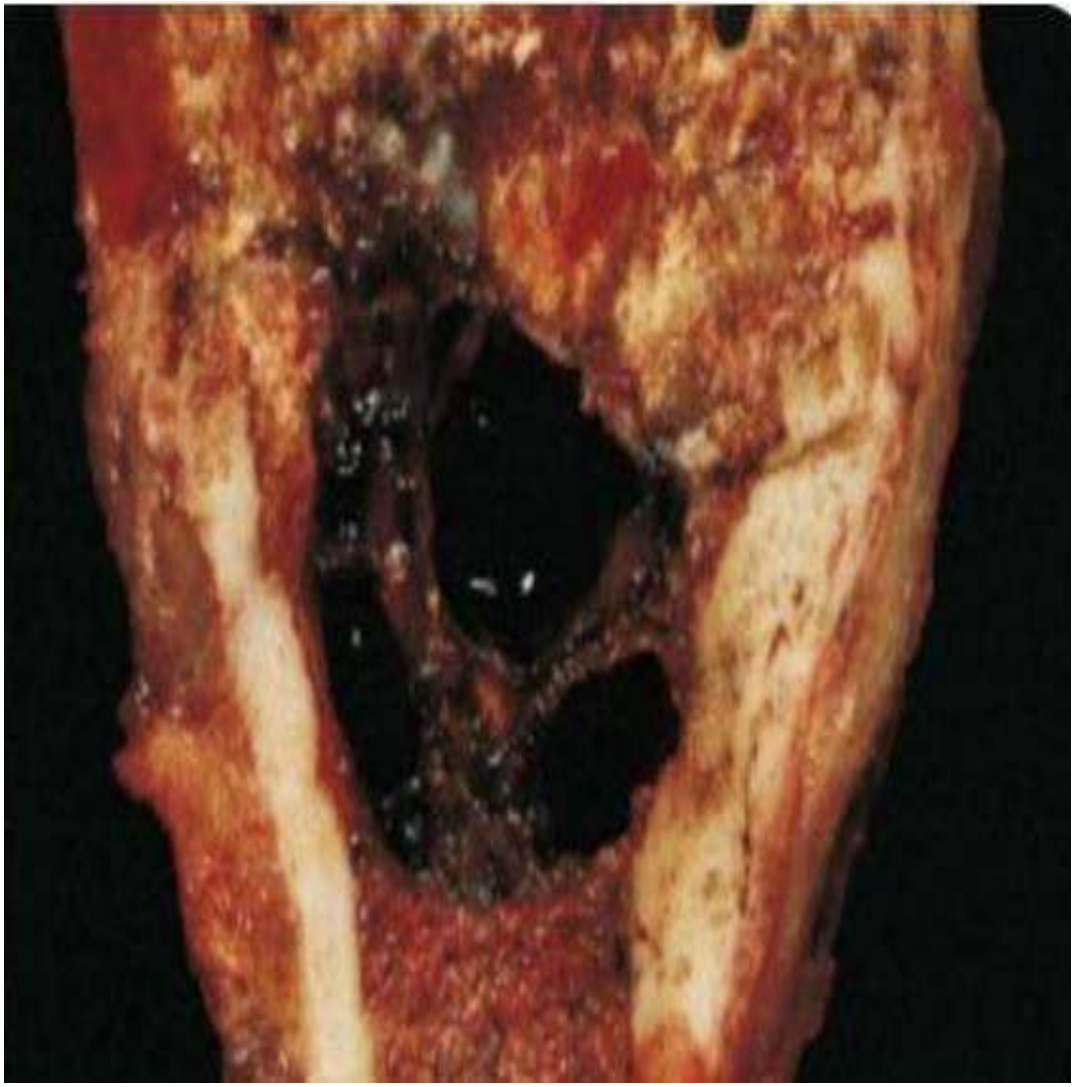
Proximal end of tibia

Proximal end of humerus

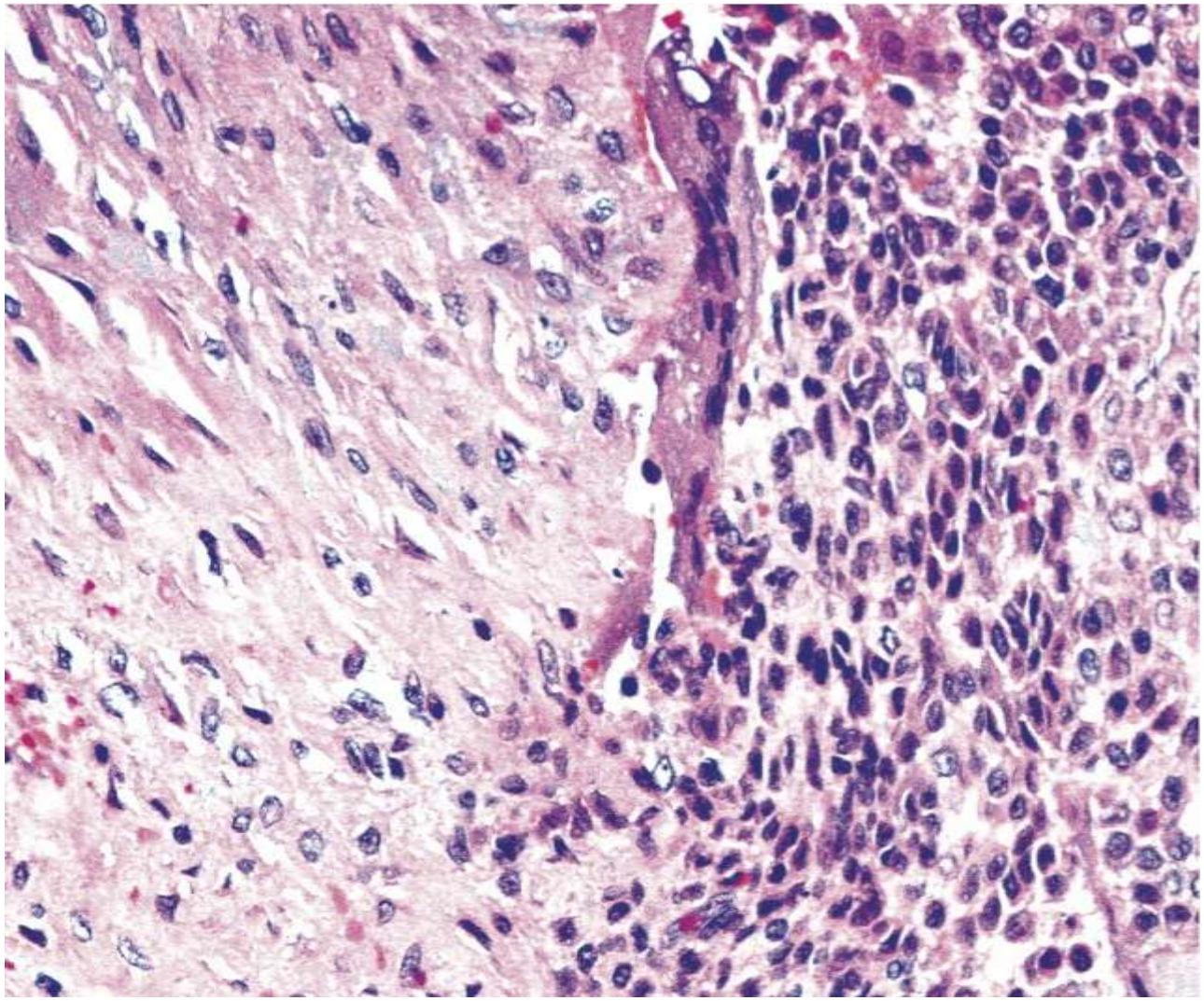
Radiograph- Intramedullary well defined tumor with sclerotic margins, radiolucent with internal calcifications



Gross-
Grey pink,well circumscribed firm tissue with gritty calcifications and hemorrhage, <5cm,sharply marginated from surrounding bone



Microscopy- Chondroid differentiation, the stroma is composed of mononuclear cells with distinct cytoplasmic boundaries and scattered benign giant cells



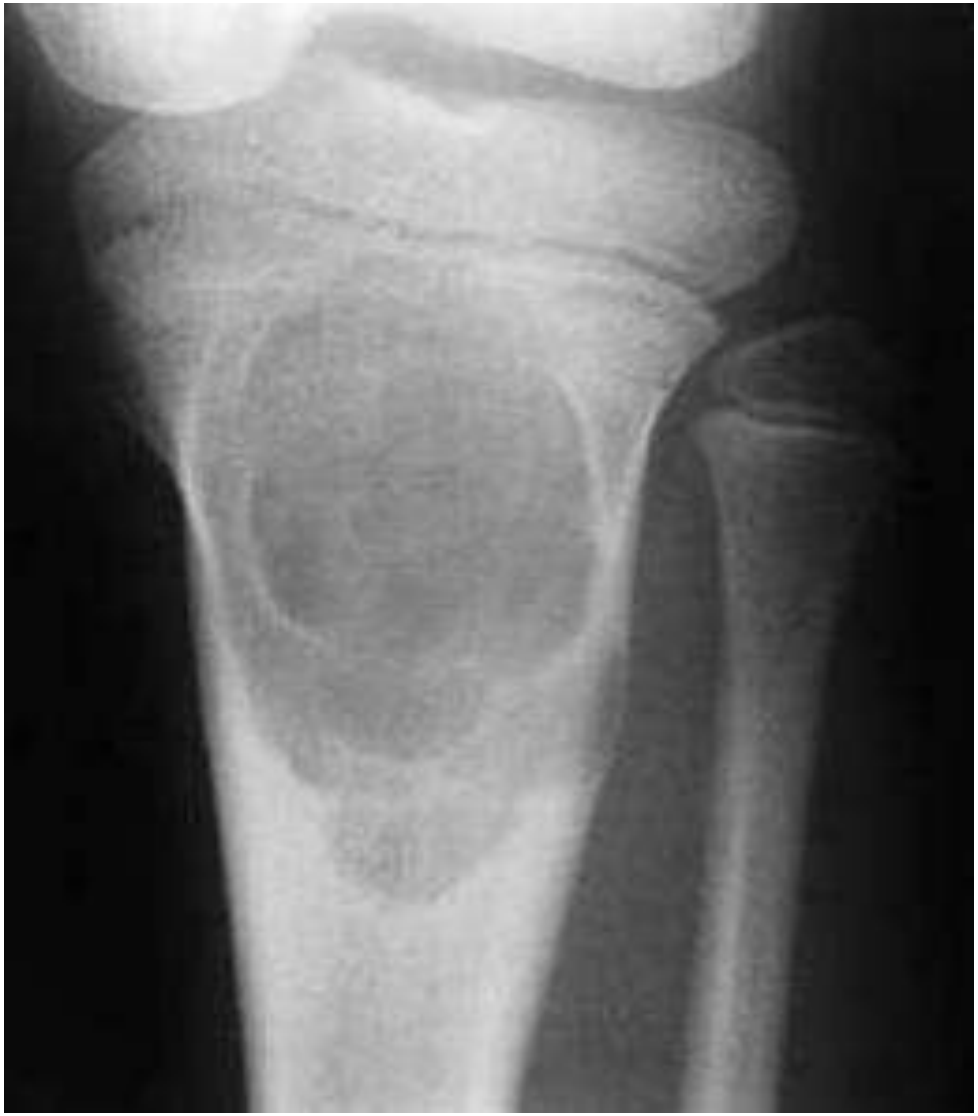
D/D-

- Giant cell tumor
- Primary Aneurysmal bone cyst
- Chondromyxoid fibroma
- Clear cell chondrosarcoma

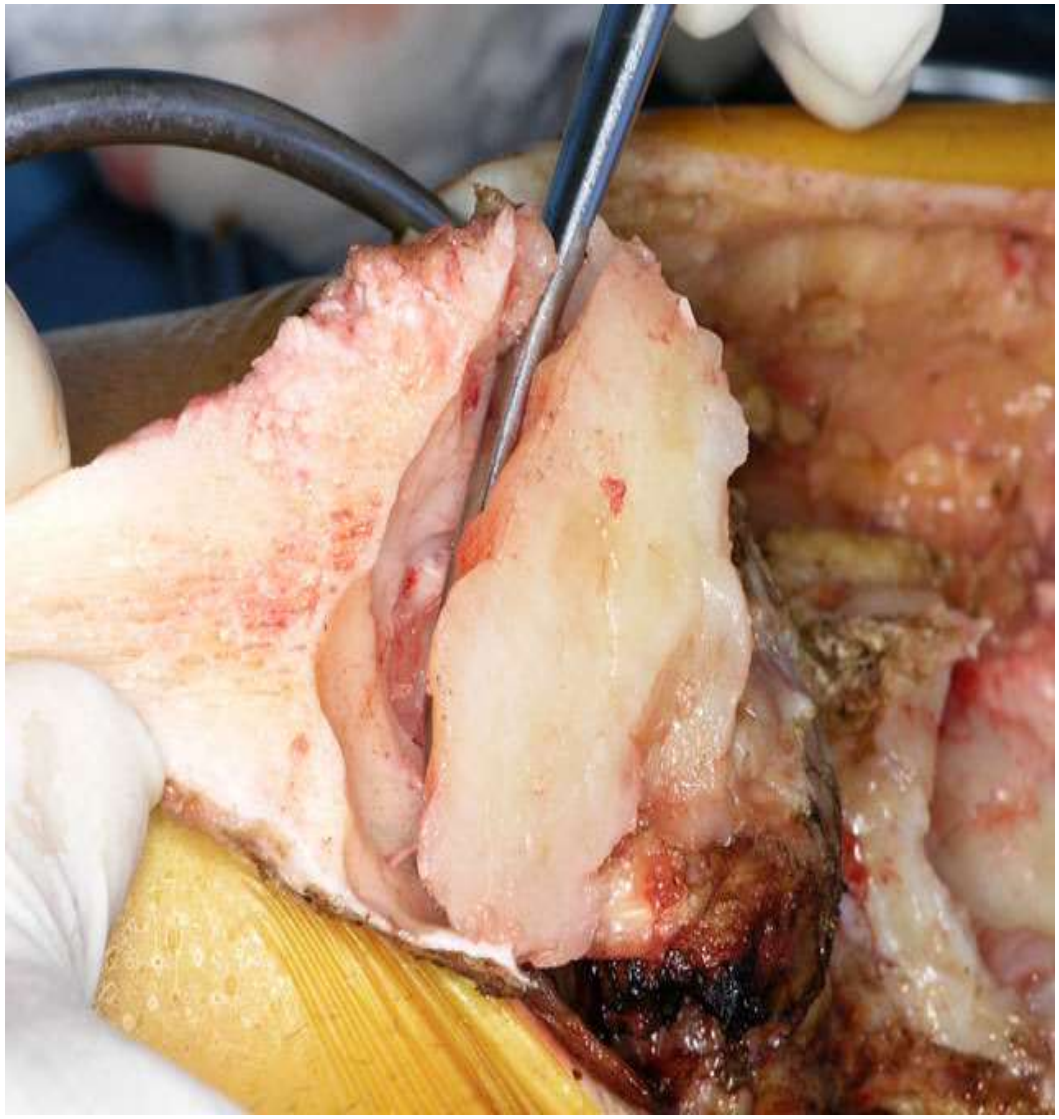
CHONDROMYXOID FIBROMA

- Rare benign tumor
- Long bones
- Young adults- 2^{nd} to 3^{rd} decade of life

Radiograph- arising within the metaphysis, sclerotic and scalloped rim of lesion

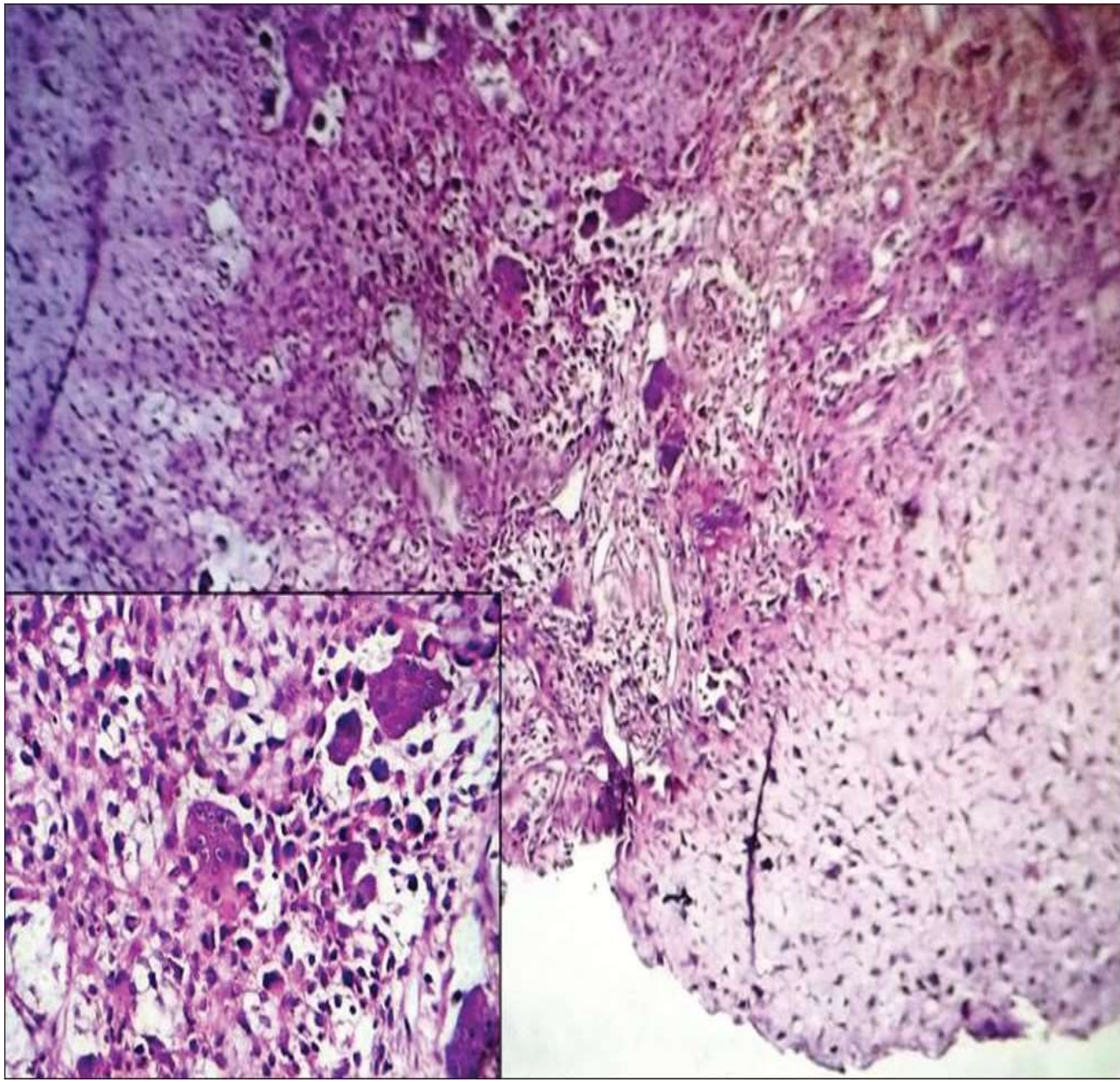


Gross-
Yellow white/grey white,lobulated apperance



Microscopy-

Low power view of a macrolobular pattern in chondromyxoid fibroma. The shape and size of the lobules vary. A hypocellular center with condensation of tumor cells towards periphery. Benign giant cells are seen at periphery of lobules (high power)



- IHC

✓S-100

✓SOX 9

Negative for Keratin

- D/D

✓Chondroblastoma

✓Enchondroma

✓Low grade chondrosarcoma

✓Chondromyxoid fibroma like osteosarcoma

✓Fibromyxoma

✓Osteochondromyxoma

MALIGNANT GIANT CELL LESIONS

OSTEOSARCOMA

- Malignant tumor in which the cancer cells produce osteoid matrix or mineralized bone
- Most common primary malignant tumor of bone
- Occurs in all age groups but has bimodal age group
- Male preponderance
- Site- Metaphyseal region of long bones
  - Lower end of femur
  - Upper end of tibia
  - Upper end of humerus

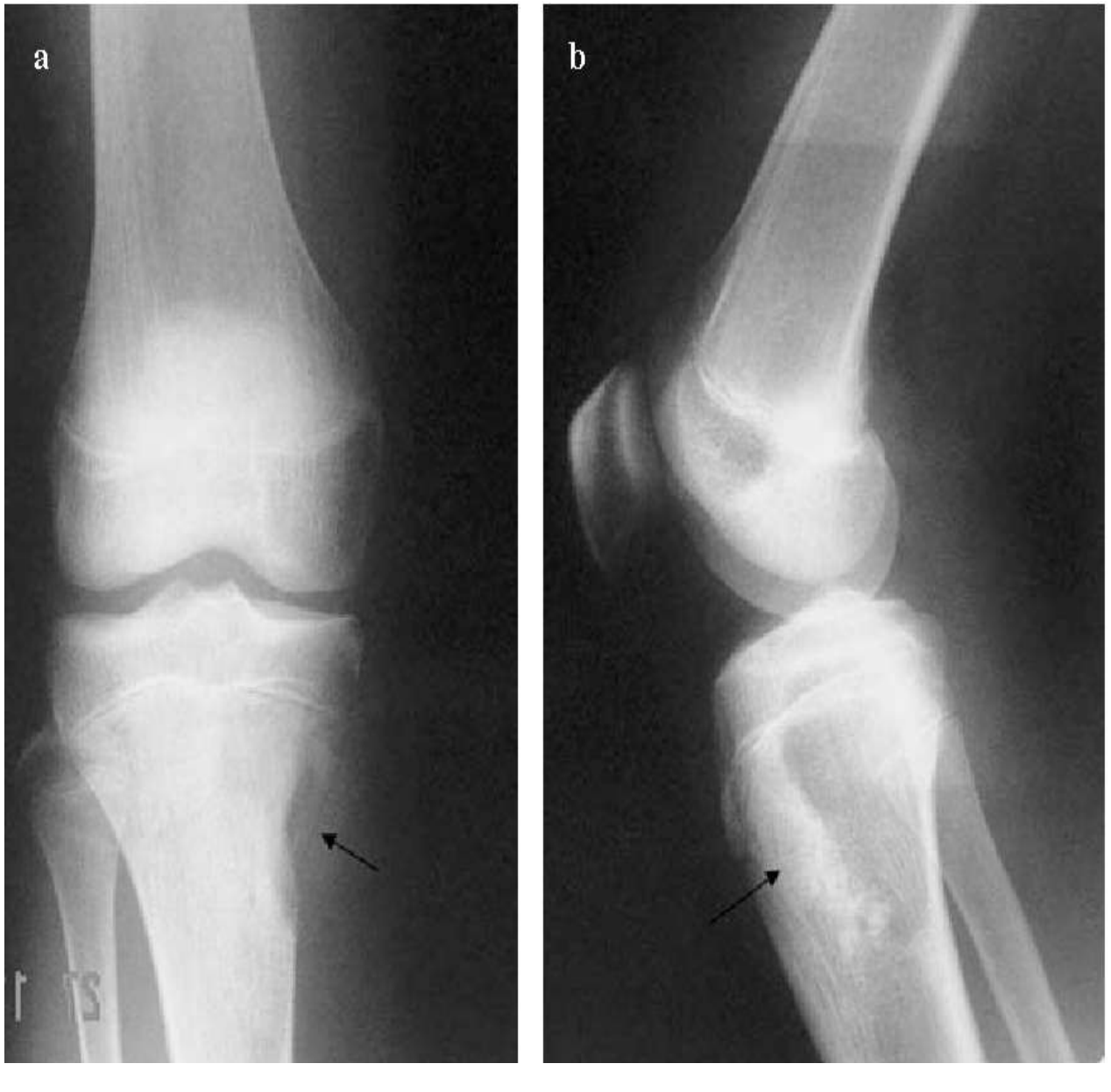
- Subtypes-
- Site of origin-Intramedullary,Intracortical,Surface
- Histologic grade- Low,High
- Primary-underlying bone is unremarkable
  Secondary-to preexisting disorders(Pagets,bone infarcts,benign tumors)
- Histologic features-
  Osteoblastic,Chondroblastic,Fibroblastic,Telengectiactic,Small cell,**Giant cell**

  The most common subtype arises in metaphysis of long bones and is Primary,Intramedullary,Osteoblastic and high grade.

Radiograph-

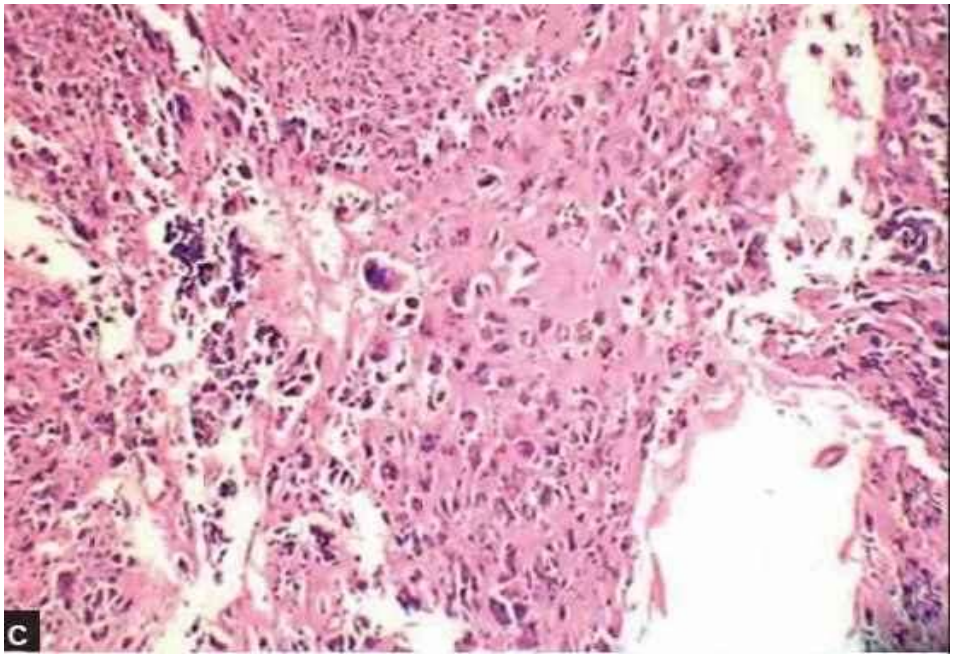
An ill-defined margin surrounds a predominantly lytic lesion of the proximal tibia of a young patient, the periosteal reaction is weak.

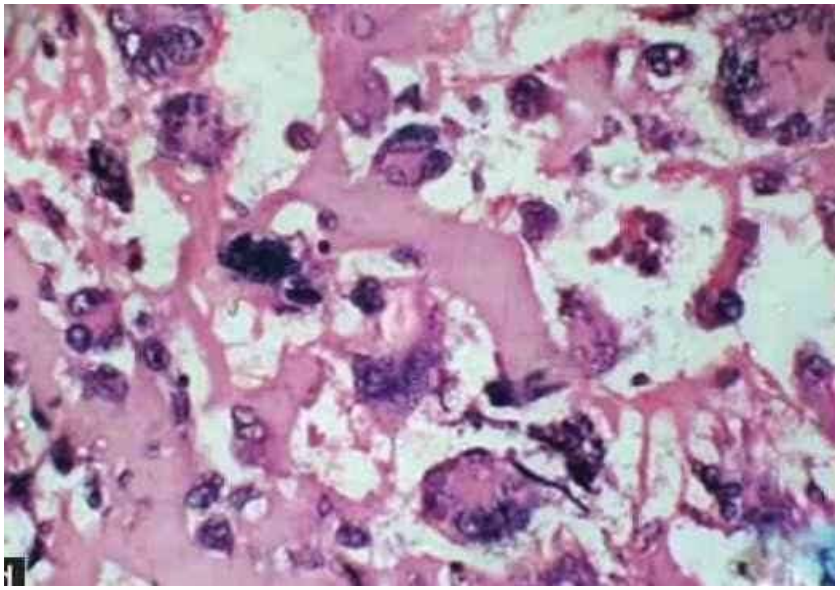
Some cases, faint onion skin-like periosteal reaction



Gross-
revealed diaphyseal bony hard growth with variegated cut surface, areas of necrosis, and few bluish areas in between

Microscopy-
numerous scattered giant cells containing large pleomorphic nuclei with irregular nuclear membrane and few showing prominent nucleoli. Malignant osteoid was seen being layered by bizarre atypical cells having scanty foamy cytoplasm, atypical nuclear morphology.



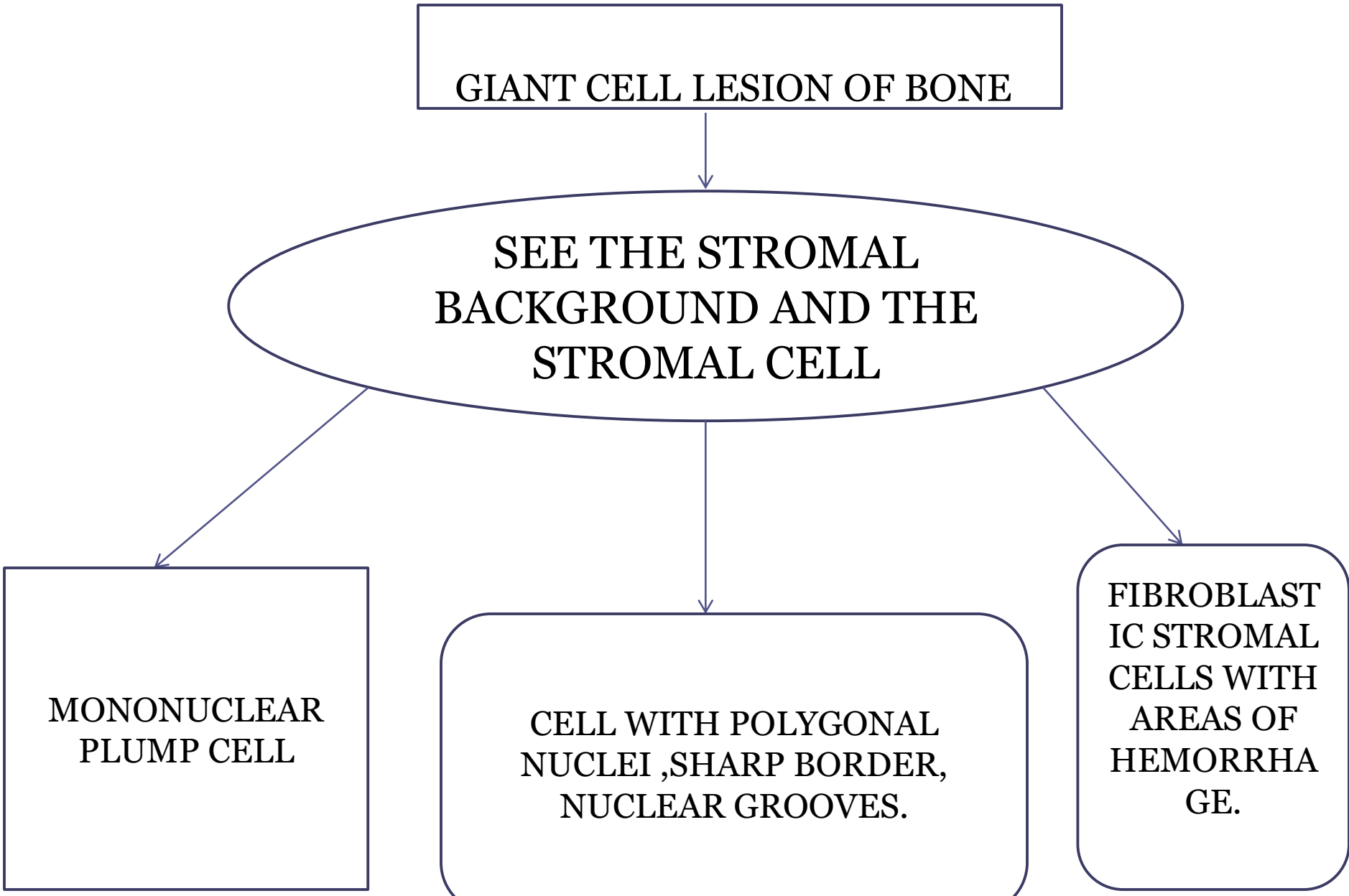


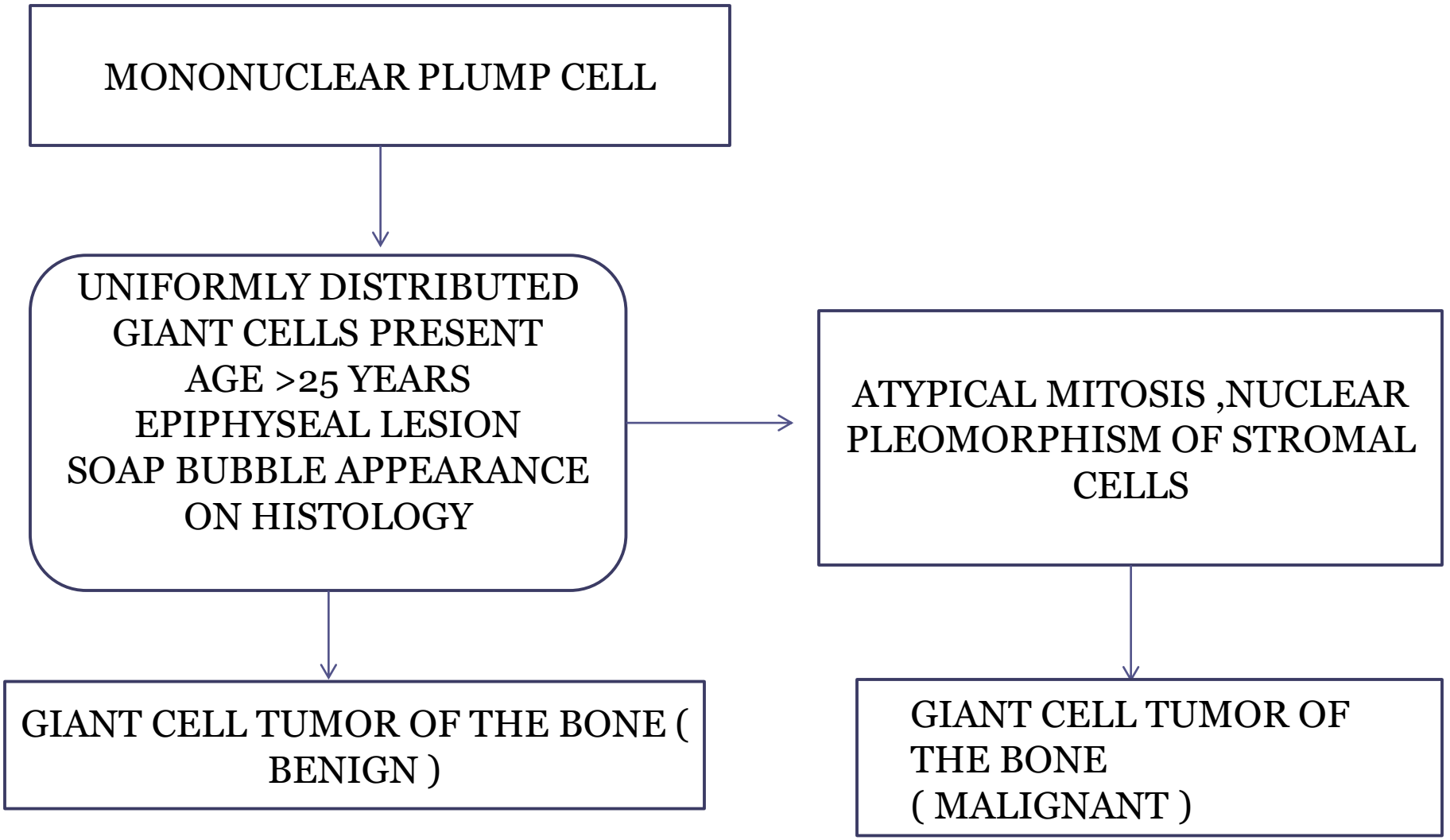
IHC-

- Strong alkaline phosphatase activity
- Immunoprofile is non specific
- SAT B2-nuclear transcription factor-stains OB-sensitive not specific
- May be positive for keratin and EMA
- Cartilagenous area-S100 positive

D/D-

- Dedifferentiated chondrosarcoma
- Fibrosarcoma
- Ewing sarcoma
- Osteoblastoma
- Undifferentiated pleomorphic sarcoma(so- called malignant fibrous histiocytoma)


GIANT CELL LESION OF BONE
SEE THE STROMAL BACKGROUND AND THE STROMAL CELL
MONONUCLEAR PLUMP CELL
CELL WITH POLYGONAL NUCLEI ,SHARP BORDER, NUCLEAR GROOVES.
FIBROBLASTIC STROMAL CELLS WITH AREAS OF HEMORRHAGE.

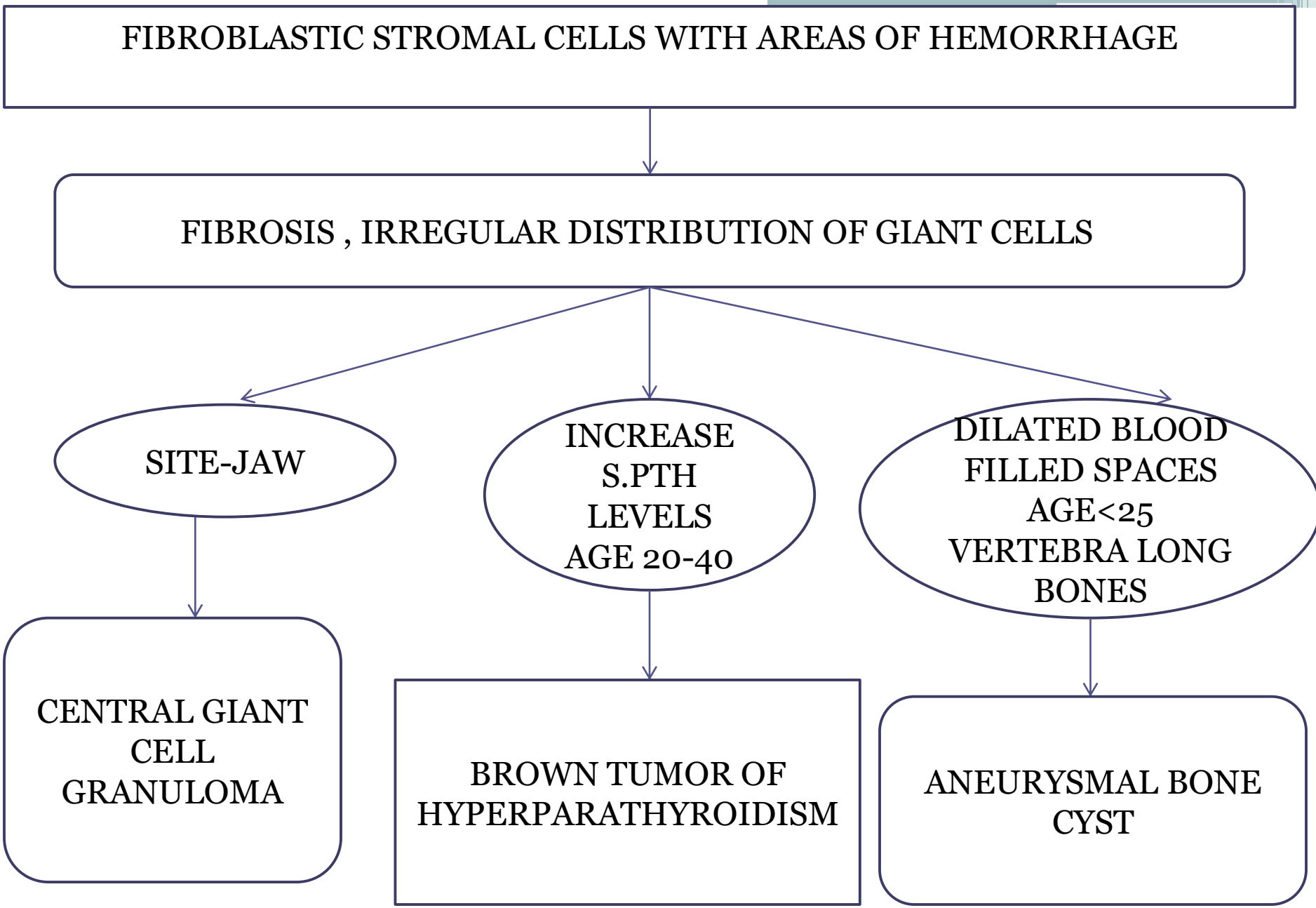

MONONUCLEAR PLUMP CELL
UNIFORMLY DISTRIBUTED
GIANT CELLS PRESENT
AGE >25 YEARS
EPIPHYSEAL LESION
SOAP BUBBLE APPEARANCE
ON HISTOLOGY
ATYPICAL MITOSIS ,NUCLEAR
PLEOMORPHISM OF STROMAL
CELLS
GIANT CELL TUMOR OF THE BONE (
BENIGN)
GIANT CELL TUMOR OF
THE BONE
(MALIGNANT)

CELL WITH POLYGONAL NUCLEI ,SHARP BORDER, NUCLEAR GROOVES.

AGE <25 YEARS , VARIABLE IRREGULAR DISTRIBUTION OF GIANT CELLS .

PERICELLULAR CHICKEN WIRE CALCIFICATION ,CELLS POSTIVE FOR S-100

CHONDROBLASTOMA


FIBROBLASTIC STROMAL CELLS WITH AREAS OF HEMORRHAGE
FIBROSIS , IRREGULAR DISTRIBUTION OF GIANT CELLS
SITE-JAW
INCREASE S.PTH LEVELS AGE 20-40
DILATED BLOOD FILLED SPACES AGE<25 VERTEBRA LONG BONES
CENTRAL GIANT CELL GRANULOMA
BROWN TUMOR OF HYPERPARATHYROIDISM
ANEURYSMAL BONE CYST

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THANK YOU