Osteosarcoma
Malignant Bone Forming Tumors

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General Information

- Osteosarcoma
  - Cancerous spindle cell tumor (sarcoma) that is derived from a mesenchymal stem cell precursor that **produces immature woven bone or osteoid**
  - It is a bone producing sarcoma

Osteosarcoma Classification (Types of Osteosarcomas)

- Intramedullary (75%)
  - Conventional
    - Osteoblastic (82%)
      - Mixed and Sclerosing
    - Chondroblastic (5%)
    - Fibroblastic (3-4%)
    - MFH-like (3-4%)
    - Osteoblastoma-like (.5%)
    - Giant Cell-rich (.5%)
    - Small-cell (1%)
    - Epithelioid (.5%)
  - Telangiectatic (3%)
  - Well-differentiated (low grade intraosseous; 4%-5%)
- Juxtacortical/Surface (7-10%)
  - Parosteal
  - Periosteal
  - High-grade surface
- Intracortical (.2%)
- Secondary (older population)
  - Pagets (67-90%); Post RT (6-22%); Bone infarct; Fibrous dysplasia; Metallic implant; Osteomyelitis
- OS with specific syndromes
  - Familial; Retinoblastoma; Rothmund-Thomson Syndrome; Multifocal; OI

General Information Osteosarcoma

- 2nd most common primary malignant tumor of bone
- Most common primary cancer of bone in children and adolescents
- 15% of all biopsied primary bone tumors
- 600 to 700 new cases of osteosarcoma in the United States per year

Clinical Presentation

- Mild Pain and swelling for weeks-months
- High serum alkaline phosphatase
- Two peak age groups (rare <6y or >60y)
  - 15-25 years: Most common
  - Over 50 years of age
    - Usually secondary to an underlying predisposing condition
      - Radiation, Pagets disease

Clinical Presentation
Conventional Osteosarcoma

- **Sites:**
  - Distal Femur: most common site
  - Proximal Tibia: Second most common site
  - Proximal Humerus: Third most common site
  - **Metaphysis** (90%); **Diaphysis** (10%)

Clinical Presentation
Conventional Osteosarcoma

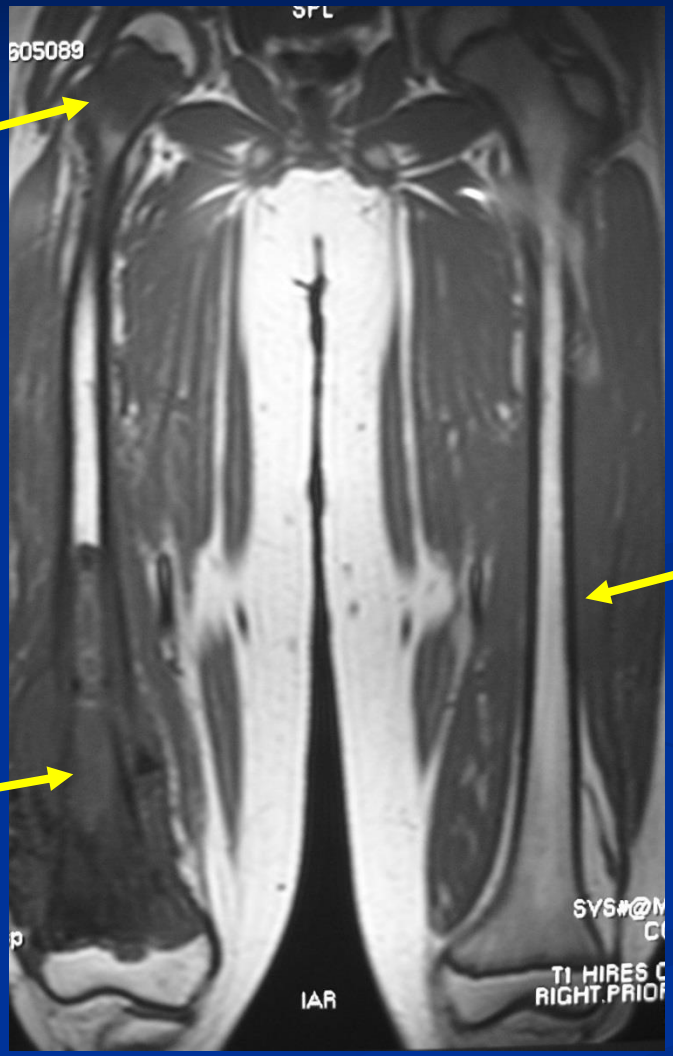
- Most patients present with Stage IIb tumors
- Metastases:
  - Lungs: Most common site
  - Bones: Second most common site
  - Liver: Rare site
- ~15%-20% detectable metastases to the lungs.

Clinical Presentation
Osteosarcoma

- **Skip metastases** occur within the same bone or across the joint in the adjacent bone. They occur through the intraosseous venous system within the bone or through the transarticular venous system.
  - Poor prognosis

MRI: Osteosarcoma of Distal Femur with Skip Metastasis to Proximal Femur

Skip Metastasis to Proximal Femur/Femoral Neck



Normal Femur

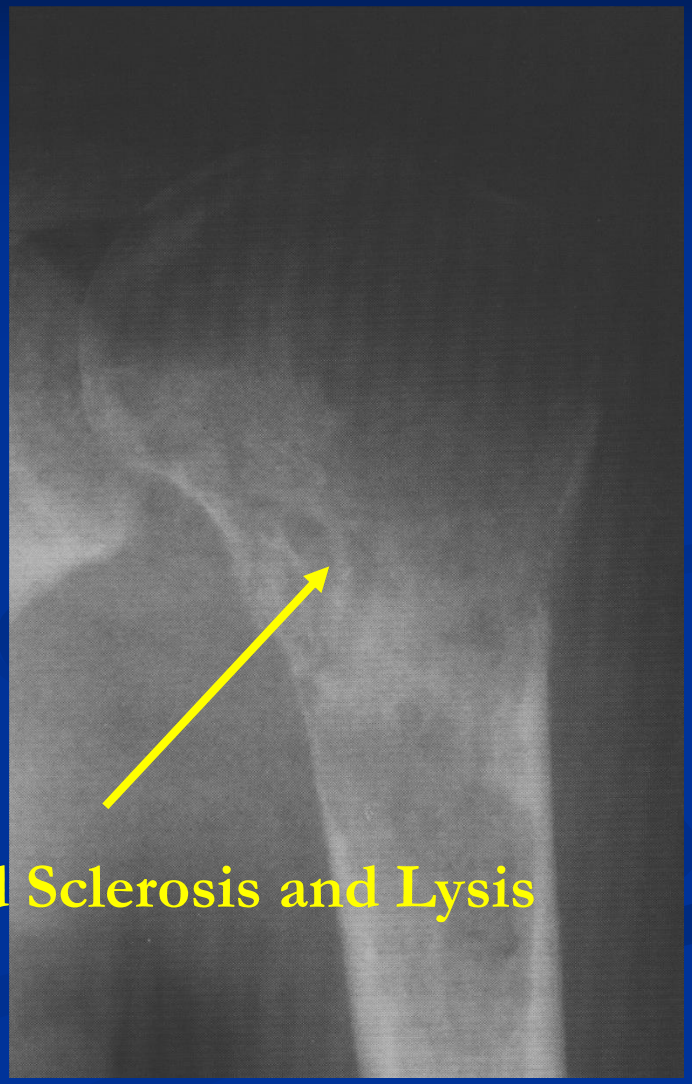
Osteosarcoma of Distal Femur

Radiographic Presentation Conventional Osteosarcoma

- Radiographic presentations: Permeative Lesions
  - Mixed Sclerotic and Lytic Permeative Lesion
    - Most common radiographic presentation
  - Purely Osteoblastic Permeative Lesion
  - Purely Lytic Permeative Lesion

Xray: Osteosarcoma of Proximal Humerus

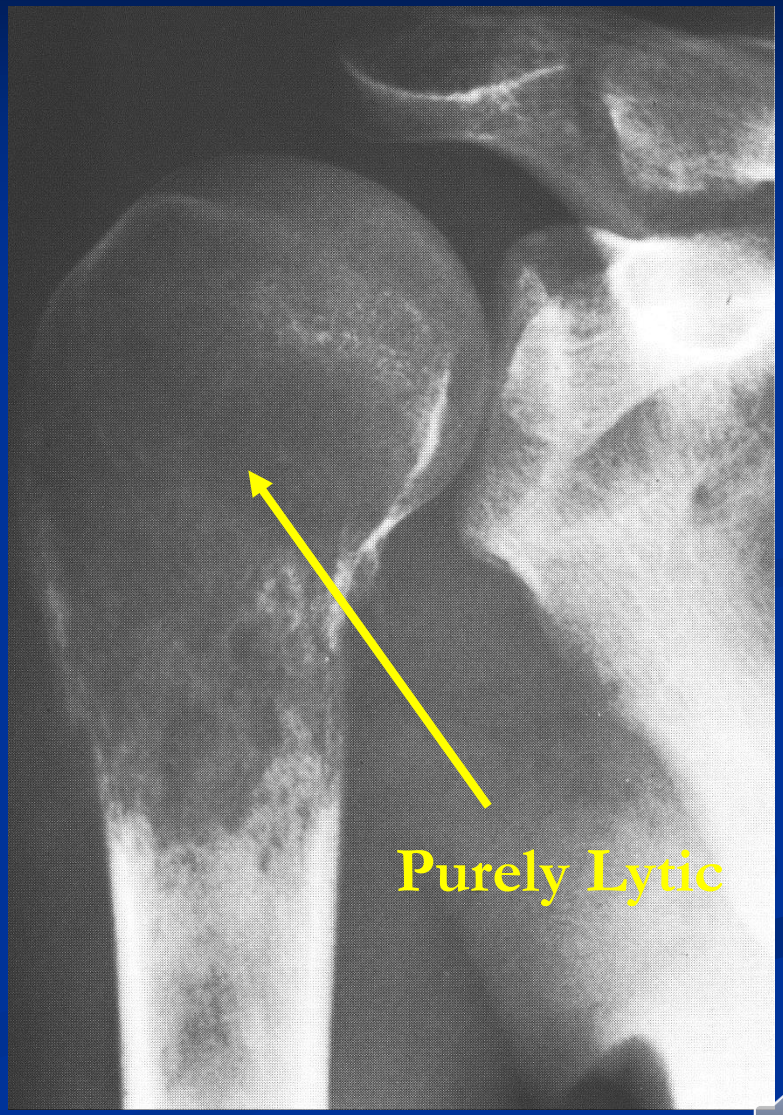
- Permative Lesion
- Metaphyseal Origin
- Mixed Lysis and Sclerosis
- Sclerosis represents calcified osteoid
- Most common radiographic presentation



Mixed Sclerosis and Lysis

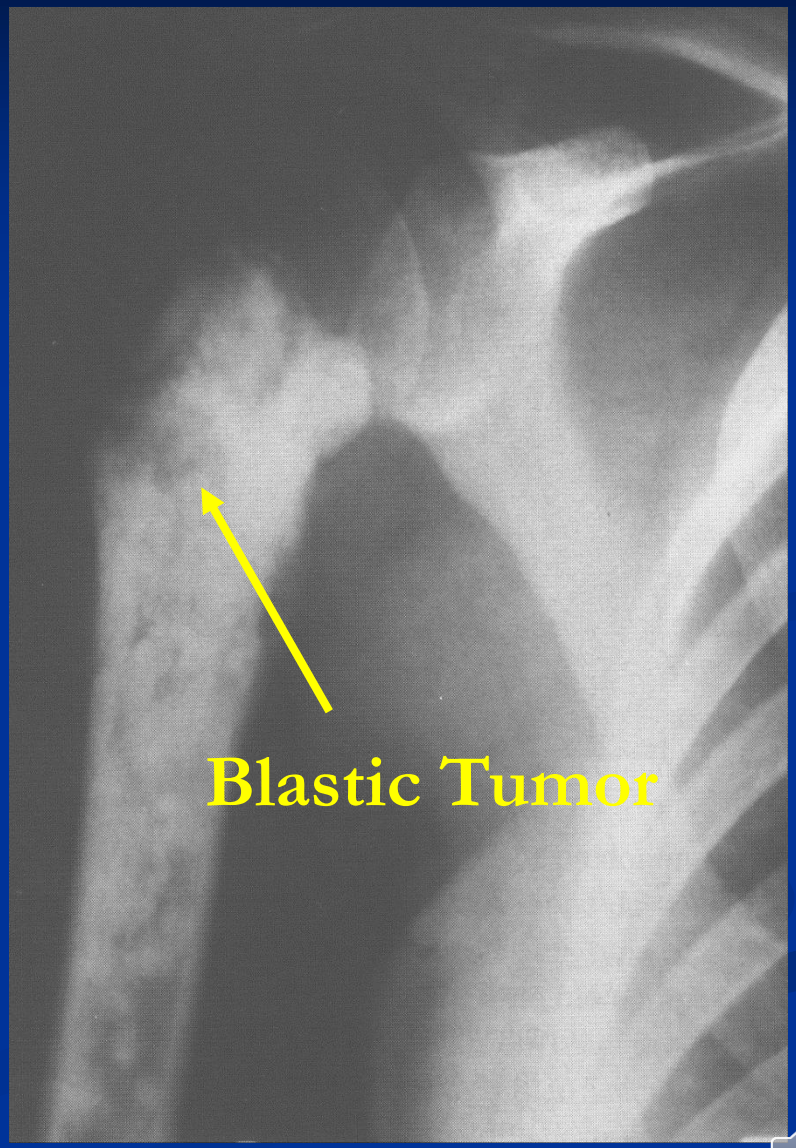
Xray: Osteosarcoma of Proximal Humerus

- Permeative Lesion
- Metaphyseal
- Cortical Destruction
- Purely Lytic
- Malignant Appearance



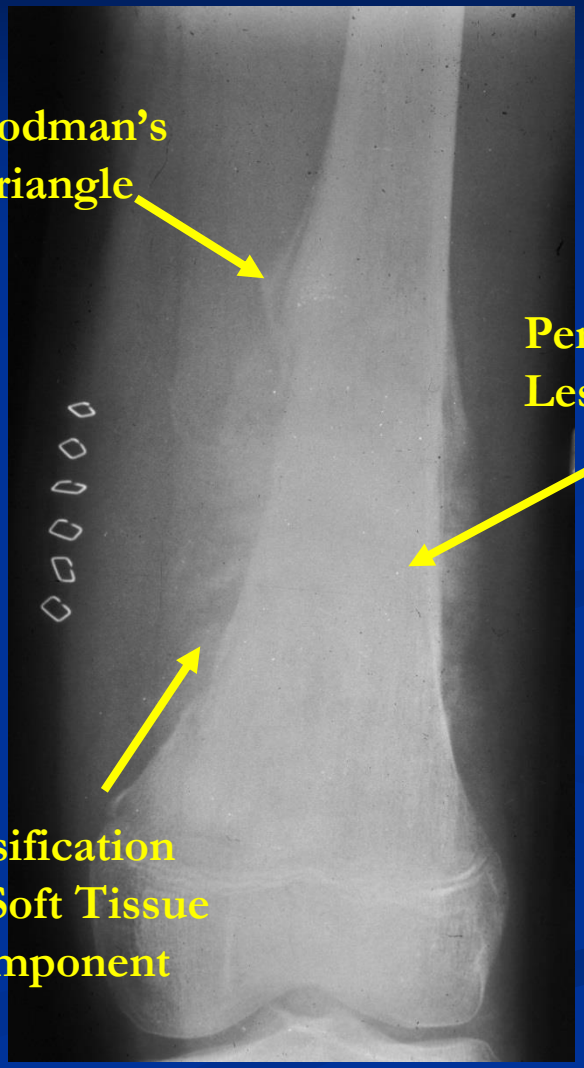
Xray: Blastic Osteosarcoma of Proximal Humerus

- Permeative Lesion
- Metaphyseal Origin
- Purely Blastic
- Heavily Calcified Osteoid



Xray: Conventional Osteosarcoma of Distal Femur

- Distal femur is most common site
- Permeative lesion with mixed lysis and sclerosis (sclerosis is calcified osteoid)
- Metaphyseal Origin
- Codman's triangle interrupted type of periosteal reaction
- Tumor extends into soft tissue and the soft tissue component is **ossified**

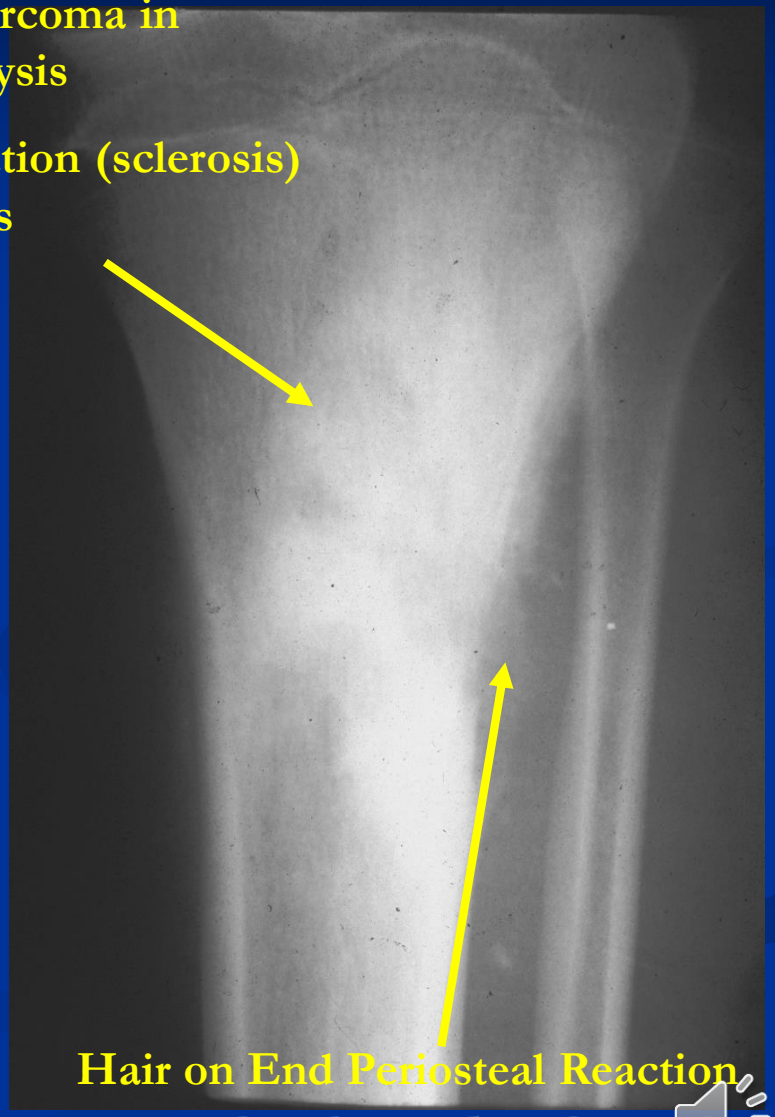


Xray: Conventional Osteosarcoma of Distal Femur

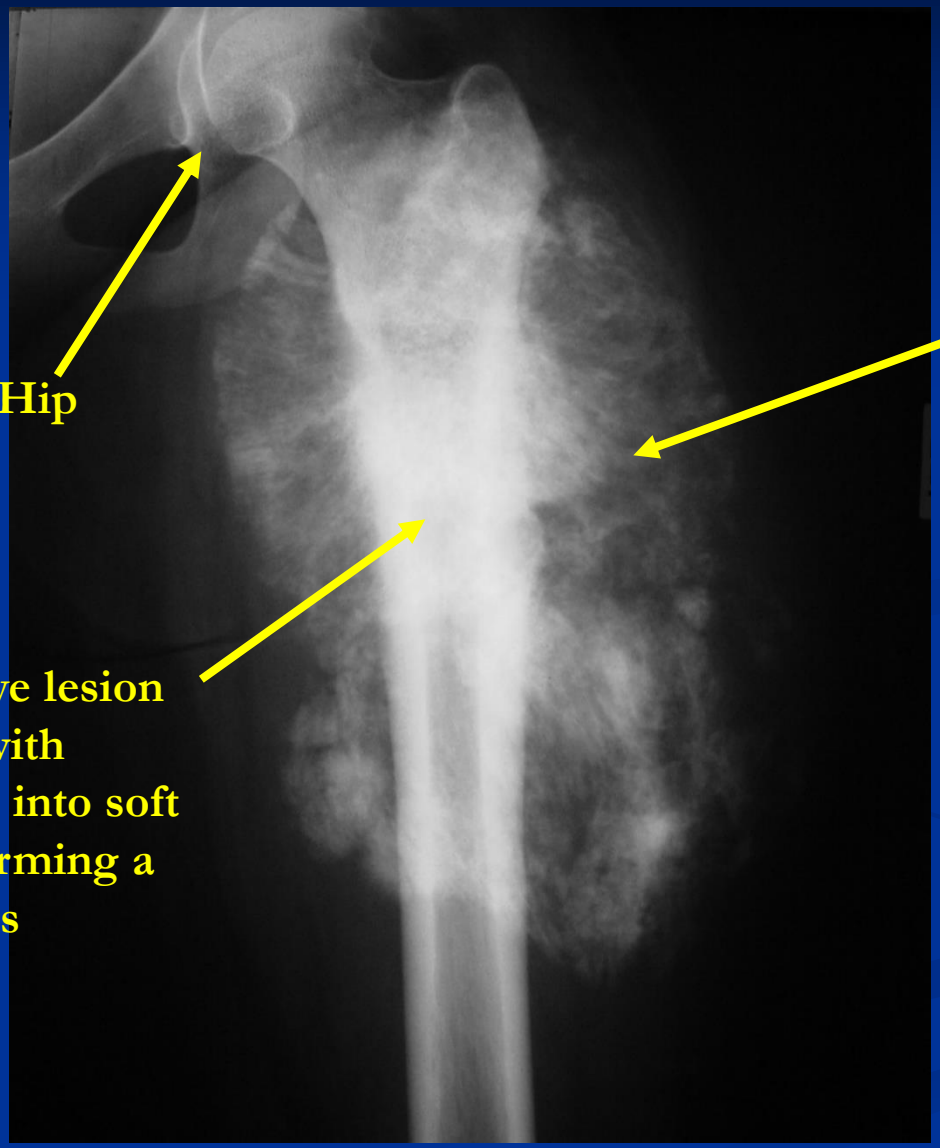
- Permeative Lesion
- Mixed Lysis and Sclerosis
- Metadiaphyseal Origin
- Ossified Soft Tissue Mass (white arrows)
- Codman's Triangle periosteal reaction

Xray: Osteosarcoma of Proximal Tibia

- Proximal tibia is second most common site for conventional osteosarcoma
- Permeative lesion with mixed lysis and sclerosis (ossification)
- Metaphyseal origin
- Soft tissue extension
- Hair on End periosteal reaction

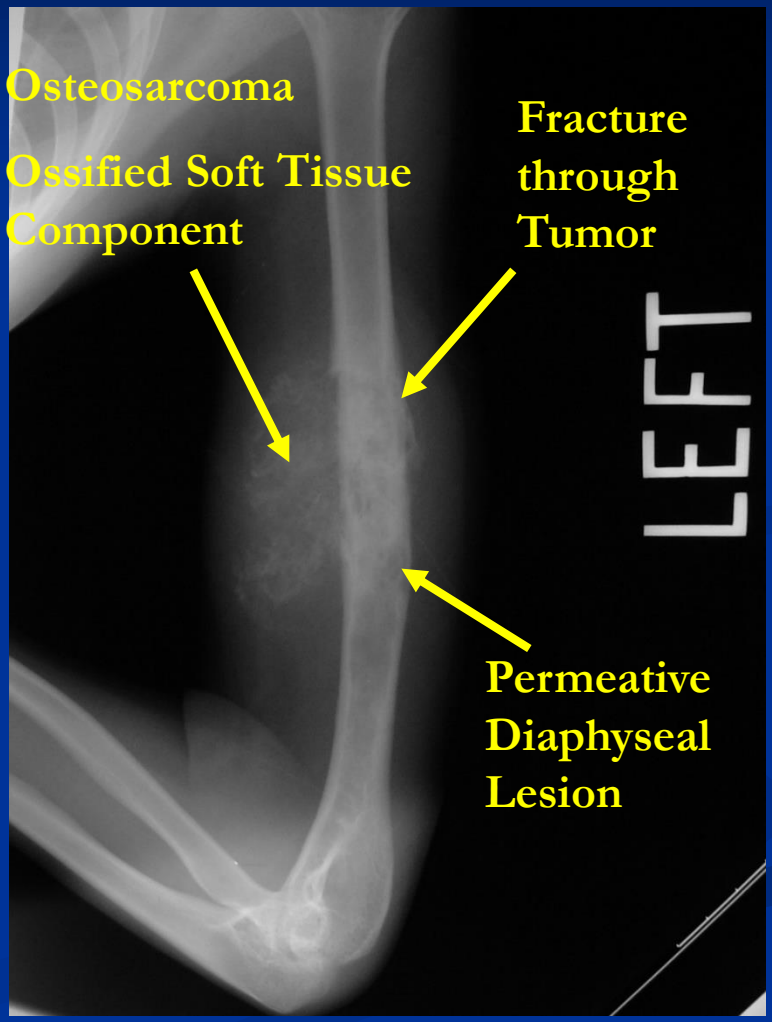


Xray: Large Osteosarcoma of Proximal Femur with Heavily Ossified Soft Tissue Component



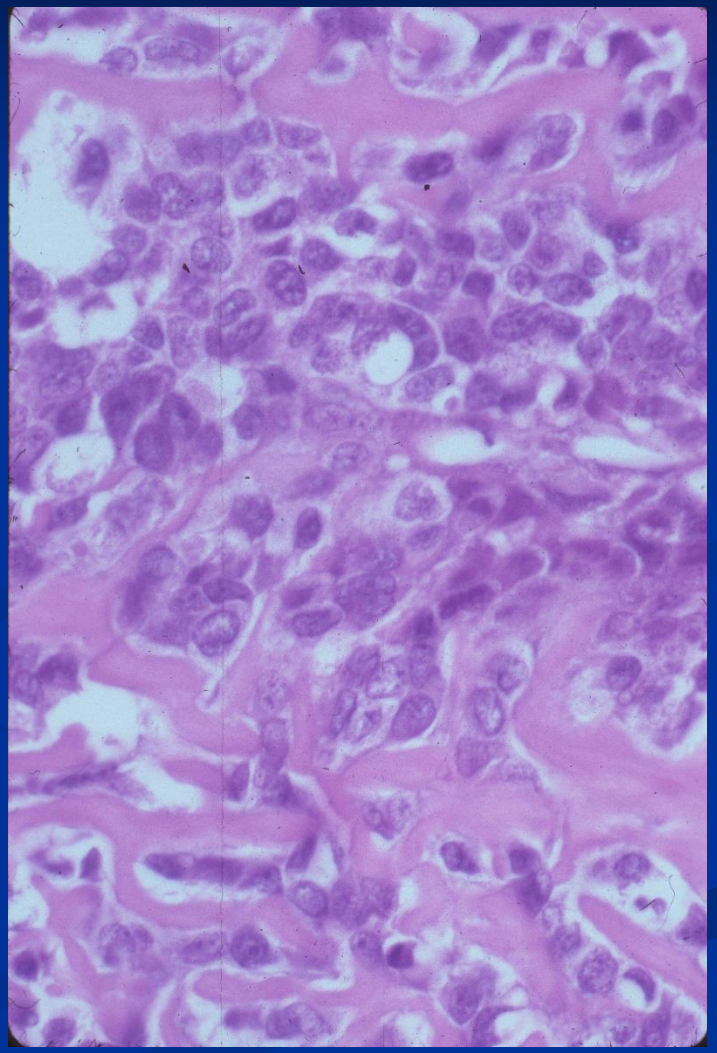
Xray: Osteosarcoma of Left Humerus
Diaphyseal Osteosarcoma

- Permeative Tumor
- Diaphyseal Origin
  - Only 10% of osteosarcomas arise from the diaphysis
- Osteoid (fluffy cloudlike densities)
- Ossification of mass and within bone
- Pathological Fracture is present (10% of osteosarcomas present with a pathological fracture)



Microscopic Pathology: Conventional Osteosarcoma

- **High Grade Anaplastic Tumor**
- **Osteoid Production**
  - Lace-like pattern (no trabeculae)
  - No osteoblastic rimming
  - The osteoid may or may not mineralize. The degree of mineralization determines how well it shows on an Xray
- Other elements such as cartilage, fibrous tissue, small round blue cells, giant cells and telangiectatic changes



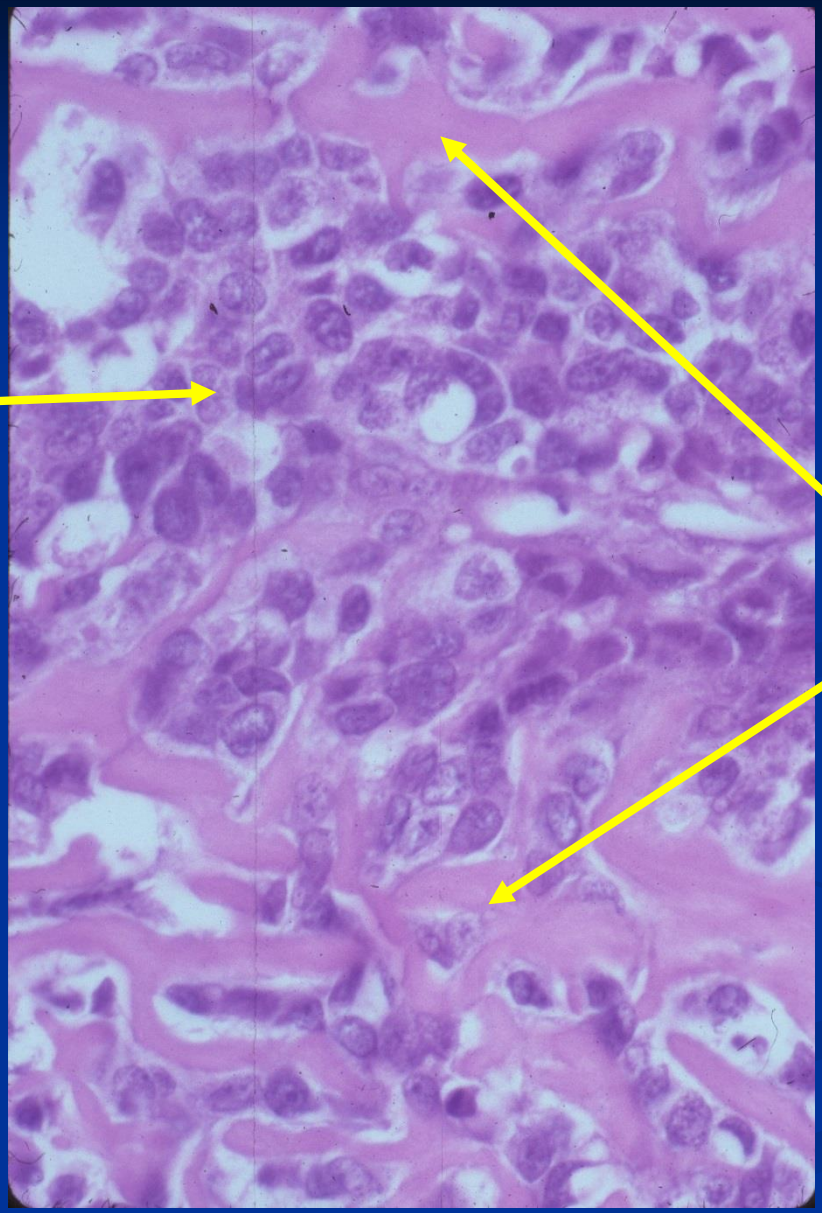
Microscopic Pathology: High Power of Conventional Osteosarcoma

Large Hyperchromatic Spindle Cells with Large Nuclei

Nuclear Pleomorphism

Cells are Crowded

No trabeculae; the osteoid is layed down in between cells

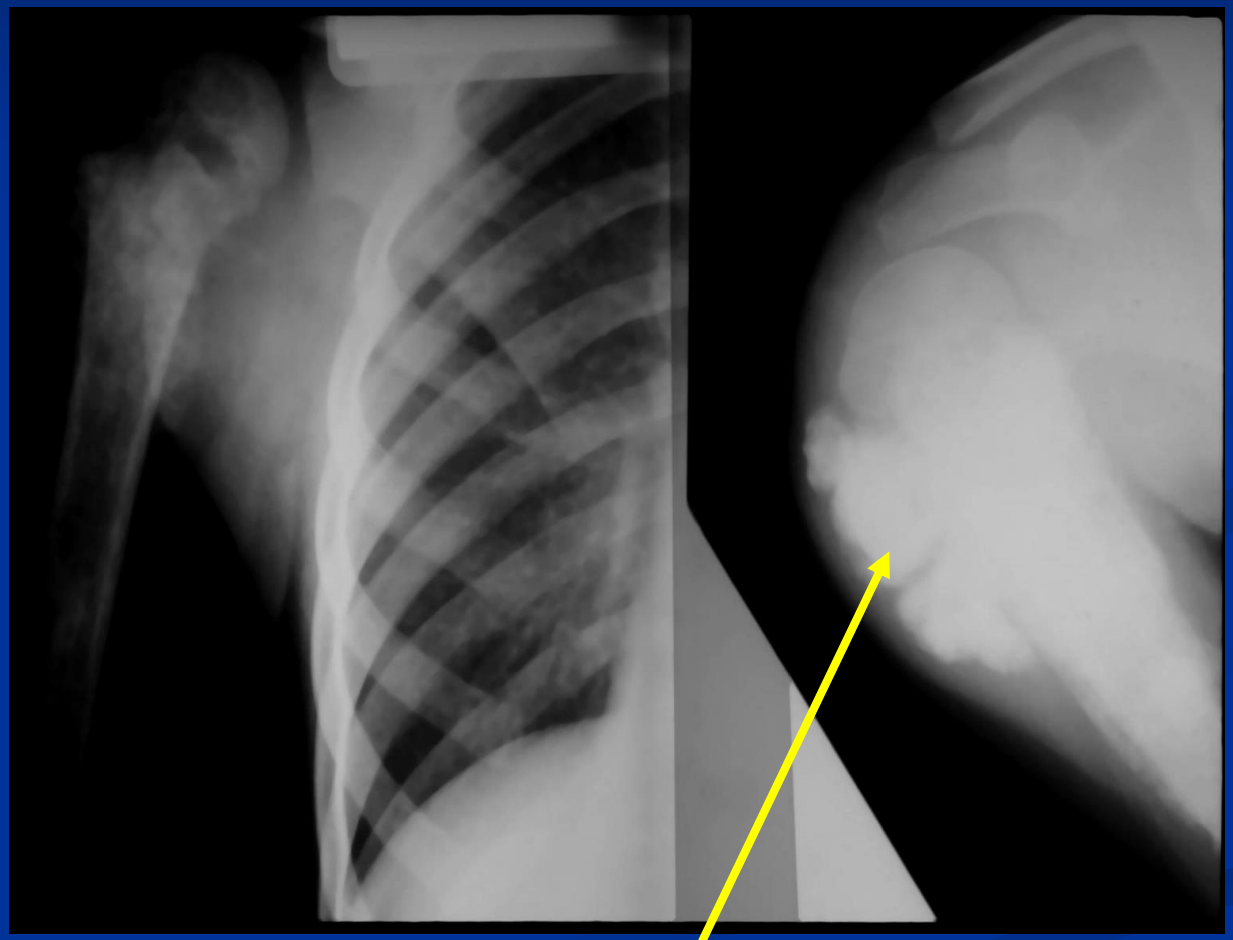


Pink Lace-like Osteoid

Treatment

- Preoperative (induction) chemotherapy:
  - Adriamycin (doxorubicin)
  - Cisplatinum (cisplatin)
  - High Dose Methotrexate (HDMTX)
  - Ifosfamide/Etoposide in some regimens
  - (Typically: 2 to 3 cycles and then surgery)
- Surgery:
  - Wide surgical resection/limb Salvage
  - Amputation (5% of extremity lesions)
- Postoperative (adjuvant) chemotherapy:
  - Same regimen as preop; usually 4 cycles

X-rays of a Proximal Humerus Osteosarcoma: before and after preoperative chemotherapy demonstrating intense ossification of the tumor indicative of a good response to the preoperative chemotherapy



Extensive Ossification Occurs when the Osteosarcoma has had a Good Response

Preoperative (Neoadjuvant) Chemotherapy

- Estimate of response to preoperative chemotherapy occurs when the specimen is analyzed by the pathologist. This estimate helps predict prognosis. A "Good Response" (usually greater than 90% of the tumor killed) has been correlated with approximately a 90% cure rate.

Prognosis of Conventional Osteosarcoma

- Localized, nonmetastatic osteosarcoma: 65% 5 yr survival.
- "Good Response" approximately a 90% chance of being cured (5 yr survival)
- There is no difference in survival rates whether a limb sparing procedure or an amputation is performed
- Patients who present with or develop metastases to the lungs have a poor prognosis (15% 5 year survival if pulmonary mets can be resected)
- Patients with bone metastases have a dismal prognosis
- Skip metastases confer a poor prognosis
- Changing the chemotherapy regimen postoperatively for patients who did not have a "Good Response" has not been shown to change prognosis as of 2010

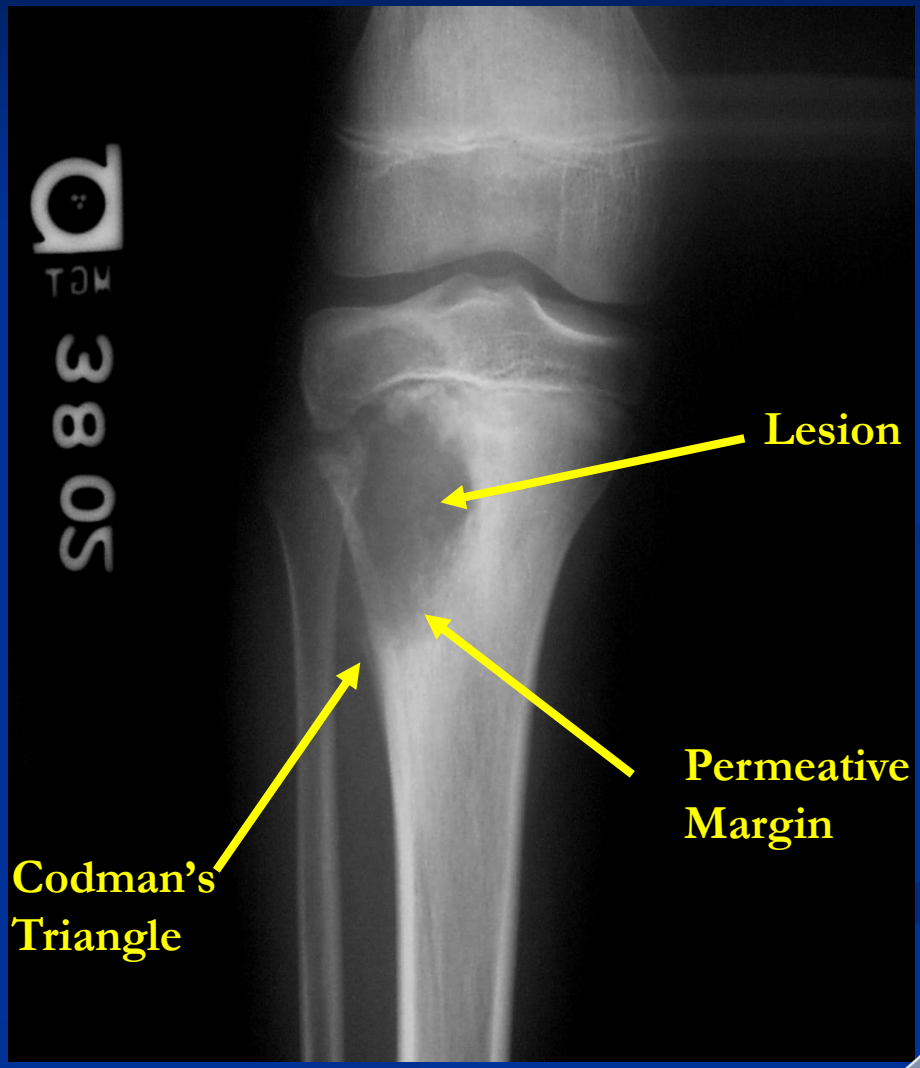
Telangiectatic Osteosarcoma

General Information

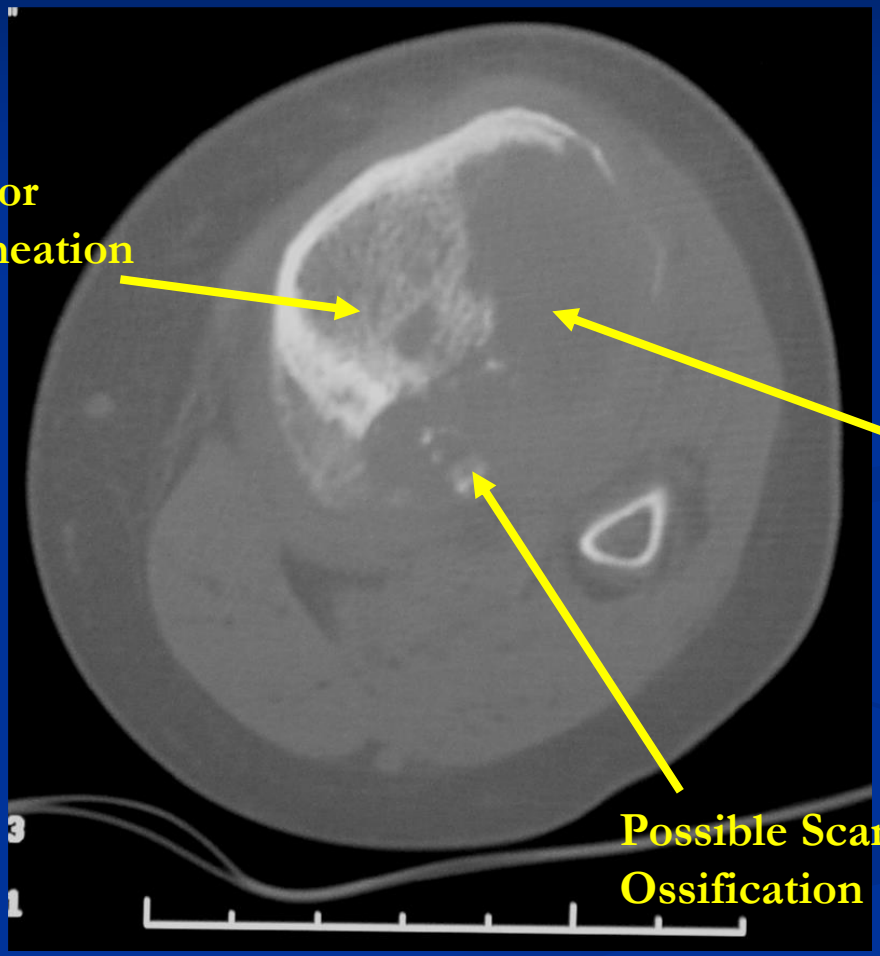
- Telangiectatic osteosarcoma is a variant of an intramedullary high grade osteosarcoma.
- Accounts for 3% of osteosarcomas
- Extremely lytic on X-rays
- Very little osteoid production.
- Cystic spaces filled with blood that are separated by thin septa.
- Fluid-Fluid Levels on MRI: Cystic spaces filled with hemorrhagic material
- ABC- like changes can sometimes lead to a misdiagnosis on X-rays and the tumor may be misinterpreted as being a benign ABC.

X-Ray: Telangiectatic Osteosarcoma of Proximal Tibia

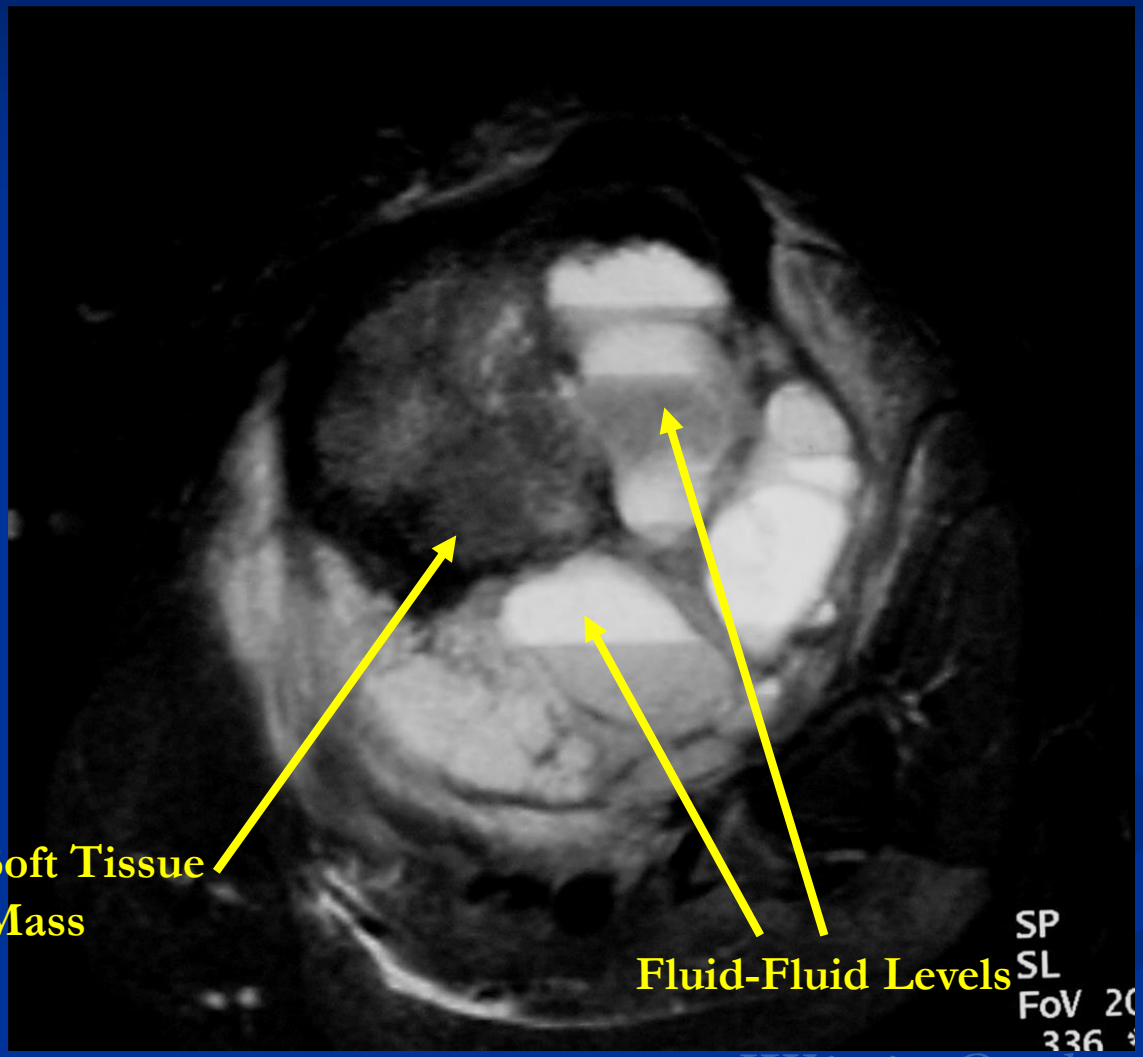
- Lytic lesion with indistinct (permeative) margin
- Metaphyseal origin
- Codman's triangle
- Cortical destruction
- No ossification detected on plain x-ray



CT Scan: Telangiectatic Osteosarcoma of Proximal Tibia

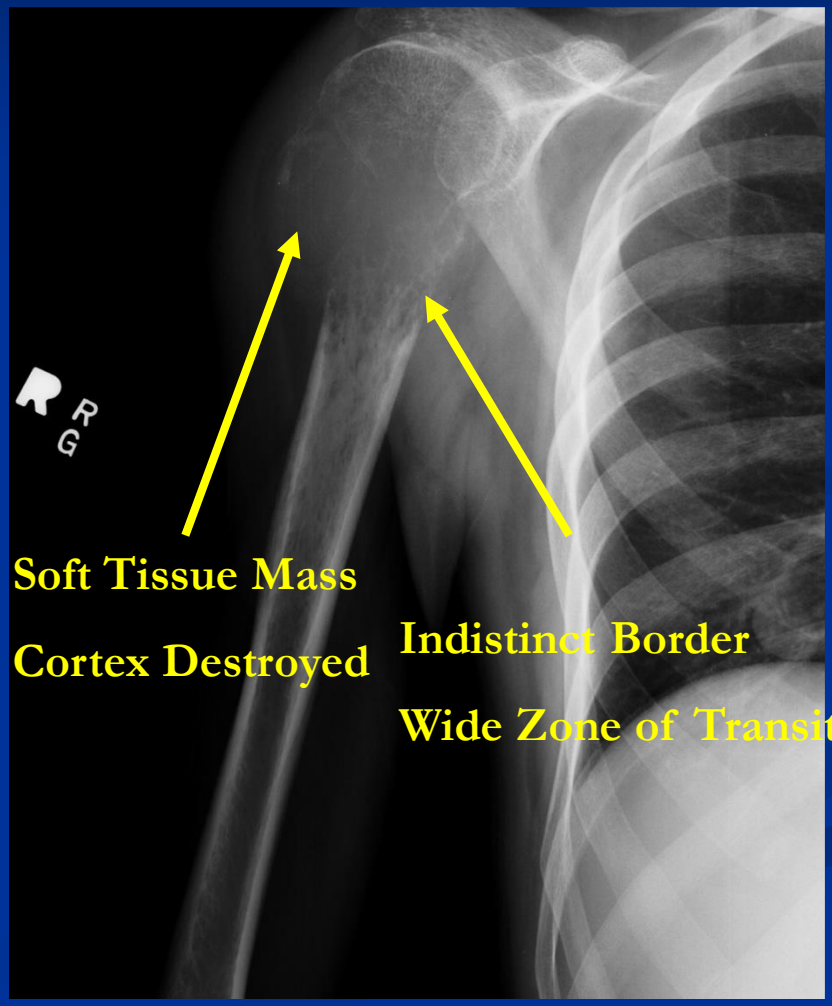


MRI: Telangiectatic Osteosarcoma of Proximal Tibia Multiple Fluid-Fluid Levels are Demonstrated



X-Ray: Telangiectatic Osteosarcoma of Proximal Humerus

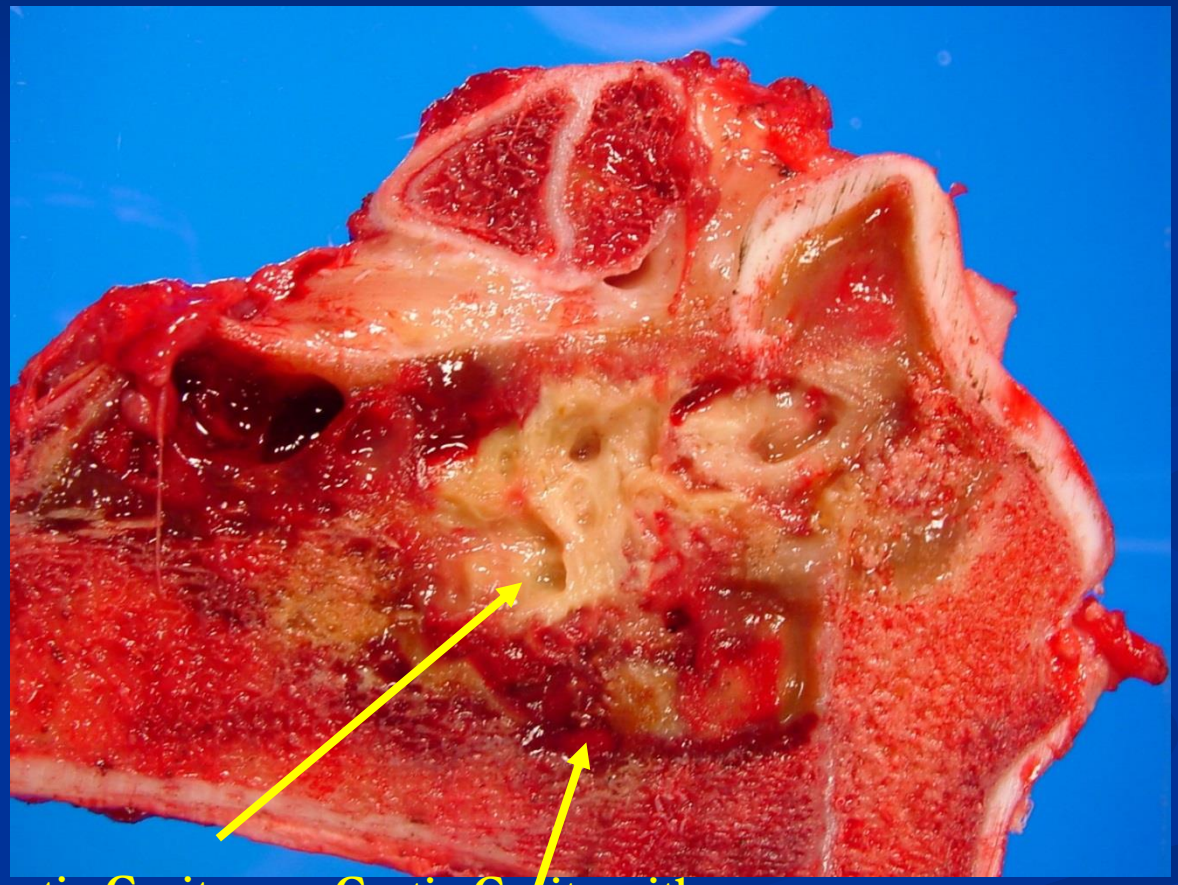
- Permeative, lytic tumor with indistinct moth-eaten border
- Cortical destruction
- Expansile lesion with soft tissue mass
- No ossification on X-ray



Gross Pathology

- Its gross appearance can mimic an aneurysmal bone cyst
- Mixture of large cystic and spongy areas

Gross Specimen: Telangiectatic Osteosarcoma of Proximal Tibia

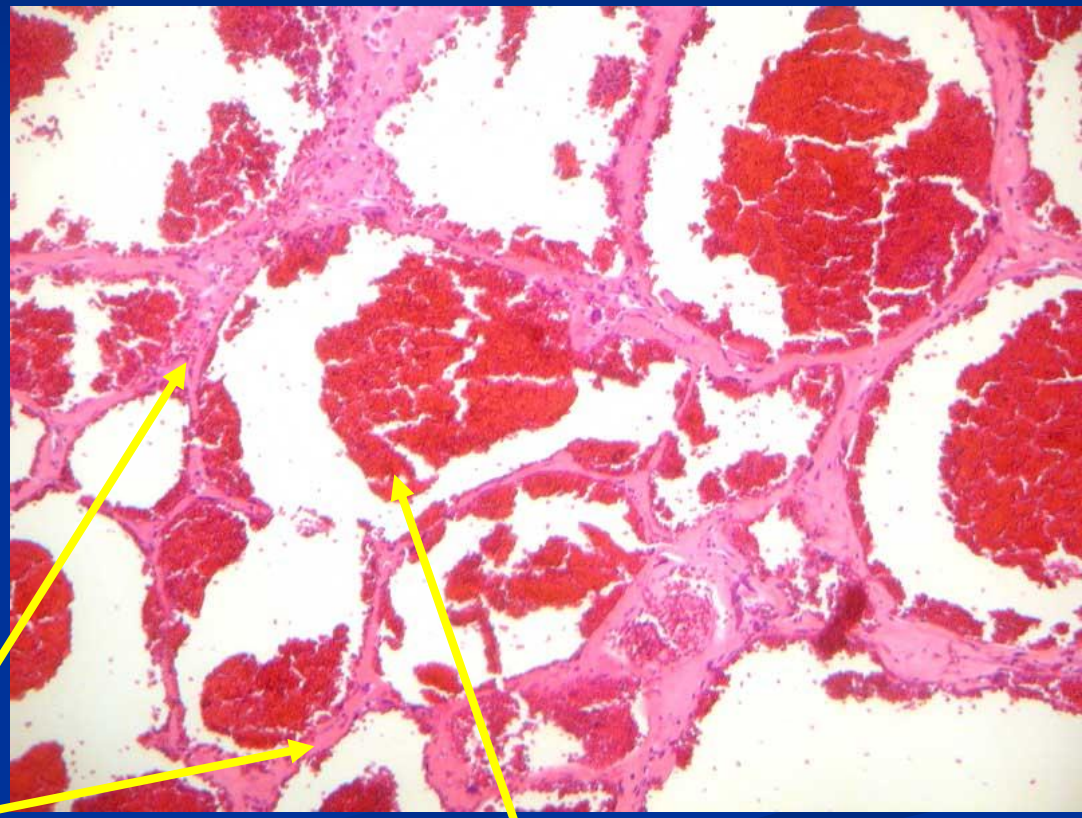


Cystic Cavity

Cystic Cavity with Hemorrhage/Blood Clot

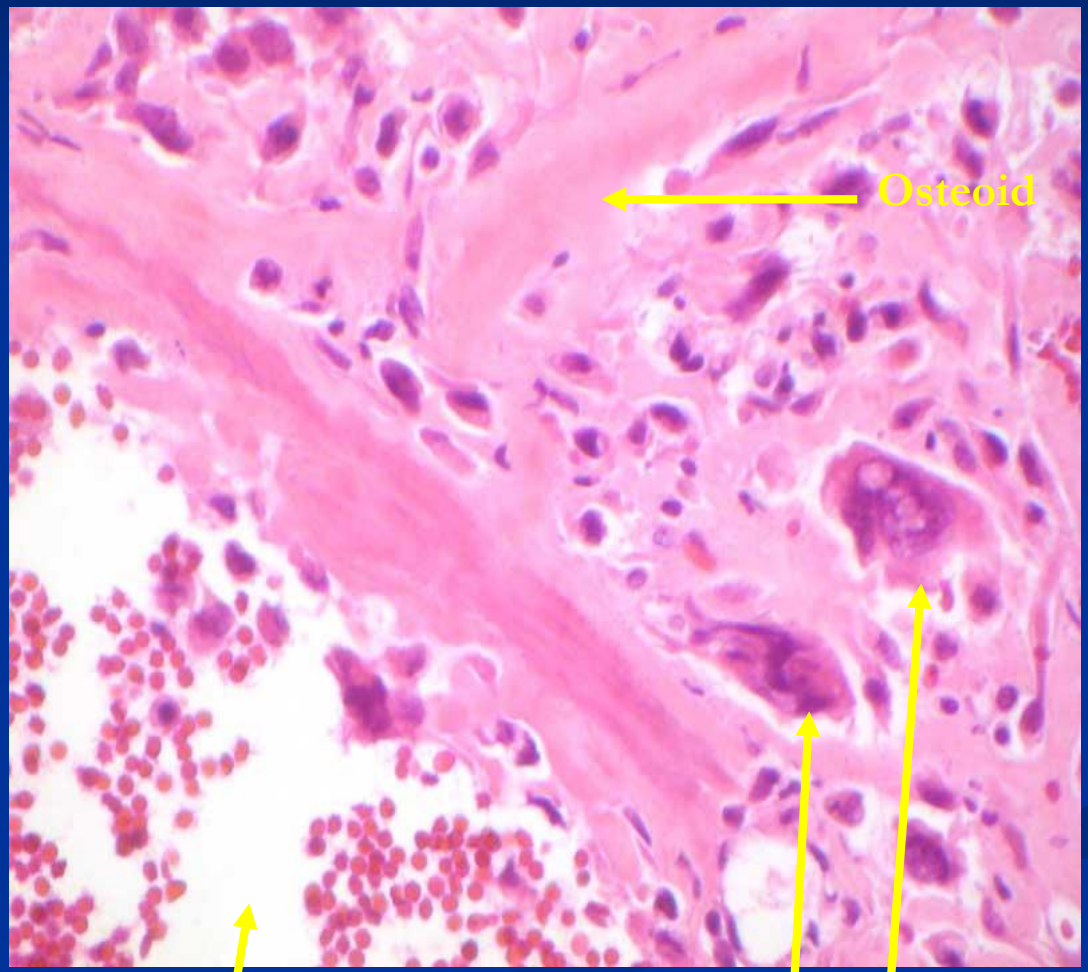
Microscopic Pathology: Telangiectatic Osteosarcoma

- Low power architecture demonstrates multiple blood filled cystic cavities separated by multiple septae



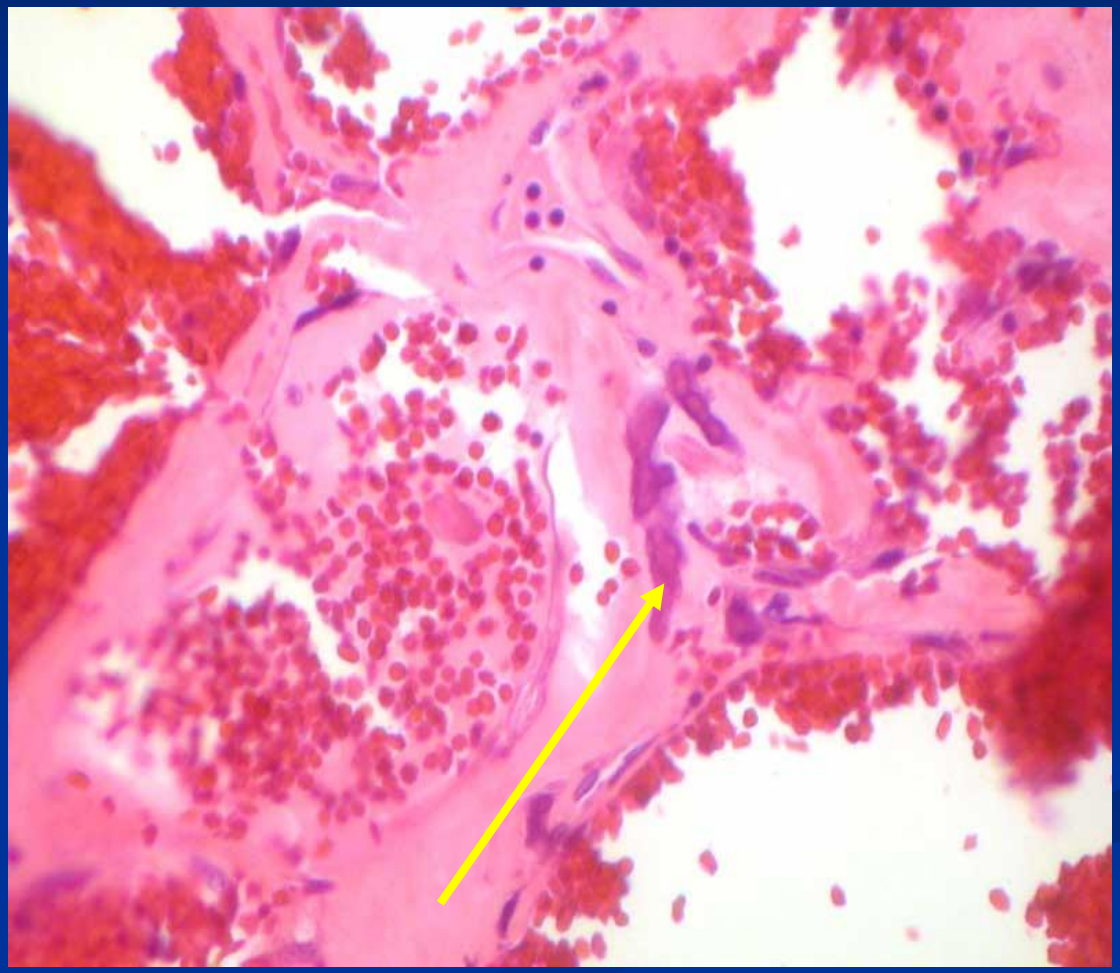
Microscopic Pathology: Telangiectatic Osteosarcoma

- High power view of septa
- Malignant appearing cells with large, hyperchromatic atypical nuclei
- Scant Osteoid



Microscopic Pathology: Telangiectatic Osteosarcoma

- High power view of septa showing malignant spindle cells in cavity wall
- Cystic cavities are filled with blood

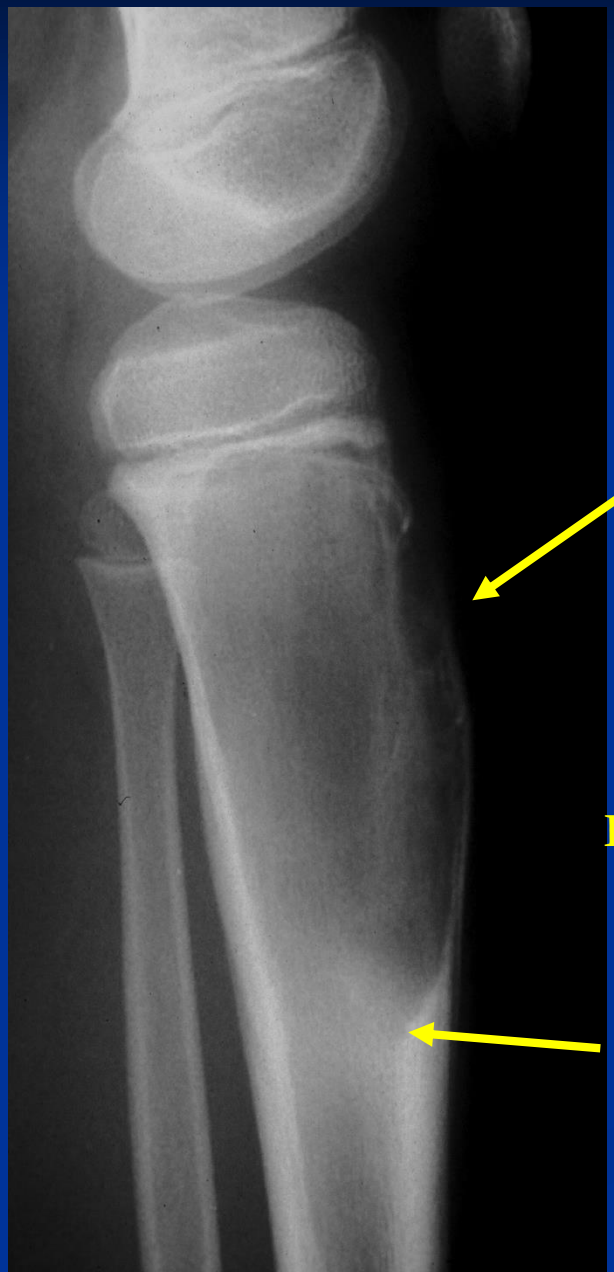


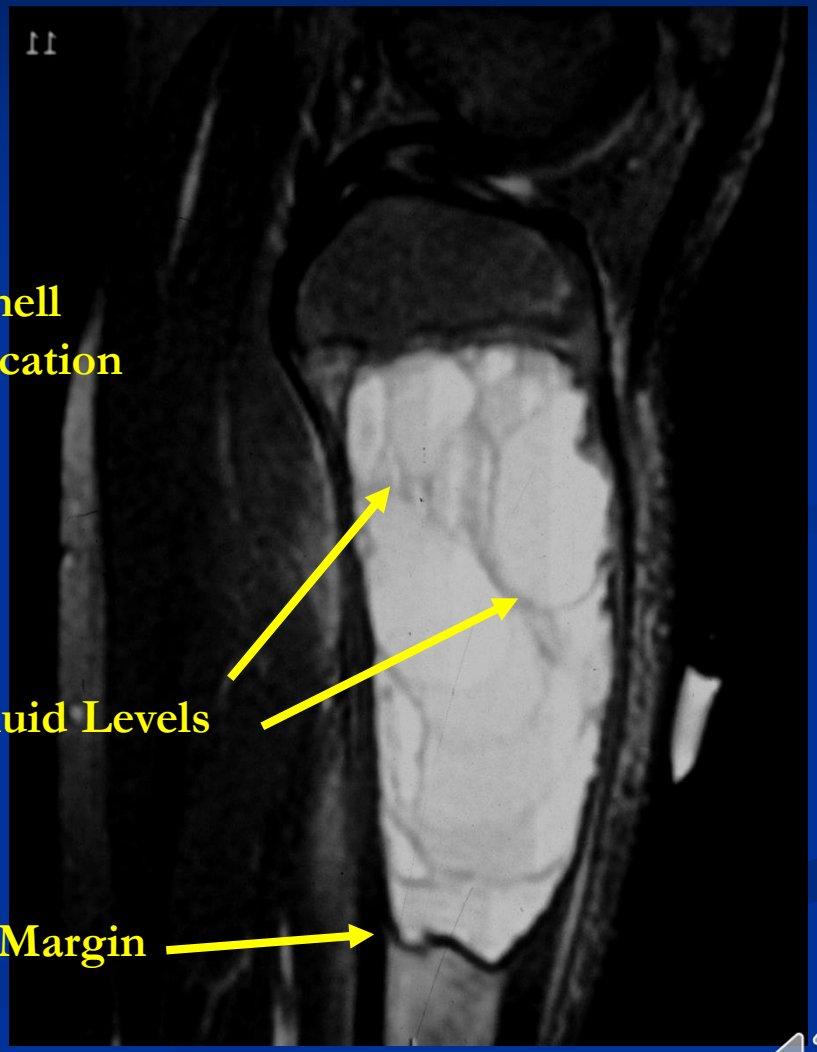
Malignant Spindle Cells

Differential Diagnosis

- Conventional osteosarcoma with dilated vascular spaces
- Aneurysmal Bone Cyst (ABC)

Aneurysmal Bone Cyst



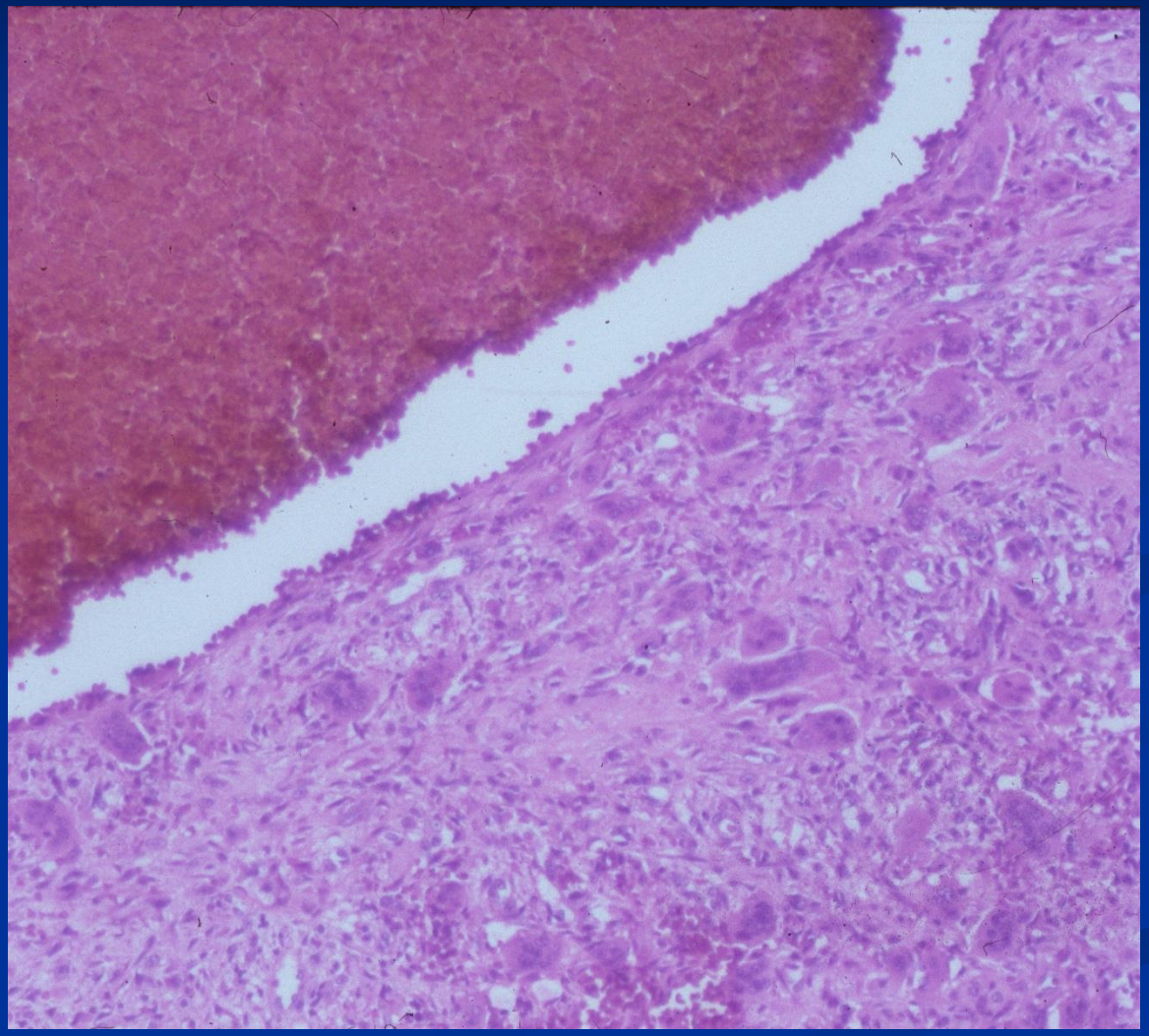


Egg Shell Calcification

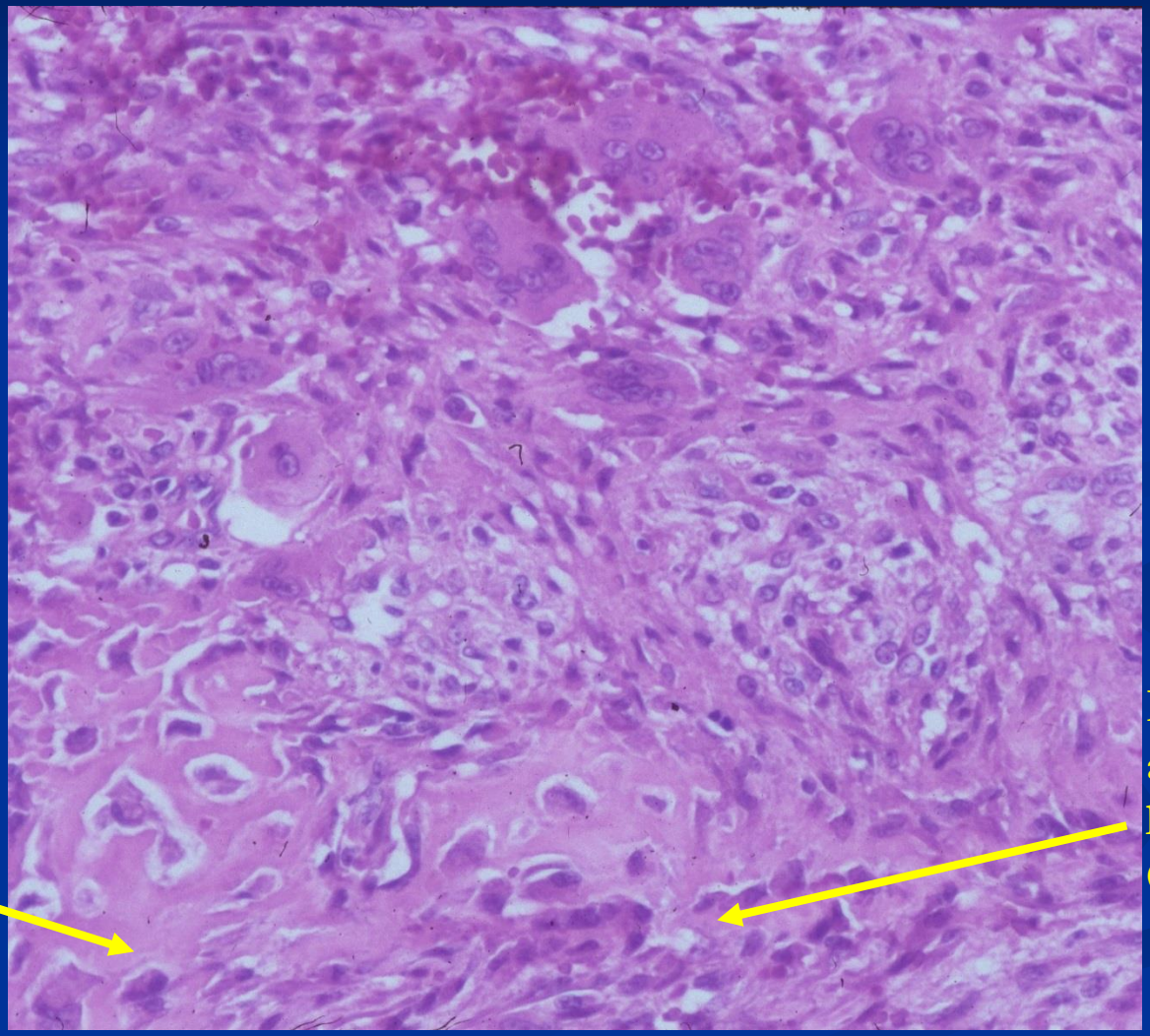
Fluid-Fluid Levels

Sharp Margin

Microscopic Pathology ABC



Microscopic Pathology ABC



Osteoid

Benign appearing cells

Benign appearing cells line up along Osteoid

Biological Behavior

- Fast growing, rapidly dividing, high grade tumor with high risk for metastases (spreading)
- Metastases (similar to conventional osteosarcoma):
  - Lungs are most common sites of metastases
  - Bones are second most common site

Treatment

- Same Treatment as Conventional Osteosarcoma
- Preop Chemo, Surgery, Postop Chemo

Prognosis

- Similar prognosis as conventional osteosarcoma
- Overall 65% 5 year survival

Low Grade Intramedullary Osteosarcoma

General Information

- Low-grade fibroblastic osteoid producing lesion arising within the medullary space of the bone
- Usually well-differentiated cells
- 1% of all osteosarcomas

Clinical Presentation

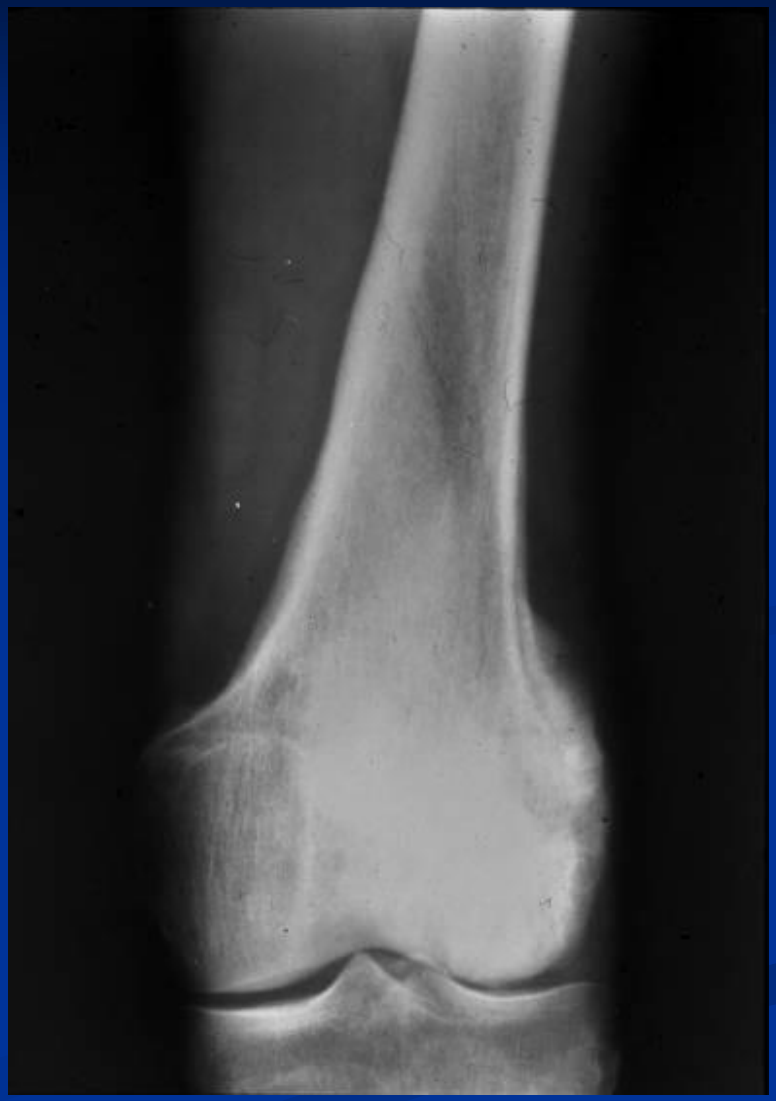
- **Signs/Sxs:** Pain in affected region for months to years

- **Age:** Peak in 20s (50% of cases)
  - Individual cases in 2nd decade and 50s

- **Sites:** Metaphysis of femur and tibia most common

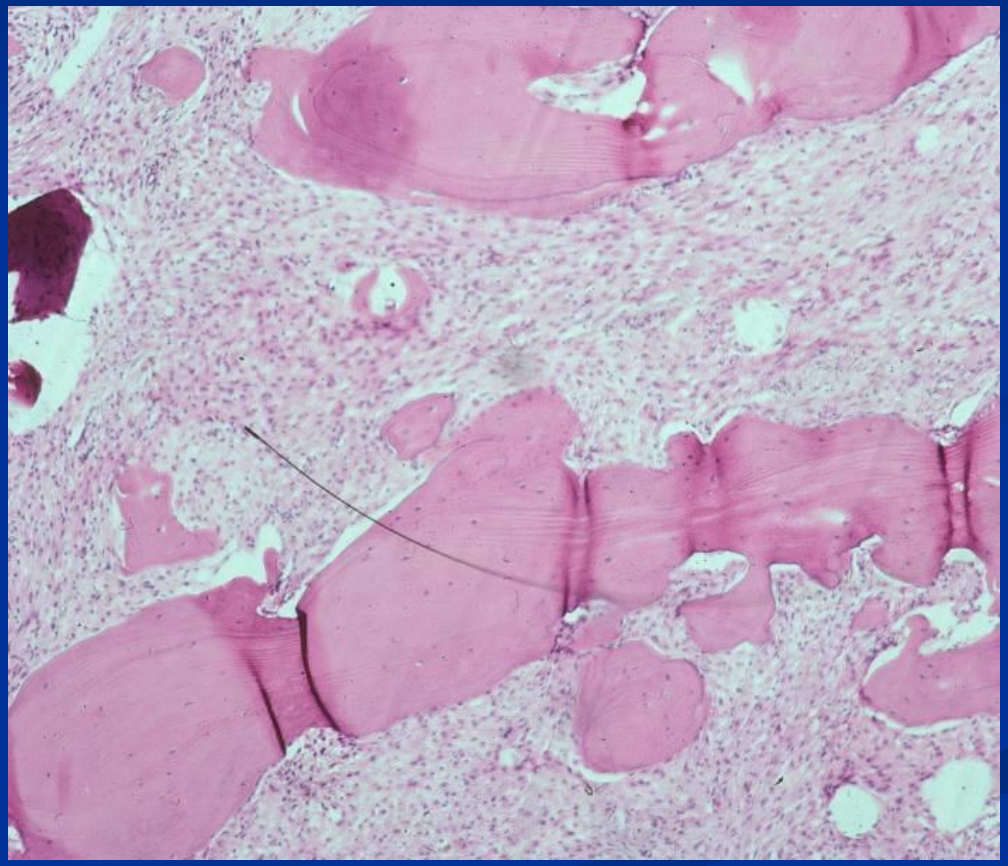
Radiographic Presentation

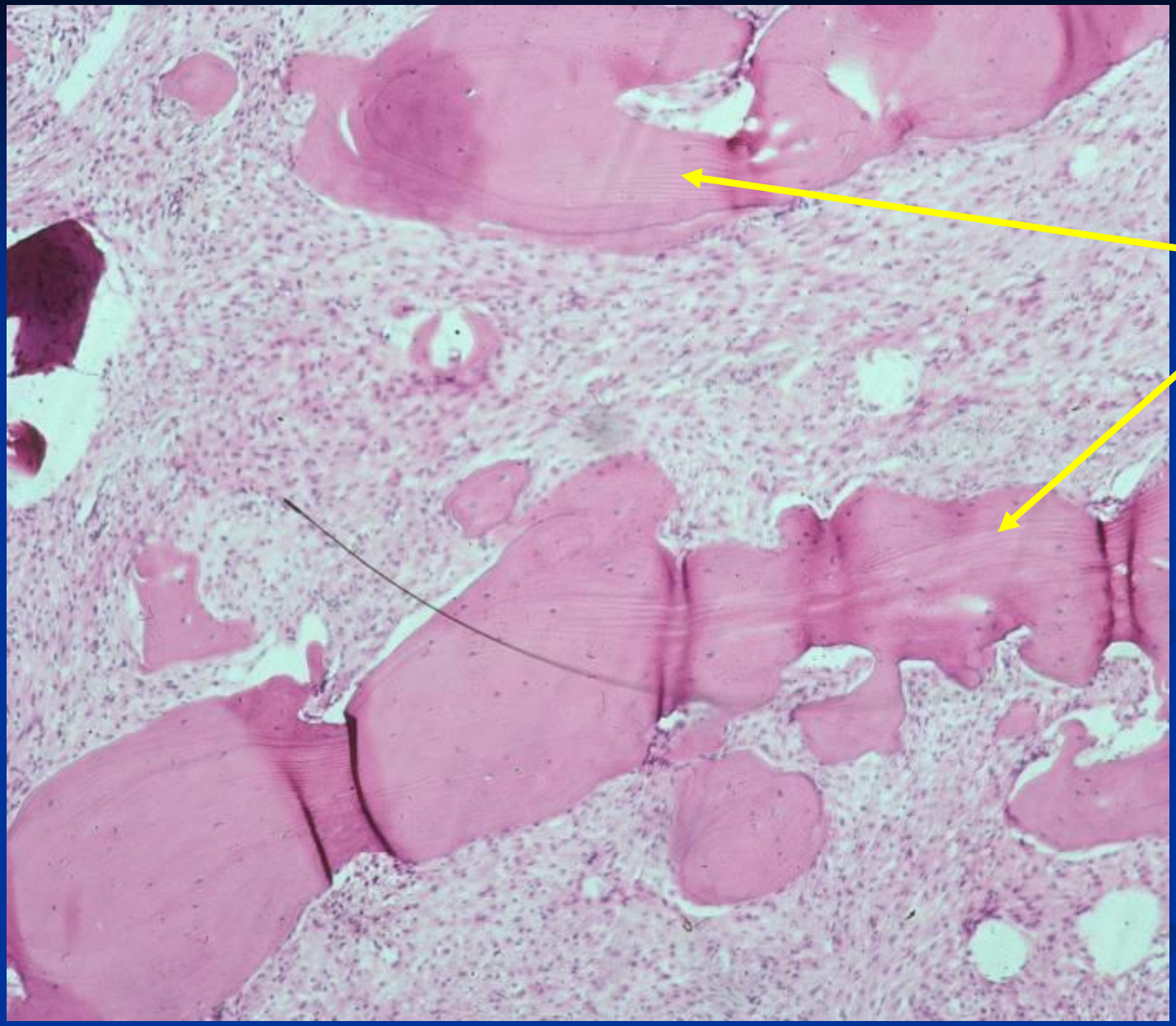
- Meta-epiphyseal
- Central ossification/sclerosis with expansile remodeling
- Ground glass density and internal trabeculation (simulates fibrous dysplasia)
- Usually no soft tissue mass and not as aggressive appearing
- Usually no periosteal reaction

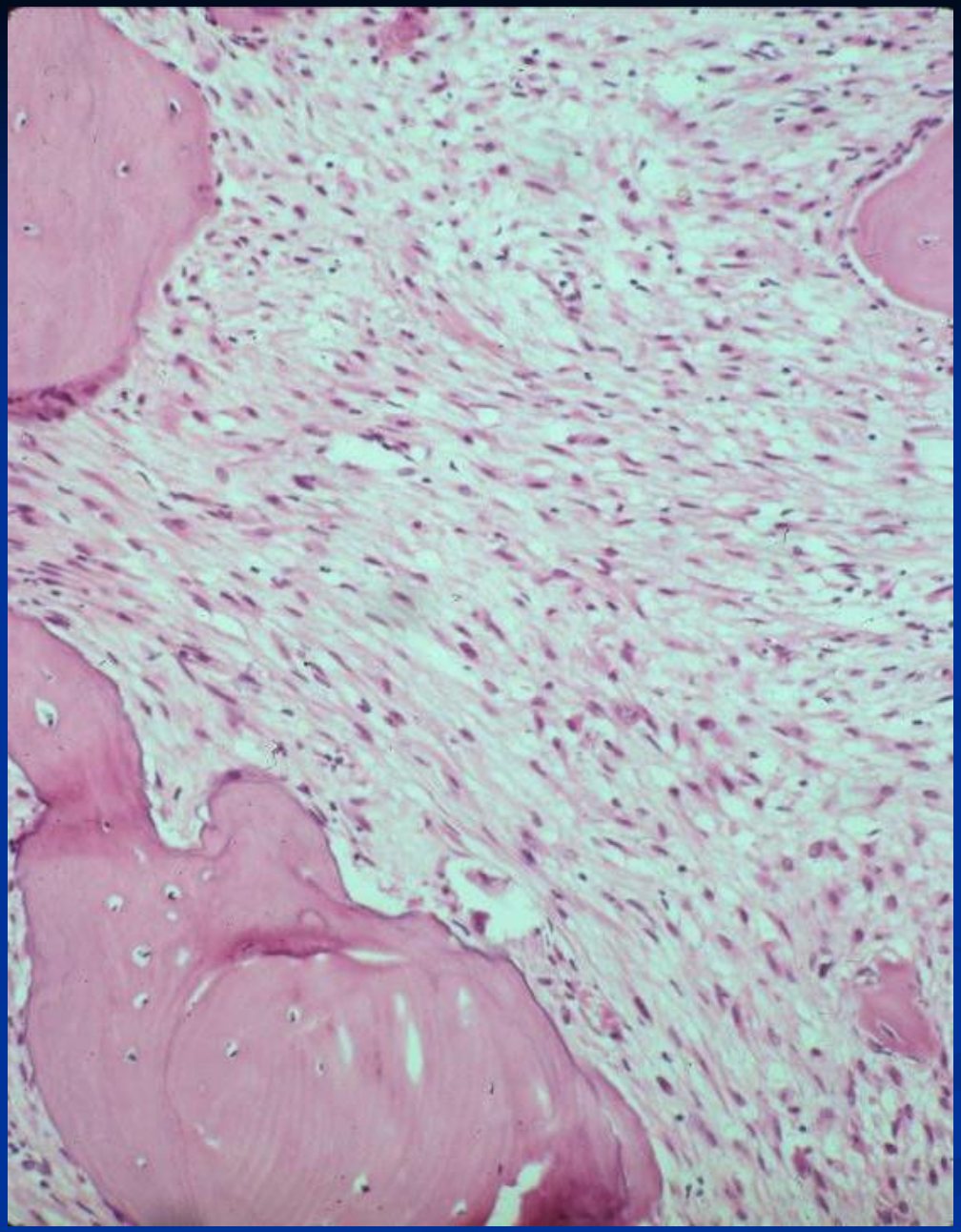


Microscopic Pathology

- Fibroblastic tumor producing bone (osteoid/immature bone)







Treatment

- Surgical resection and reconstruction
- No chemotherapy unless dedifferentiation is present

Prognosis

- 90% cure rate (<10% metastatic rate) with surgical resection alone if entirely low grade and no areas of dedifferentiation

Surface/Juxtacortical Osteosarcomas

Parosteal Osteosarcoma

Periosteal Osteosarcoma

High Grade Surface Osteosarcoma

Parosteal Osteosarcoma
General Information

- **Parosteal osteosarcoma** is a low grade, well differentiated fibroblastic tumor that produces bone/osteoid (immature woven bone)
- **Outer layer** of the periosteum.
- **Slow growing** and slow to metastasize.
- Most common type of juxtacortical/surface osteosarcoma
- 5% of all types of osteosarcomas

General Information

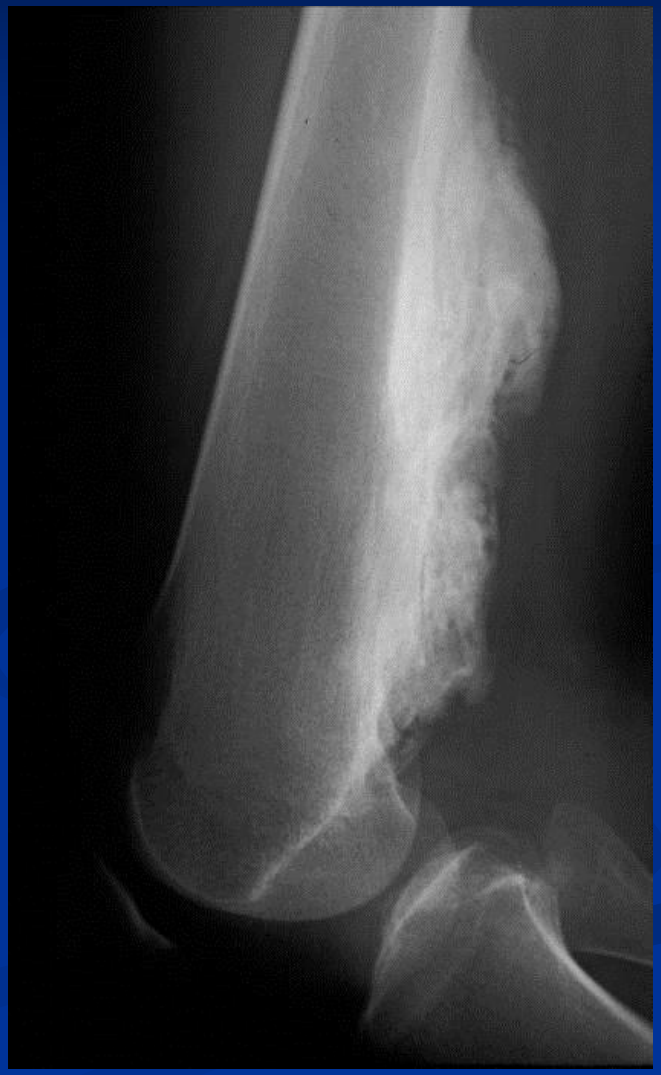
- **Dedifferentiation** refers to a portion of the tumor changing and becoming a high grade type of sarcoma. Long standing tumors
- Parosteal osteosarcomas that are present for a prolonged period of time may invade the bone (medullary canal) that it arose from.

Clinical Presentation

- **Signs/Symptoms:** Painless slowly enlarging firm immobile mass in an extremity
- **Prevalence:** Female>Male 2:1
- **Age:** 20-40 yrs
- **Sites:**
  - Posterior distal femur metaphysis (65%)
    - Presents as a mass in popliteal fossa
  - Proximal humerus (15%); Tibia (10%); Fibula (3%)

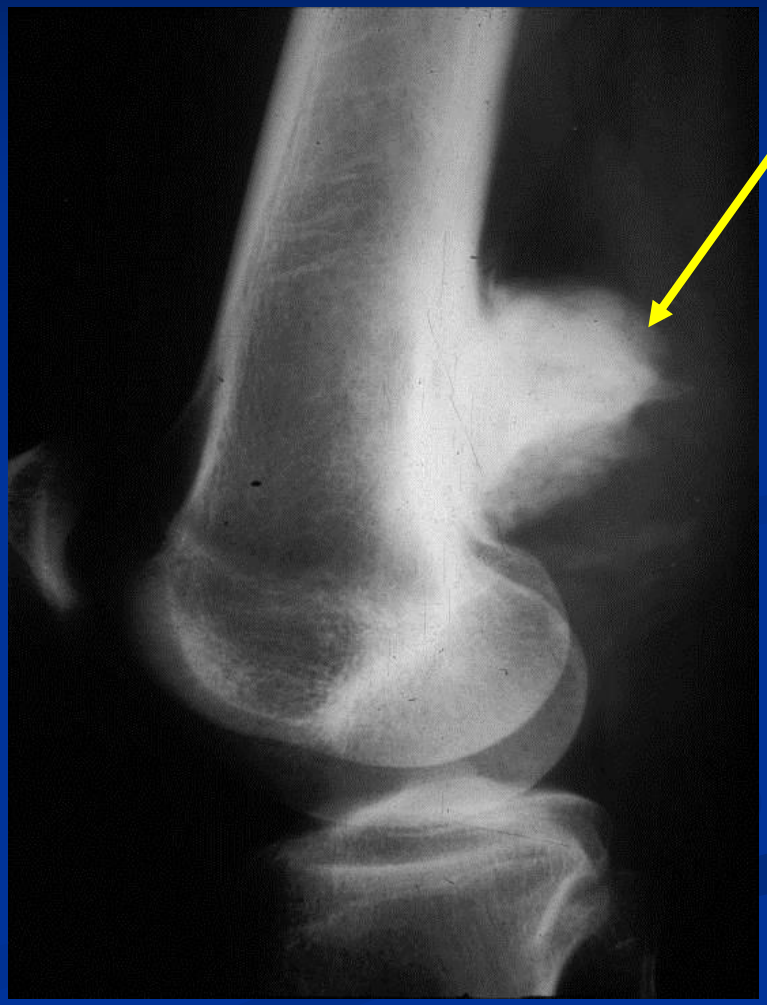
Radiographic Presentation

- **X-Rays:**
  - Lobulated and ossified exophytic mass (cauliflower like)
  - **Radiodense** Centrally
  - **Radiolucies** Peripherally represent low grade cartilaginous lobules, fibrous tissue or fat
  - No periosteal reaction.
  - **String Sign:** Cleft between exophytic base and cortex at periphery (Cleft is often only identifiable on CT scan)

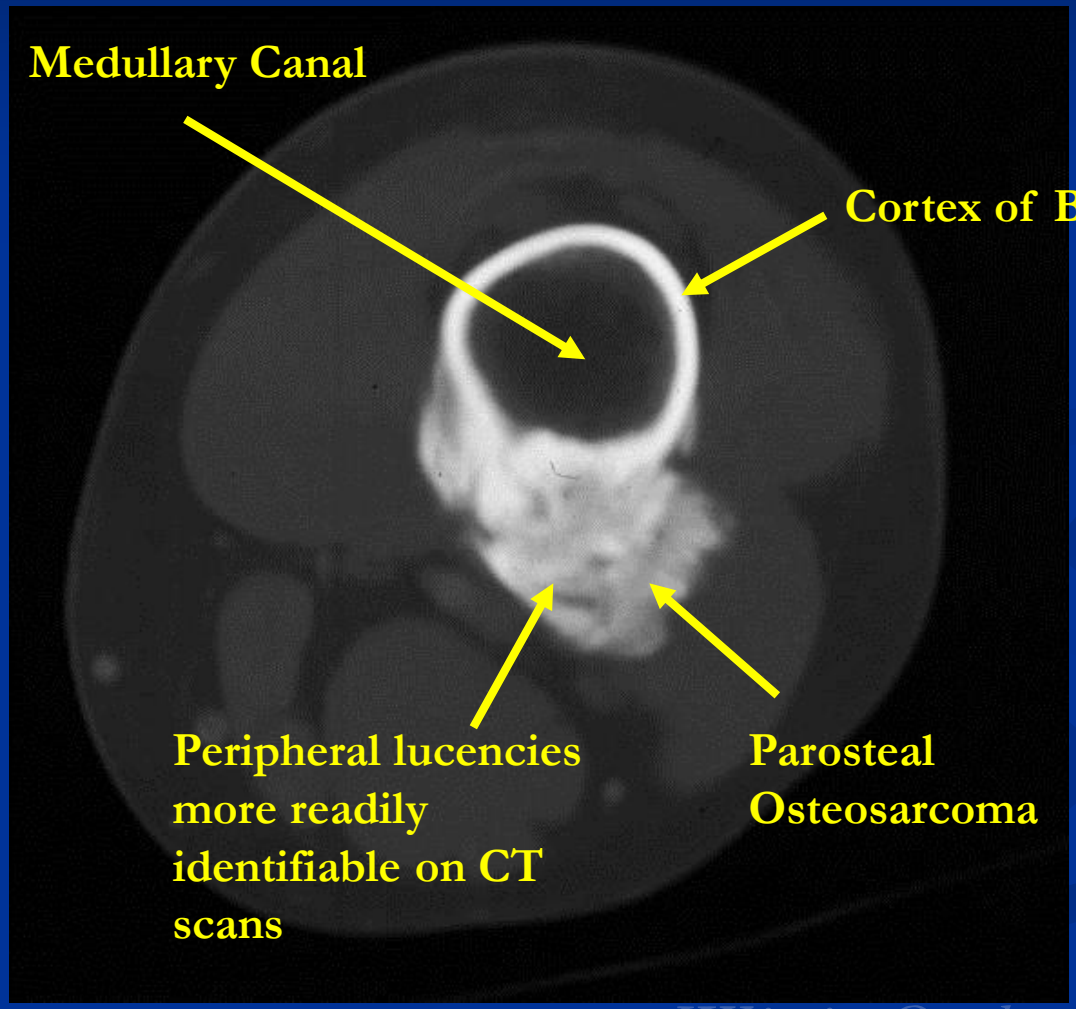


X-ray of Parosteal Osteosarcoma of Distal Femur

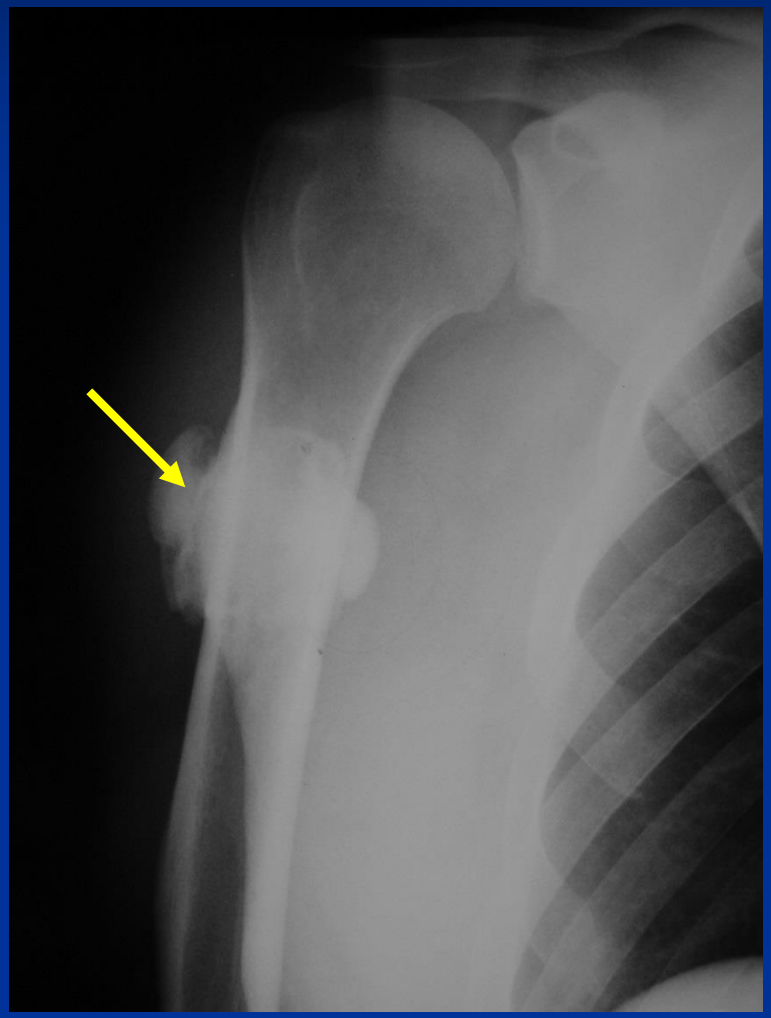
- Parosteal osteosarcoma arising from posterior distal femur
- Mass is exophytic and arising from surface of bone
- The mass is heavily ossified
- The cortex appears intact along the deep surface of lesion

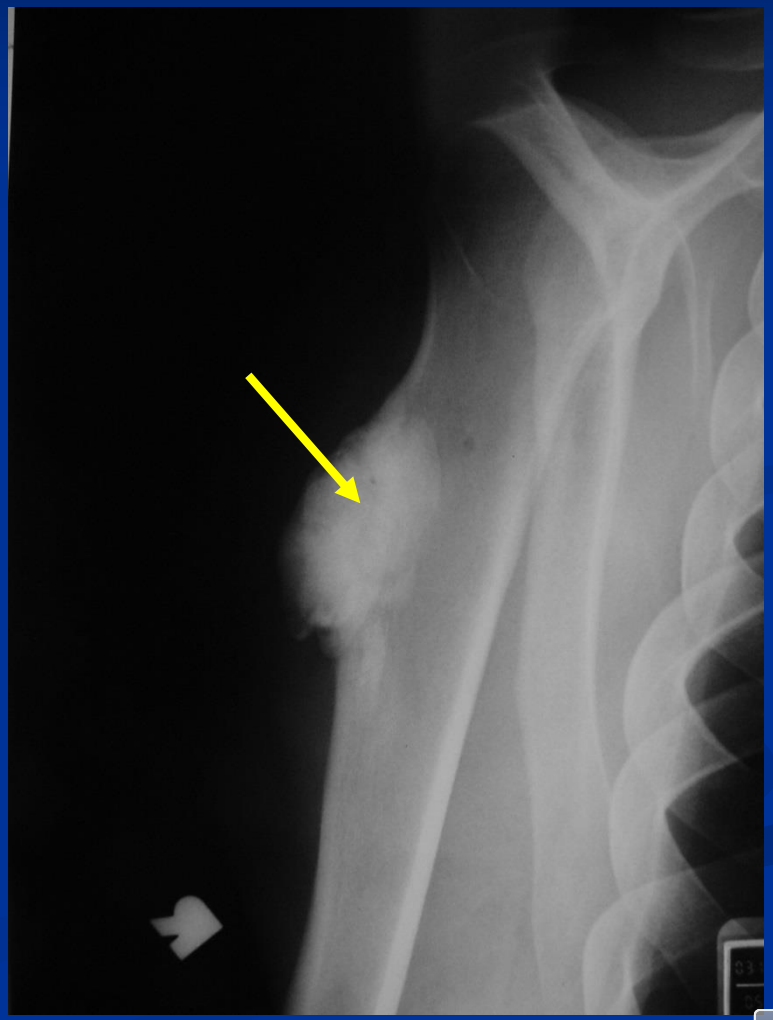


CT Scan of Distal Femur Parosteal Osteosarcoma



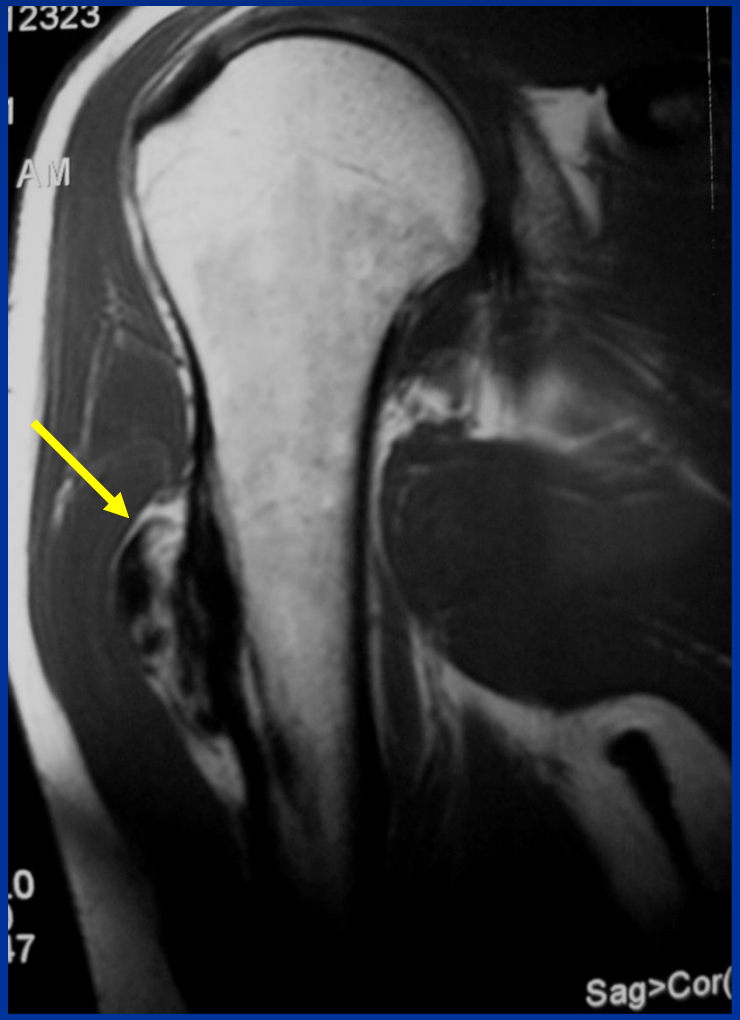
X-Ray: Parosteal Osteosarcoma of Proximal Humerus

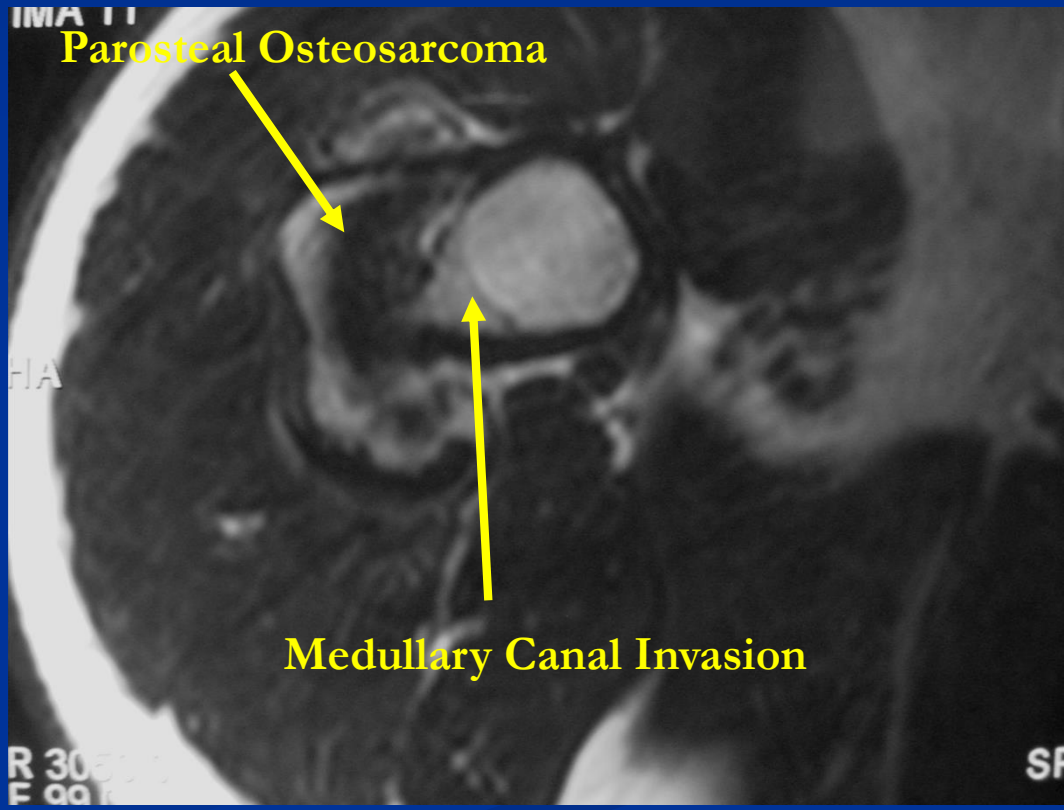




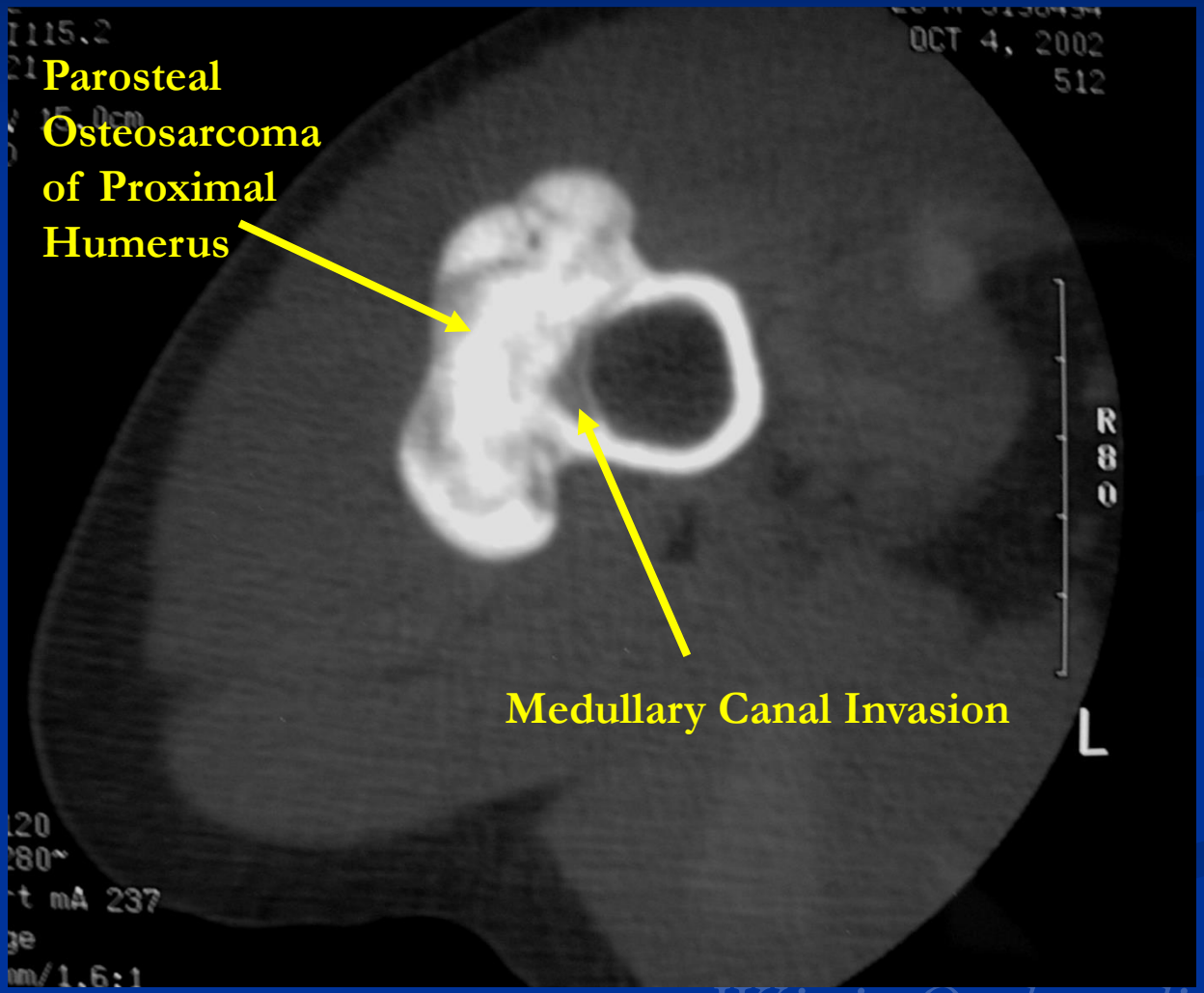
MRI Parosteal Osteosarcoma of Proximal Humerus

The tumor appears to have invaded the medullary canal

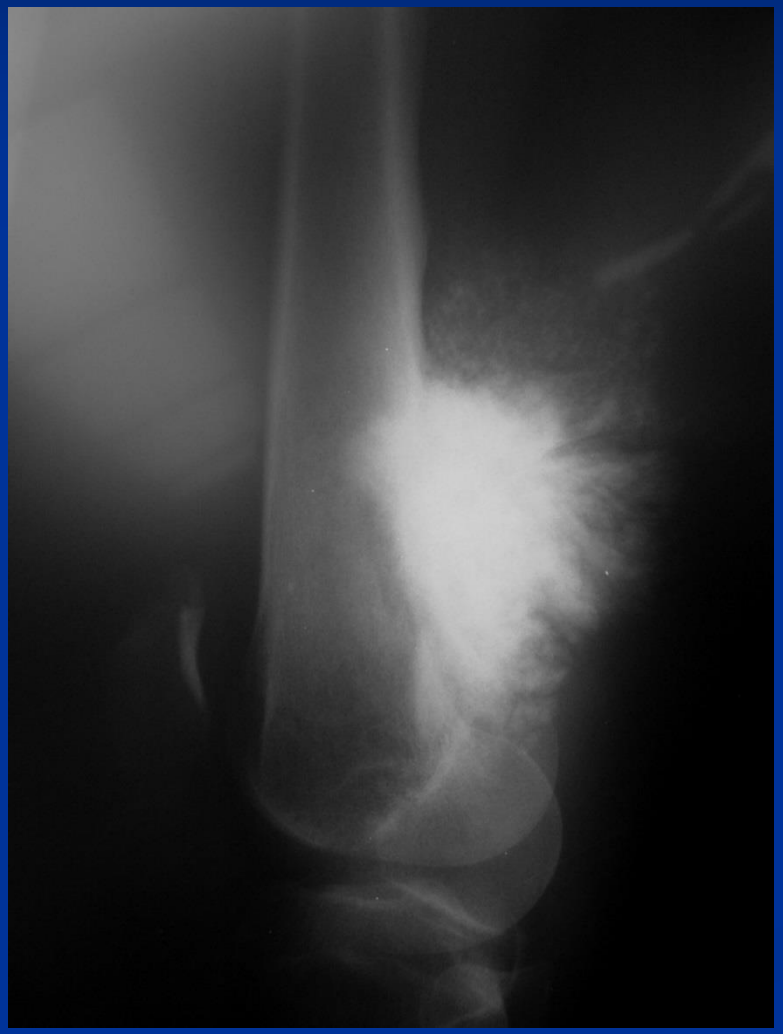


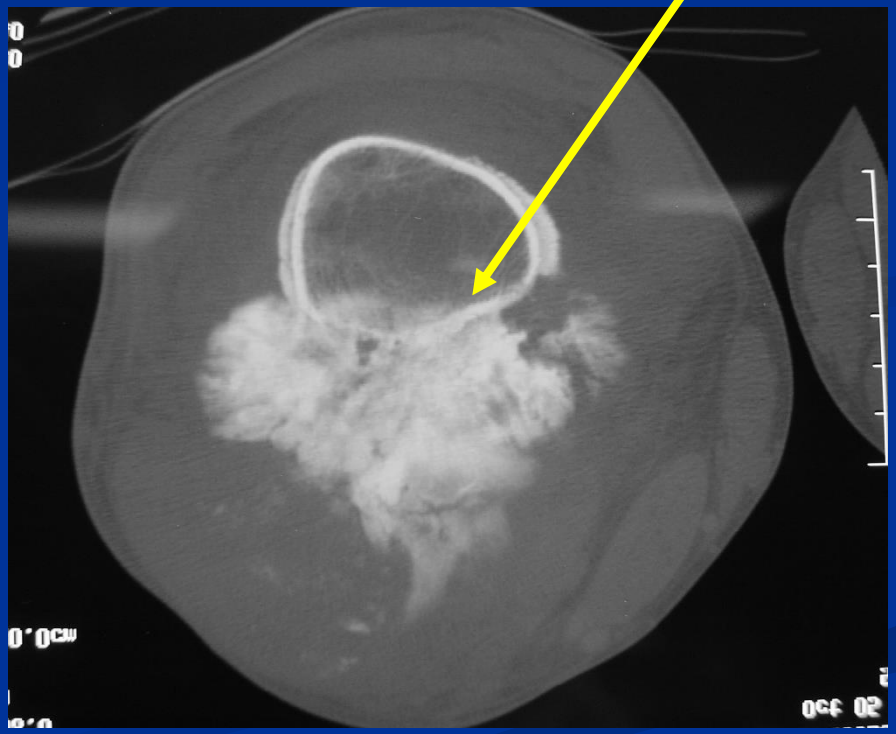


CT Scan of Parosteal Osteosarcoma of Proximal Humerus



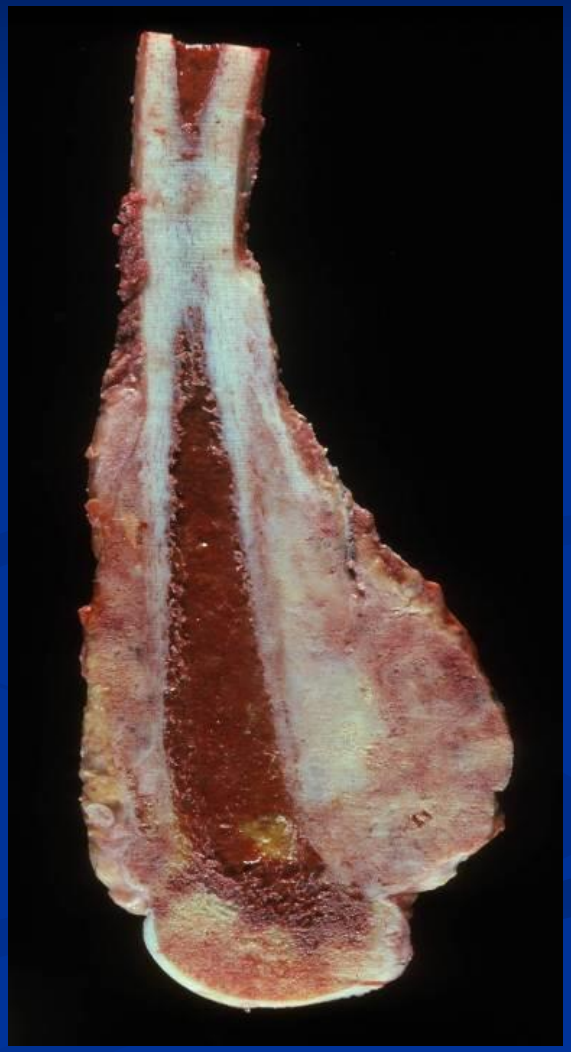
Plain X-ray and CT Scan of Parosteal Osteosarcoma of Distal Posterior Femur





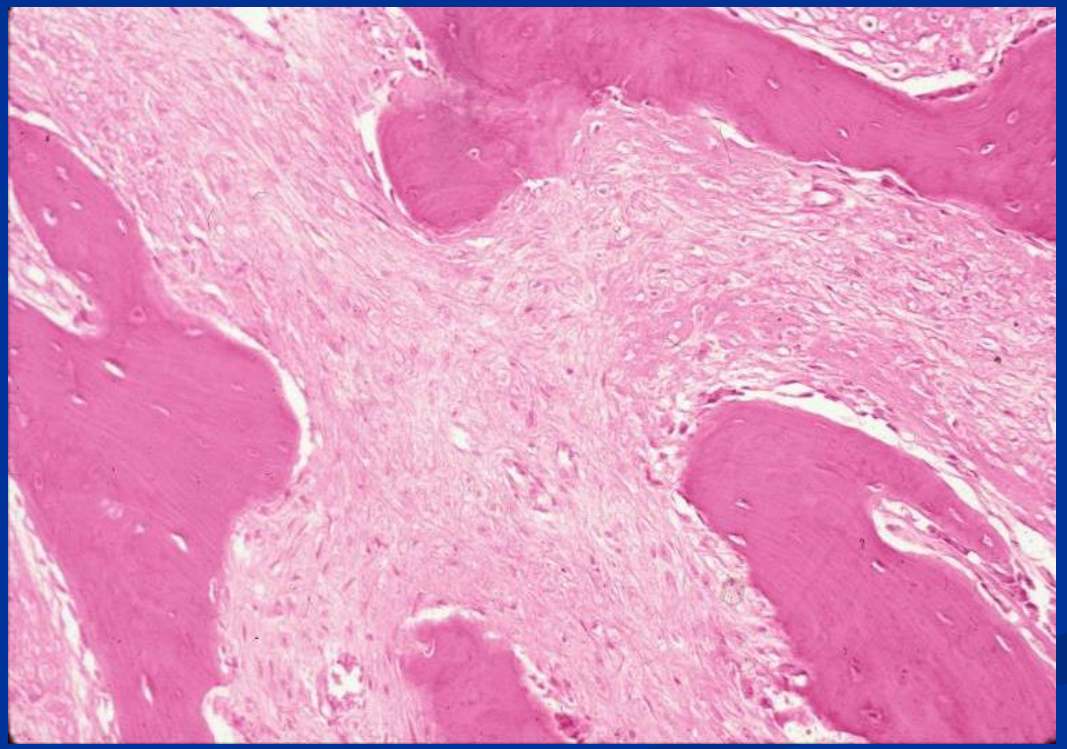
Gross Pathology

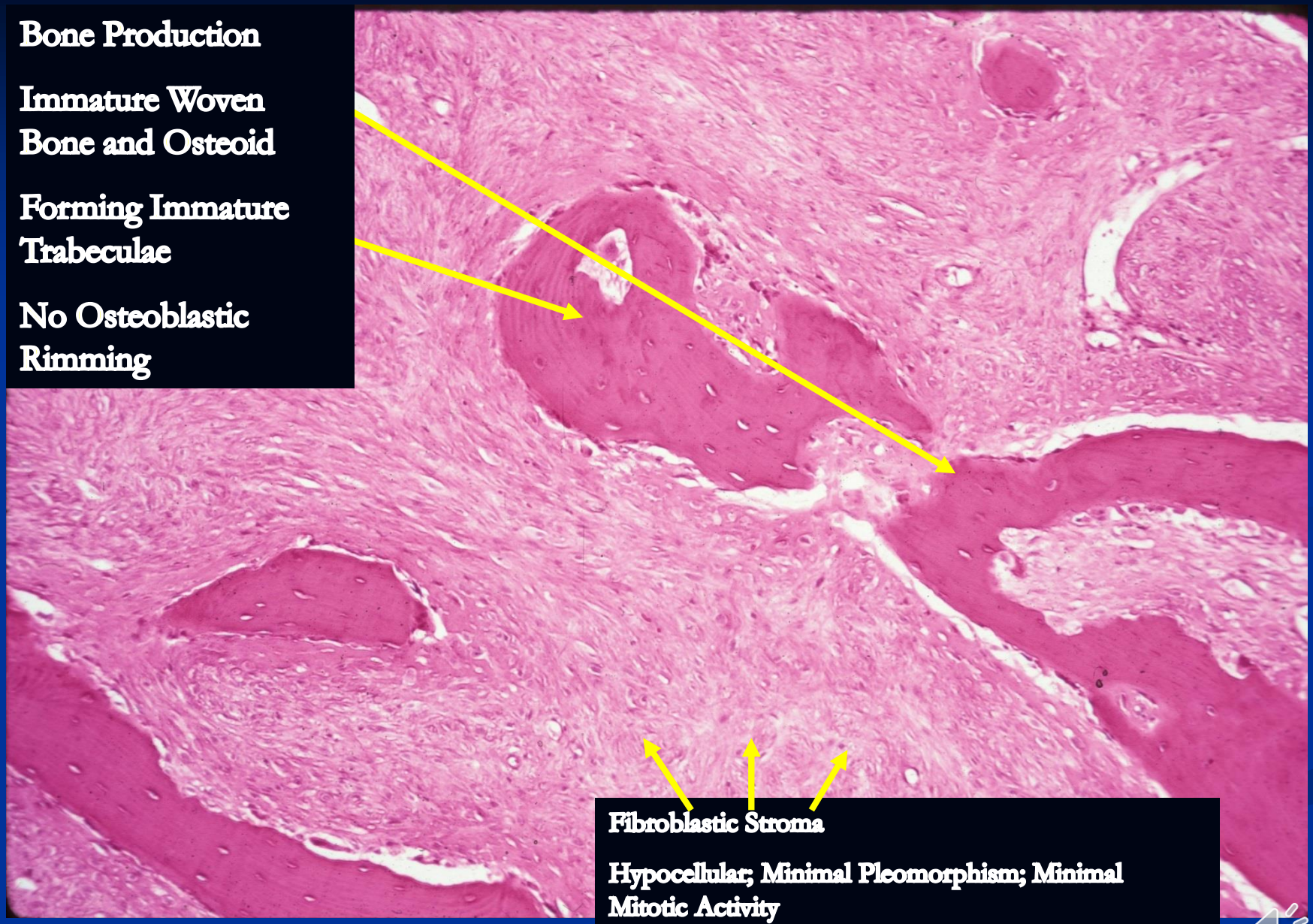
- Firm, exophytic bony mass fixed to cortex by means of a broad base
- If it has grown through the cortex there may be an intramedullary component
- May encircle bone or invade medullary canal



Microscopic Pathology: Parosteal Osteosarcoma

- Islands of immature trabeculae of woven bone admixed in fibrous tissue
- None to minimal osteoblastic lining of trabeculae
- Fibroblastic tissue that is bland (hypocellular, minimal pleomorphism; minimal mitoses)





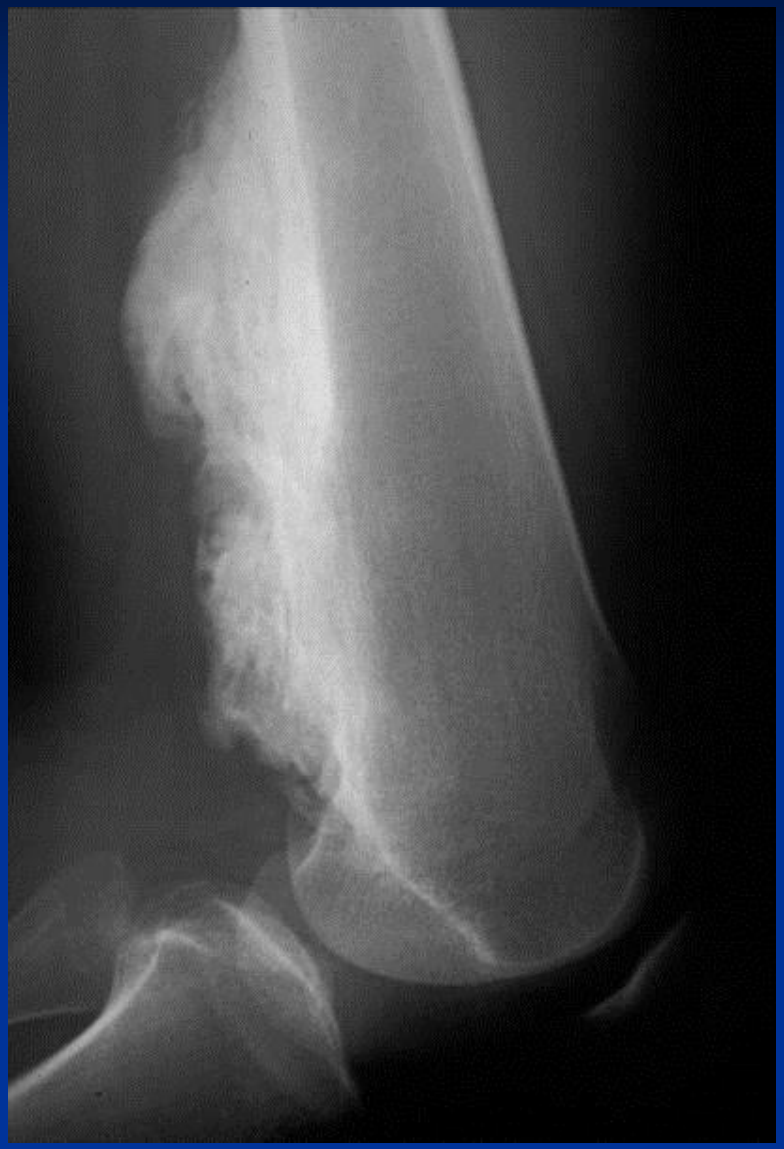
Treatment

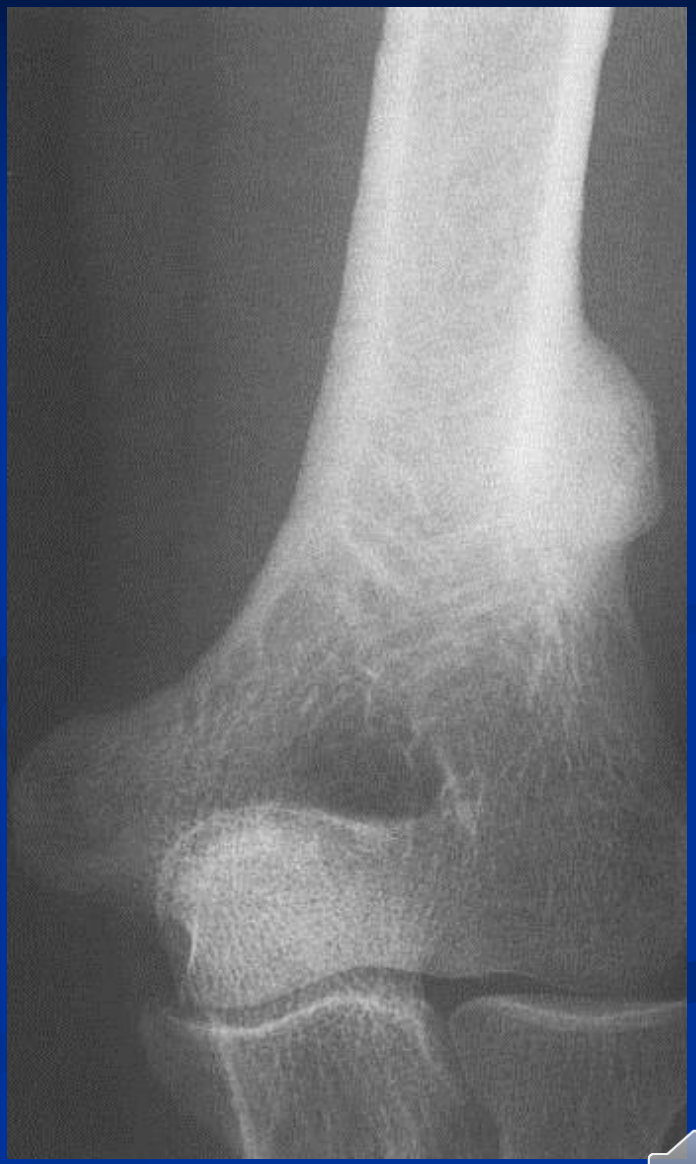
- Wide surgical resection and reconstruction
- No chemotherapy or radiation

Prognosis

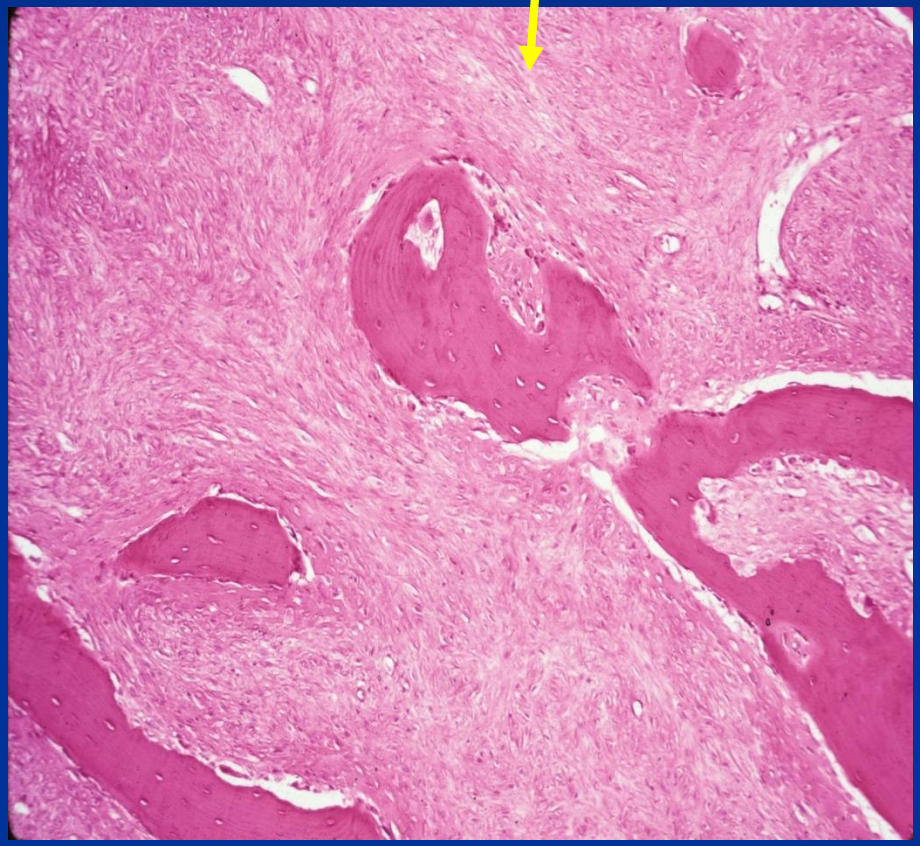
- 80-90% cure rate for low grade parosteal osteosarcomas treated with surgery alone
- Metastases more common with medullary invasion, high grade components (grade 3) and dedifferentiation (grade 3 tumors)

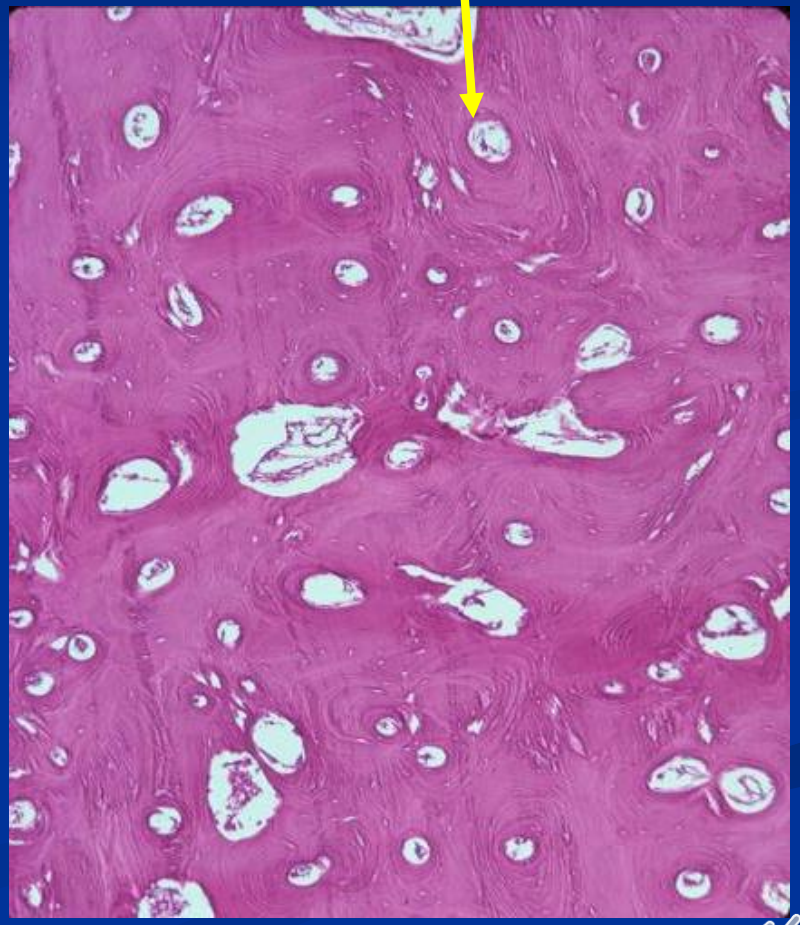
Parosteal Osteosarcoma vs Osteoma



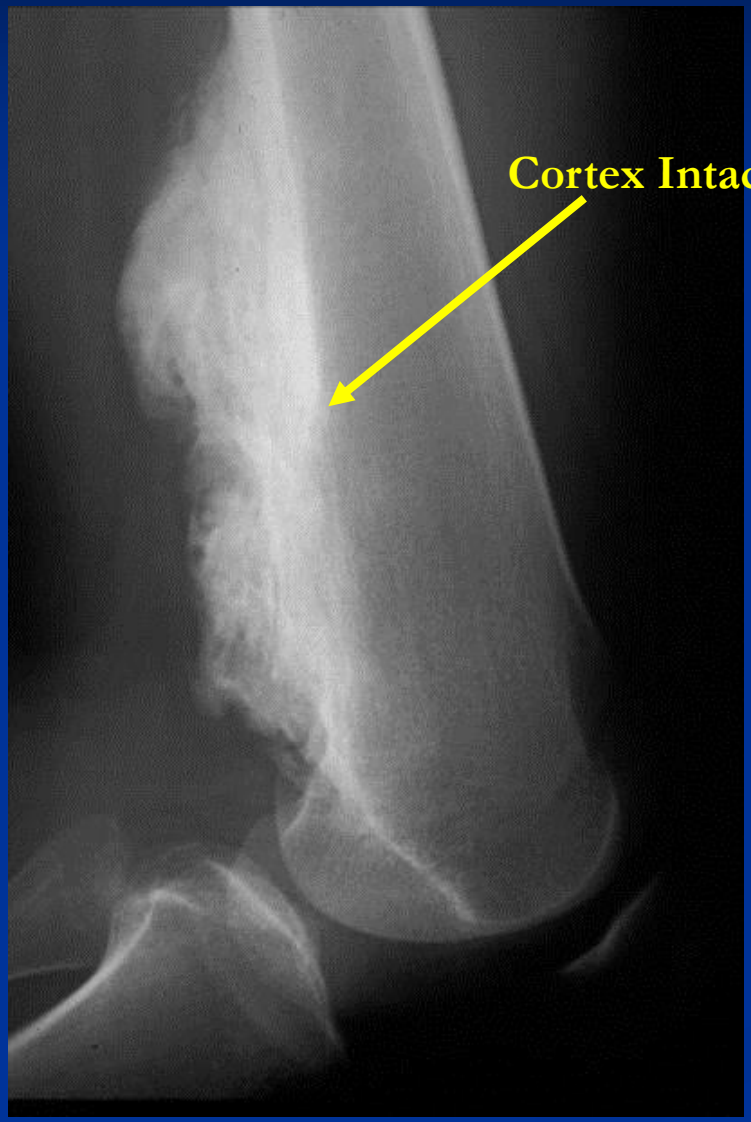


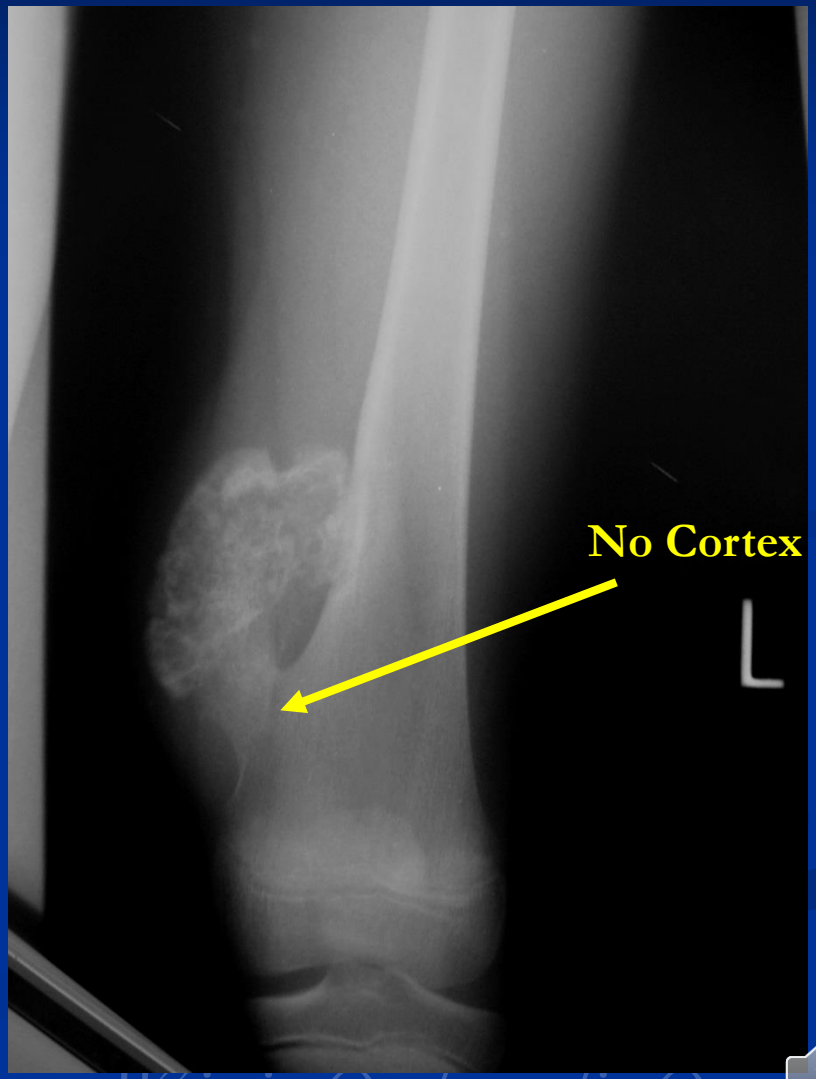
Parosteal Osteosarcoma vs Osteoma



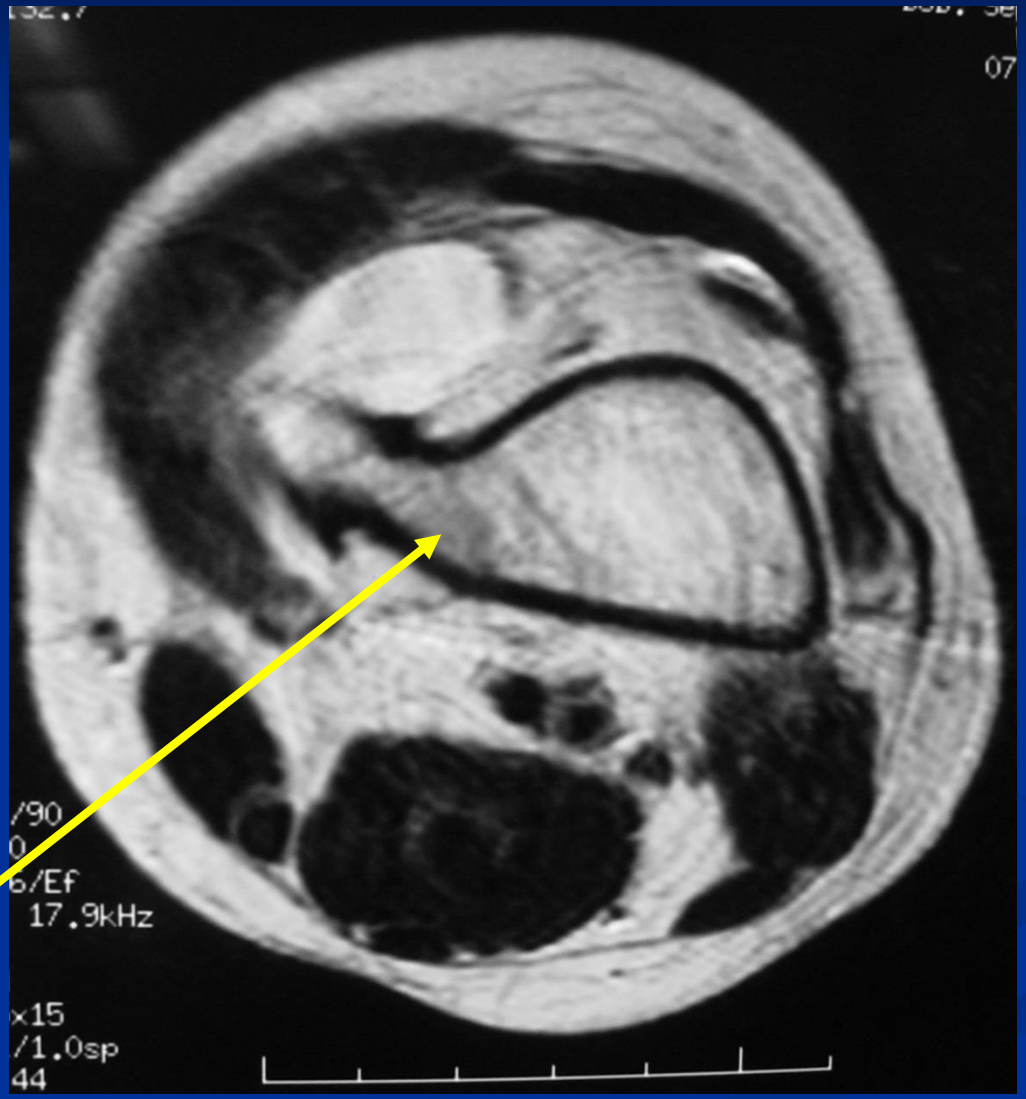


Parosteal Osteosarcoma vs. Osteochondroma





MRI of Osteochondroma



Medullary Cavity is Continuous with Osteochondroma

Cortex Expands into Osteochondroma

Periosteal Osteosarcoma

General Information

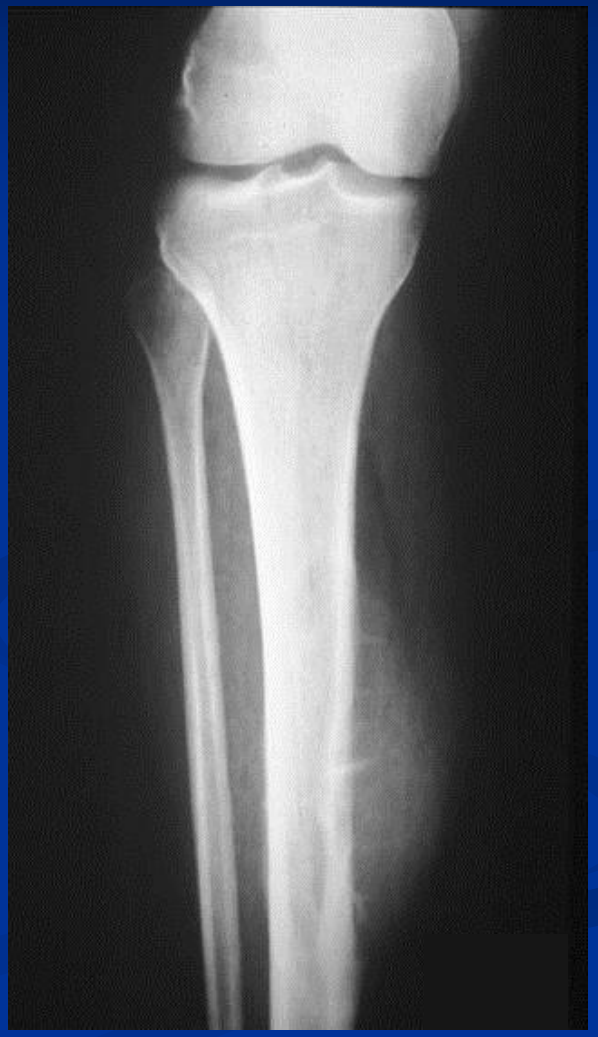
- <2% of all osteosarcomas
- Inner layer of the periosteum and therefore elevates the periosteum and produces a periosteal reaction
- Chondroblastic tumor that produces osteoid or bone
- Diaphysis of the tibia
- Intermediate grade tumors as compared to conventional (most common type) osteosarcomas that are high grade.
- Better prognosis than conventional osteosarcomas.

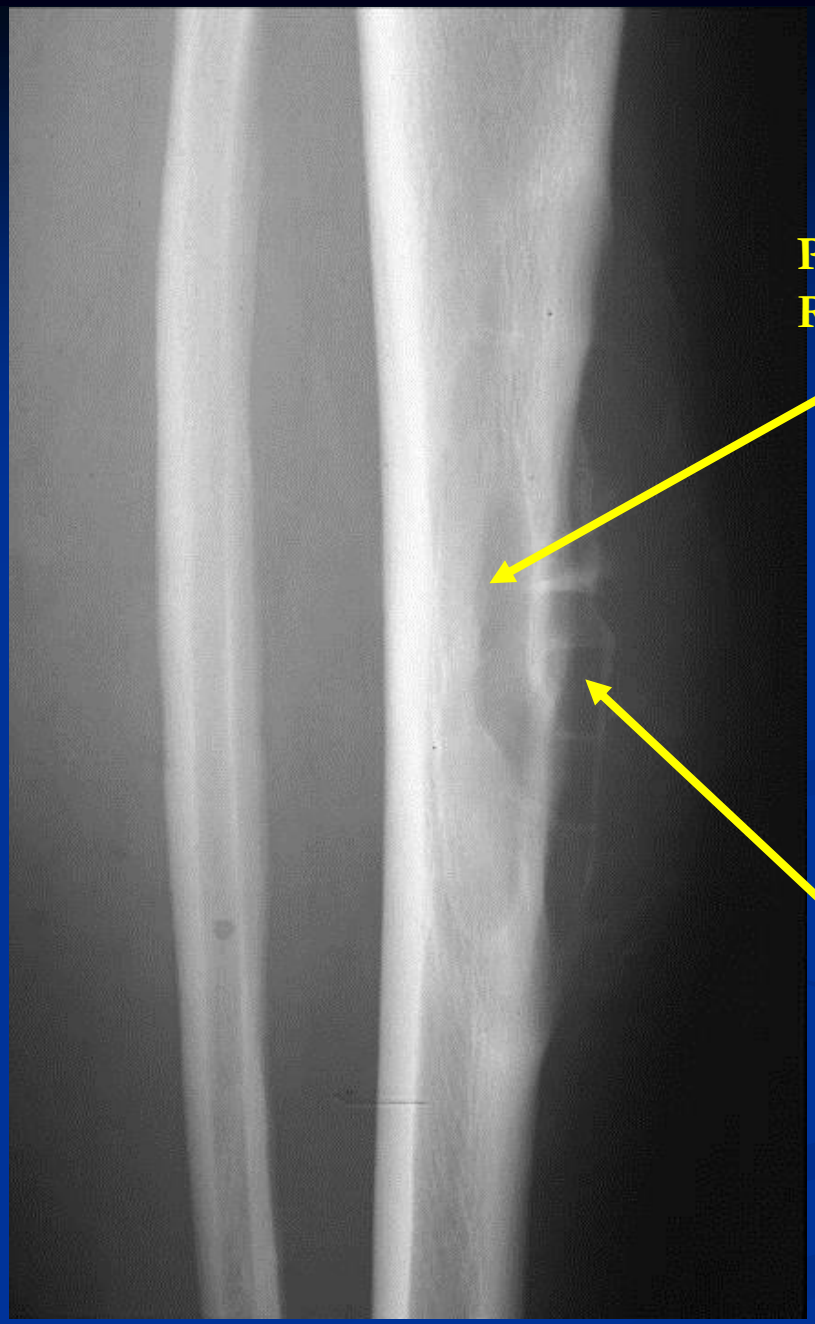
Clinical Presentation

- **Age:** Most patients are 10-20 years of age
- **Sites:** Tibia or Femur (>85%); Humerus, Radius, Ulna

Radiographic Presentation

- **Plain X-Rays:**
  - Diaphyseal lesion on external surface of bone; medullary canal uninvolved
  - **Radiolucent**
  - Saucerized cortex
  - **Periosteal reaction** (Hair on End or Sunburst)
  - Partial matrix mineralization may be seen
  - Rare intramedullary invasion



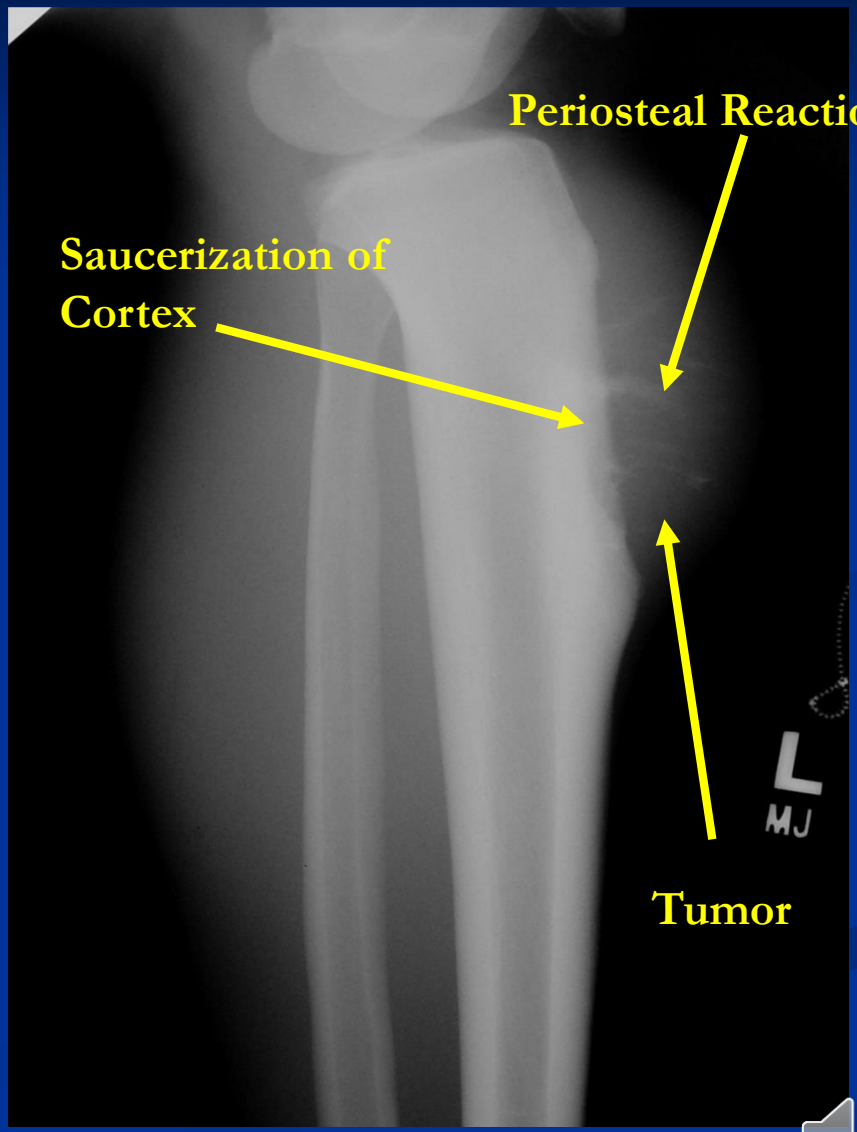


Primarily Cartilaginous and Radiolucent on X-rays

Hair on End Periosteal Reaction

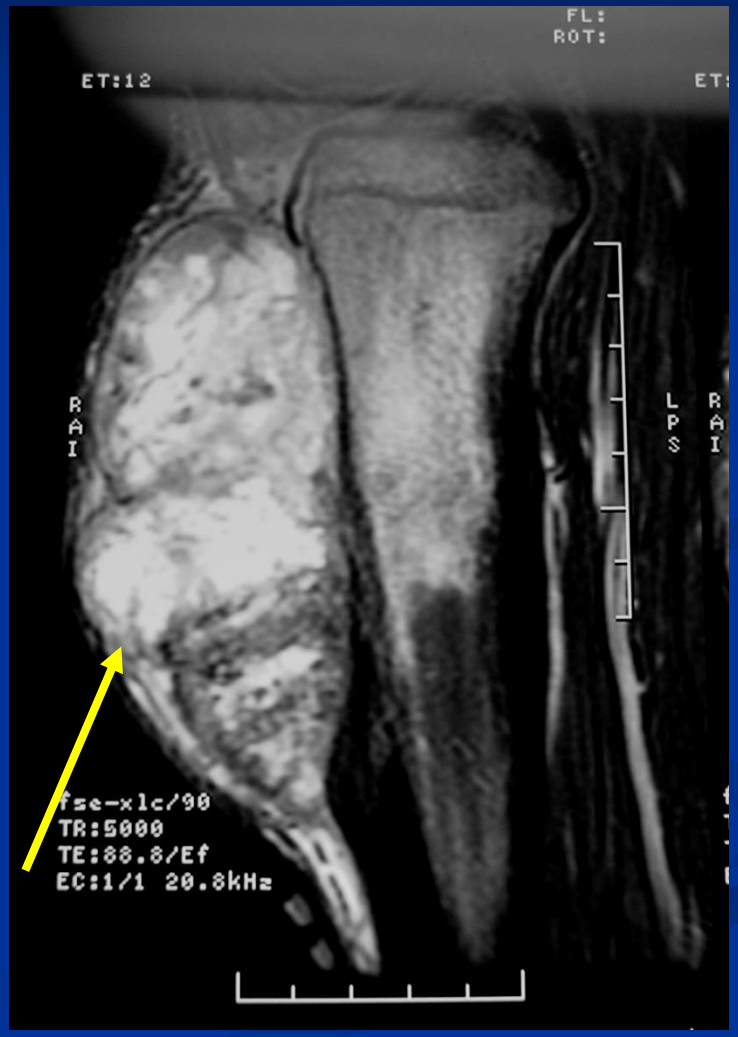
X-Ray of Periosteal Osteosarcoma of Tibia

- Surface tumor from tibia
- Tumor is mostly cartilaginous with little mineralization and therefore is radiolucent
- Hair on End Periosteal Reaction
- Saucerization (minor erosion) of underlying cortex of bone

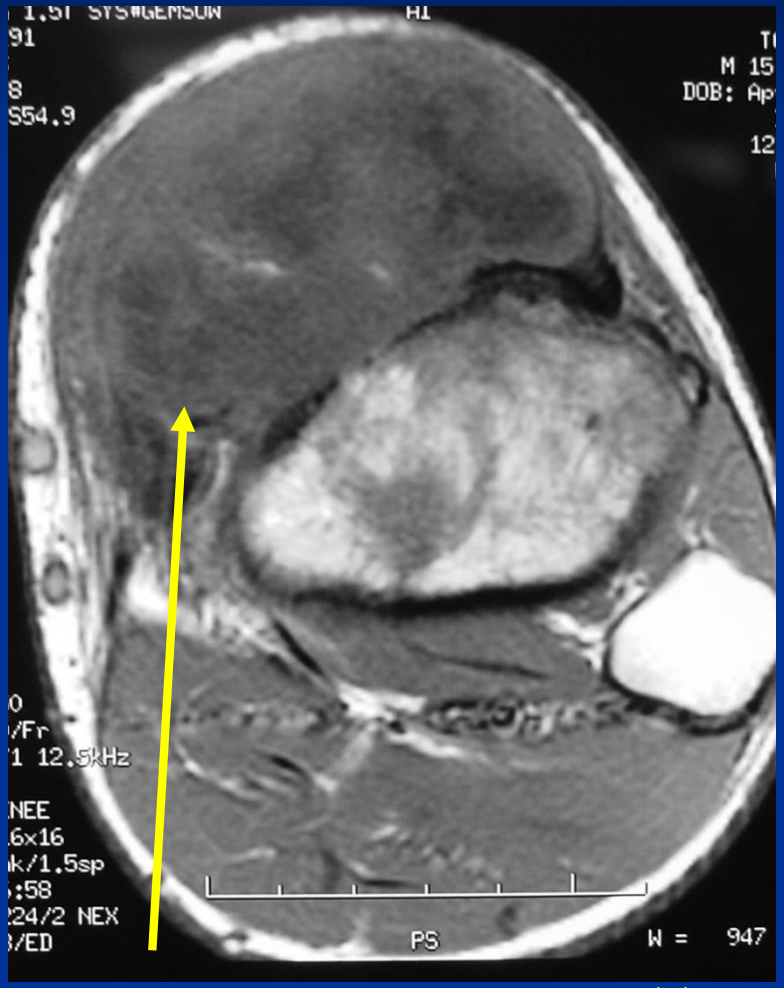


MRI of Periosteal Osteosarcoma of Tibia

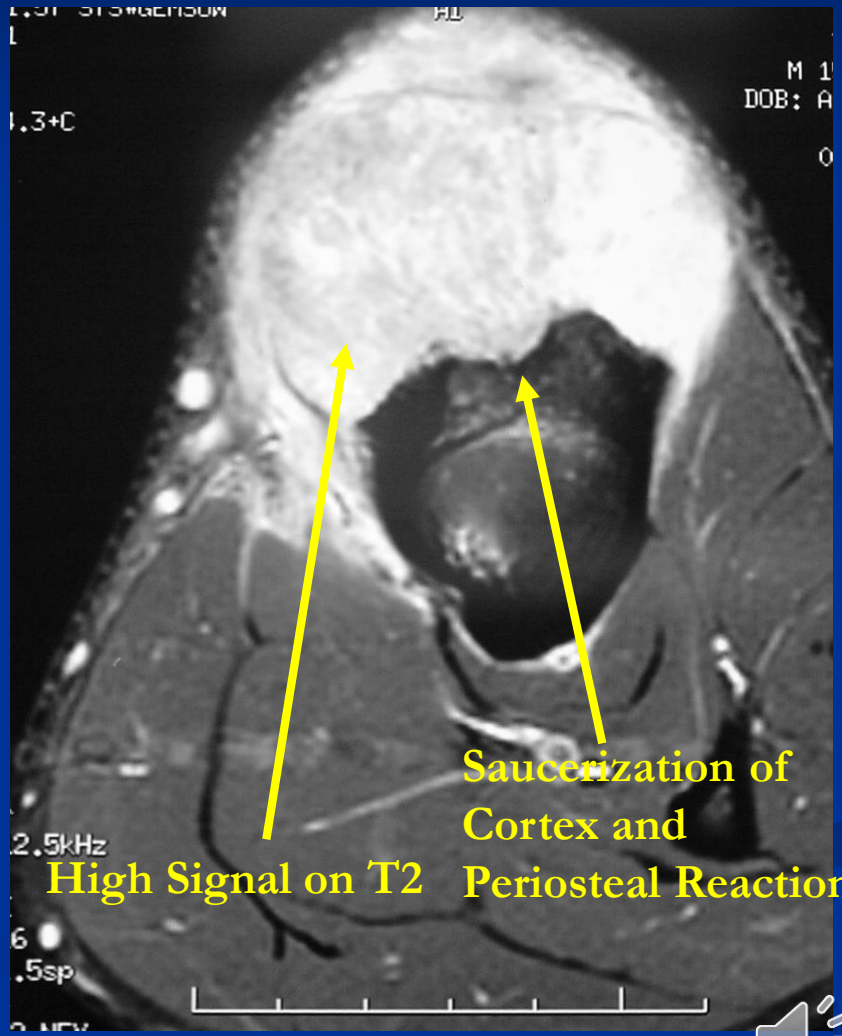
- Tumor is on surface of bone
- Mild saucerization of underlying cortex
- Large mass
- No intramedullary invasion
- Primarily high signal on T2 weighted images consistent with cartilage



MRI: Axial T1 and T2 Weighted Images of Periosteal Osteosarcoma of Tibia



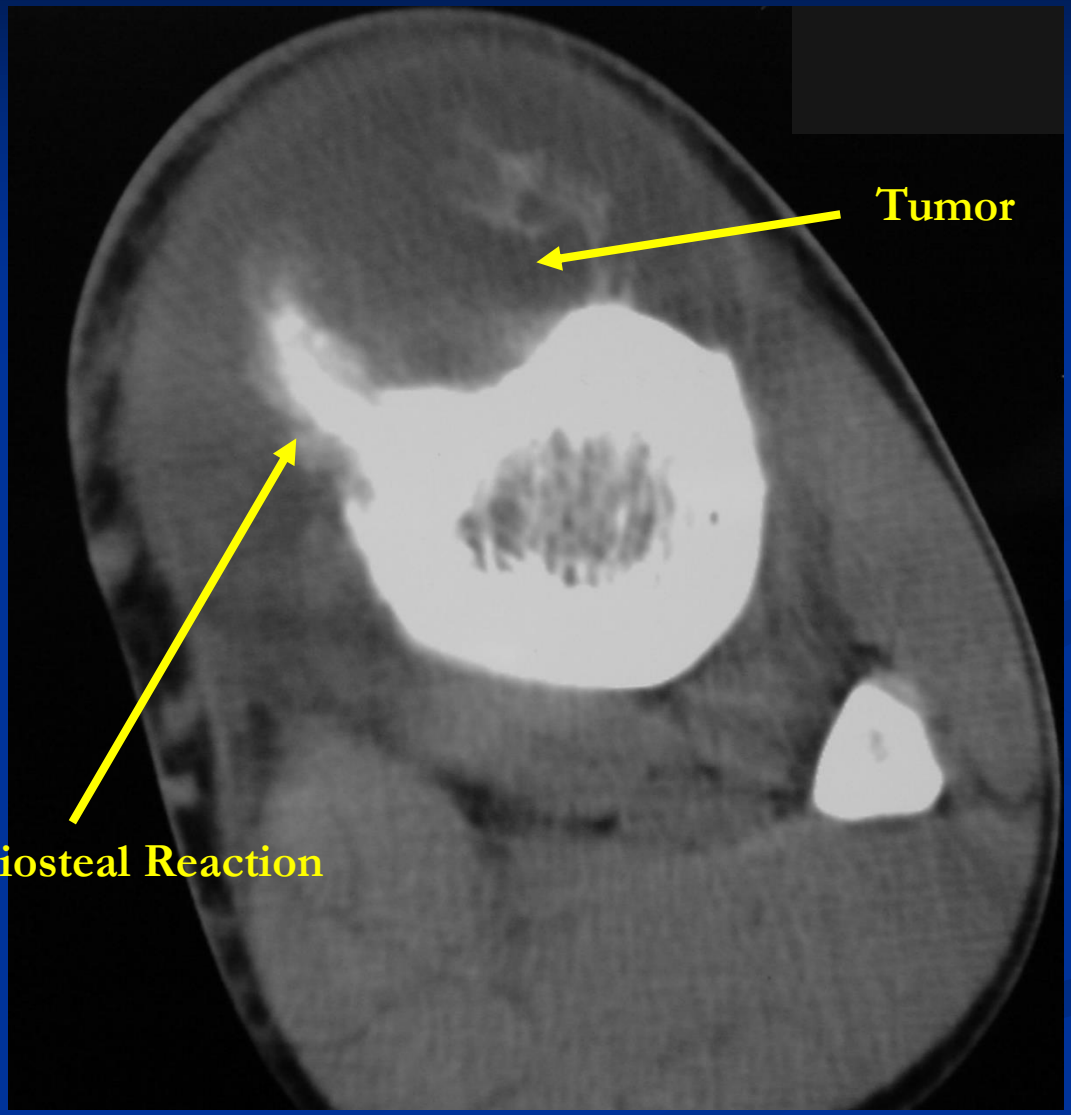
Mass is Intermediate Signal on T1



High Signal on T2

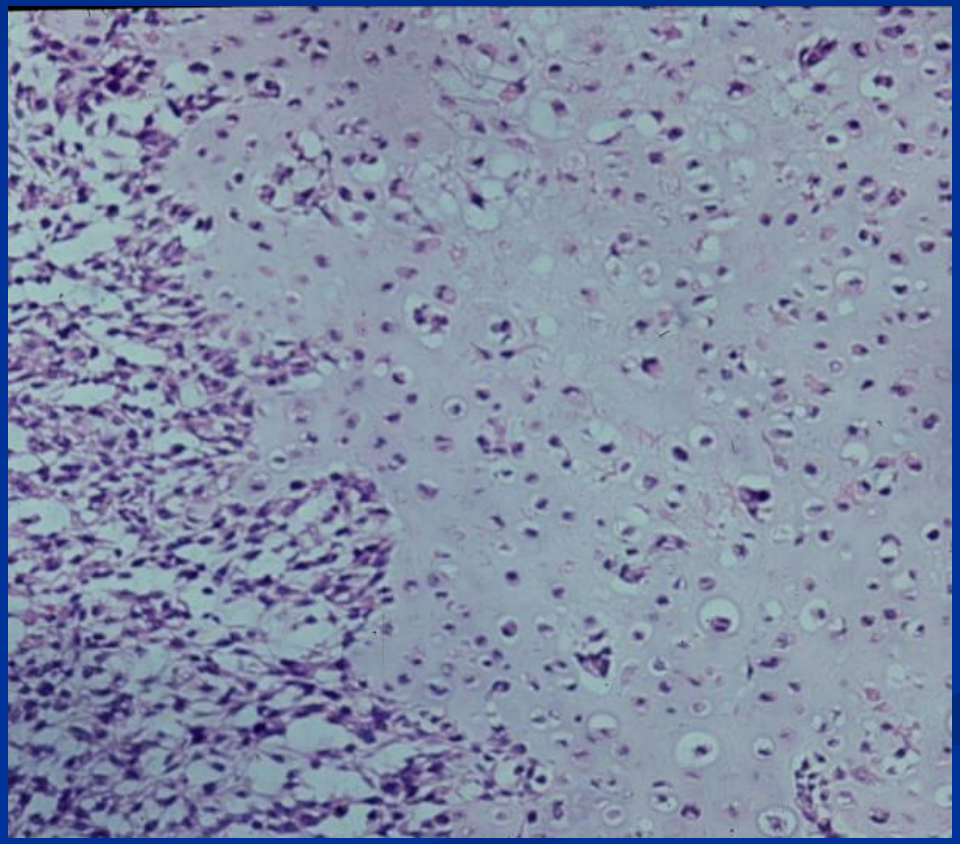
Saucerization of Cortex and Periosteal Reaction

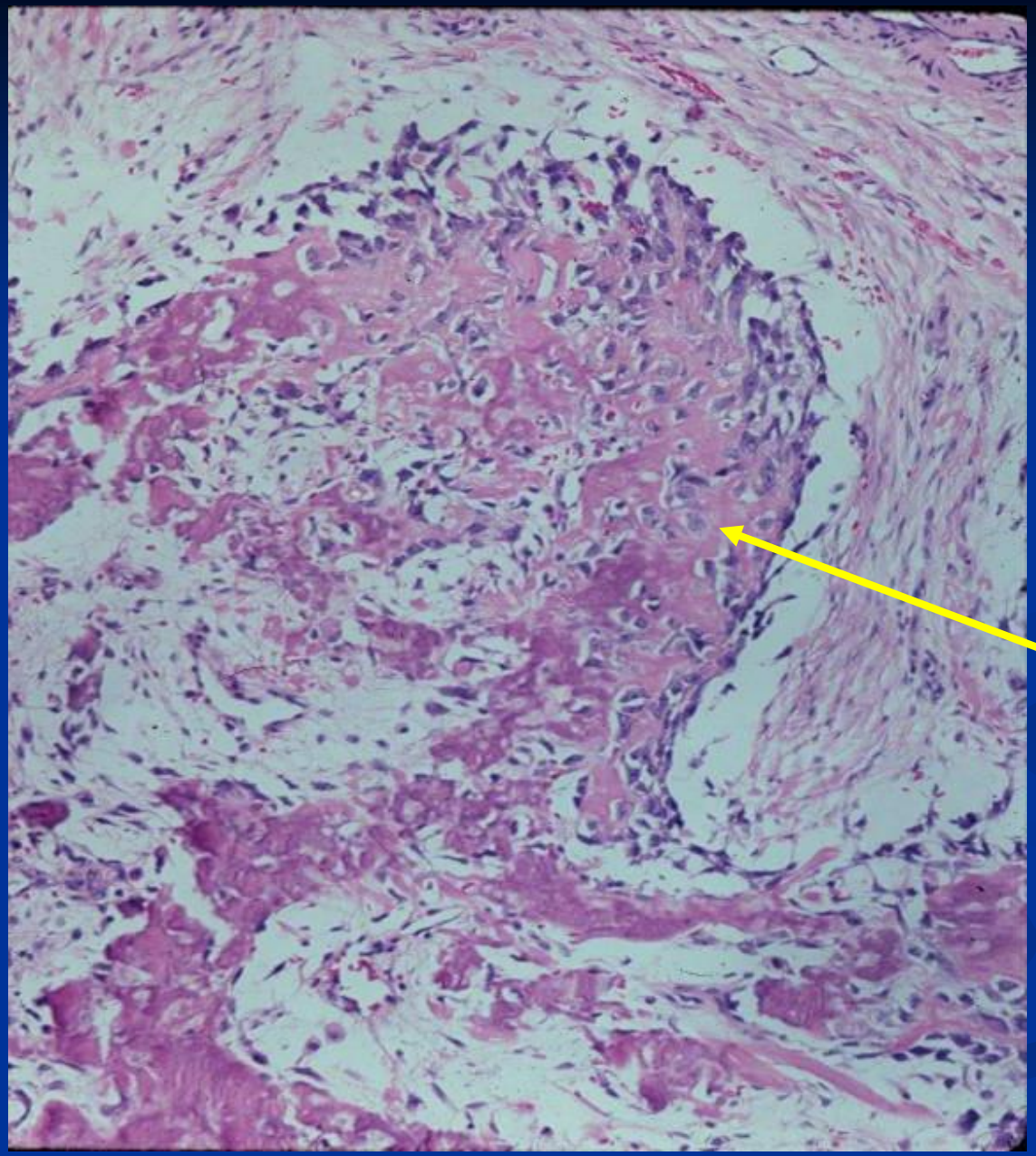
CT scan of Periosteal Osteosarcoma of Tibia



Microscopic Pathology

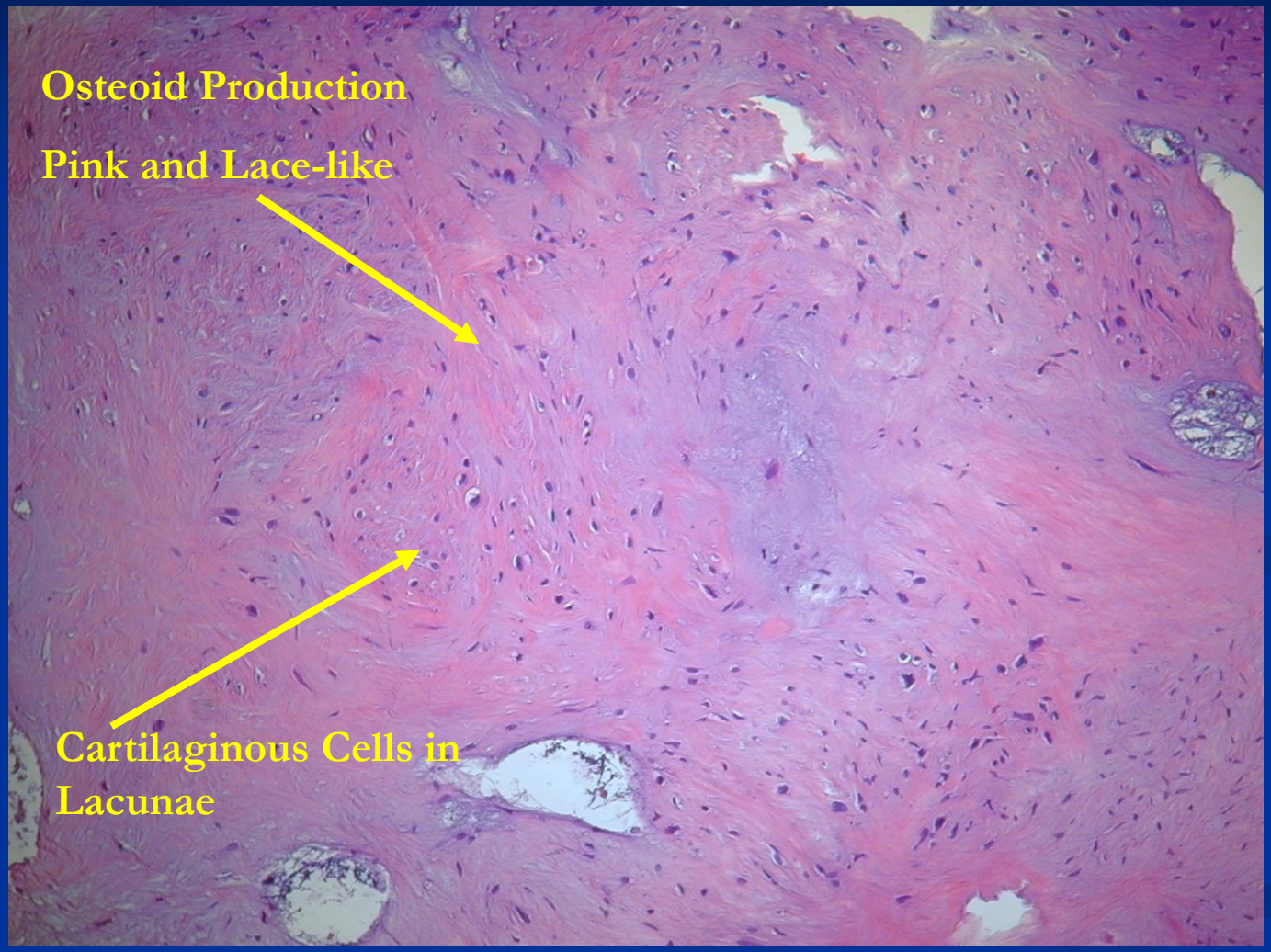
- **Chondroblastic tumor**
  - Poorly differentiated **lobules of cartilage** separated by **malignant appearing spindle cells**
- **Osteoid production** by neoplastic cells is present
  - Deposited in lace-like manner in between malignant spindle cells





Osteoid Production Identified in Various Areas of Tumor

Pathology of Periosteal Osteosarcoma



Biological Behavior

- Periosteal Osteosarcomas have a 15% metastatic rate
- Most metastasize primarily to the lungs

Treatment

- Treatment usually includes preop and postop chemotherapy and surgery, although the benefit of chemotherapy is controversial

Prognosis

- 15-25% metastatic rate to lungs
- 85-90% 5 year survival
- Survival is much better than conventional osteosarcoma

High Grade Surface Osteosarcoma

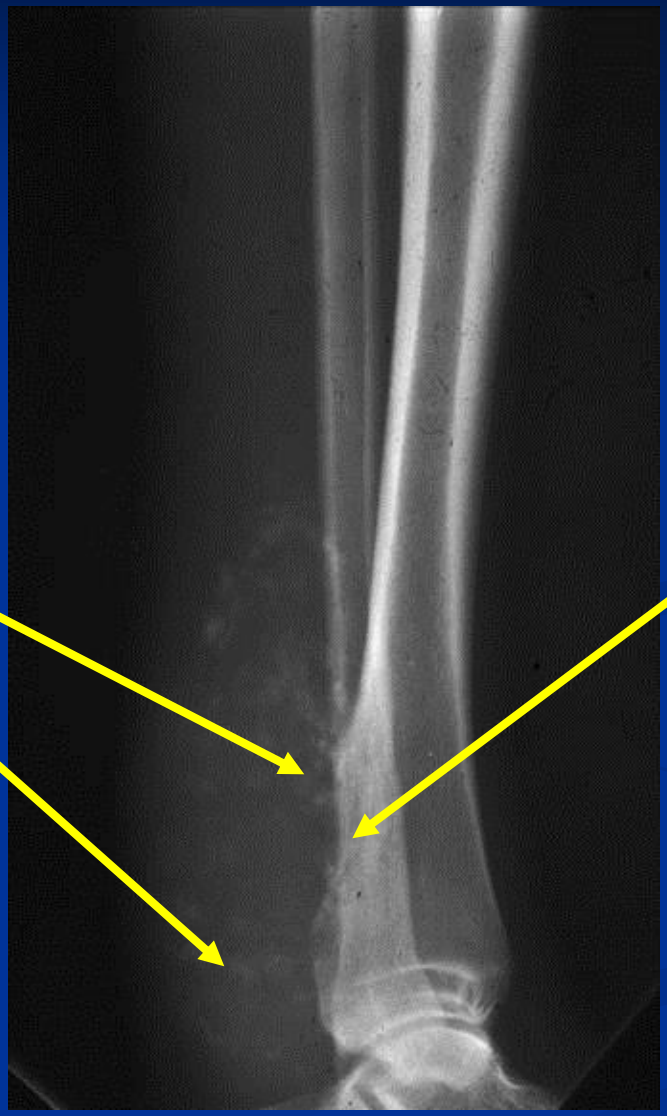
General Information

- Type of high grade osteosarcoma that develops on the surface of the bone from the outer cortex. There is none to minimal medullary involvement
- Microscopic pathology same as a conventional osteosarcoma
- High potential for metastasizing.
- Least common type of surface osteosarcoma
- Very rare <1% of all osteosarcomas

Clinical Presentation

- **Sites:** Femur (45%); Humerus (26%); Fibula (10%)
- Diaphysis or metadiaphysis of the bone most common

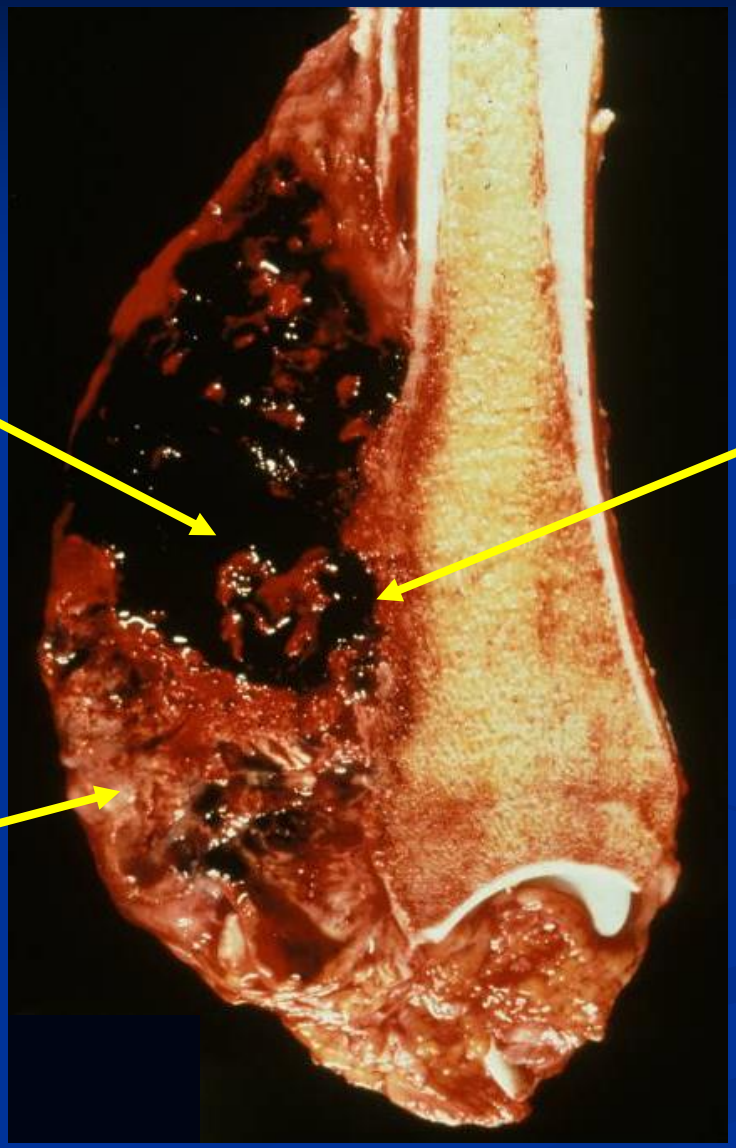
Plain X-Ray: High Grade Surface Osteosarcoma of Distal Tibia



Ossification in Tumor

Subtle Cortical Erosion

Gross Pathology of High Grade Surface Osteosarcoma of Distal Tibia



Necrotic Cystic Cavity

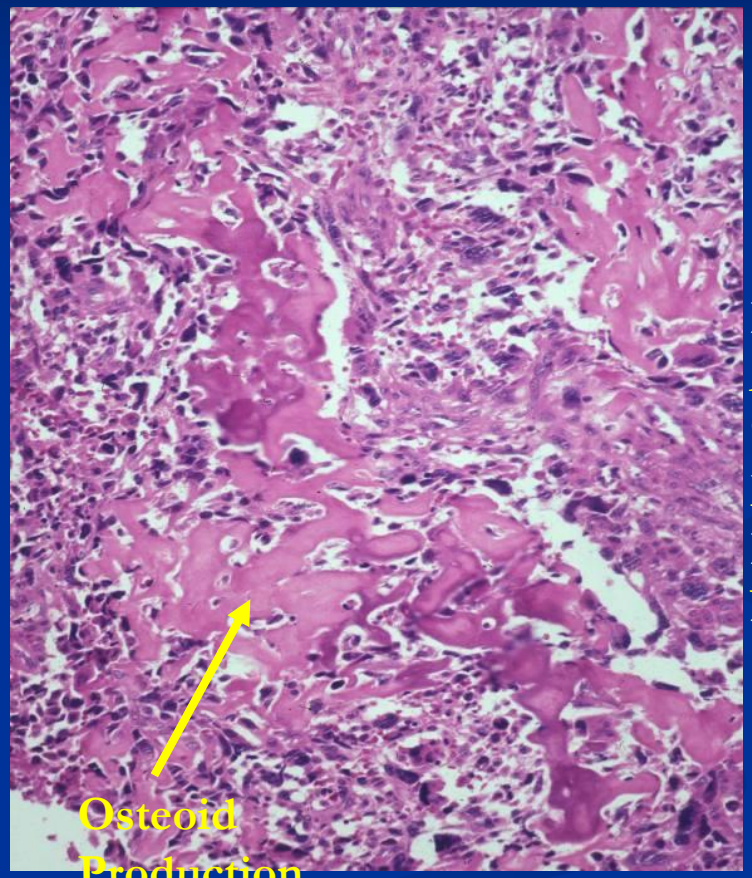
Areas of Cortical Erosion

Fleshy Area

Tumor is arising from Surface of Distal Tibia

Microscopic Pathology

- The pathology of a high grade surface osteosarcoma is indistinguishable from conventional medullary osteosarcoma
- The lack of medullary involvement distinguishes this tumor from a conventional intramedullary osteosarcoma
- It consists of high grade, anaplastic, pleomorphic spindle cells producing osteoid, and immature bone that is deposited in a lace-like manner



High Grade Anaplastic Spindle Cells with Large Hyperchromatic Nuclei

Treatment/Prognosis

- Same as conventional osteosarcoma

Prognosis

- Survival is similar to conventional intramedullary osteosarcoma.

Intracortical Osteosarcoma

General Information

- Intracortical osteosarcoma is an extremely rare type of high grade osteosarcoma that arises within and is usually confined to the cortex of the bone
- Differential: osteoid osteoma, bone abscess, non ossifying fibroma, osteoblastoma or adamantinoma

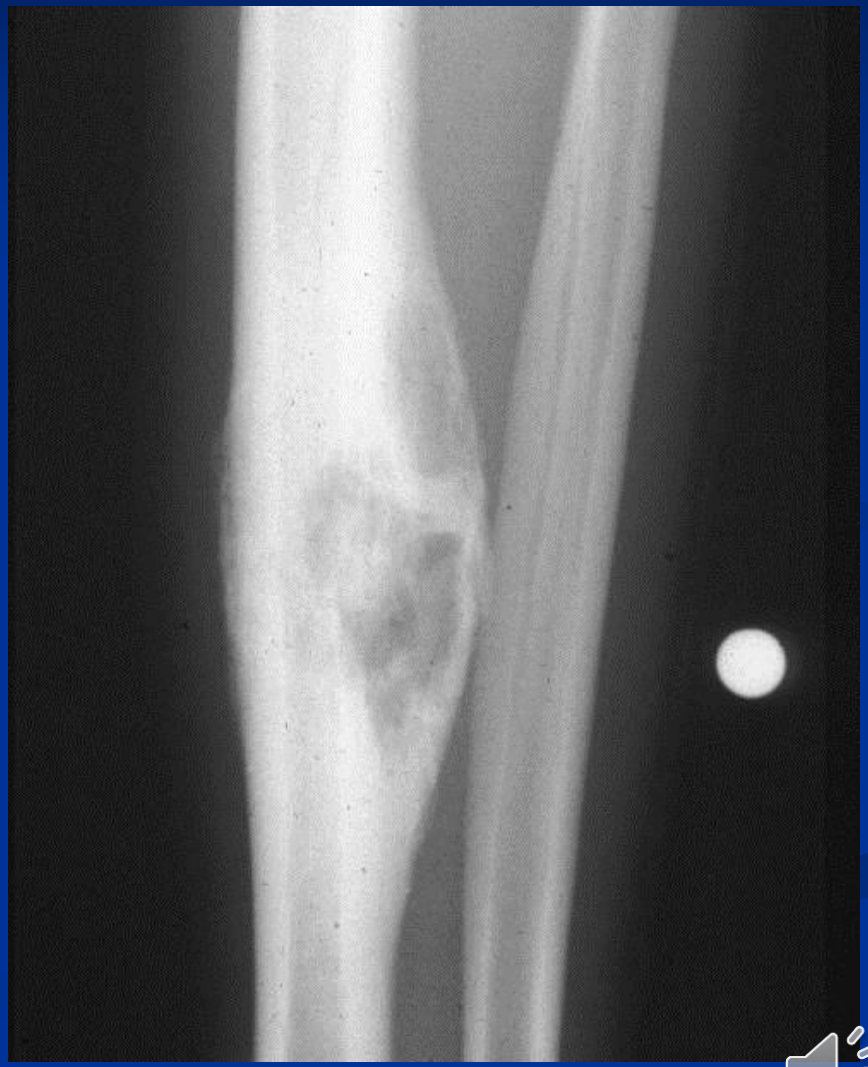
Clinical Presentation

- **Age:** 10-30 years

- **Sites:**
  - Diaphysis of femur or tibia most common sites

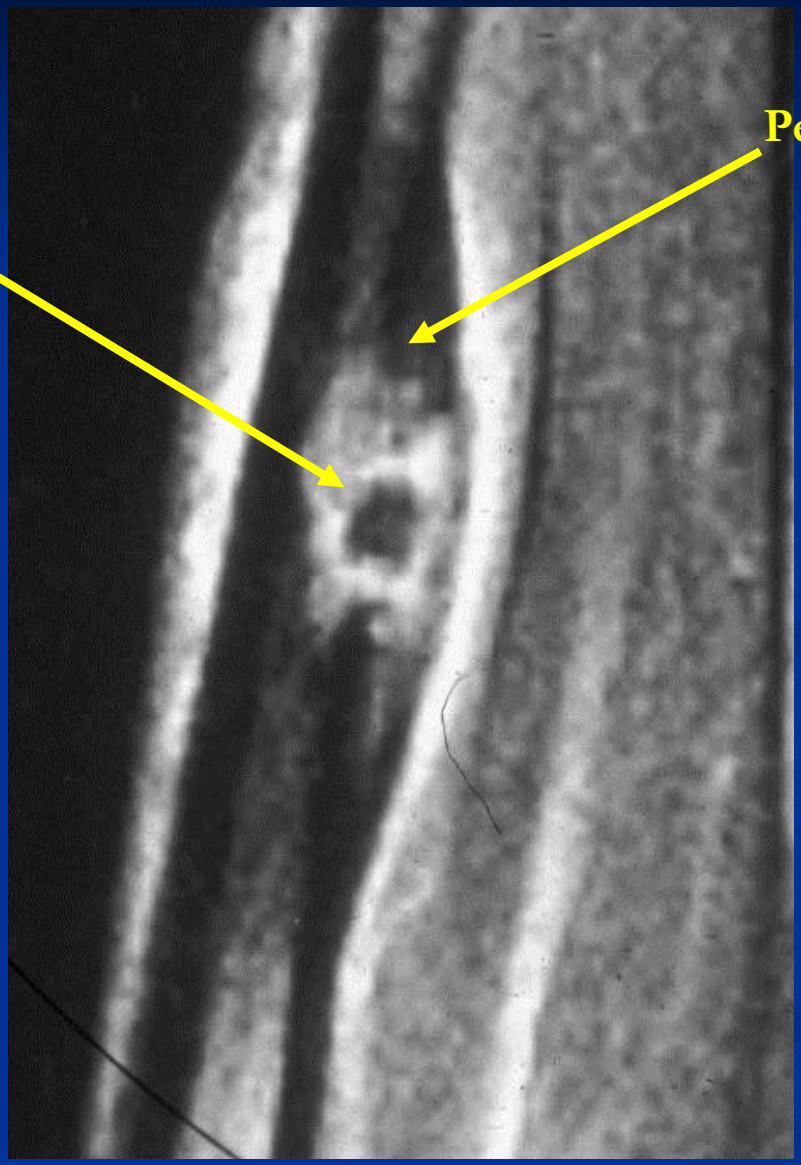
Radiographic Presentation

- **Plain Radiographs:**
  - Intracortical irregular lytic lesion with surrounding sclerosis
  - The junction of the lesion with the normal bone is usually irregular but sharply demarcated
  - Permeation of cortex
  - Lesion may demonstrate ossification or mineralization within it
  - Minimal or no periosteal reaction



MRI of Intracortical Osteosarcoma

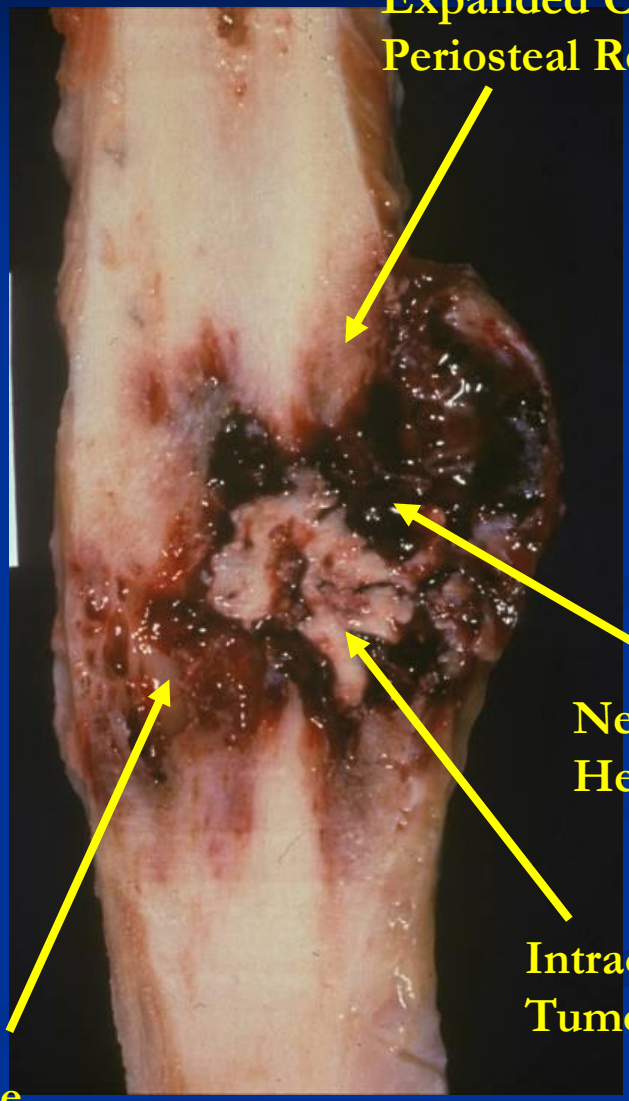
Intracortical Tumor with Surrounding Edema



Periosteal Reaction

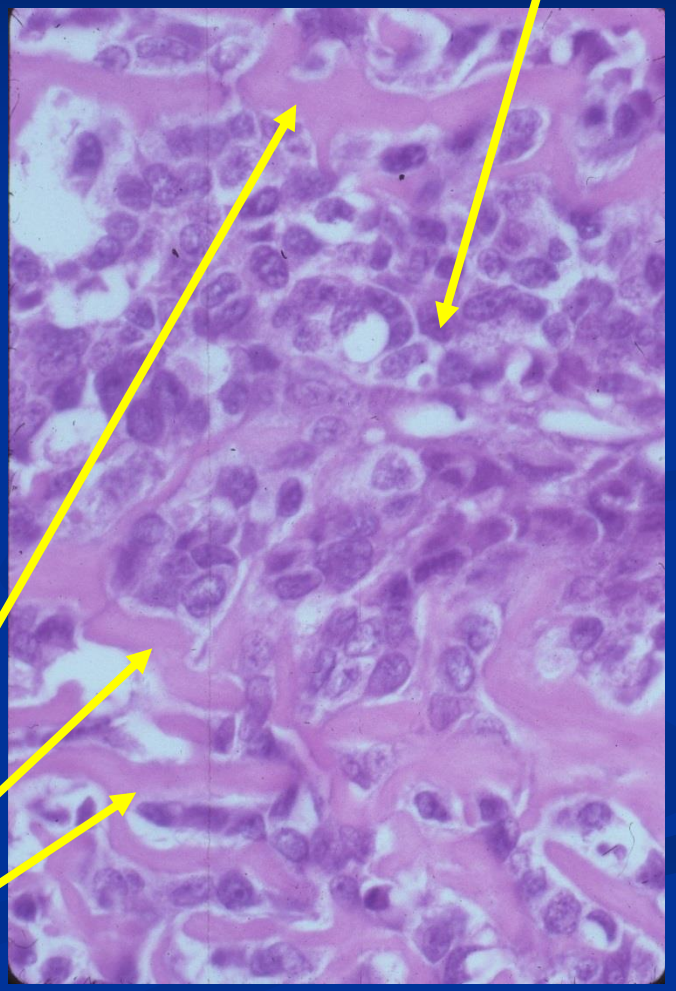
Gross Pathology

- Intracortical, well defined tumor with very thick expanded cortex
- Irregular borders
- Thick and expanded cortex
- Tumor is grey/tan/yellow and gritty from mineralized osteoid or bone production



Microscopic Pathology

- Malignant spindle cell tumor producing osteoid
- Malignant cells have large nuclei, minimal cytoplasm, nuclear pleomorphism, mitoses
- They appear crowded and haphazard
- The osteoid is layed down in lace-like manner in between malignant cells



Differential Diagnosis

- Osteoid Osteoma
- Brodie's Abscess
- Osteoblastoma
- Nonossifying fibroma
- Eosinophillic Granuloma
- Osteofibrous Dysplasia
- Adamantinoma

Treatment

- En bloc Resection/Limb Sparing Surgery whenever feasible
- Efficacy of chemotherapy is uncertain given the small number of cases, but would be treated same as conventional osteosarcoma

Thank You!