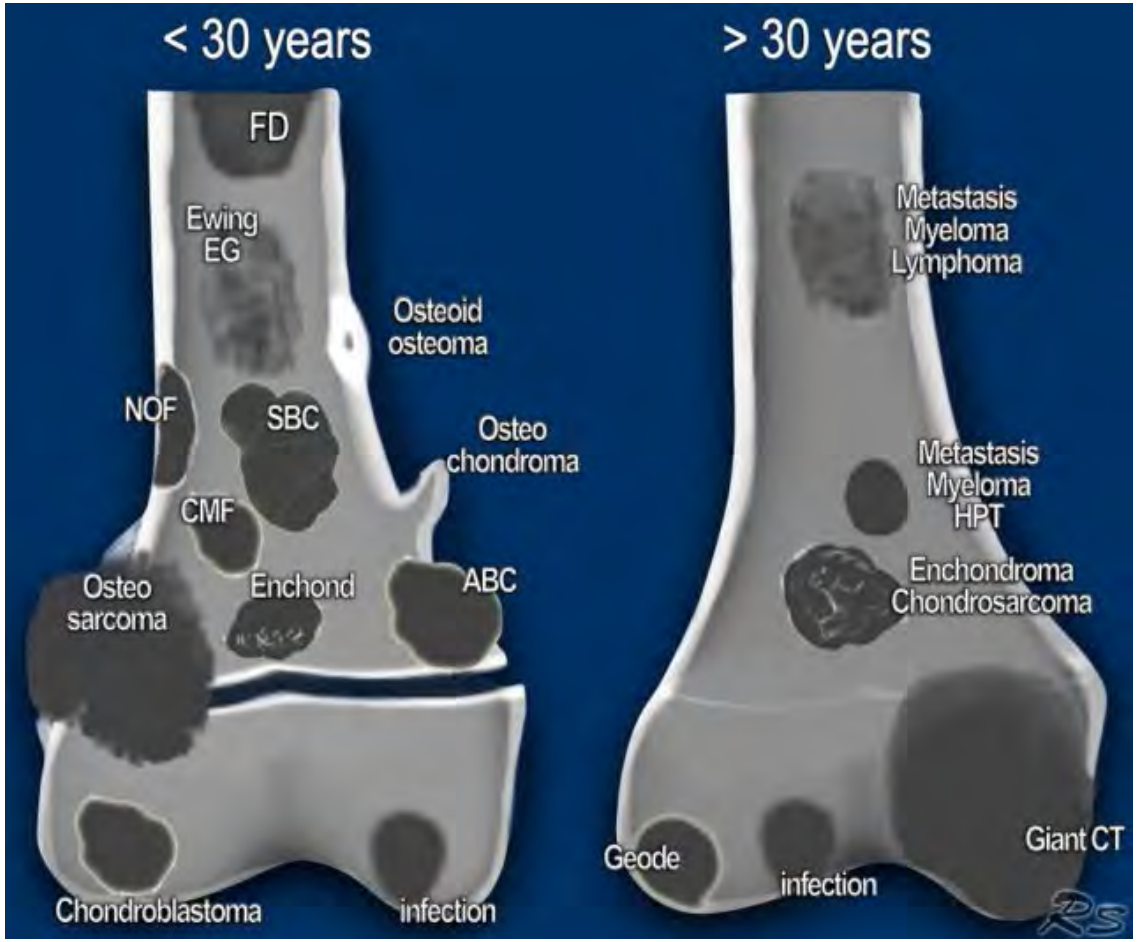
A COMPREHENSIVE OVERVIEW OF COMMON MUSCULOSKELETAL TUMORS

Dr. Nicholas Okumu



What are Sarcomas?

- **Sarcomas** are cancers that arise from **mesenchymal cells** (connective tissues like bone, cartilage, muscle, fat).
- Two main types:
  - **Bone Sarcomas** (e.g., Osteosarcoma)
  - **Soft Tissue Sarcomas** (e.g., Liposarcoma, Rhabdomyosarcoma)
- **Characteristics**:
  - Can occur anywhere in the body, most commonly in **extremities**, **abdomen**, and **chest**.
  - **Aggressive** with potential to invade nearby tissues and metastasize (often to the lungs).
- **Treatment**:
  - Requires a **multimodal approach**: Surgery, chemotherapy, and radiotherapy.

Introduction

Scope of the Presentation

- In-depth focus on four common musculoskeletal tumors
- Covering epidemiology, pathophysiology, genetic mutations, diagnostic workup, and treatment strategies

Importance in Oncology

- These tumors represent a significant burden due to their aggressive nature and the need for multimodal treatment approaches

Key Aspects Of a Multi-Disciplinary Approach to Care

Osteosarcoma – Overview

Epidemiology

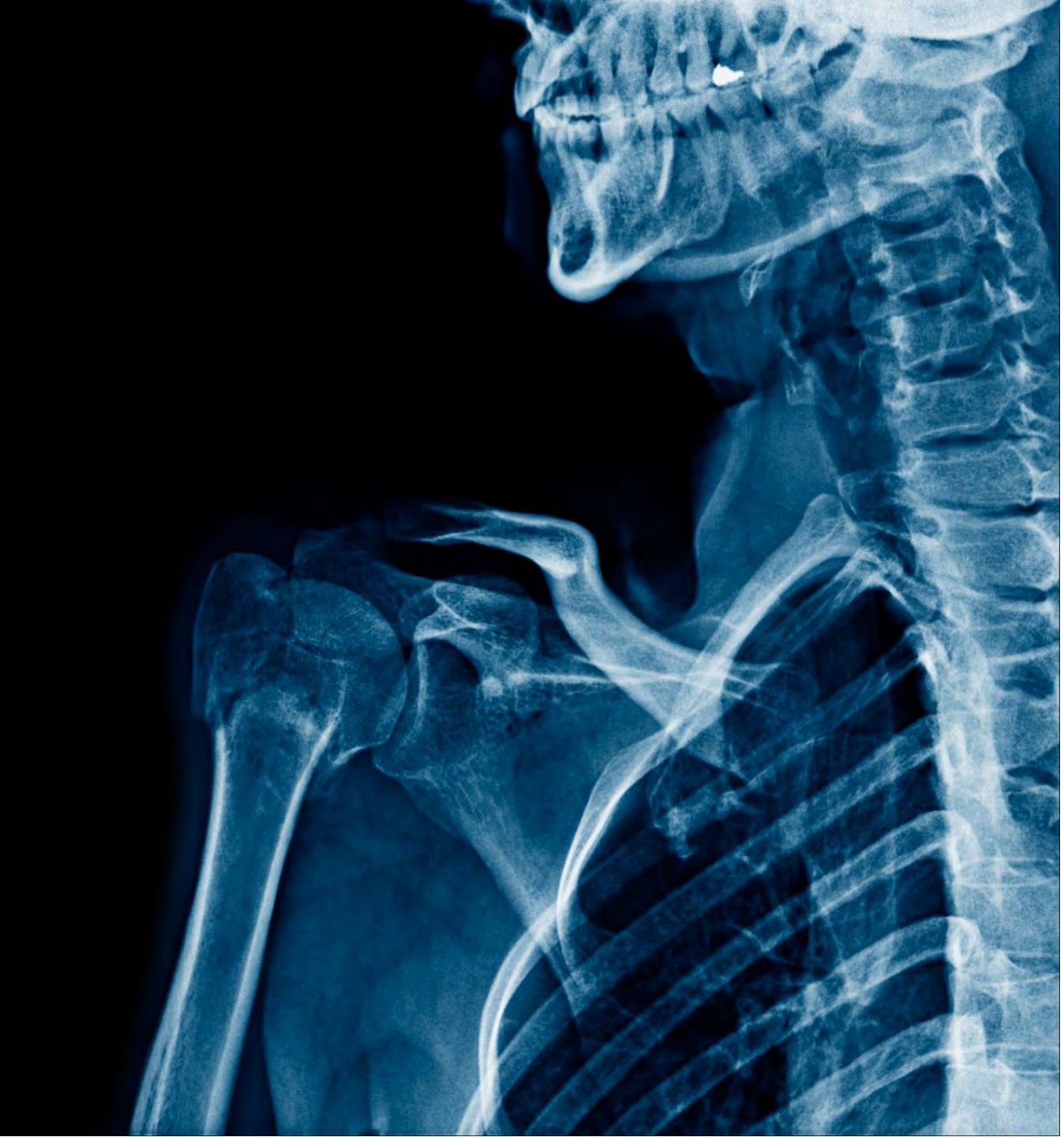
- Most common primary bone cancer, typically affecting adolescents and young adults
- Peak incidence: 10-20 years

Genetic Mutations

- TP53, RB1, and RECQL4 mutations
- Li-Fraumeni syndrome association

Clinical Presentation

- Pain and swelling, often in metaphyseal regions of long bones
- Pathological fractures in advanced cases



Osteosarcoma – Staging & Workup

- Staging: Based on the Enneking system
  - Stage IA/B: Low-grade, confined to the bone
  - Stage IIA/B: High-grade, without/with soft tissue extension
  - Stage III: Metastasis
- Workup
  - Imaging: X-ray , MRI , CT/PET
  - Biopsy: Core needle or open biopsy for histopathological confirmation

Osteosarcoma – Histology & Imaging

Histology

Osteoid production by malignant osteoblasts

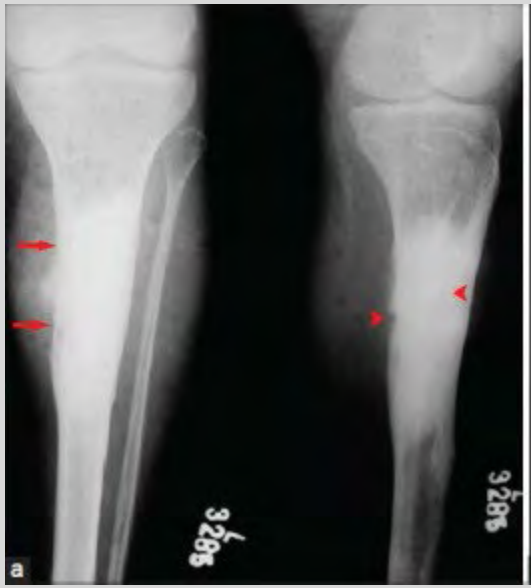
High mitotic rate and atypical spindle cells

Imaging Findings

X-ray: Codman's triangle, sunburst pattern

MRI: Enhances soft tissue involvement; T1/T2 sequences for tumor boundaries

CT: Best for pulmonary metastasis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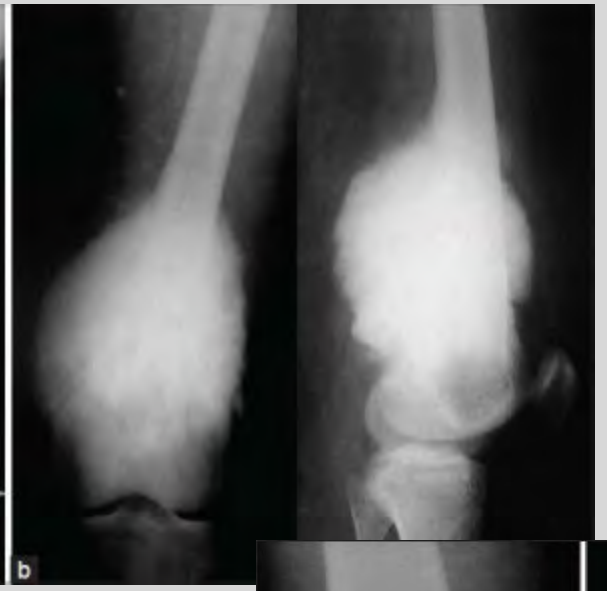
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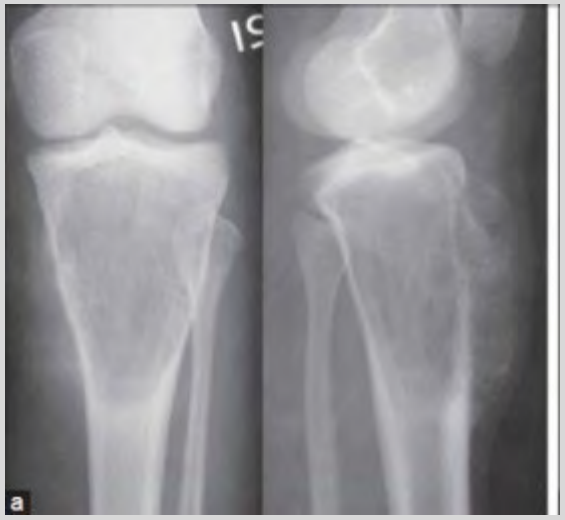
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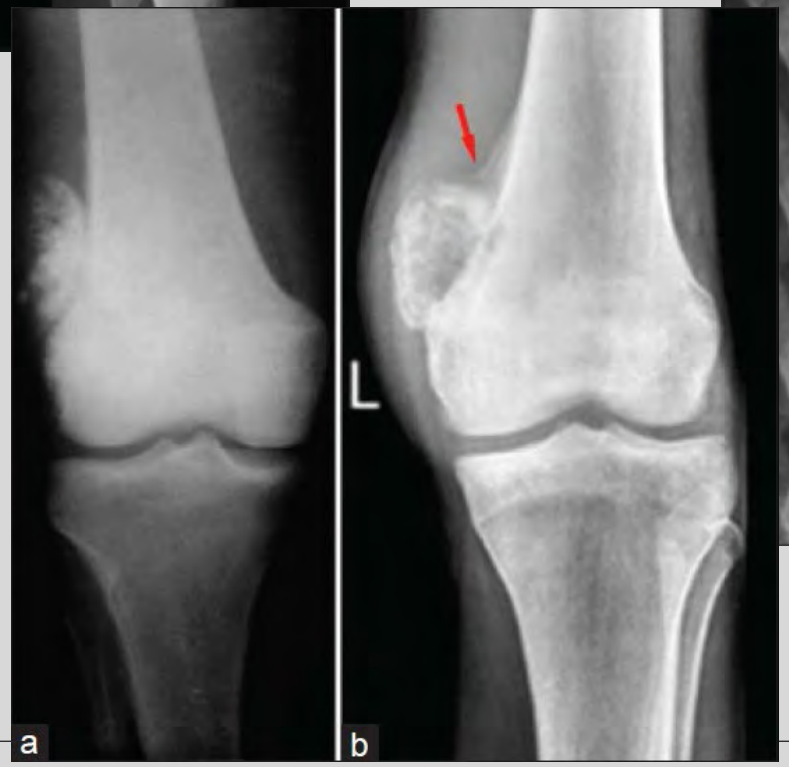
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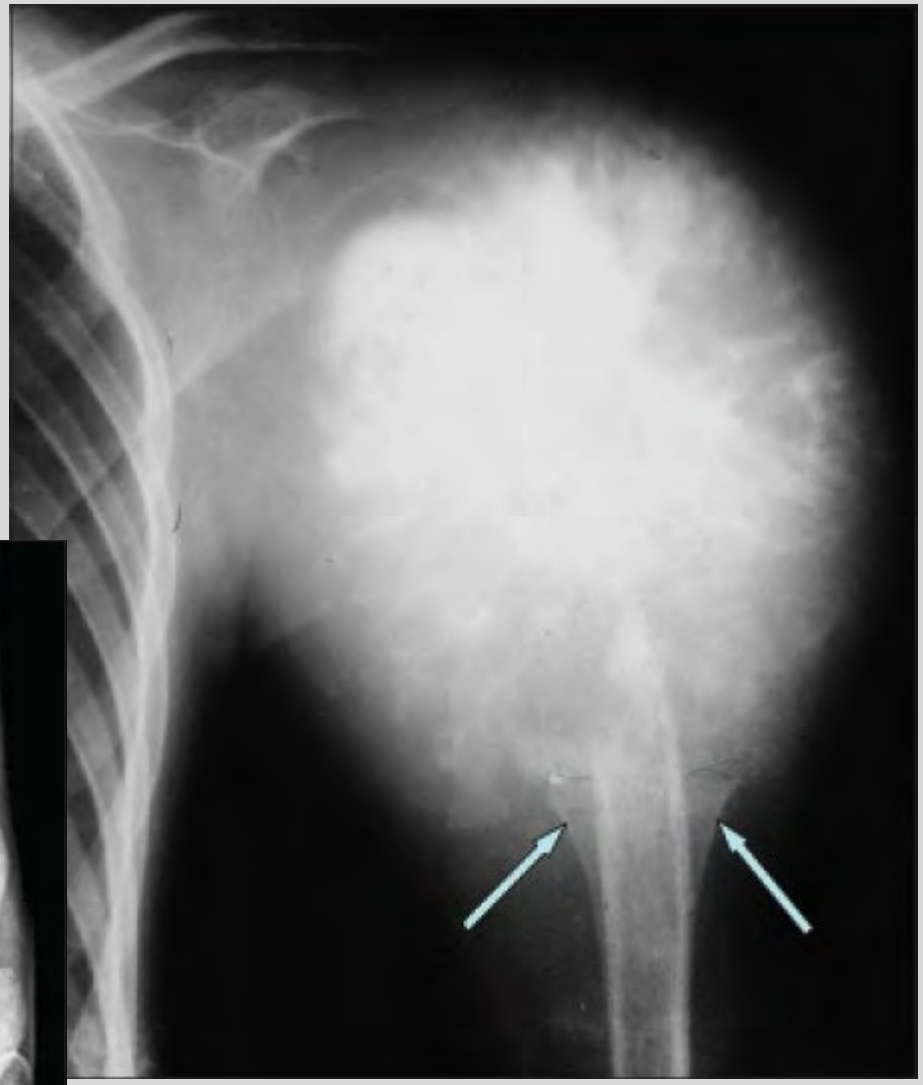
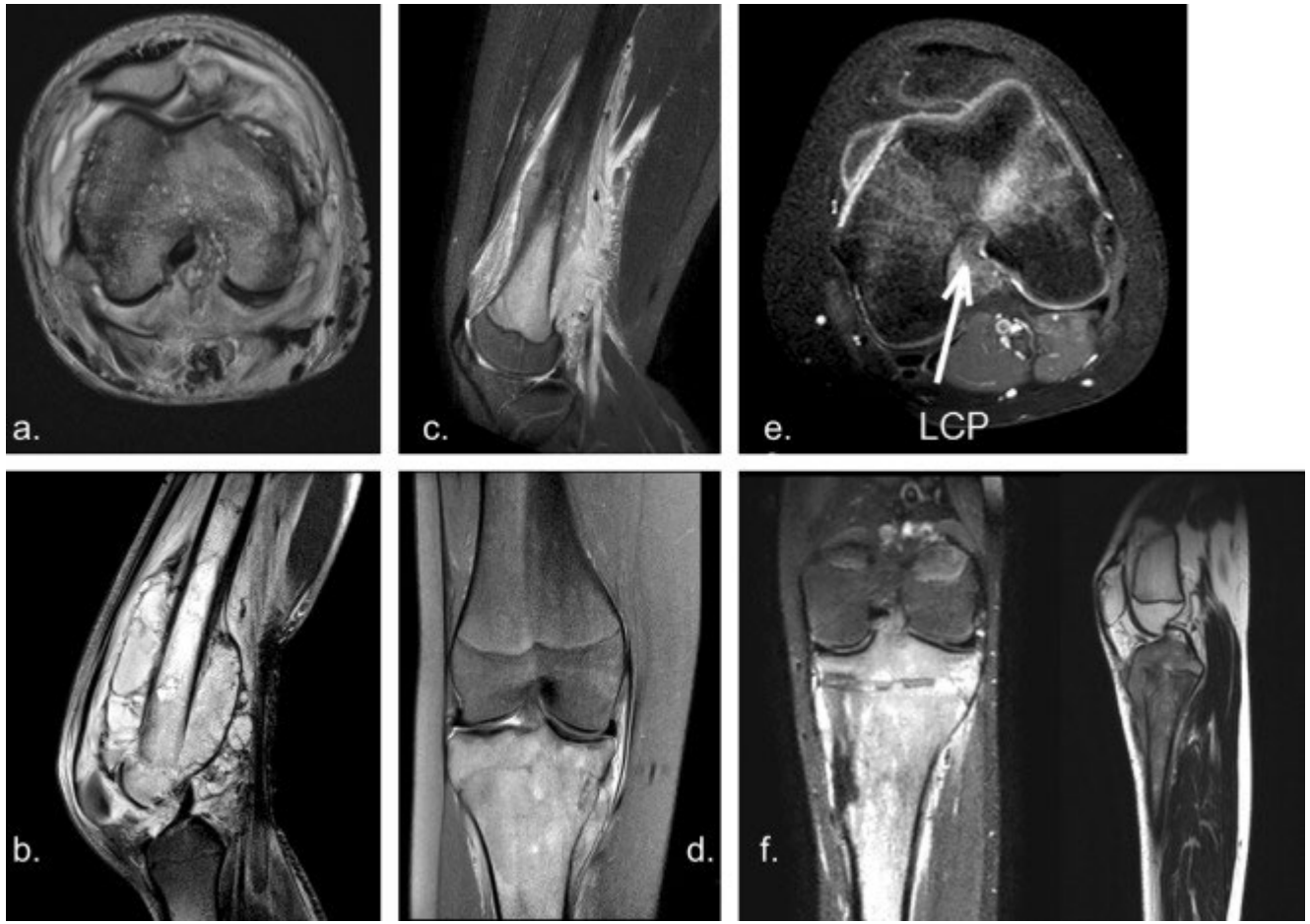
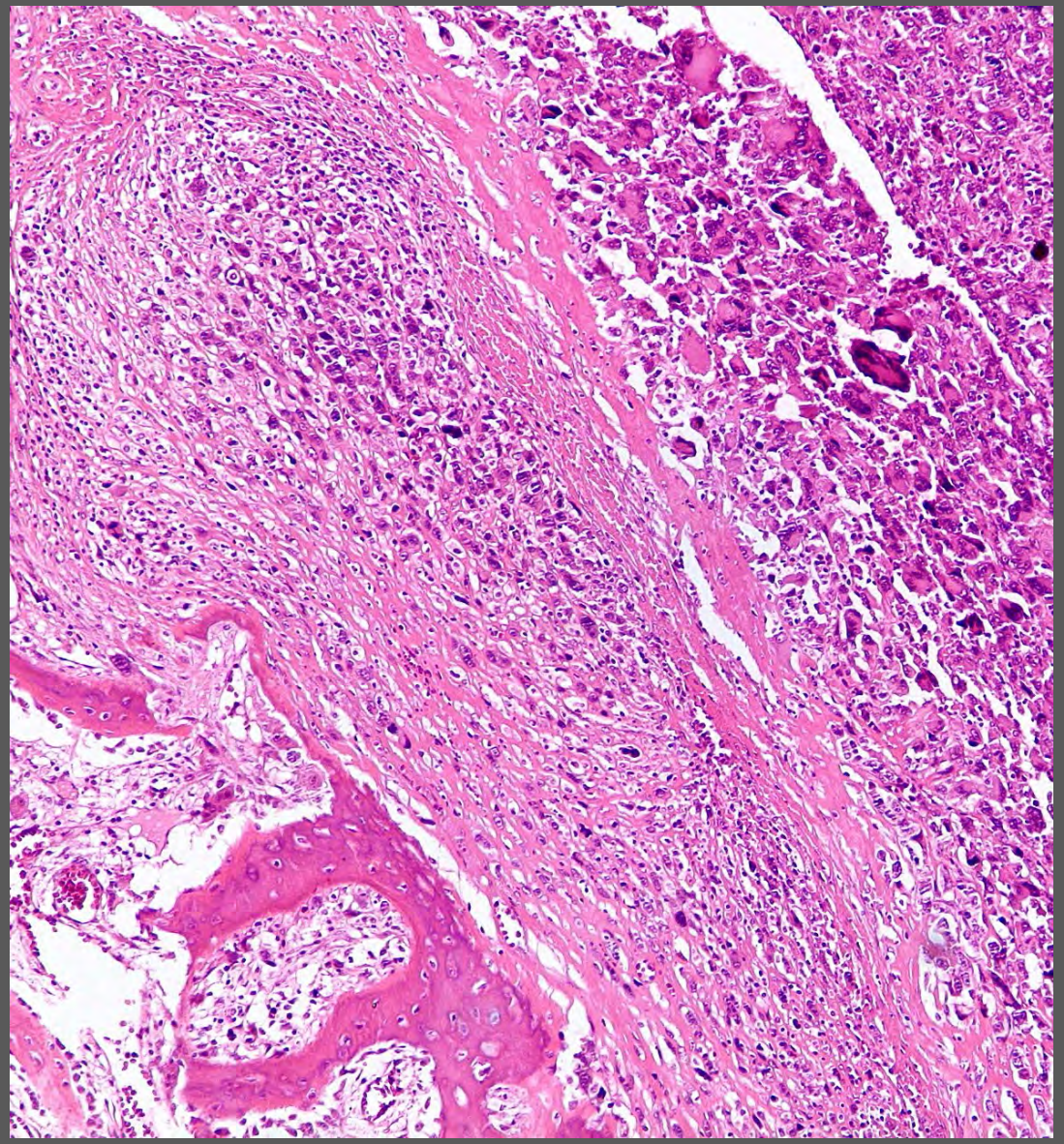
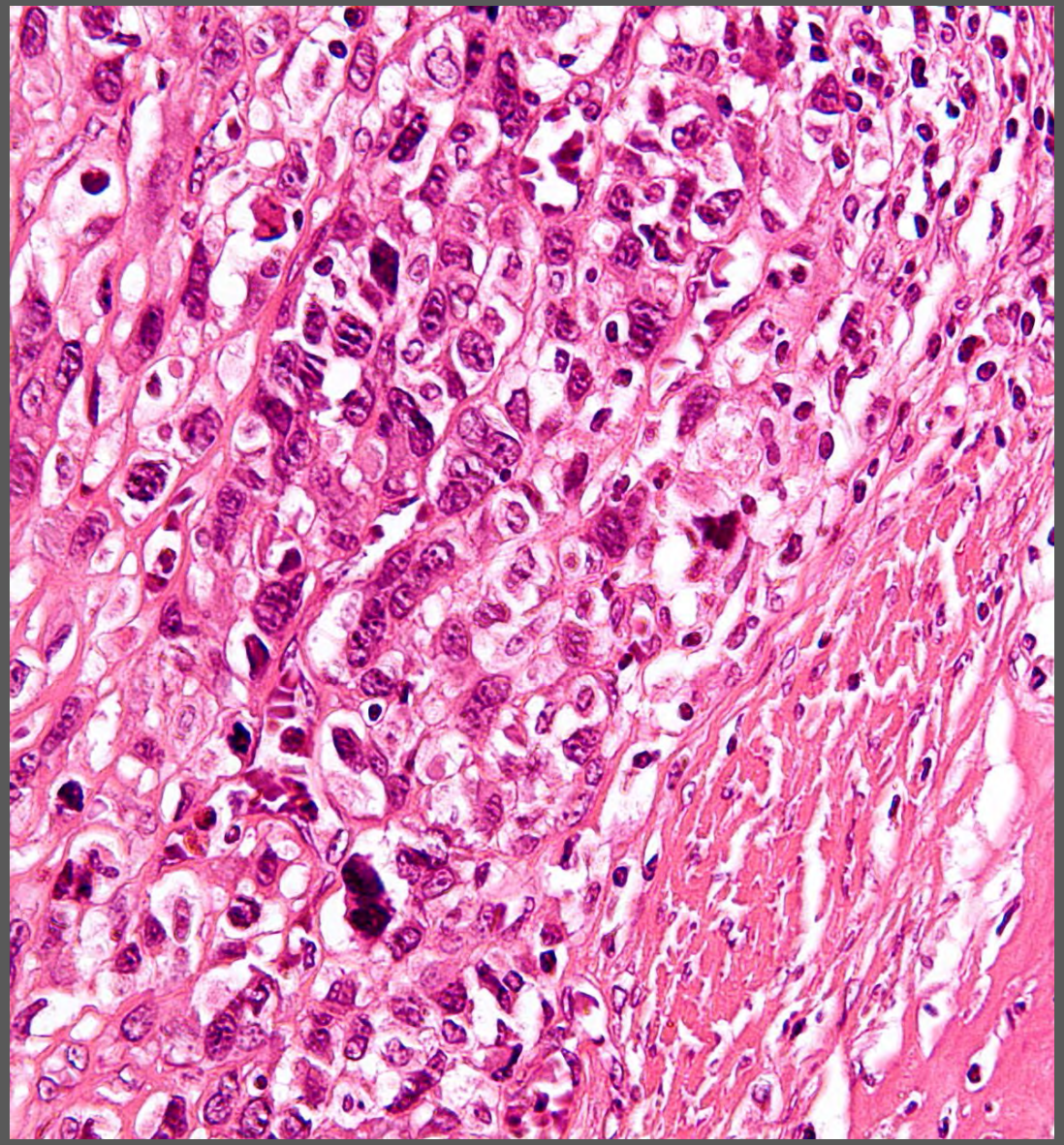




Bone sarcomas are usually iso- to hypointense to muscle on T1-weighted images, and heterogeneously hyperintense on T2 DIXON or STIR images, due to the presence of hemorrhage and necrosis.

On T1-weighted images, osteosarcoma usually shows a sharp transition from normal fatty marrow to hypointense tumor marrow involvement.





HISTOLOGICAL SUBTYPES

Primary osteosarcomas

Conventional-intramedullary/central high grade (most common) further sub-typed as:

- Osteoblastic (50%)
- Chondroblastic (25%)
- Fibroblastic (25%)

Small cell

Telangiectatic

Low grade central

Surface osteosarcomas:

- Parosteal
- Periosteal
- High grade surface

Secondary osteosracomas can occur in Paget's disease and after radiation exposure.[1,2]

Unusual forms of osteosarcoma given below are viewed as subtypes of conventional osteosarcoma because their biological behavior is similar.[2]

- Osteoblastic osteosarcoma-sclerosing type
- Osteosarcoma resembling osteoblastoma
- Chondromyxoid fibroma-like osteosarcoma
- Chondroblastoma-like osteosarcoma
- Clear-cell osteosarcoma
- Malignant fibrous histiocytoma-like osteosarcoma
- Giant cell rich osteosarcoma
- Epithelioid osteosarcoma

Osteosarcoma – Treatment Modalities

Surgical Resection

Limb-sparing surgery preferred; amputation in cases of extensive soft tissue invasion

Importance of achieving negative margins

Chemotherapy

Neoadjuvant: High-dose methotrexate, doxorubicin, cisplatin

Adjuvant: Same regimen post-surgery to target micrometastatic disease

Radiotherapy

Limited role, used in non-resectable tumors or palliation

Chondrosarcoma – Overview

Epidemiology

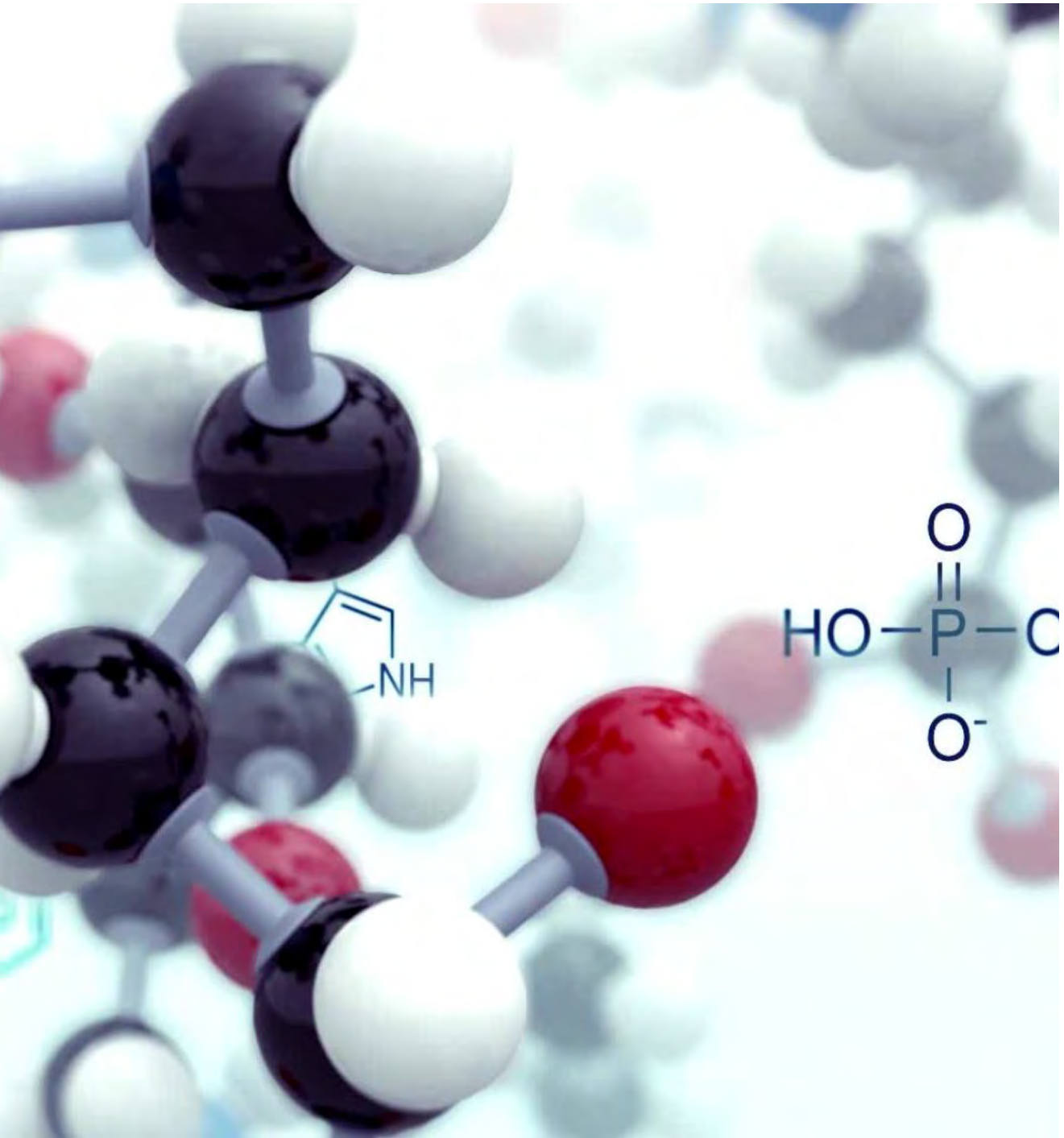
- Second most common primary bone cancer, typically seen in adults aged 40-70 years
- Arises in pelvis, ribs, and long bones
- Typically slow growing and metastasise late – variants exist

Genetic Mutations

- IDH1, IDH2 mutations
- Tumor often arises de novo or from benign cartilaginous lesions

Clinical Presentation

- Pain and swelling at tumor site
- Slow-growing but locally aggressive tumor



- Majority are sporadic (primary chondrosarcomas), but they may develop from the malignant transformation of osteochondromas or enchondromas (secondary chondrosarcomas)
- **Primary chondrosarcoma**
  - **conventional type**
    - account for >90% of all chondrosarcomas
    - can be central intramedullary (99%) or juxtacortical / periosteal (~1%)
  - **non-conventional**
    - dedifferentiated chondrosarcoma (<10%)
    - clear cell chondrosarcoma (<5%)
    - mesenchymal chondrosarcoma (<1%)
- **Secondary chondrosarcoma**
  - osteochondroma
    - account for the majority (>80%) of secondary chondrosarcomas
    - solitary osteochondromas have <1% risk of malignant transformation
    - multiple hereditary exostosis (5-10% risk of malignant transformation)
  - enchondromas (1% to 9% risk of malignant transformation)
    - Ollier's disease (25-30% risk of malignant transformation)
    - Maffucci's (>50% risk of malignant transformation)
  - histologically indistinguishable from conventional chondrosarcoma

Chondrosarcoma – Staging & Workup

Staging

Enneking

Stage IA/B: Low-grade, localized

Stage IIA/IIB: Intermediate to high-grade, without metastasis

Stage III: High-grade, with metastasis

Workup

Imaging: X-ray , MRI for soft tissue involvement, CT for bony details

Biopsy: Necessary for definitive diagnosis and grading

Chondrosarcoma – Histology & Imaging

Histology

Lobules of hyaline cartilage, with atypical chondrocytes in lacunae

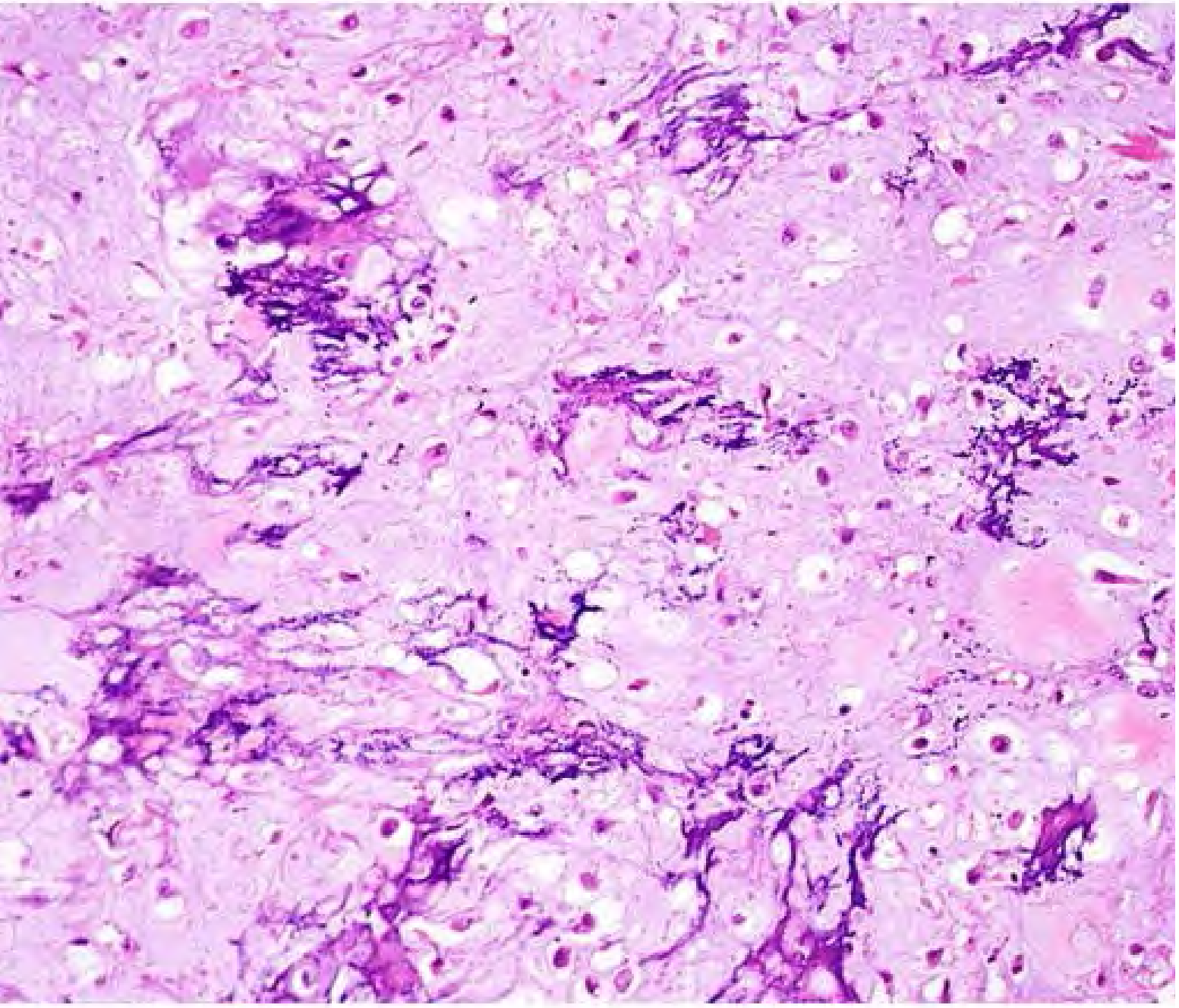
Increased cellularity, binucleation in high-grade tumors

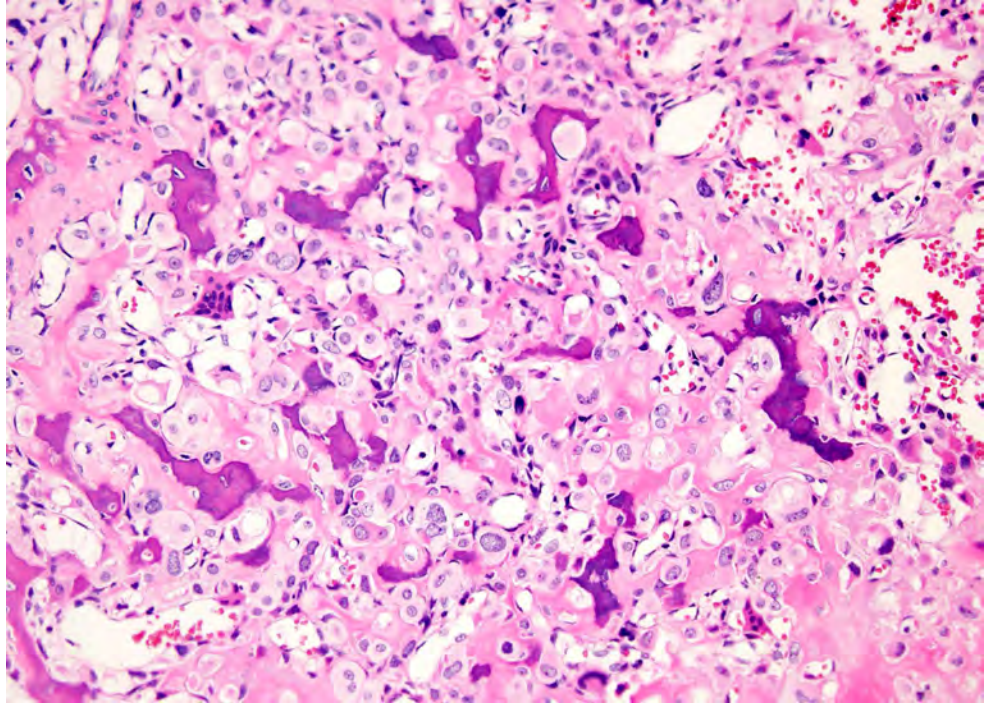
Imaging Findings

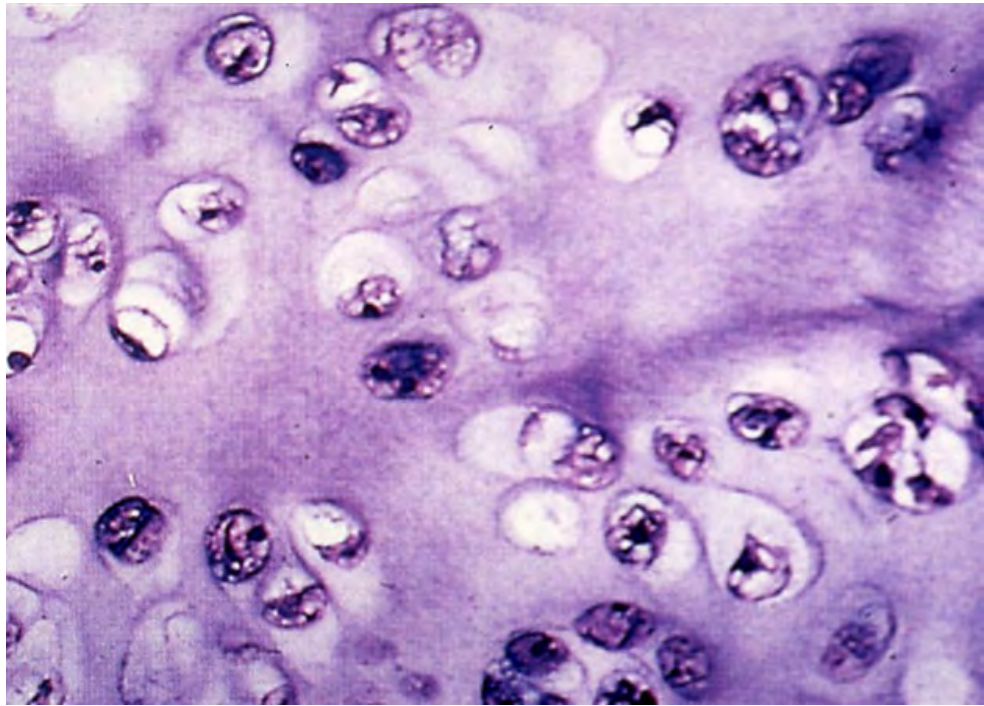
X-ray: Popcorn-like calcifications

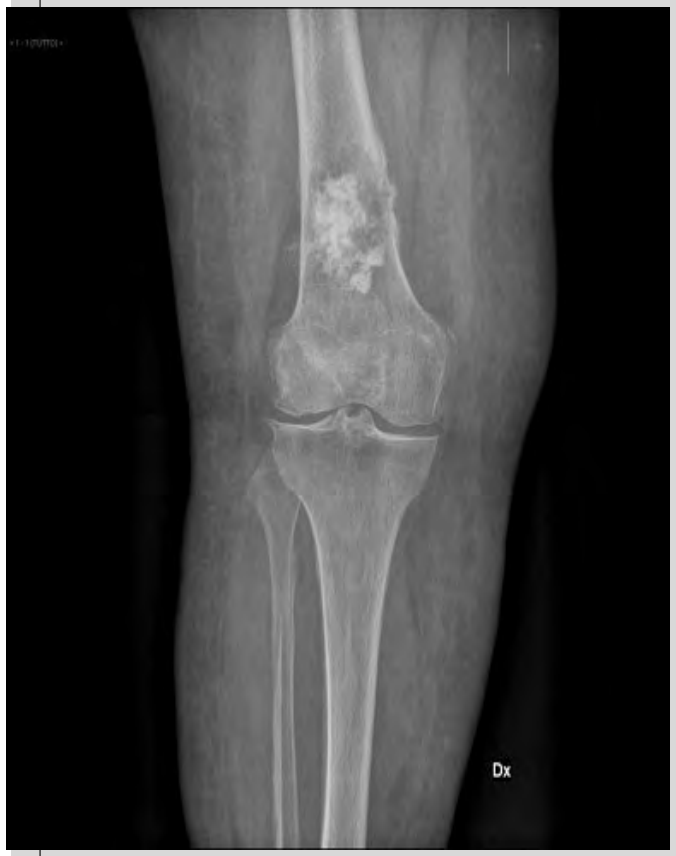
MRI: Defines extent of medullary and soft tissue involvement

CT: Essential for evaluating bone destruction





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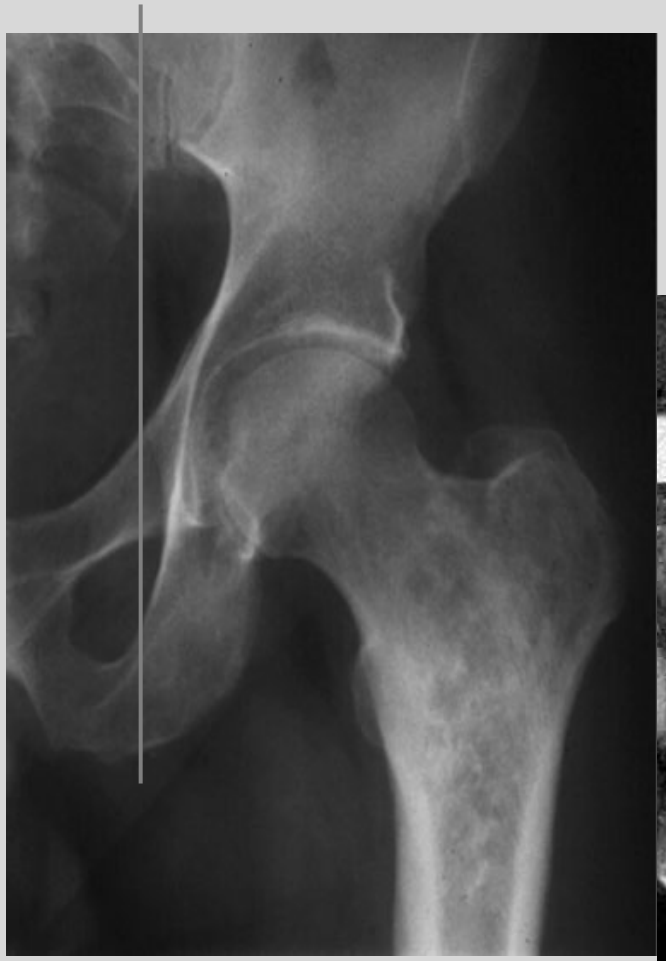
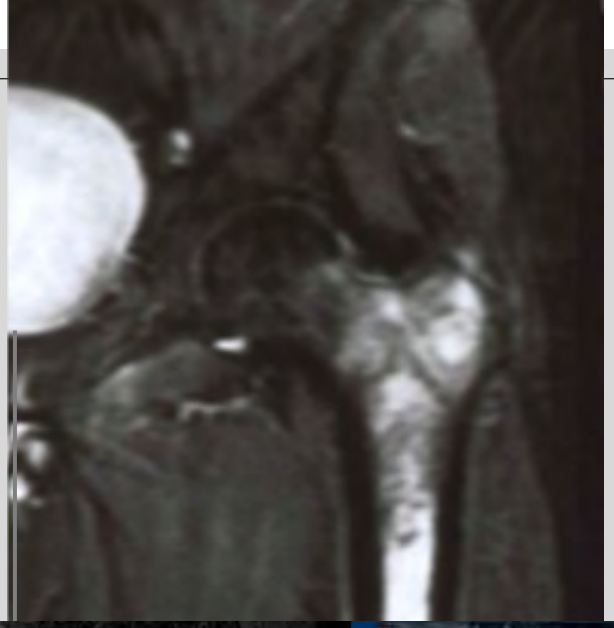
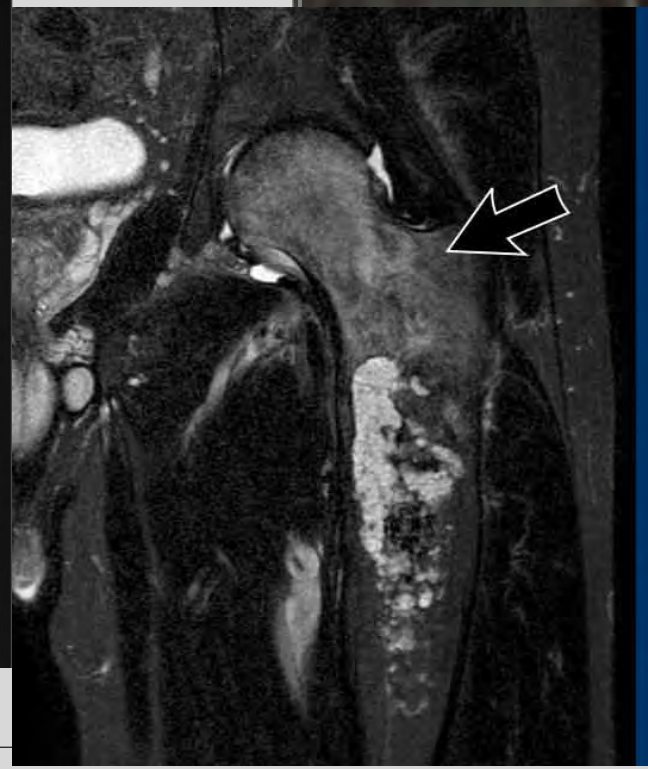
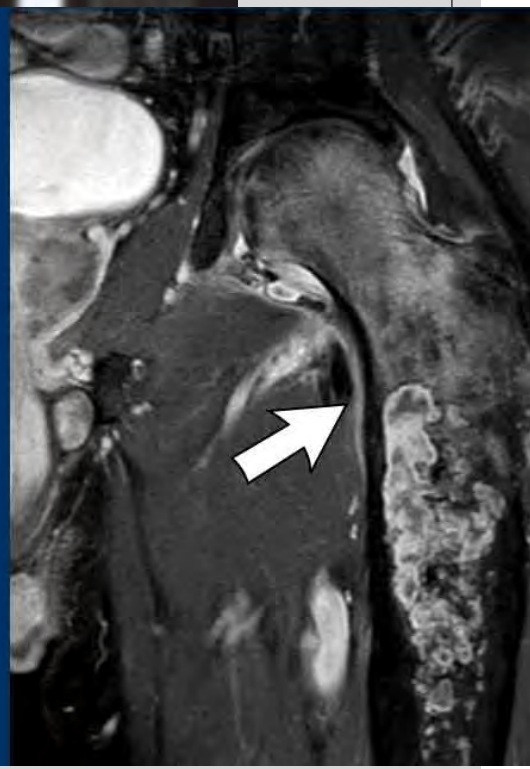








Chondrosarcoma – Treatment Modalities

Surgical Resection

Wide en bloc resection is the primary treatment

Margins are critical due to local aggressiveness

Chemotherapy

Not effective in conventional chondrosarcoma

Dedifferentiated Chondrosarcoma: Can respond to chemotherapy

Radiotherapy

Limited role due to poor radiosensitivity; reserved for inoperable cases

Ewing's Sarcoma – Overview

Epidemiology

- Aggressive tumor primarily affecting children and adolescents
- Common sites: pelvis, femur, ribs

Genetic Mutations

- t translocation leads to EWSR1-FLI1 fusion protein

Clinical Presentation

- Pain and swelling, often with systemic symptoms
- Commonly involves diaphysis of long bones

Ewing's Sarcoma – Staging & Workup

Staging

- Enneking: Similar to osteosarcoma, involving tumor size, lymph node status, and metastasis
- Localized: Confined to the primary site
- Metastatic: Involves lungs, bones, or bone marrow

Workup

- Imaging: X-ray , MRI for soft tissue mass, PET/CT for metastasis
- Bone Marrow Biopsy: To check for marrow involvement

Ewing's Sarcoma – Histology & Imaging

Histology

Small round blue cells with scant cytoplasm

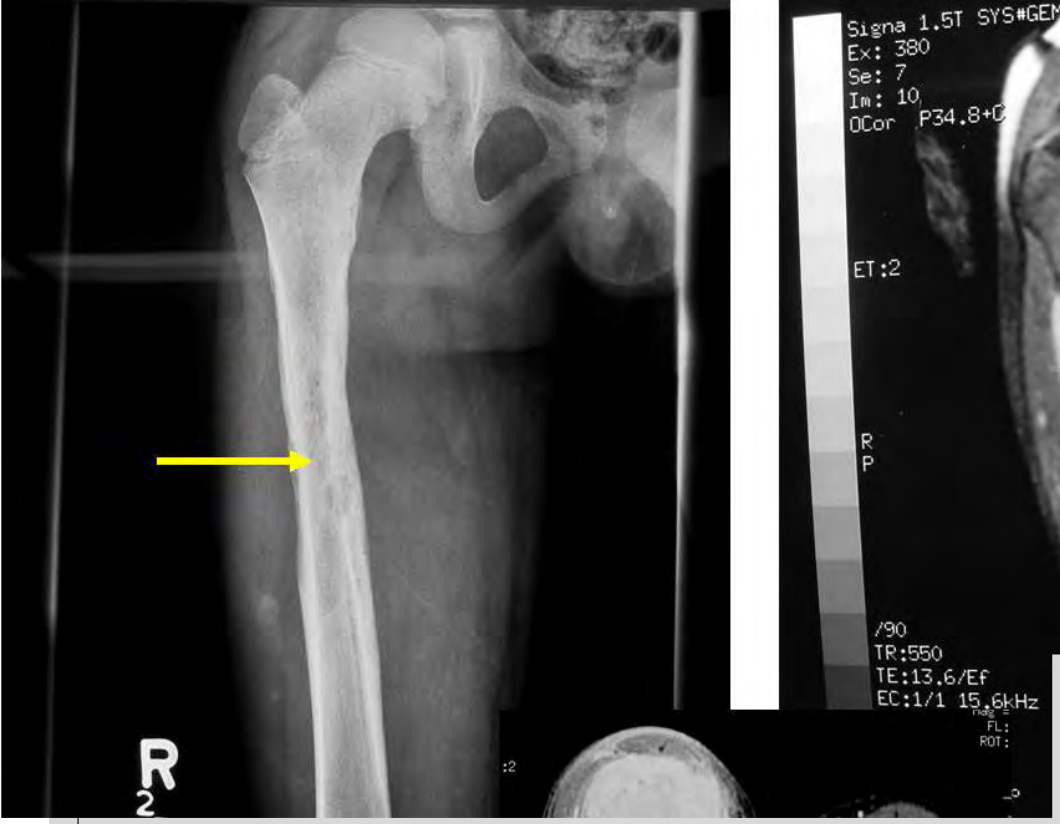
Immunohistochemistry: Positive for CD99

Imaging Findings

X-ray: Onion-skinning periosteal reaction

MRI: Large soft tissue component

PET/CT: For systemic disease spread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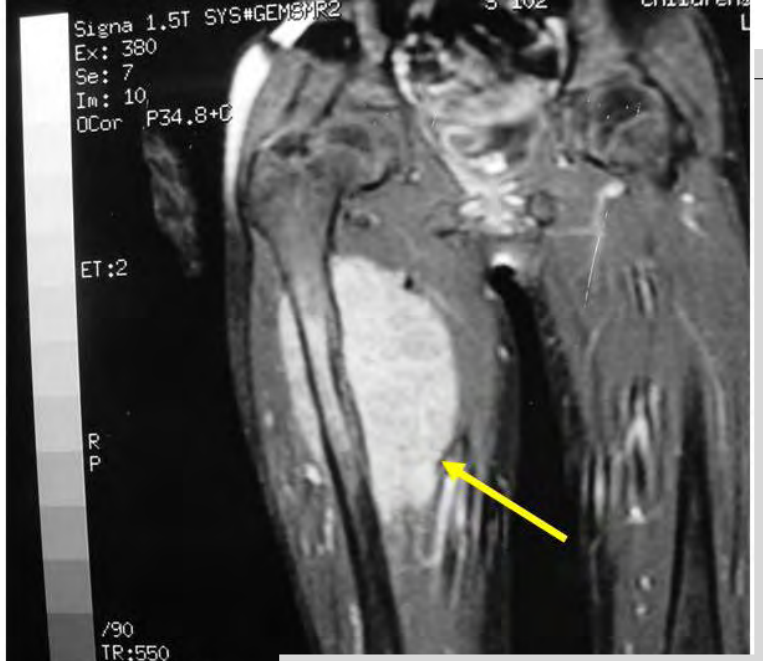
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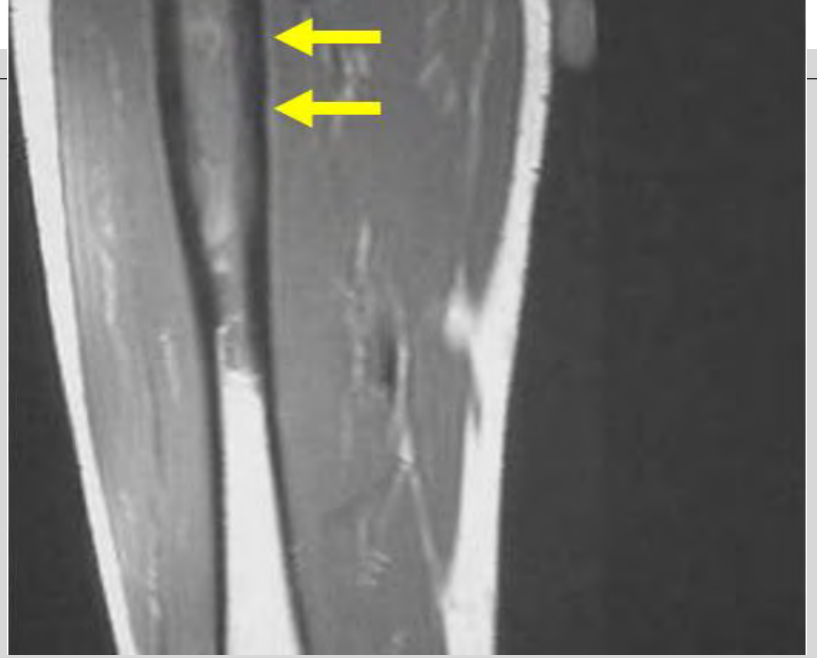
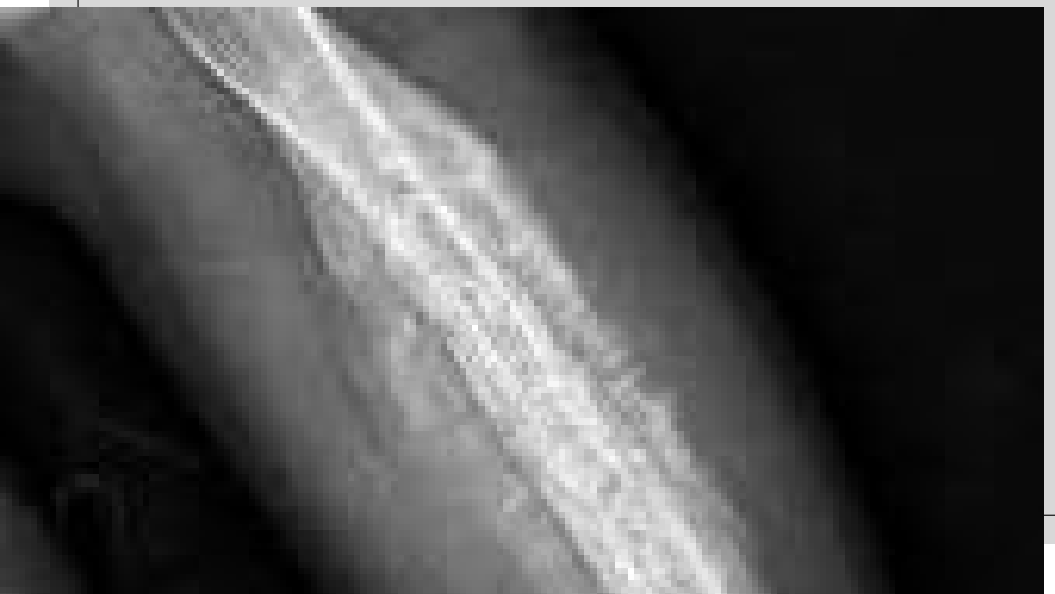
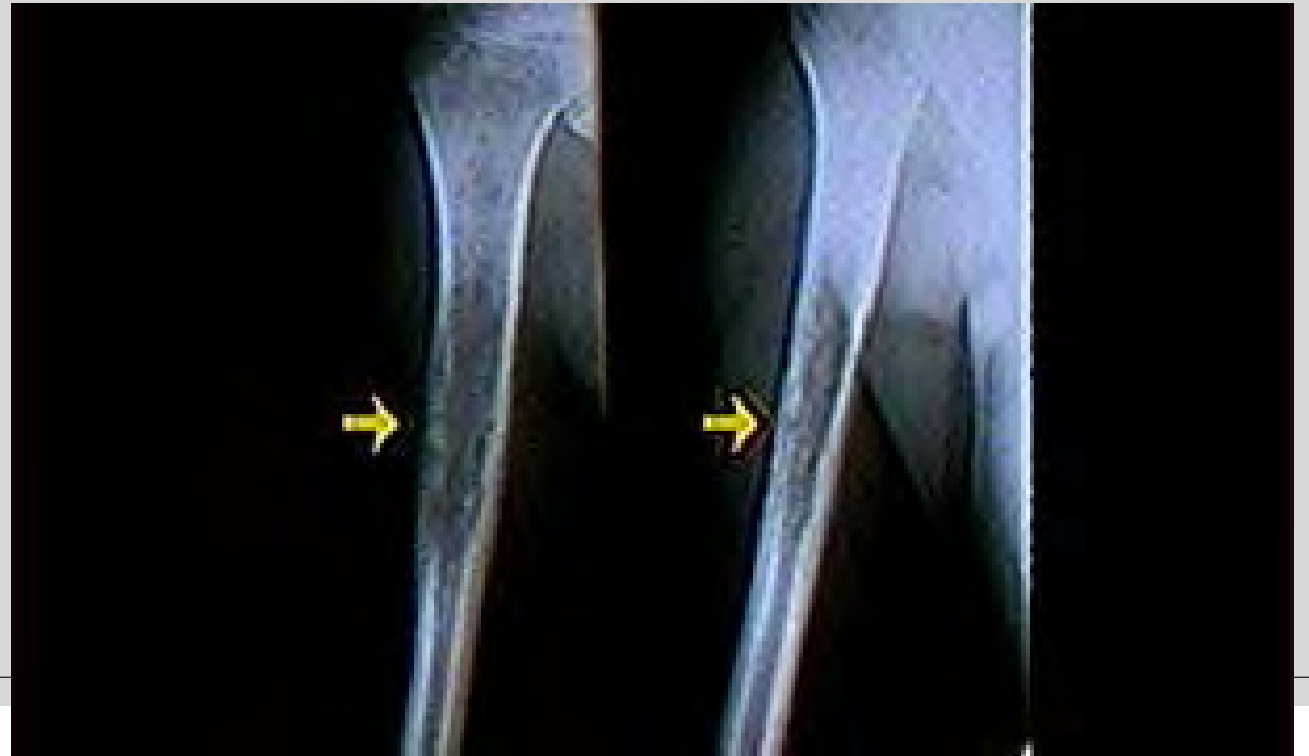
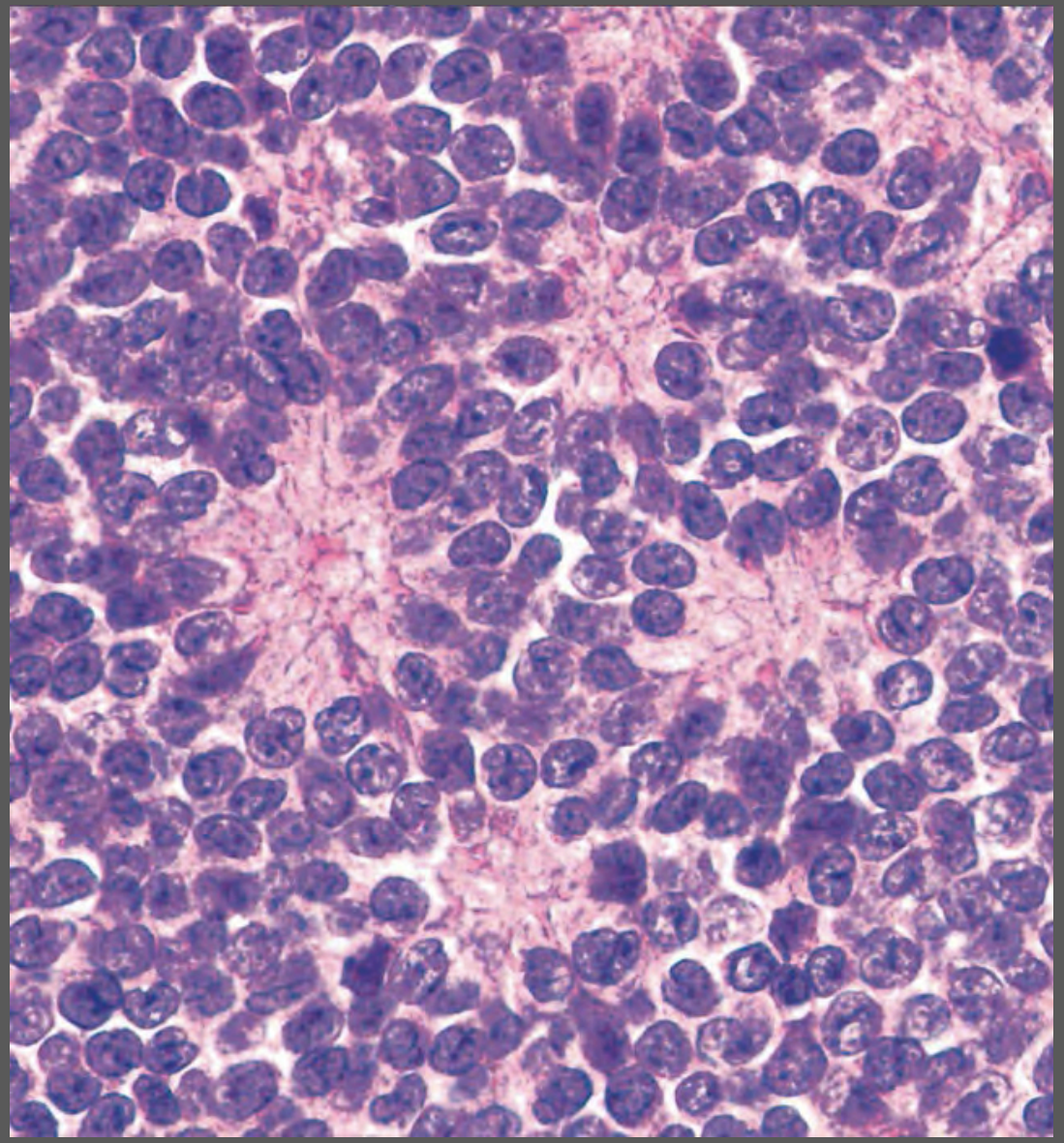
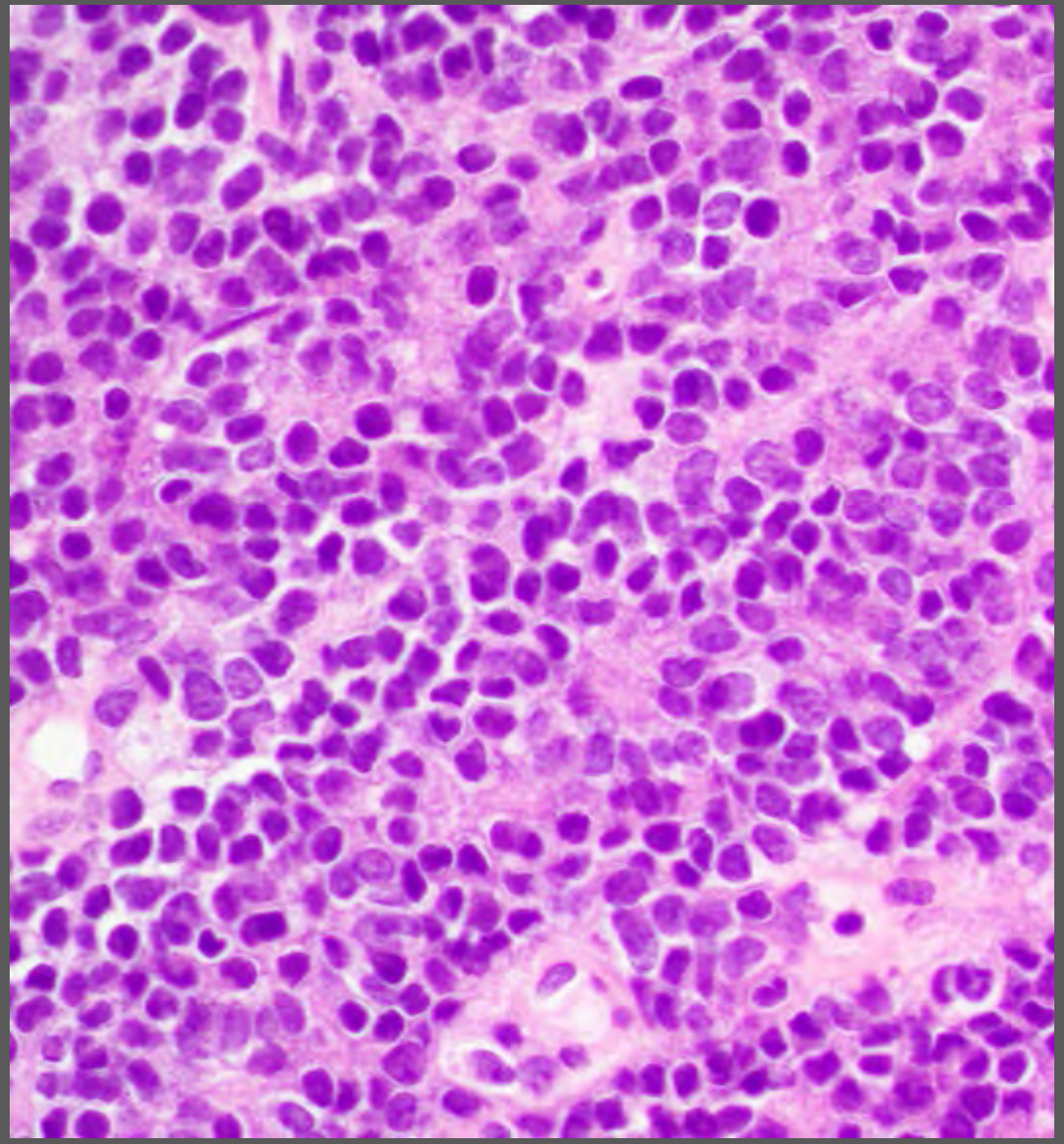






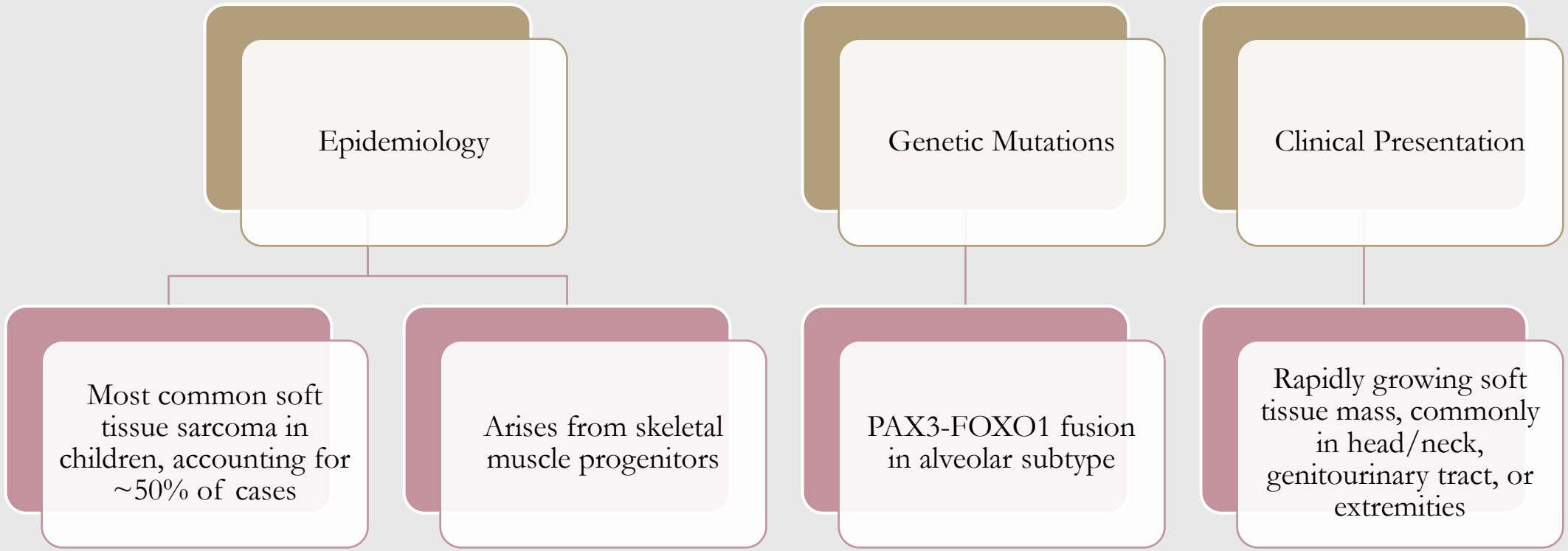


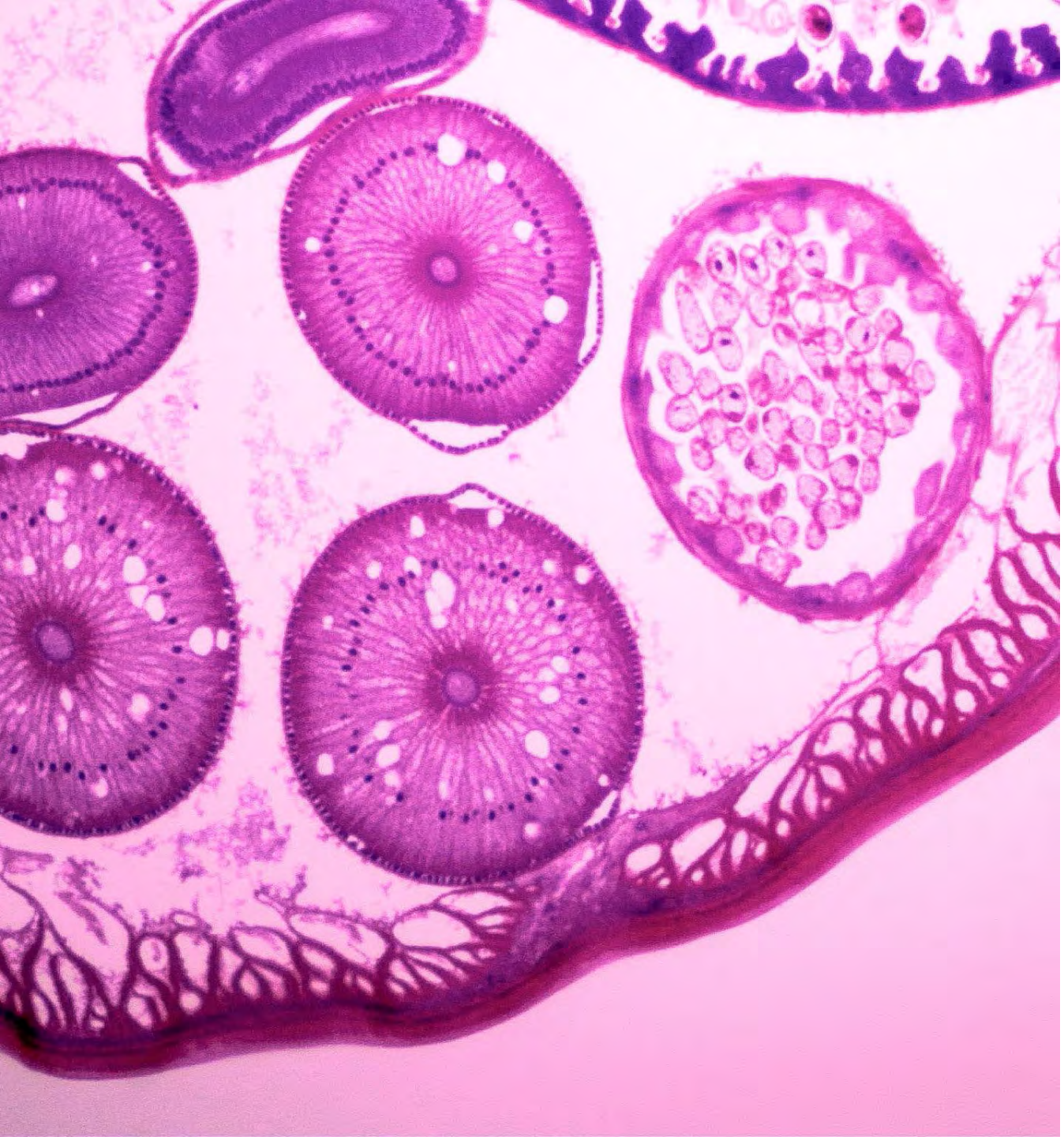


Ewing's Sarcoma – Treatment Modalities

Surgical Resection	Limb-sparing surgery when possible, with negative margins
Chemotherapy	VAC/IE regimen Neoadjuvant and adjuvant chemotherapy
Radiotherapy	Crucial for localized tumors, particularly when surgery is not possible High doses for localized control

Rhabdomyosarcoma – Overview





Rhabdomyosarcoma – Staging & Workup

- Workup
  - Imaging: MRI for soft tissue involvement, CT for distant metastasis
  - Bone Marrow Biopsy: Mandatory in suspected metastatic cases

TNM

Tumor (T)	T1	Tumor confined to site of origin
	T1a	< 5 cm
	T1b	≥5 cm
	T2	Tumor extending into surrounding tissue
	T2a	< 5 cm
	T2b	≥5 cm
Node (N)	N0	No lymph node involvement
	N1	Clinical involvement of lymph nodes
	NX	Unknown lymph node status
Metastasis (M)	M0	No metastasis
	M1	Metastasis present

PRE-TREATMENT STAGING

Stage	Sites	T	Size	N	M
1	Orbit, head/neck (no parameningeal involvement), genitourinary (no bladder/prostate involvement)	T1 or T2	< 5 cm or ≥5 cm	N0 or N1 or Nx	M0
2	Bladder/prostate, extremity, cranial, head/neck parameningeal, other (trunk, retroperitoneum, thorax)	T1 or T2	< 5 cm	N0 or Nx	M0
3	Bladder/prostate, extremity, cranial, head/neck parameningeal, other (trunk, retroperitoneum, thorax)	T1 or T2	< 5 cm	N1	M0
			≥5 cm	N0 or N1 or Nx	M0
4	Any	T1 or T2	< 5 cm or ≥5 cm	N0 or N1	M1

Post-surgical staging

- The Intergroup Rhabdomyosarcoma Study Group (IRSG) postsurgical pathologic grouping is as follows:
- Group I - Localized disease, completely resected (clear margins, negative regional nodes)
- Group II - Microscopic disease remaining (at margins or in regional nodes)
- Group III - Incomplete resection or biopsy findings indicating gross residual disease (locally or in regional nodes)
- Group IV - Distant metastases present at onset

Several studies have suggested that a cutoff tumor size of 5 cm may not be the best tool for staging pediatric RMS. Owing to variations in the body surface area (BSA) of children, the tumor size in relation to the patient's BSA and volumetric measurements may be more useful in staging.

Rhabdomyosarcoma – Histology & Imaging

Histology

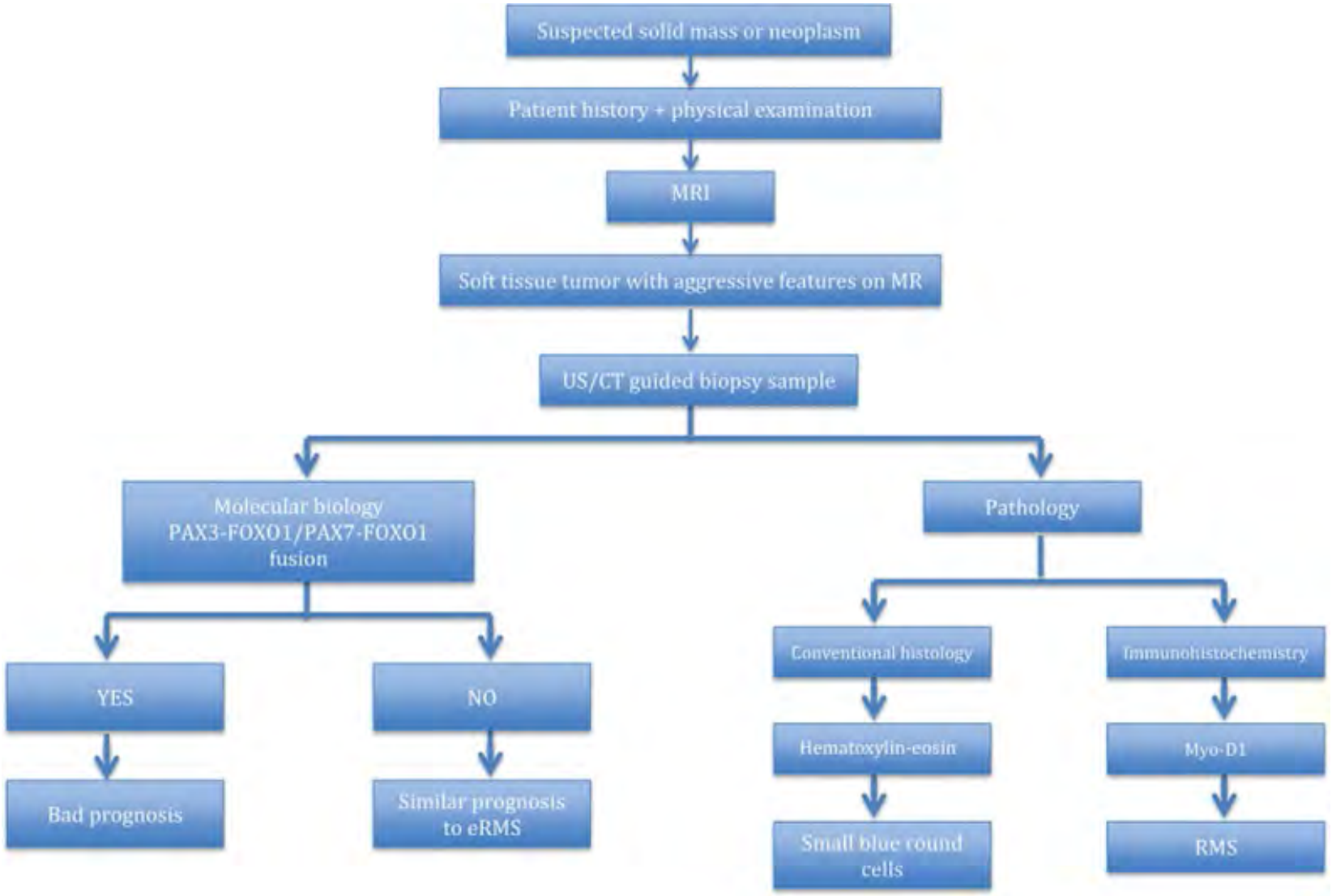
Alveolar Type: PAX3-FOXO1 fusion, sheets of small round blue cells

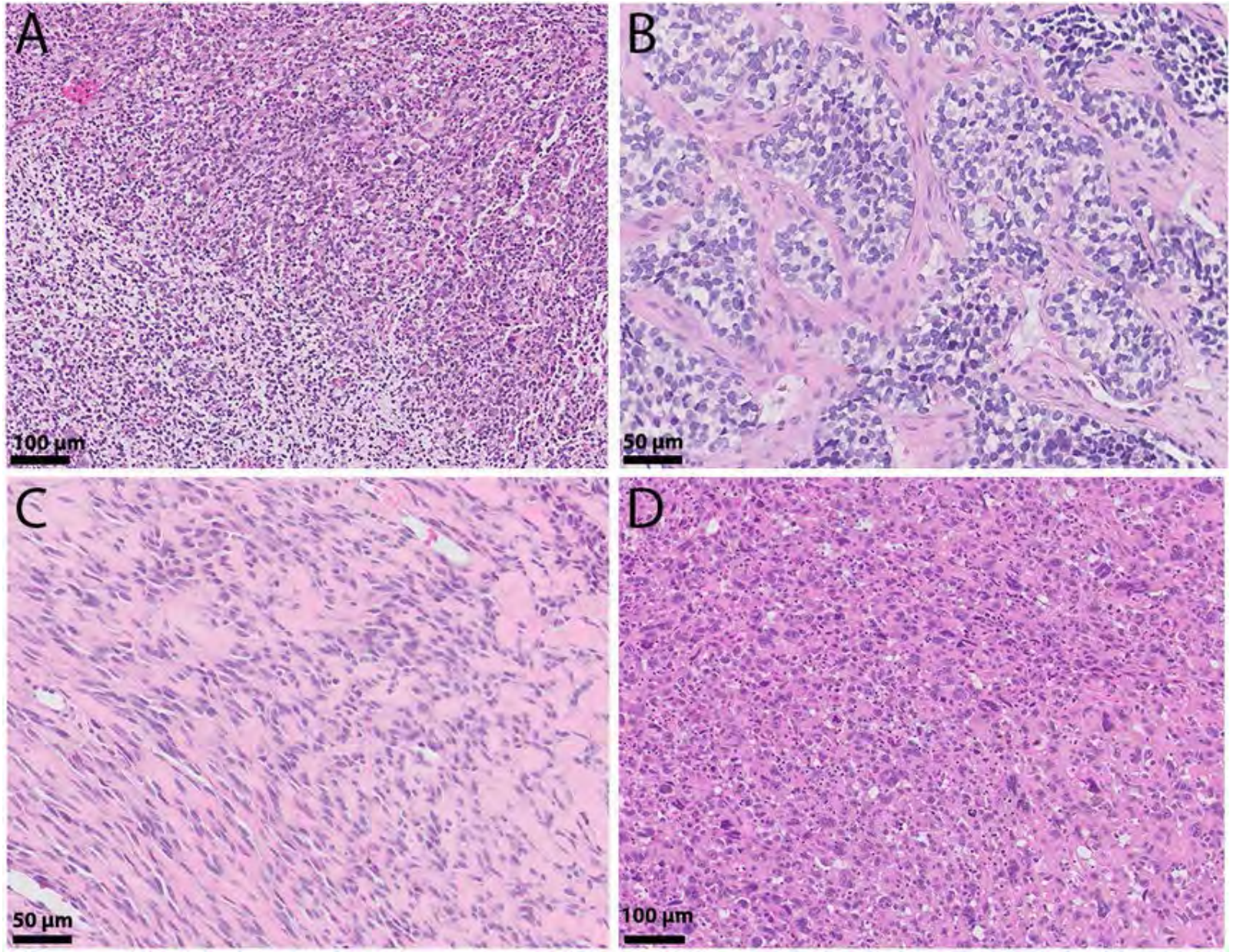
Embryonal Type: Spindle cells, less aggressive than alveolar

Imaging Findings

MRI: Best for local soft tissue involvement

CT: To evaluate distant spread, especially in lungs


Suspected solid mass or neoplasm
Patient history + physical examination
MRI
Soft tissue tumor with aggressive features on MR
US/CT guided biopsy sample
Molecular biology
PAX3-FOXO1/PAX7-FOXO1
fusion
YES
Bad prognosis
NO
Similar prognosis
to eRMS
Pathology
Conventional histology
Hematoxylin-eosin
Small blue round
cells
Immunohistochemistry
Myo-D1
RMS



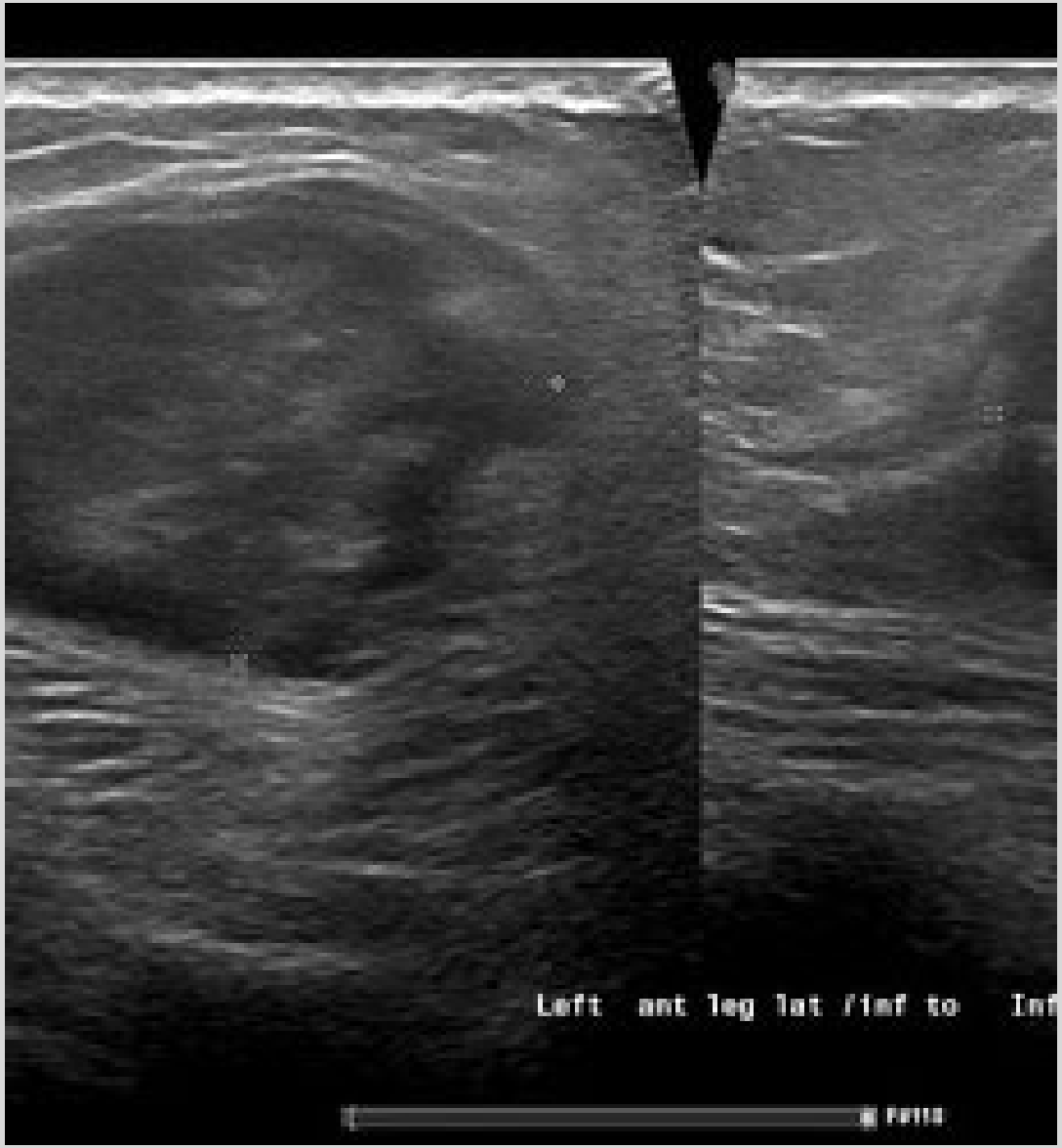
Histologic landscape of rhabdomyosarcoma.

(A) Embryonal rhabdomyosarcoma composed of primitive round and spindled cells reminiscent of skeletal muscle cells .

(B) Alveolar rhabdomyosarcoma: Nests composed of hyperchromatic round cells intervened by fibrous septae, giving it an alveolar appearance.

(C) Spindle/sclerosing rhabdomyosarcoma shows tumor cells arranged in cords that are set in a densely hyalinized eosinophilic background stroma.

(D) Pleomorphic rhabdomyosarcoma presents with epithelioid tumors exhibiting significant nuclear pleomorphism with occasional cross striations and multinucleated cells (←).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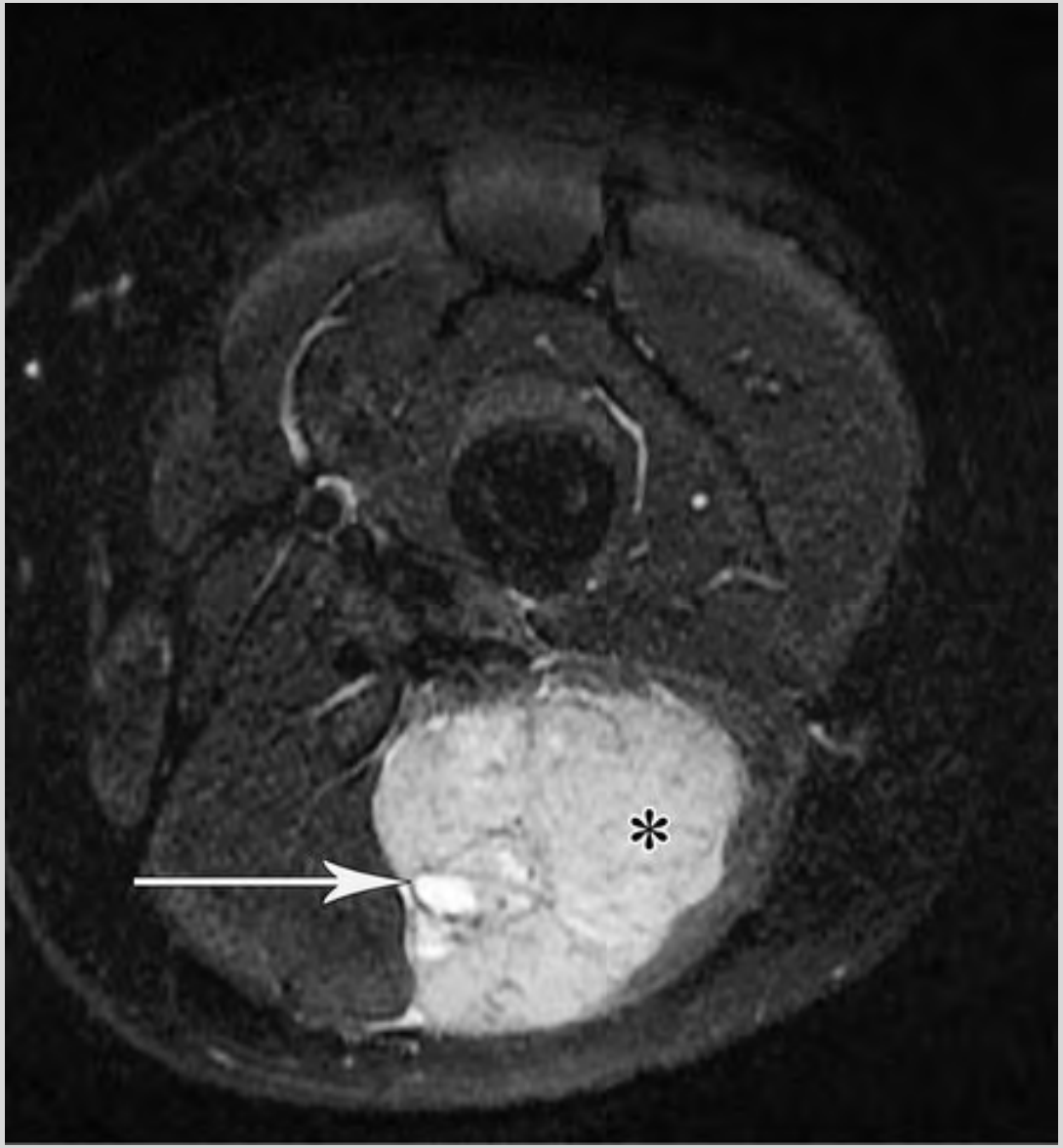

Rhabdomyosarcoma – Treatment Modalities

Surgical Resection

Complete resection with negative margins

Chemotherapy

VAC Regimen: Vincristine, Actinomycin, Cyclophosphamide

Used in both alveolar and embryonal subtypes

Radiotherapy

Important for residual disease after surgery or in unresectable tumors

Multidisciplinary Approach – Tumor Board

- **Collaborative Decision Making**:
  - **Oncologists**: Lead systemic therapy decisions.
  - **Surgeons**: Plan and perform tumor resections.
  - **Radiologists**: Provide imaging interpretation for staging and planning.
  - **Pathologists**: Confirm diagnosis through biopsy analysis.
  - **Rehabilitation Specialists**: Focus on recovery and quality of life.

Summary of Clinical Decision Pathways

- **Key Decision Points**:
  - **Limb-sparing surgery** vs. **amputation**.
  - **Neoadjuvant vs. adjuvant chemotherapy**.
  - Multimodal therapy: Integrating surgery, chemotherapy, and radiotherapy.
  - **Follow-up and surveillance**: Imaging to detect recurrence (e.g., X-ray, PET).

The Importance of Biopsy

- **Biopsies for Musculoskeletal Tumors**
- **Core Needle Biopsy**:
  - Preferred method, minimally invasive.
  - Used to extract small tissue samples for diagnosis.
- **Incisional Biopsy**:
  - Small portion of the tumor is surgically removed.
  - Used when core biopsy is insufficient.
- **Excisional Biopsy**:
  - Complete tumor removal, usually for small, accessible tumors.
- **Key Considerations**:
  - Biopsy track should be planned with the surgical team to prevent tumor seeding and compromise of future surgical approaches.
  - Imaging guidance (CT, MRI) is often used for deeper tumors.
  - Essential for **accurate diagnosis** and treatment planning.

Conclusion

- Key Takeaways
  - Multidisciplinary approach is critical for managing musculoskeletal tumors
  - Advances in genetics, imaging, and treatment modalities are improving survival outcomes
  - Collaboration across surgical, medical, and radiation oncology is essential for optimal care