XXXII International Academy of Pathology Congress
14-18 October 2018
Amman, Jordan

PITFALLS IN DIAGNOSIS OF BONE LESIONS

Fouad Al Dayel, MD, FRCPA, FRCPath
Professor and Chairman
Department of Pathology and Laboratory Medicine
King Faisal Specialist Hospital and Research Centre
Riyadh, Saudi Arabia

Location

- Location and age of patient most important parameters in classifying a primary bone tumor.
- Location is determined from plain radiographs.

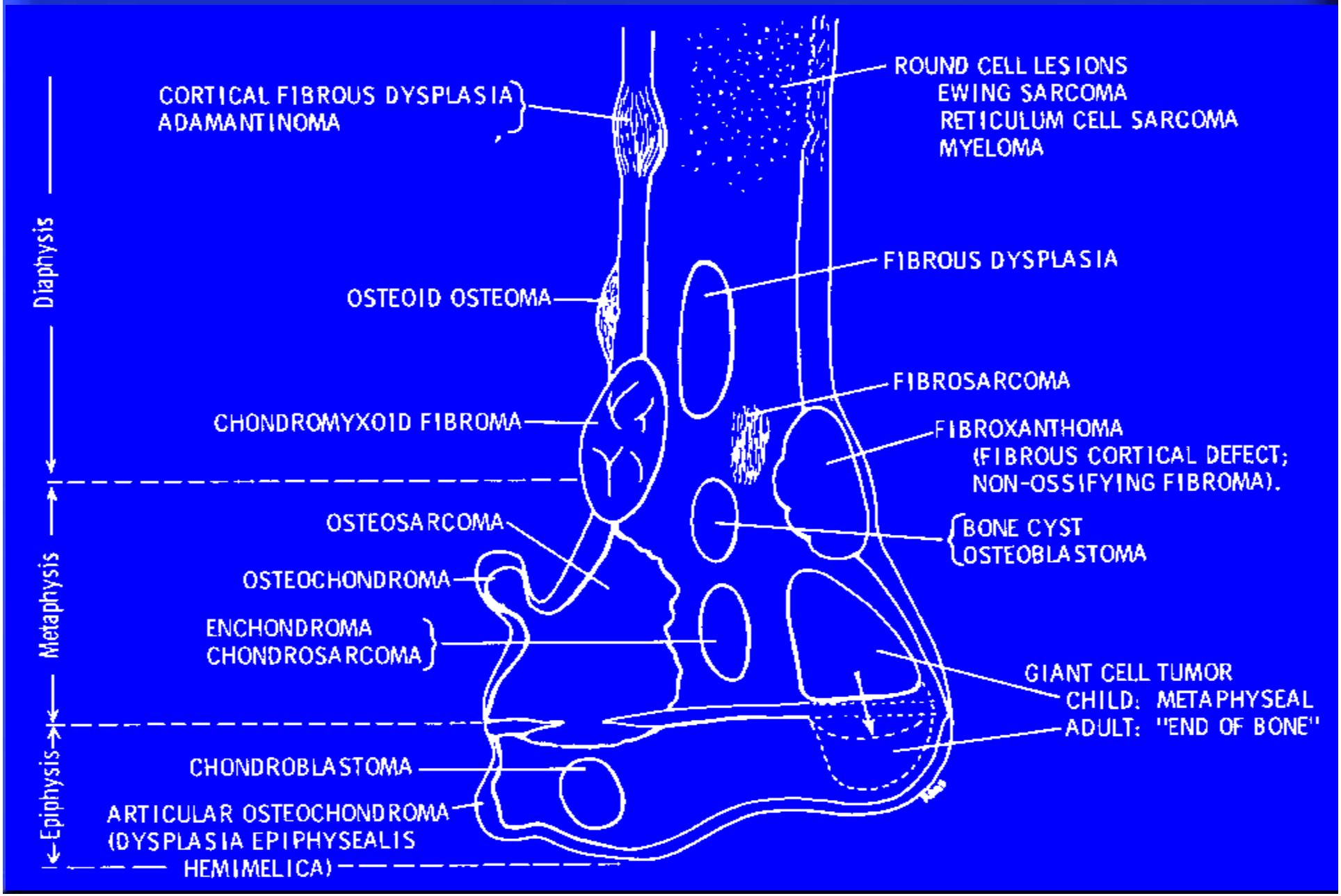
Bone Tumors

	Benign	Malignant	Other
Birth – 5 yrs	Eosinophilic Granuloma	Leukemia	Osteomyelitis
	Unicameral Bone Cyst	Metastatic	Healing/stress fracture
		Neuroblastoma	
6-18 yrs	Unicameral Bone Cyst	Ewing's Sarcoma	Osteomyelitis
	Aneurysmal Bone Cyst	Osteosarcoma	Fibrous Dysplasia
	Nonossifying Fibroma		Osteofibrous
	Eosinophilic Granuloma		
	Enchondroma		
	Chondroblastoma		
	Chondromyxoidfibroma		
	Osteoblastoma		

Bone Tumors

	Benign	Malignant	Other
19-40 yrs	Giant Cell Tumor	Ewing's Sarcoma	
	Eosinophilic granuloma		
40 yrs	Metastases (lung, breast, prostate, renal, thyroid,colon)	Multiple Myeloma Lymphoma	Hyperparathyroidism Osteomyelitis
		Osteosarcoma	Paget's
		Chondrosarcoma	
		Fibrosarcoma/	
		Malignant Fibrous	
		Histiocytoma	

Location


CORTICAL FIBROUS DYSPLASIA
ADAMANTINOMA
ROUND CELL LESIONS
EWING SARCOMA
RETICULUM CELL SARCOMA
MYELOMA
FIBROUS DYSPLASIA
OSTEOID OSTEOMA
FIBROSARCOMA
CHONDROMYXOID FIBROMA
FIBROXANTHOMA
(FIBROUS CORTICAL DEFECT;
NON-OSSIFYING FIBROMA).
OSTEOSARCOMA
BONE CYST
OSTEOBLASTOMA
OSTEOCHONDROMA
ENCHONDROMA
CHONDROSARCOMA
GIANT CELL TUMOR
CHILD: METAPHYSEAL
ADULT: "END OF BONE"
CHONDROBLASTOMA
ARTICULAR OSTEOCHONDROMA
(DYSPLASIA EPIPHYSEALIS
HEMIMELICA)
Diaphysis
Metaphysis
Epiphysis

Multiple vs Solitary

- Multiple
  - metastatic
  - congenital
    - fibrous dysplasia
  - acquired
    - Paget
- Solitary
  - metastatic
  - primary bone tumor, malignant or benign

Multiple

- 50+ y/o
  - known malignancy?
  - myeloma, get SPEP
  - otherwise, do metastatic work-up
- Child to early adult
  - known malignancy?
  - EG?
  - polyostotic fibrous dysplasia?
  - otherwise, do metastatic work-up

Conditions that simulate primary bone tumors

- Metastatic carcinoma/sarcomas
- Fibrous and fibro-osseous proliferations of bone
- Cystic lesions of bone
- Non neoplastic osteoid forming lesion (pseudosarcomas)

Metastasis to Bone

"herald" metastasis:

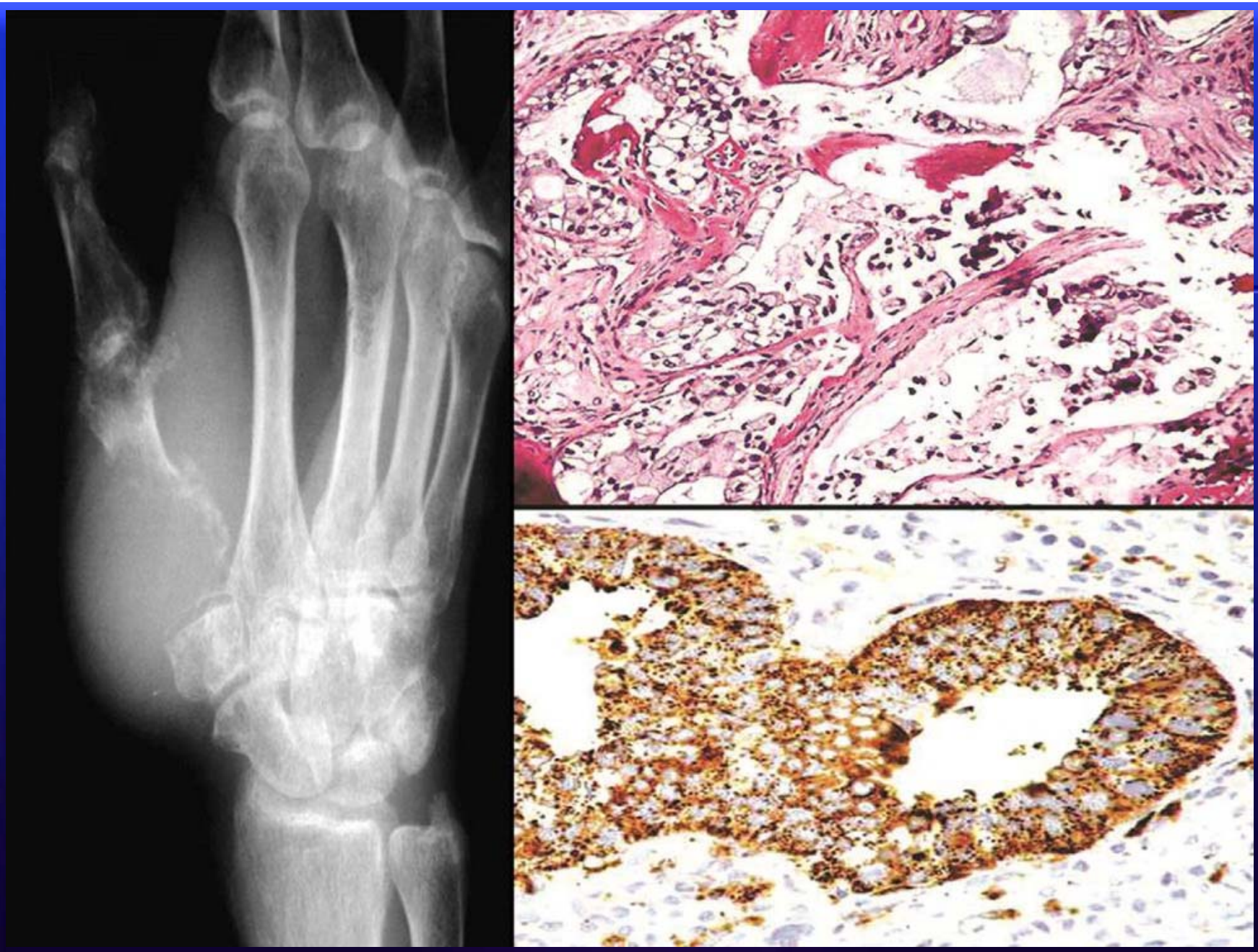
Solitary bone lesion as initial manifestation of internal malignancy.

- Metastasis grow faster than primary
- Additional metastasis within few weeks
- Clinical history is extremely important

Metastasis to Bone

Metastasis is more common than primary in bone, mainly adenocarcinomas

- Breast - osteoblastic
- Prostate- osteoblastic
- Lung - cytic, small bones of hands
- Thyroid - latent
- Kidney - lytic
- Unknown origin



Seminars in Diagnostic Pathology 31 (2014), 53-65

Metastasis to Bone

- Small cell neoplasms (adults)
  - Small cell carcinoma
    - DD: Ewing sarcoma
      - Small cell osteosarcoma
      - Lymphoma
      - Mesenchymal chondrosarcoma

Markers for small cell carcinoma:
Keratin +ve, TTF1 +ve, FLI-1(±), CD99 –ve, chromogranin +, synaptophysin +, Ki-67 high

Metastasis to Bone

- Small cell neoplasm (pediatric)
  - Neuroblastoma
    - younger age group (25 % congenital and 90% by age of 5 years)
    - neuropil, Homer Wright Rosettes, ganglion cells
    - positive for NSE, PGP 9.5, neurofilament, chromogranin
    - negative for CD99
- Other pediatric tumors with bone metastasis
  - RMS
  - Retinoblastoma
  - Wilm's tumor

Metastasis to Bone

Undifferentiated large cell tumor

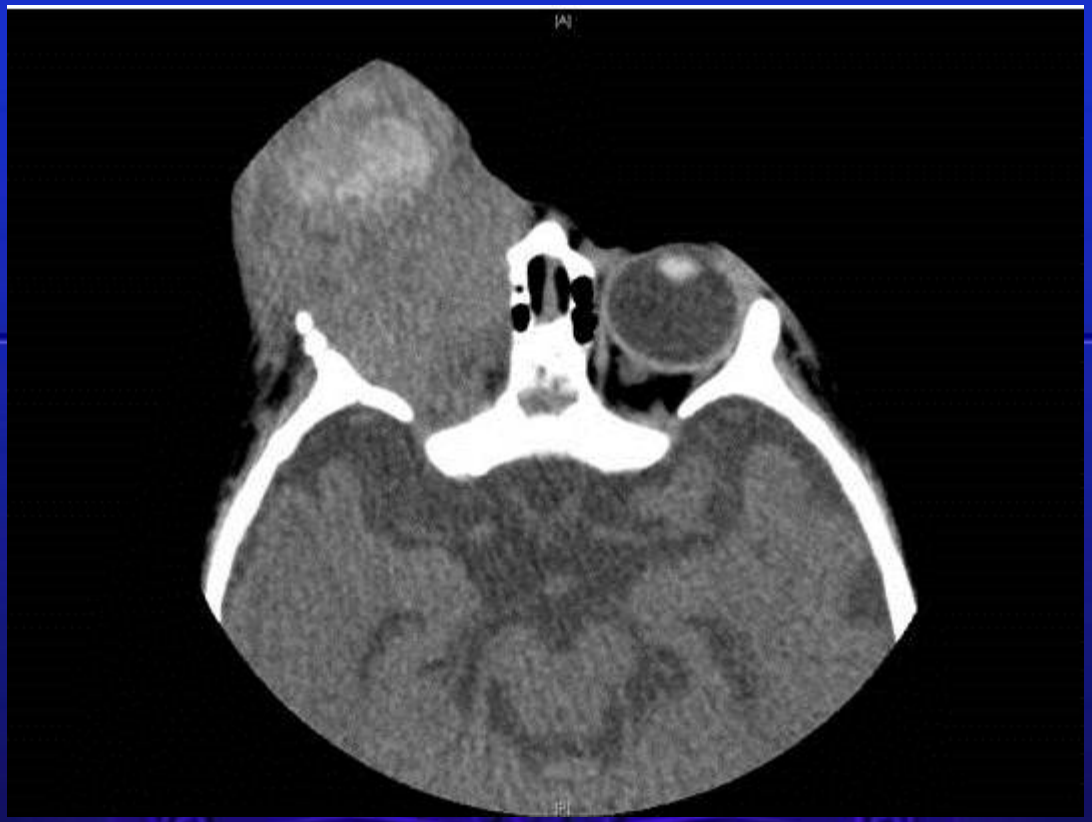
- lung carcinoma
- kidney carcinoma
- malignant melanoma

DD:

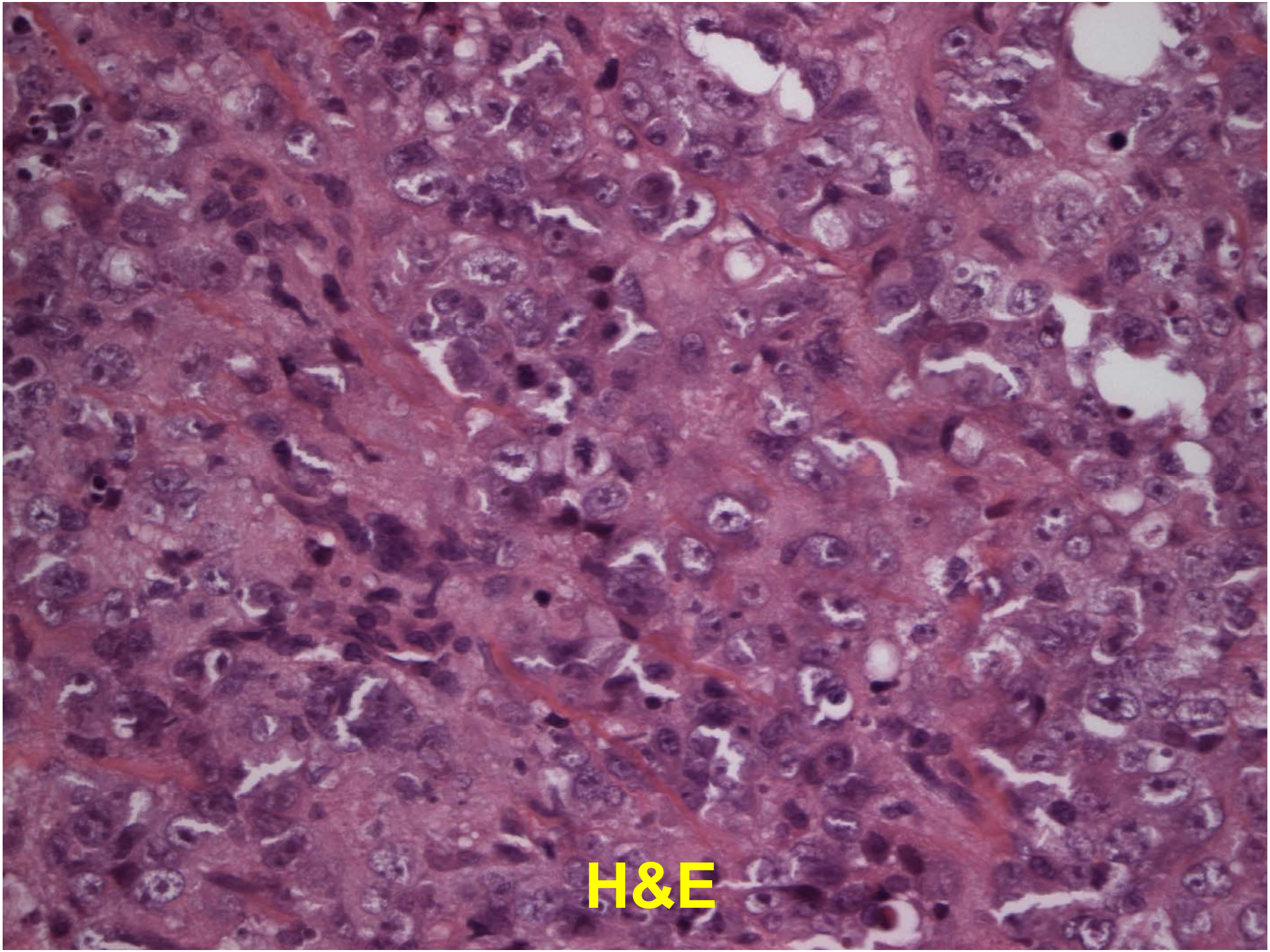
- epithelioid sarcoma (keratin +, EMA+, CD34+ [50%] 1N11 –ve)
- adamantinoma (D2-40 positive)
- epithelioid hemangioendothelioma
- epithelioid angiosarcoma (CD31+, CD34+, FLI-1+, ERG+)
- Epithelioid leiomyosarcoma
- chordoma (brachyury+, EM +, CK8+, CK19+, S100 protein +)
- epithelioid osteoblastoma

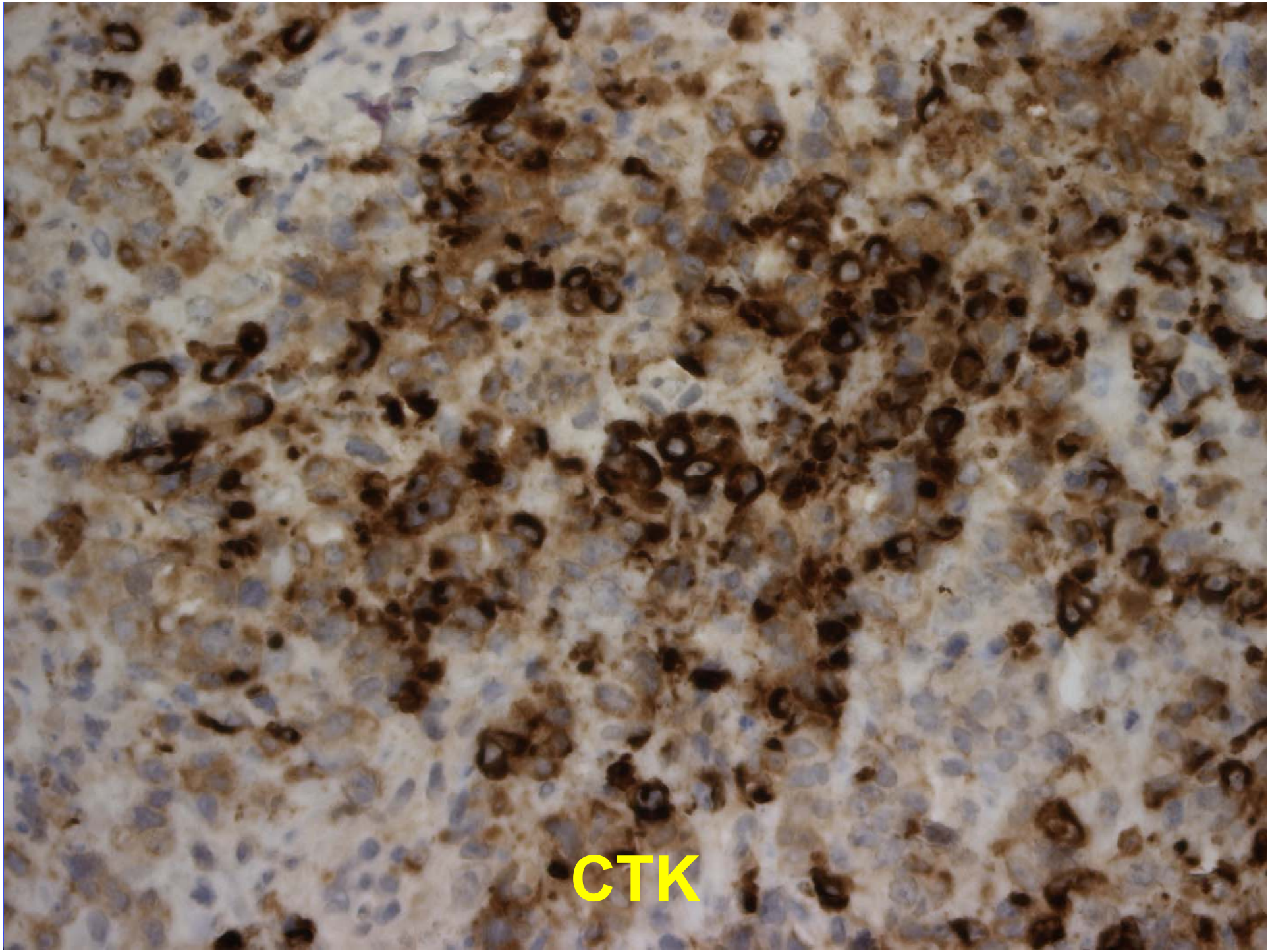
- **Clinical History:**

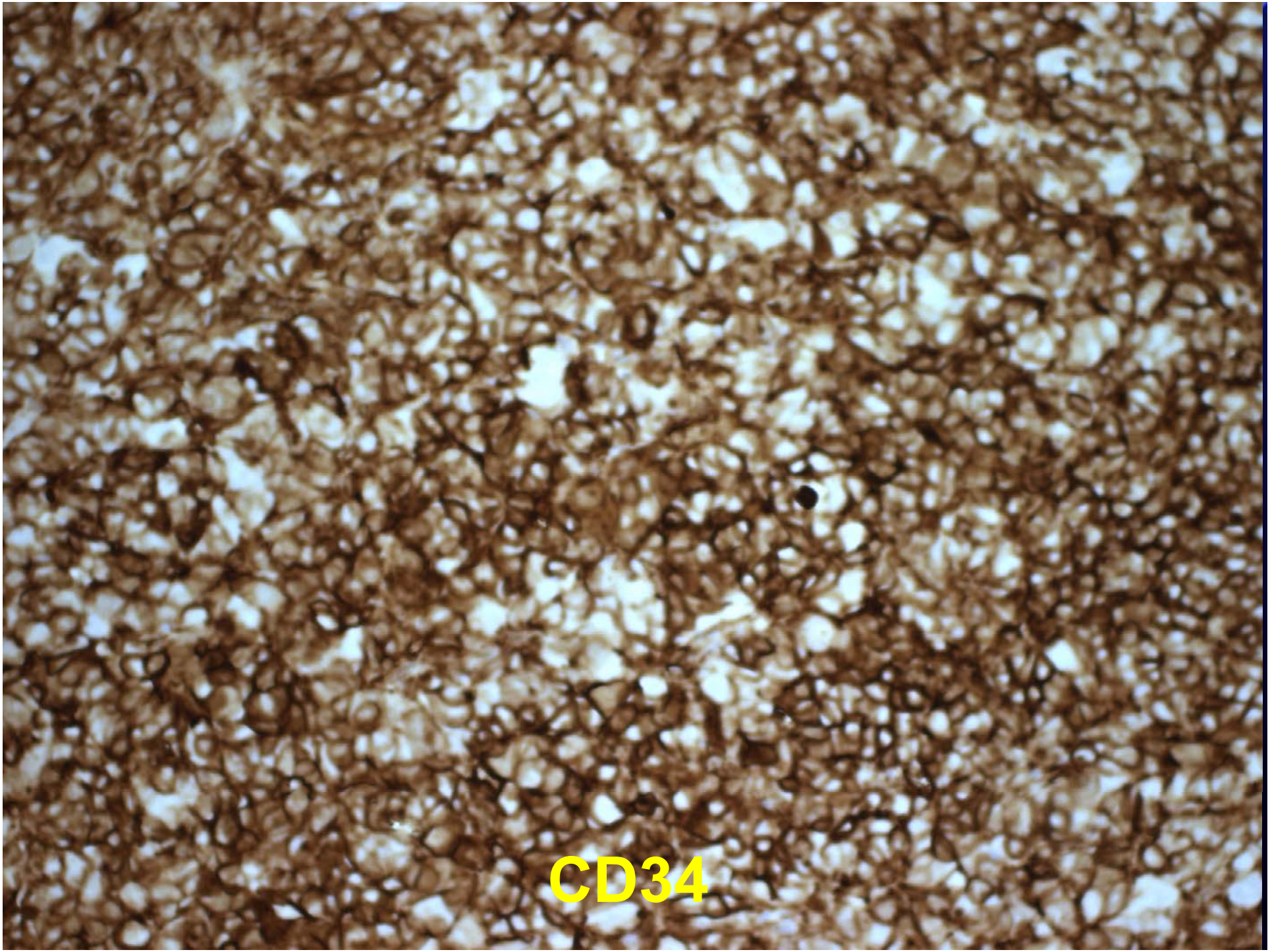
  Five months old referred from outside hospital with right eye swelling and proptosis, irritability and pain.



There is massive orbital right side tumour with severe and actual completely extra-orbital ocular displacement and distortion with invasion of the globe posterior sclera. Without comparison to the previous examination, the interval post radiation changes are not evaluated.


H&E


CTK


CD34

Diagnosis

- Epithelioid Sarcoma

Differential Diagnosis

Granulomatous Processes

- Particularly granuloma annulare
- Lacks infiltrative or invasion growth
- Lacks coagulative tumor cell necrosis
- Negative for keratin and EMA
- Retained nuclear INI1 expression

Squamous Cell Carcinoma

- Overlying in situ component may be identifiable
- Prior clinical history may be present
- Usually more pleomorphic than ES
- CK5/6(+) and p63(+)
- Negative for CD34
- Retained nuclear INI1 expression

Differential Diagnosis

Extrarenal Rhabdoid Tumor

- Can show significant morphologic overlap with proximal-type ES
- Most common in infants and young children
- Keratin(+) but less prominent than in ES
- Consistent loss of nuclear INI1 expression
- Mutation of *SMARCB1* gene

Melanoma

- Junctional component or prior clinical history may be present
- Usually larger, more pleomorphic cells than classic ES
- S100 protein(+), SOX10(+); variable HMB45(+) or MART-1(+)
- Retained nuclear INI1 expression

Differential Diagnosis

Epithelioid Angiosarcoma

- Can show significant morphologic overlap with proximal-type ES
- Foci of vasoformation often present at least focally
- CD31(+), CD34(+), FLI1(+)
- May be keratin (+), though usually not diffuse
- Retained nuclear INI1 expression

Pseudomyogenic (Epithelioid Sarcoma-Like) Hemangioendothelioma

- Commonly involves multiple tissue planes
- Predominantly spindled morphology
- Neutrophilic infiltrate characteristic
- Keratin (+), CD31(+)
- Negative for CD34
- Retained nuclear INI1 expression

Differential Diagnosis

Malignant Myoepithelioma (Myoepithelial Carcinoma)

- Can show significant morphologic overlap with proximal-type ES
- Myxoid stroma common
- Keratin (+), EMA (+), S100 protein (+)
- Loss of nuclear INI1 expression in subset of cases

Cellular Fibrous Histiocytoma (Dermatofibroma)

- Can show morphologic overlap with predominantly spindled forms of ES
- Negative for keratin
- Retained nuclear INI1 expression

Sarcomas with cytokeratin expression

- **True** (epithelial differentiation)
  - synovial sarcoma (CK7, CK19)
  - epithelioid sarcoma (CK5, CK6)

- **Anomalous** (no epithelial differentiation)
  - sarcomas with epithelioid morphology (epithelioid OS, epithelioid leiomysarcoma, epithelioid angiosarcoma, etc.)
  - small round cell tumors
    - ❖ Ewing's sarcoma
    - ❖ RMS
    - ❖ Wilms
    - ❖ DSRCT

- Other sarcomas: e.g. chondrosarcomas

Metastasis to Bone

Malignant spindle cell and pleomorphic tumors

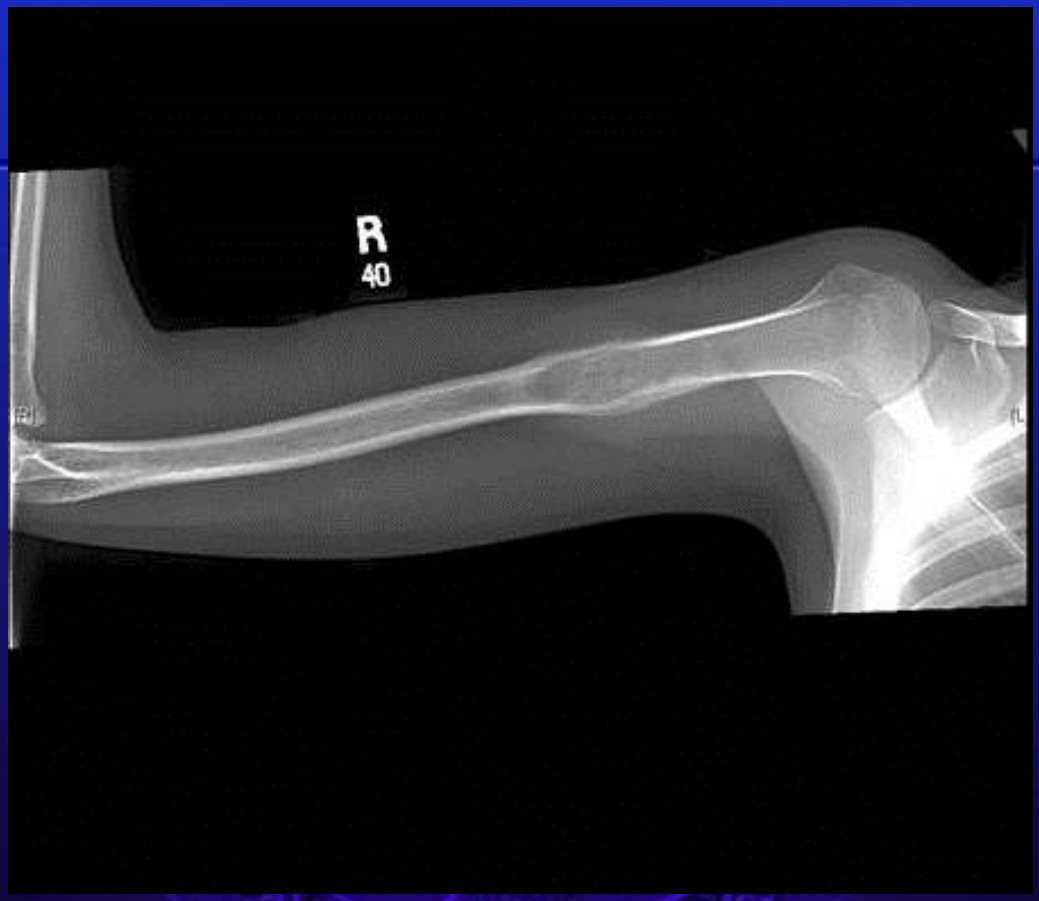
- sarcomatoid renal cell carcinoma
- sarcomatoid lung carcinoma

Cystic Lesions of Bone Simulating Neoplasm

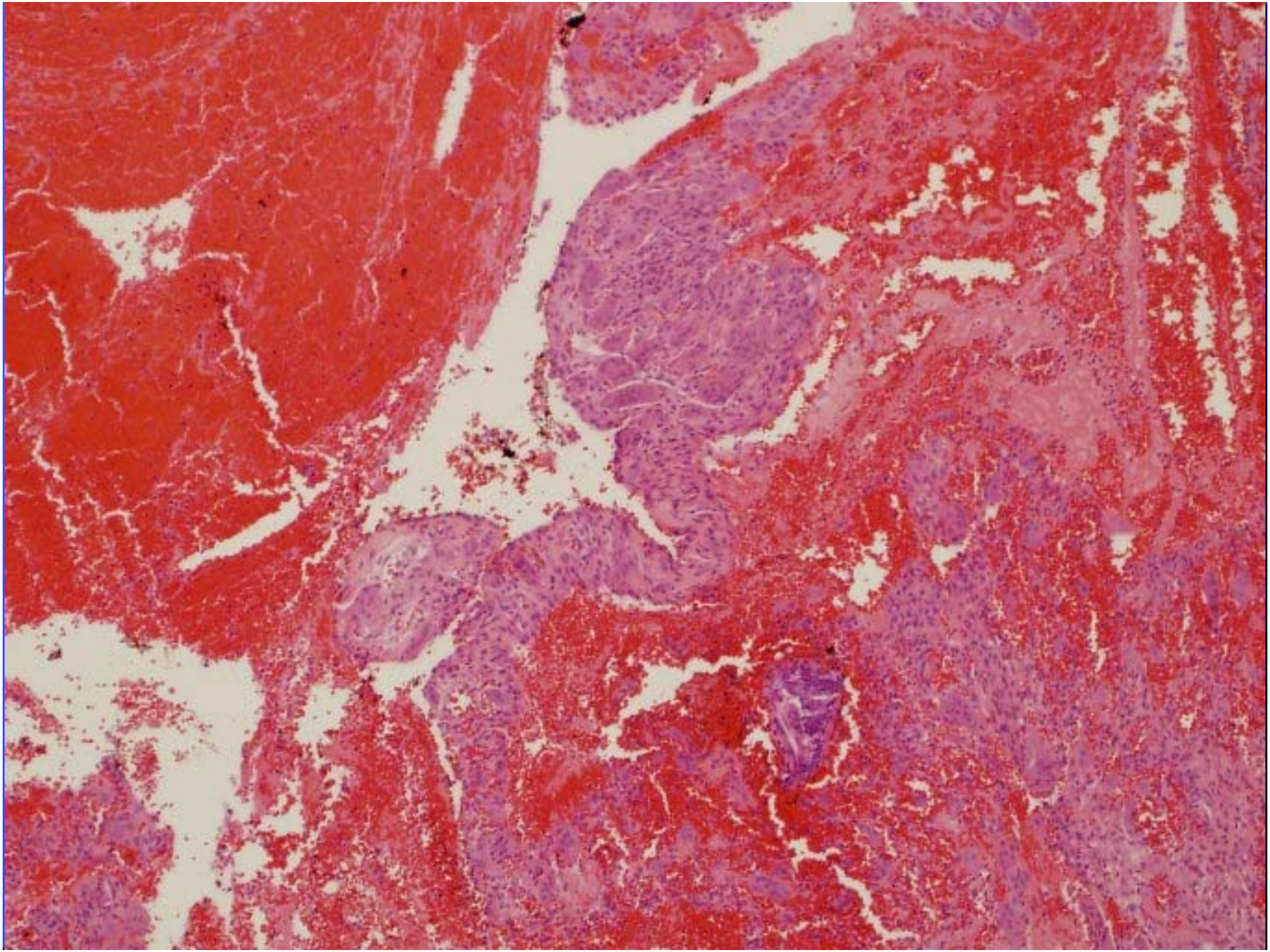
Aneurysmal bone cyst

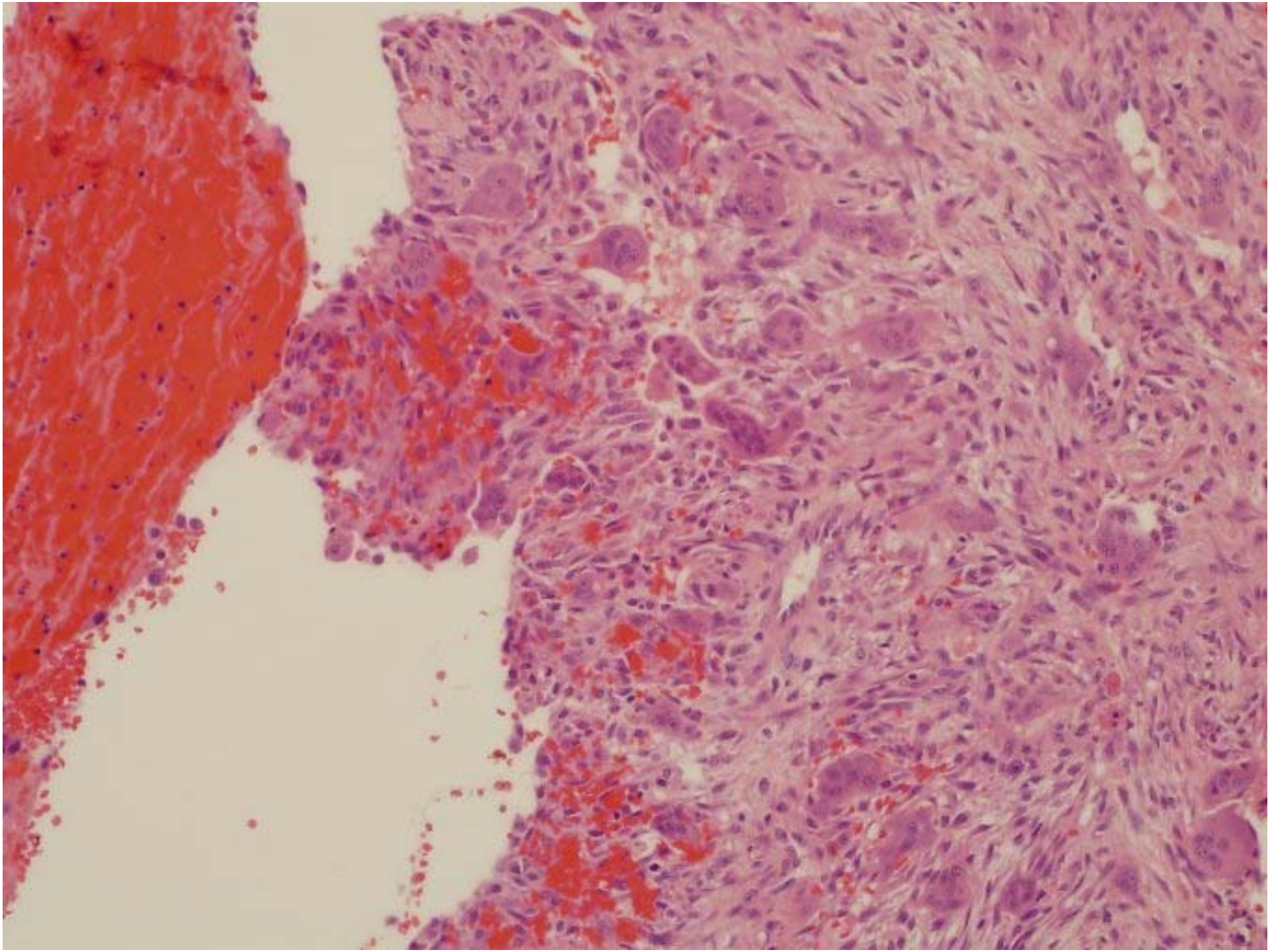
- Metaphysis of long bones or vertebra (posterior elements)
- Young, before 3rd decade
- Solid variant of "ABC" (giant cell reparative granuloma)
- Secondary ABC
  - chondroblastoma
  - osteosarcoma
  - osteoblastoma
  - CMF
  - GCT
- DD: Telangiectatic OS
  Low grade central OS

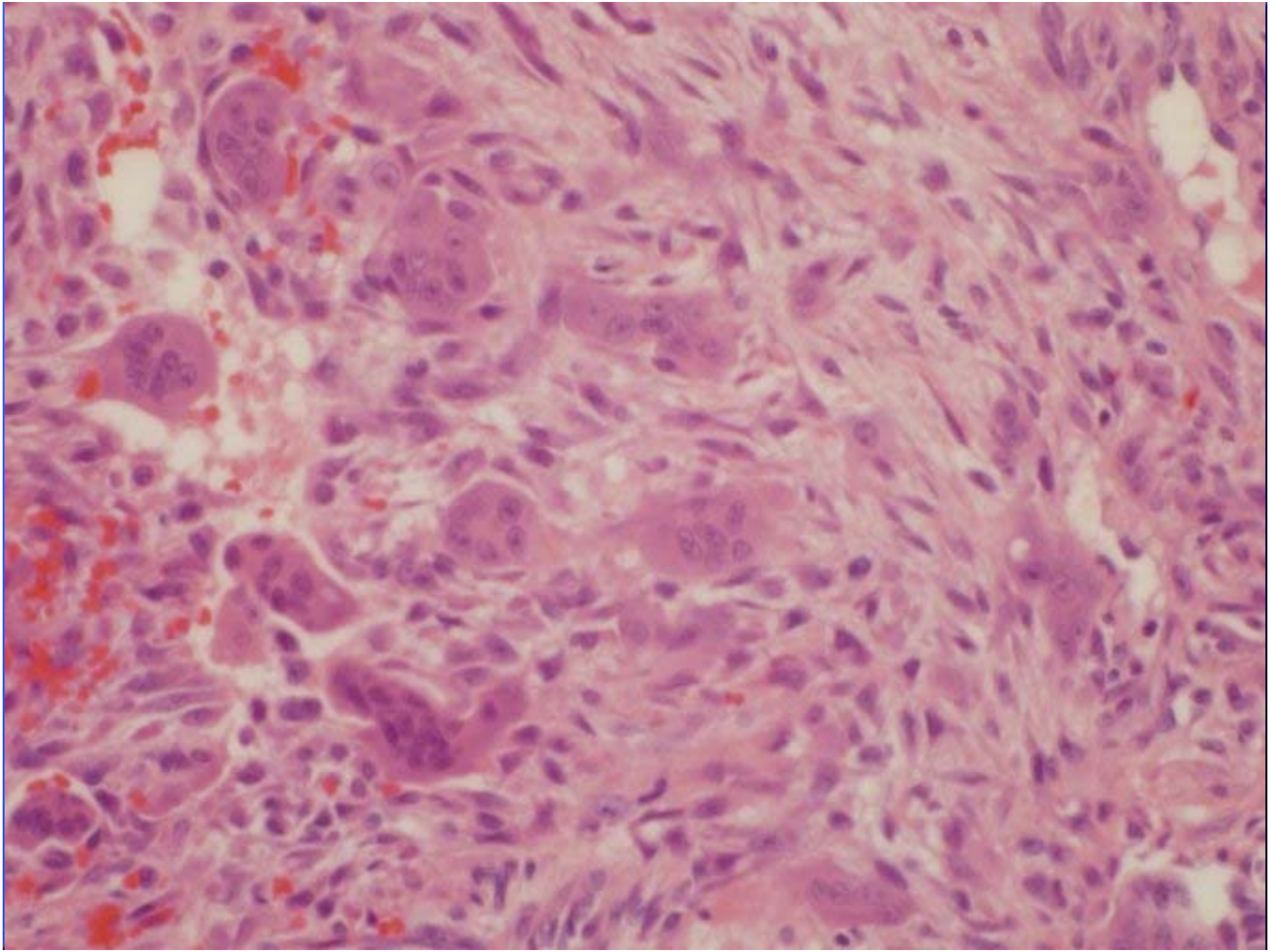
Aneurysmal bone cyst

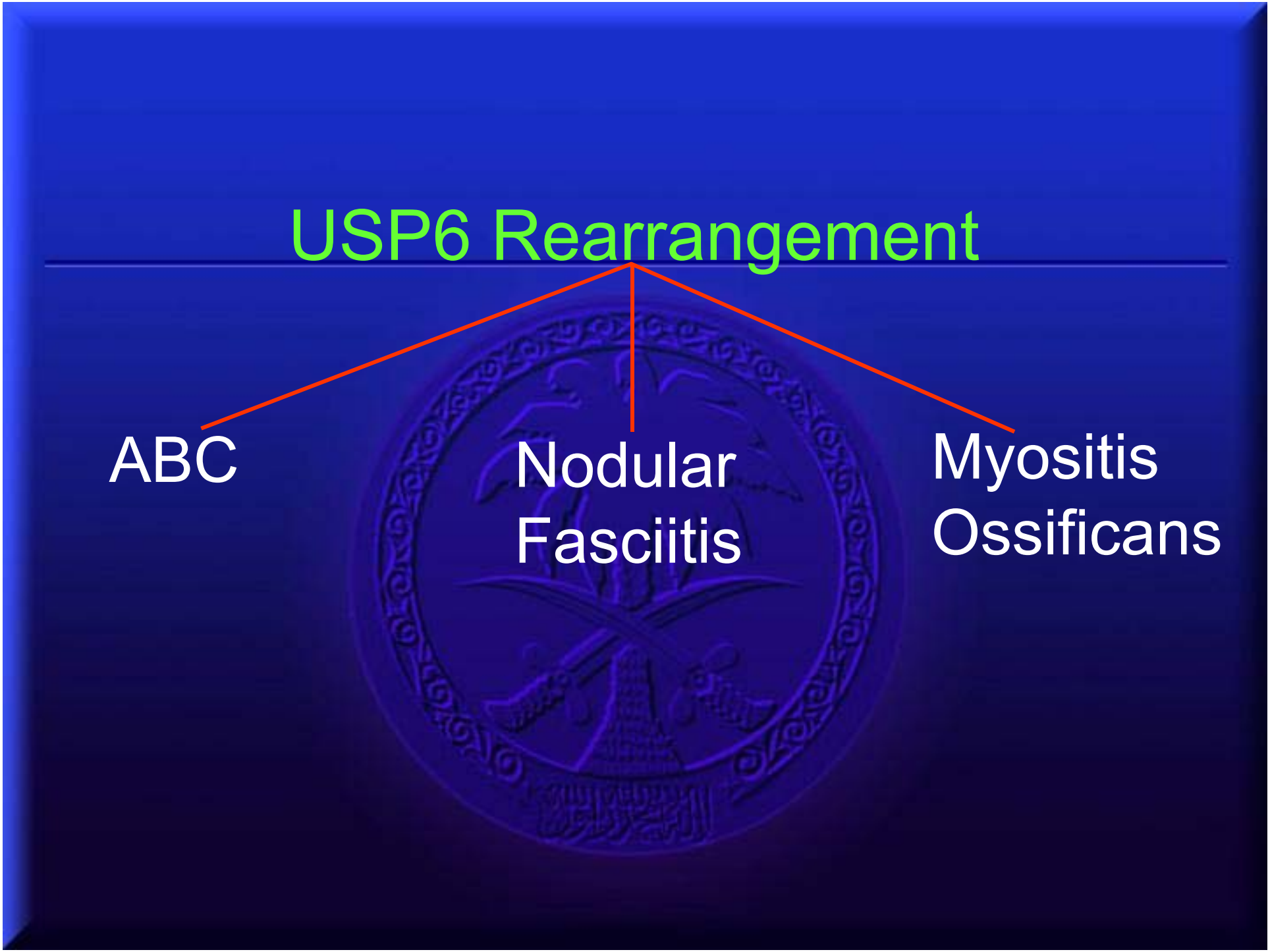


There is a small lytic lesion at the mid shaft of the right humerus, which shows no interval change in size.







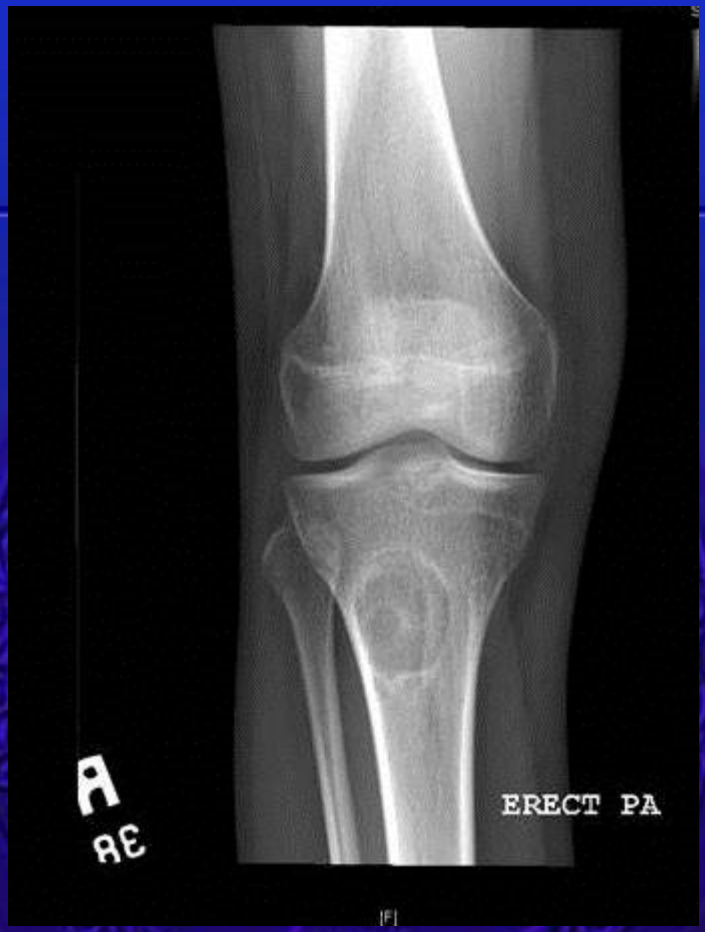

USP6 Rearrangement
ABC
Nodular Fasciitis
Myositis Ossificans

Cystic Lesions of Bone Simulating Neoplasm

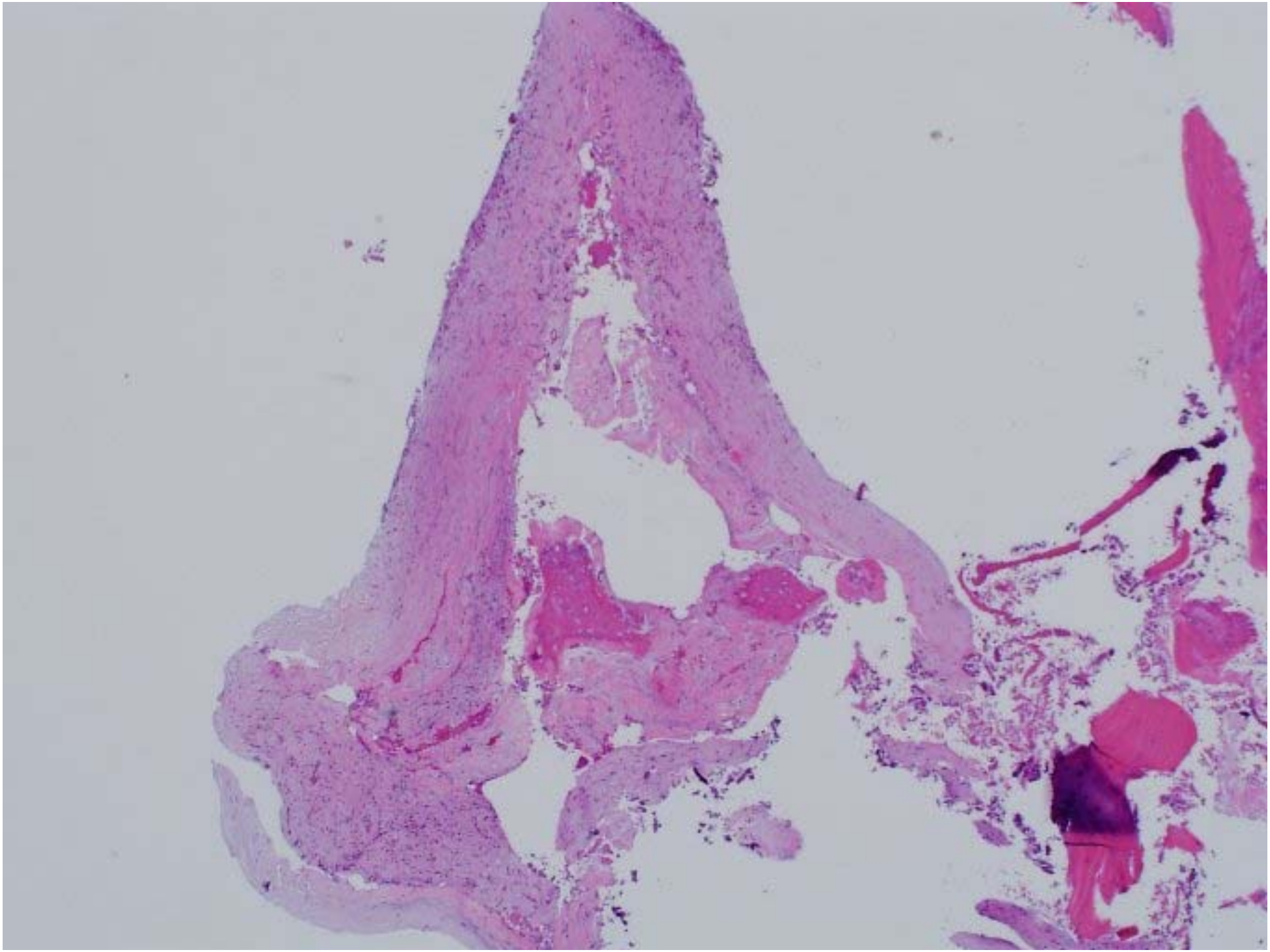
Simple Cyst (unicameral bone cyst)

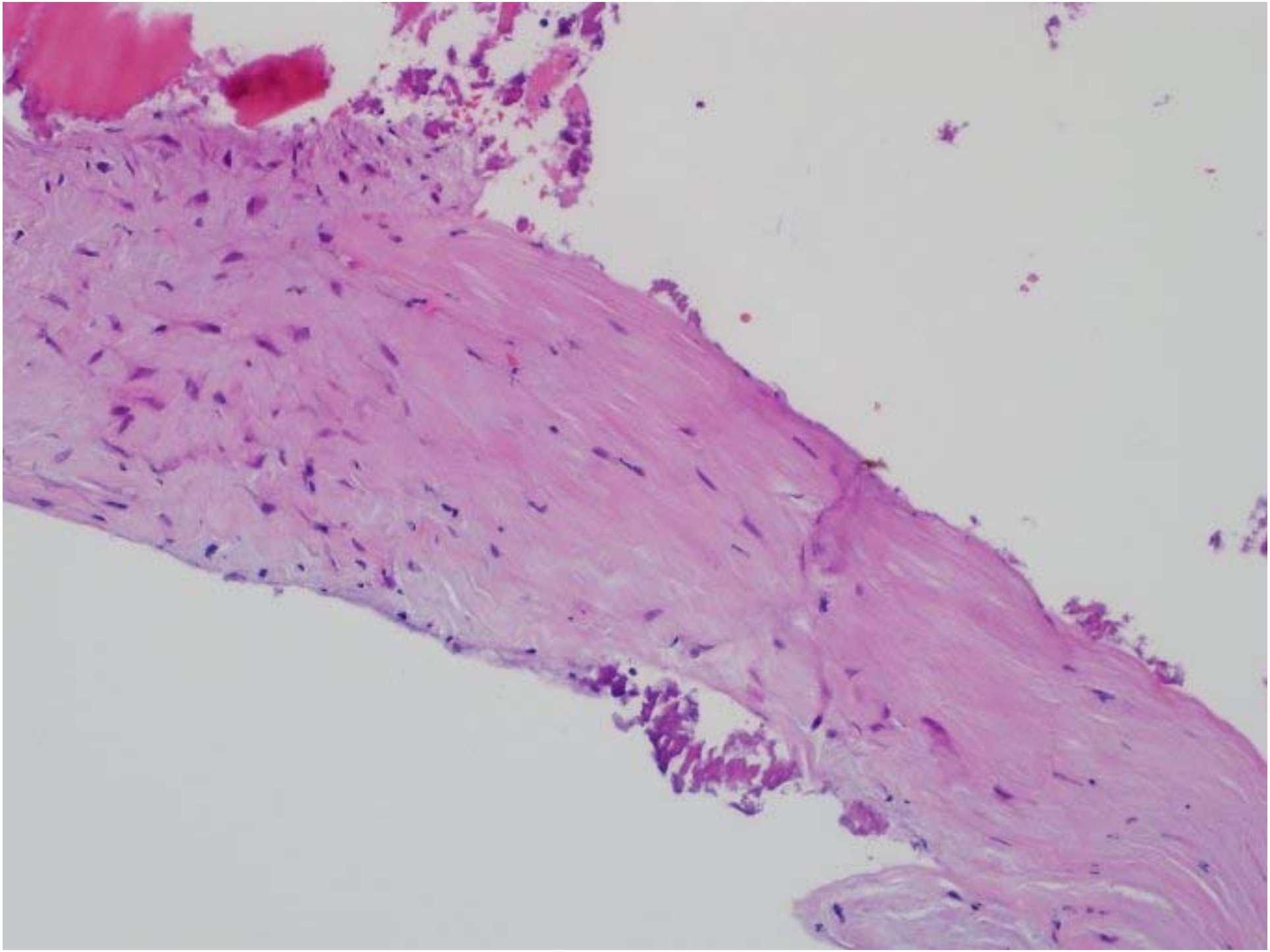
- First two decades of life
- Intramedullary, unilocular
- Pathological fracture
- Proximal humerus and femur (children)
  Calcaneus and ilium (adults)

Simple bone cyst x-ray



There is a lytic lesion seen in proximal right tibia metaphysis eccentric with narrow zone of transition and sclerotic margin not associated with periosteal reaction or soft tissue component, likely benign. Differential diagnosis include chondromyxoid fibroma and non-ossifying fibroma.



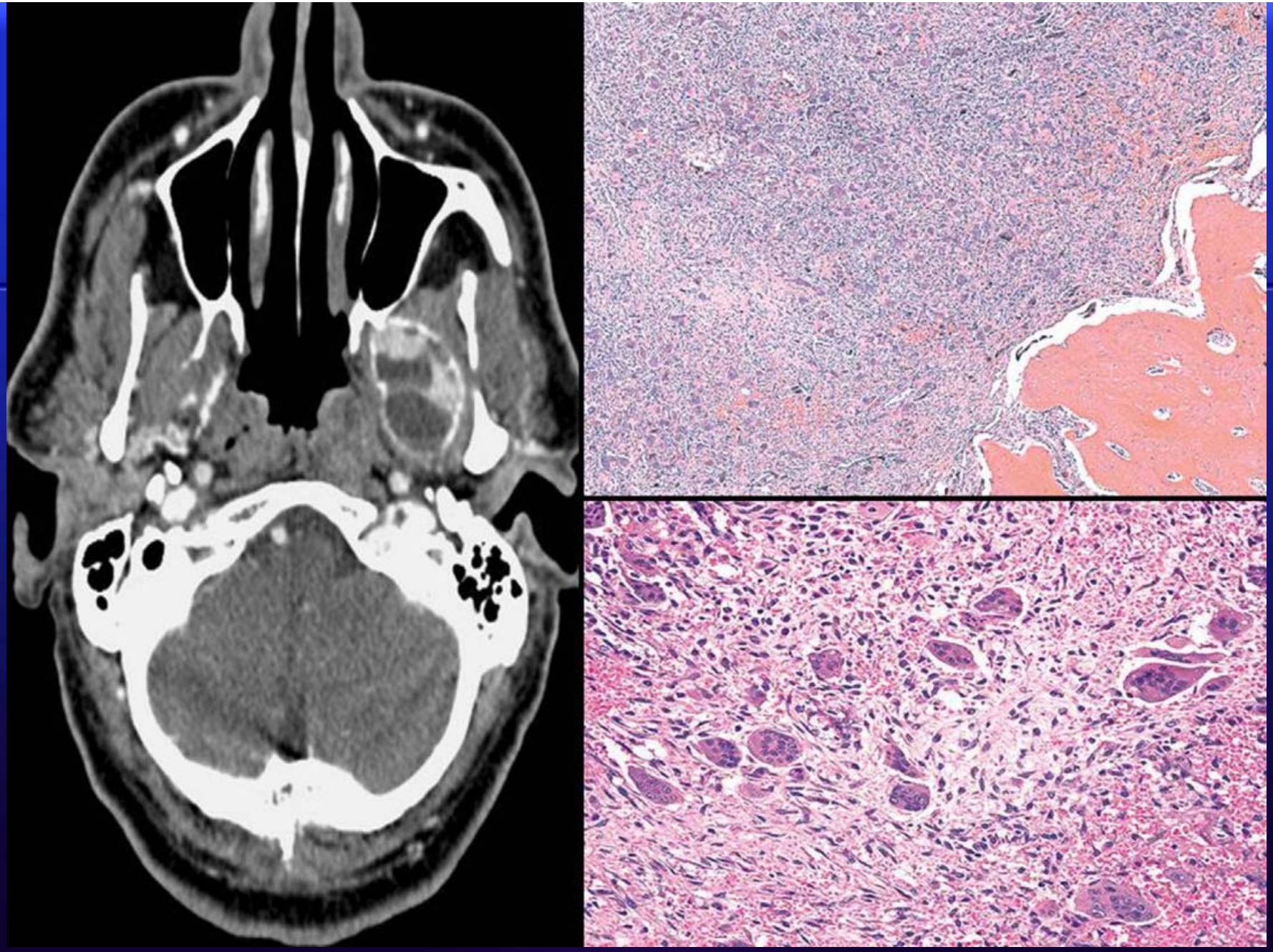


Cystic Lesions of Bone Simulating Neoplasm

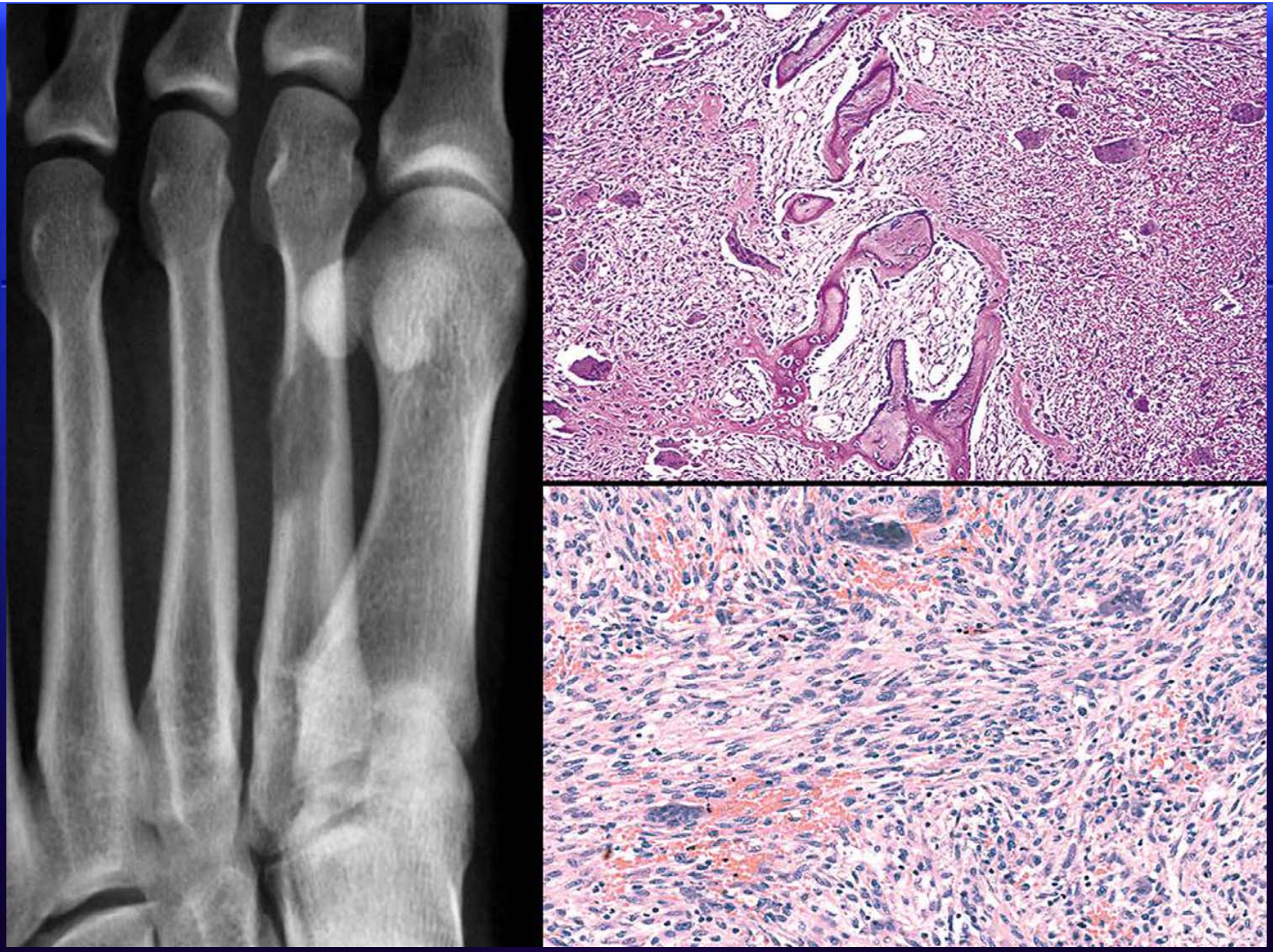
Giant cell reparative granuloma

- Jaw bone (mainly mandible)
- Small bones of hands and feet
- Can be multiple “cherubism”
- DD: 1) Giant cell tumor of bone
  - epiphyseal involvement
  - regular distribution of giant cells
  - mononuclear cell background resembling the nuclei of giant cells

  2) Brown tumor of hyperparathyroidism
  - diffuse osteopenia of hands and feet on x-ray
  - abnormal chemistry
  - identical histology to GCRG



Seminars in Diagnostic Pathology 31 (2014), 53-65

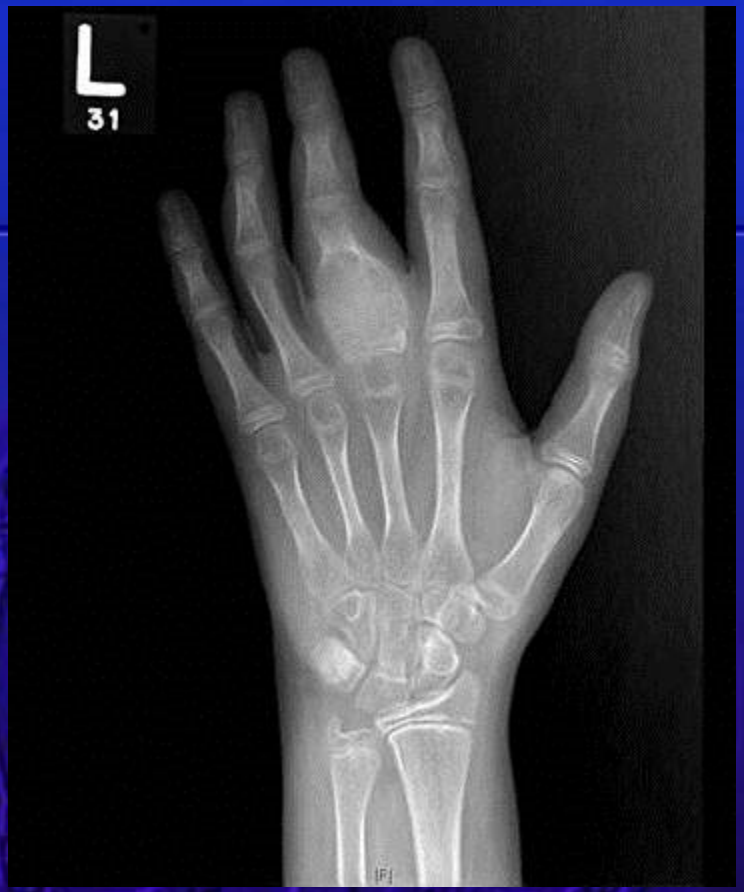


Seminars in Diagnostic Pathology 31 (2014), 53-65

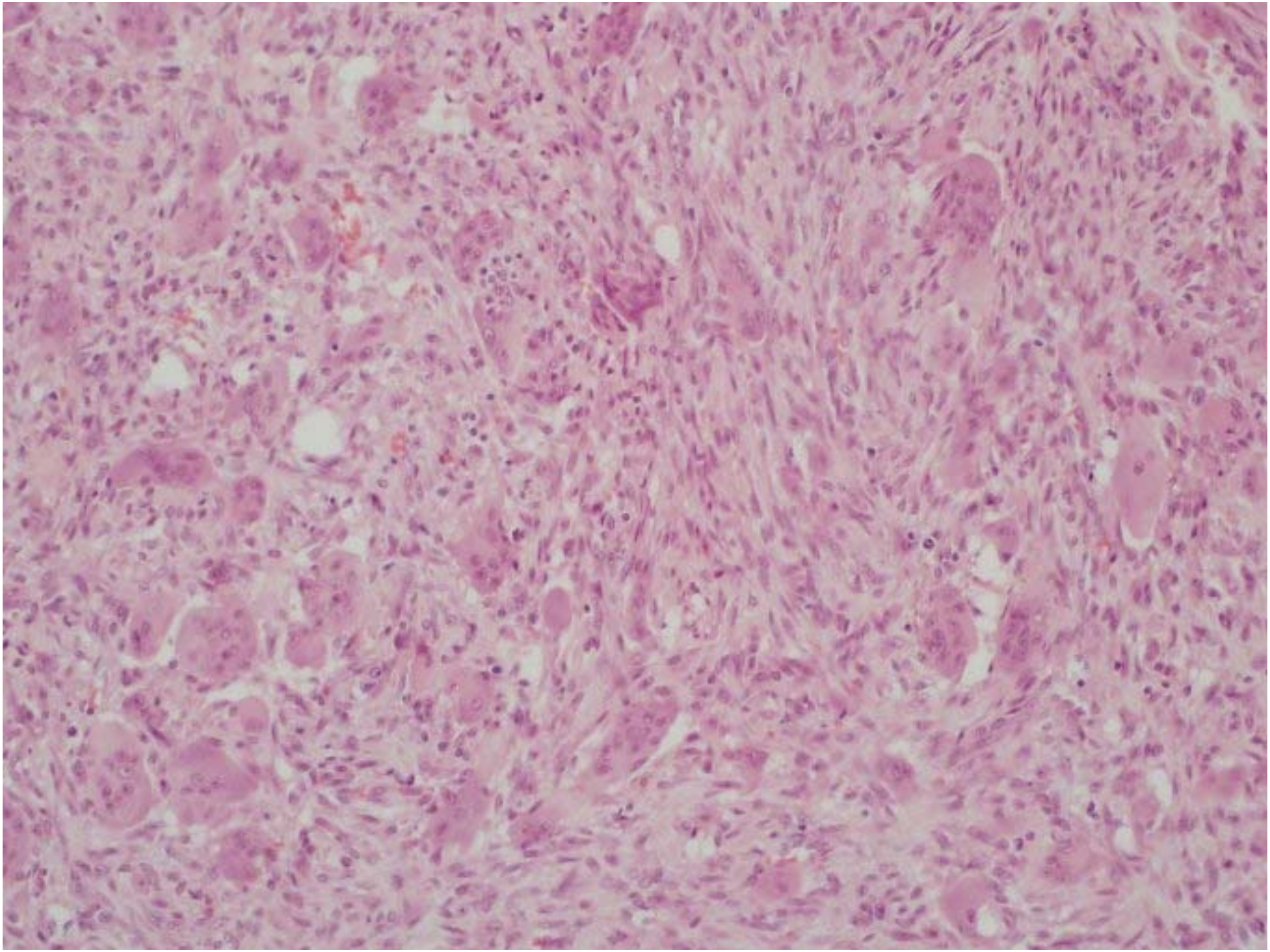
Giant cell reparative granuloma

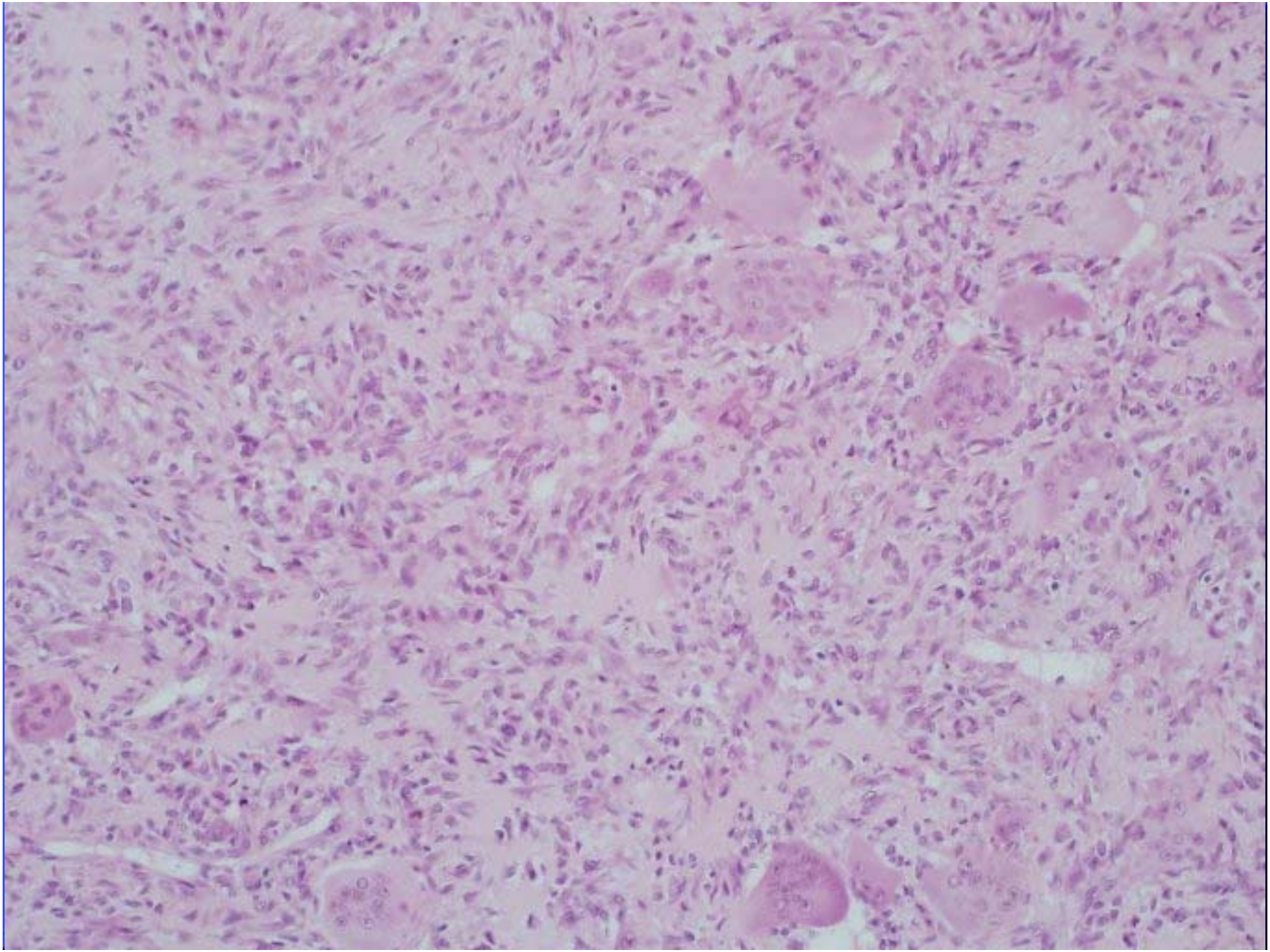
- 13 years old boy with swelling of left middle finger

Giant cell reparative granuloma



There is lytic expansile lesion in the proximal metadiaphyseal region of the proximal phalanx of the left middle finger. The lesion measures 2.6 x 2.2 cm and has thin sclerotic margins with intact cortex. The overlying soft tissues appears slightly swollen by the effect of the tumor. The remainder of the bones appear unremarkable.





Cystic Lesions of Bone Simulating Neoplasm

Intraosseous ganglion

- Hip, tibia, fibulae, carpal bones

Epidemoid cyst

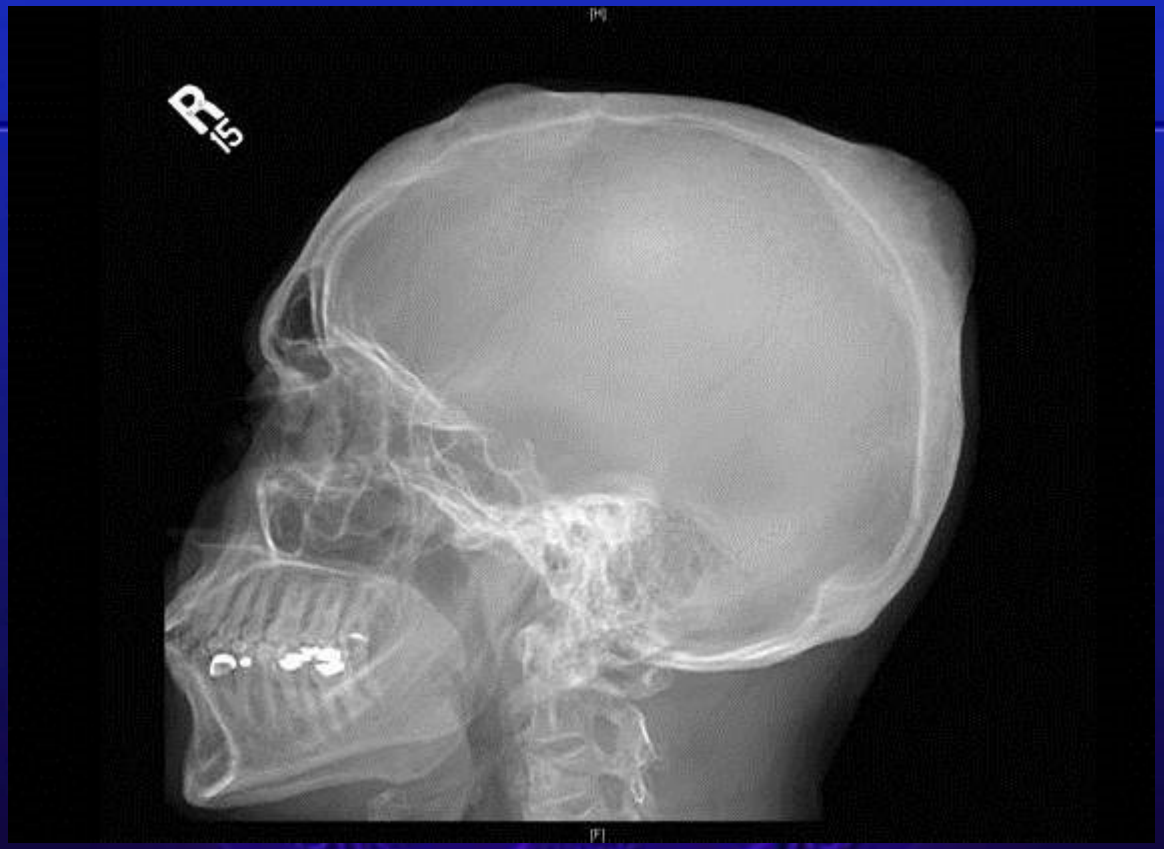
- Skull, distal phalanges

Fibrous and Fibro-esseous Proliferative of the Bone

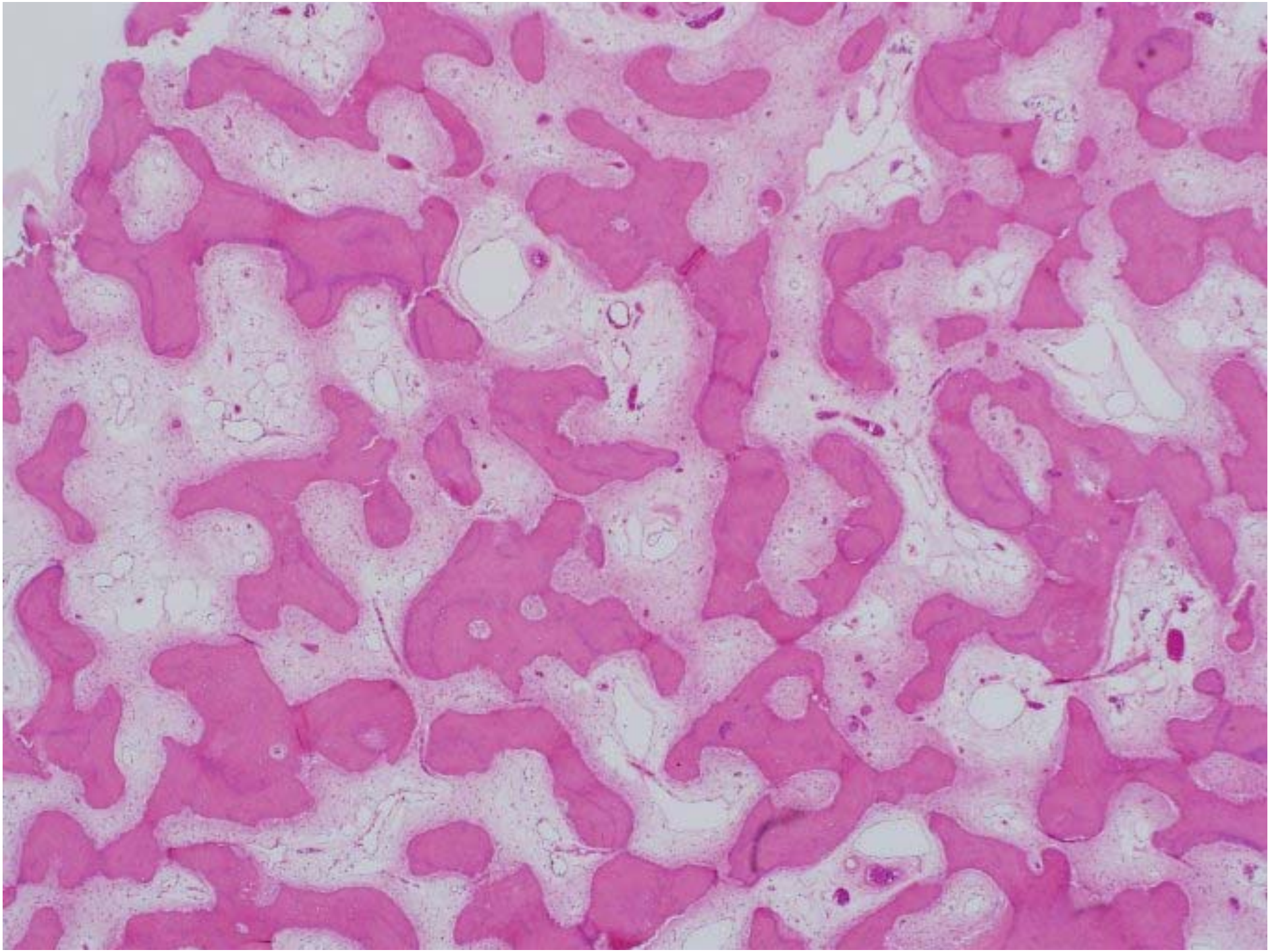
Fibrous Dysplasia

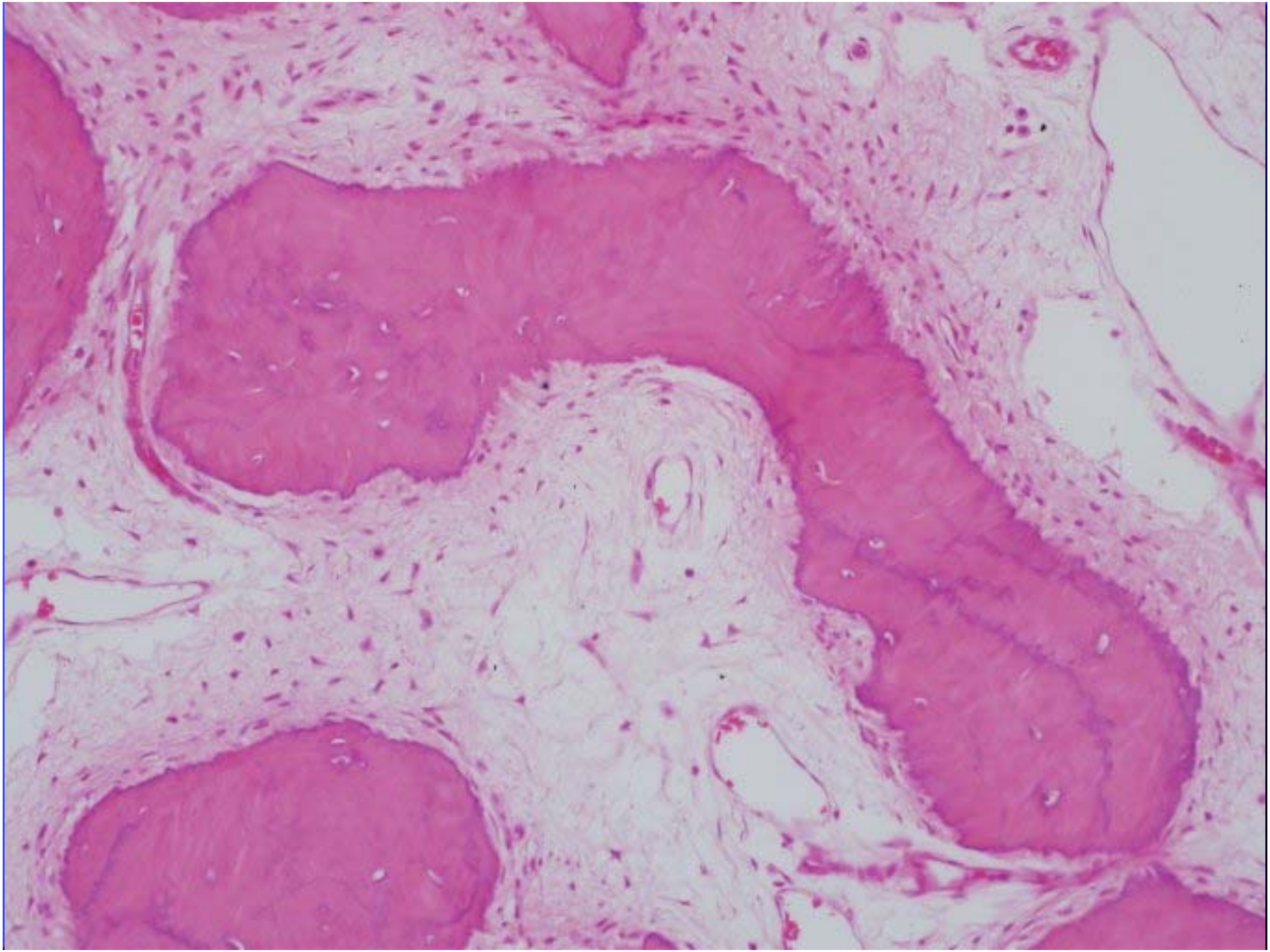
- Monostotic
- Polyostotic (can be Albright disease)
- Craniofacial bones, long bones, pelvis
- Risk of malignant transformation
- DD: - LGCO (MDM2⊕, CDK4⊕)
  - solid ABC
  - desmoplastic fibroma

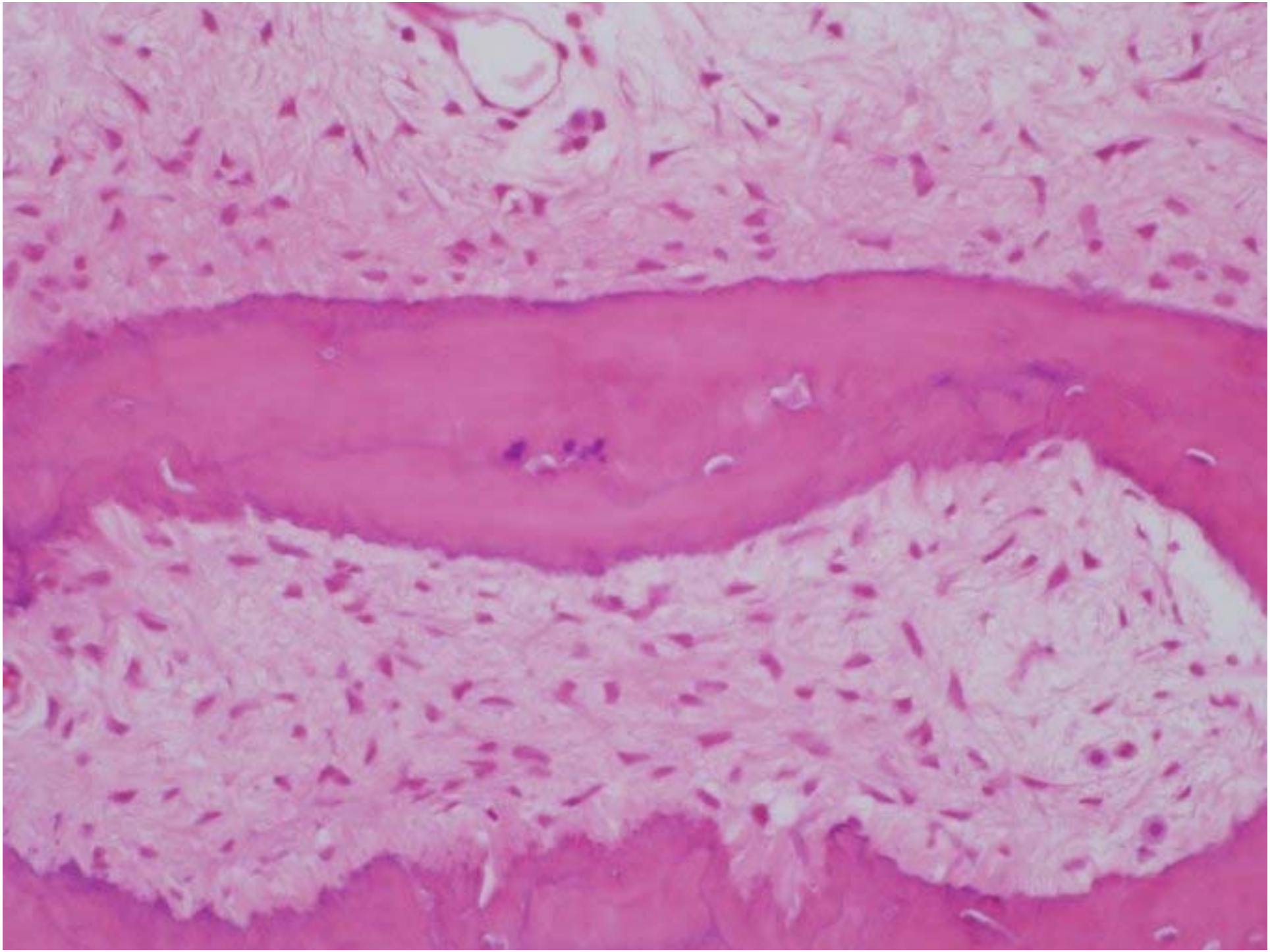
20-year-old
Fibrous dysplasia

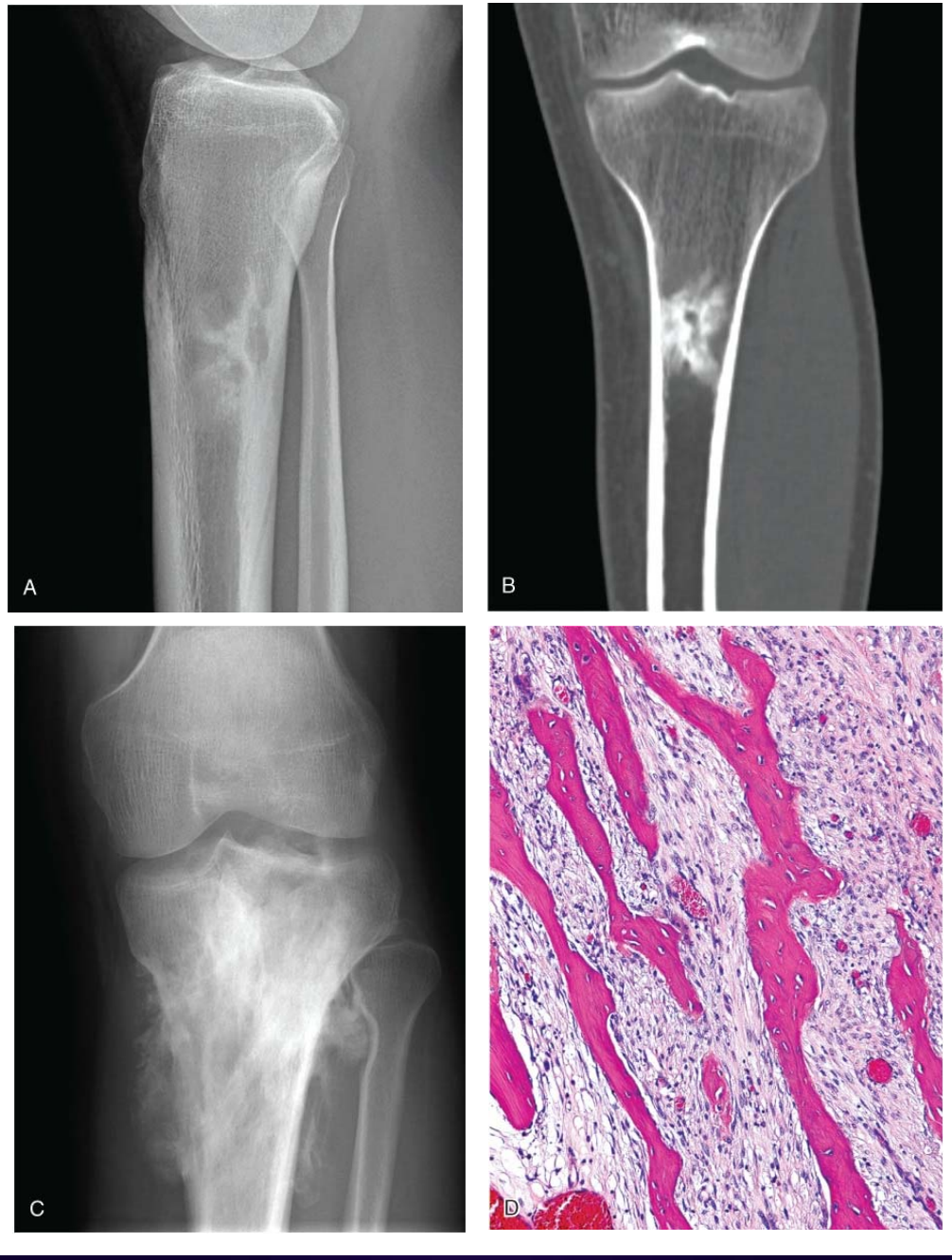


Two areas of bony prominence, which are projecting outside the skull with intact inner table of skull. In frontal bone just anterior to the coronal suture is about 45 mm long. One is located posteriorly anterior to the lamboid suture and measures 56 mm. Change is most likely due to a benign process with a history of 15-year-old lesion and this most likely fibrous dysplasia.









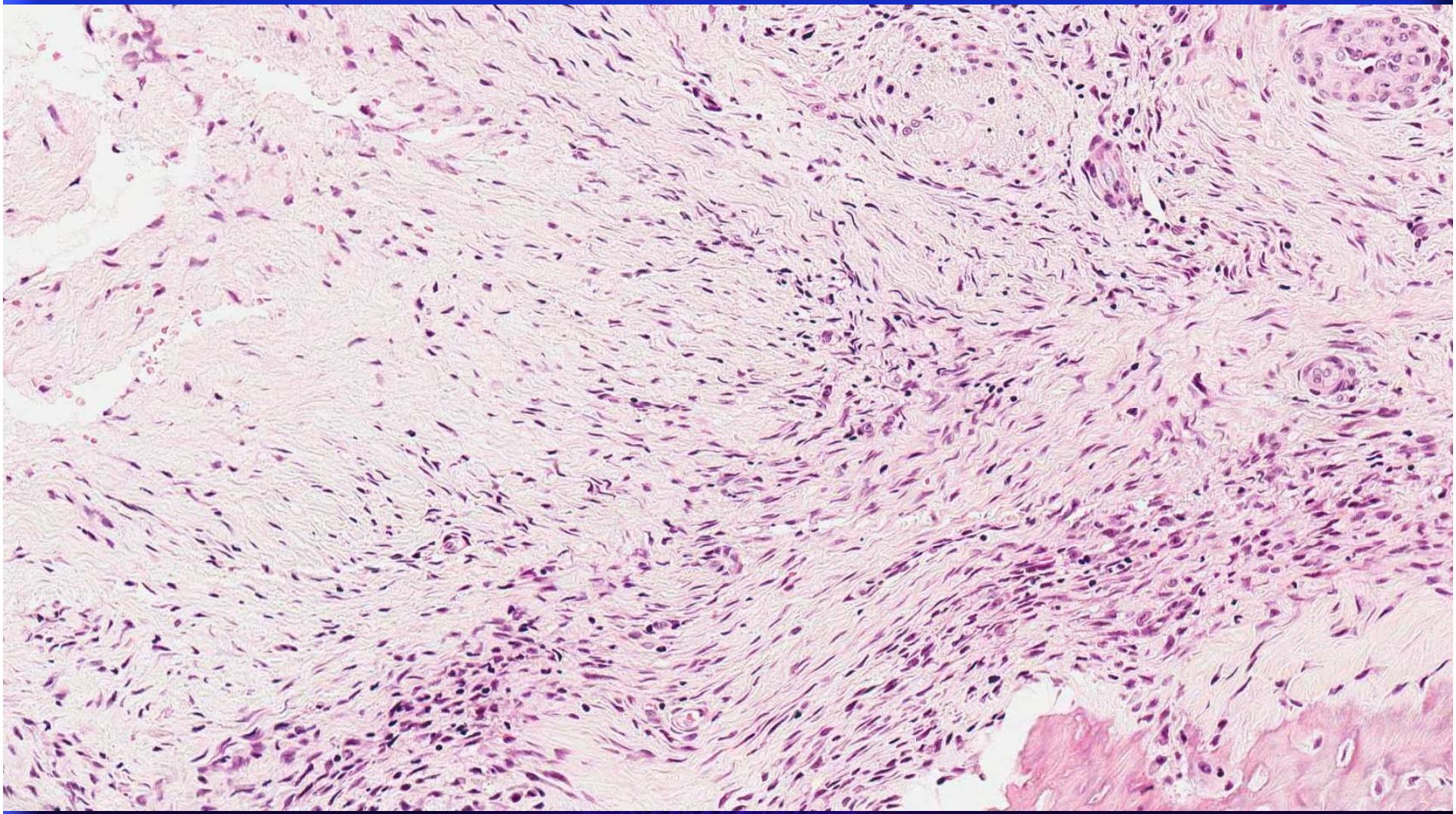
Dorfman and Czerniak's, Bone Tumors, Second Edition

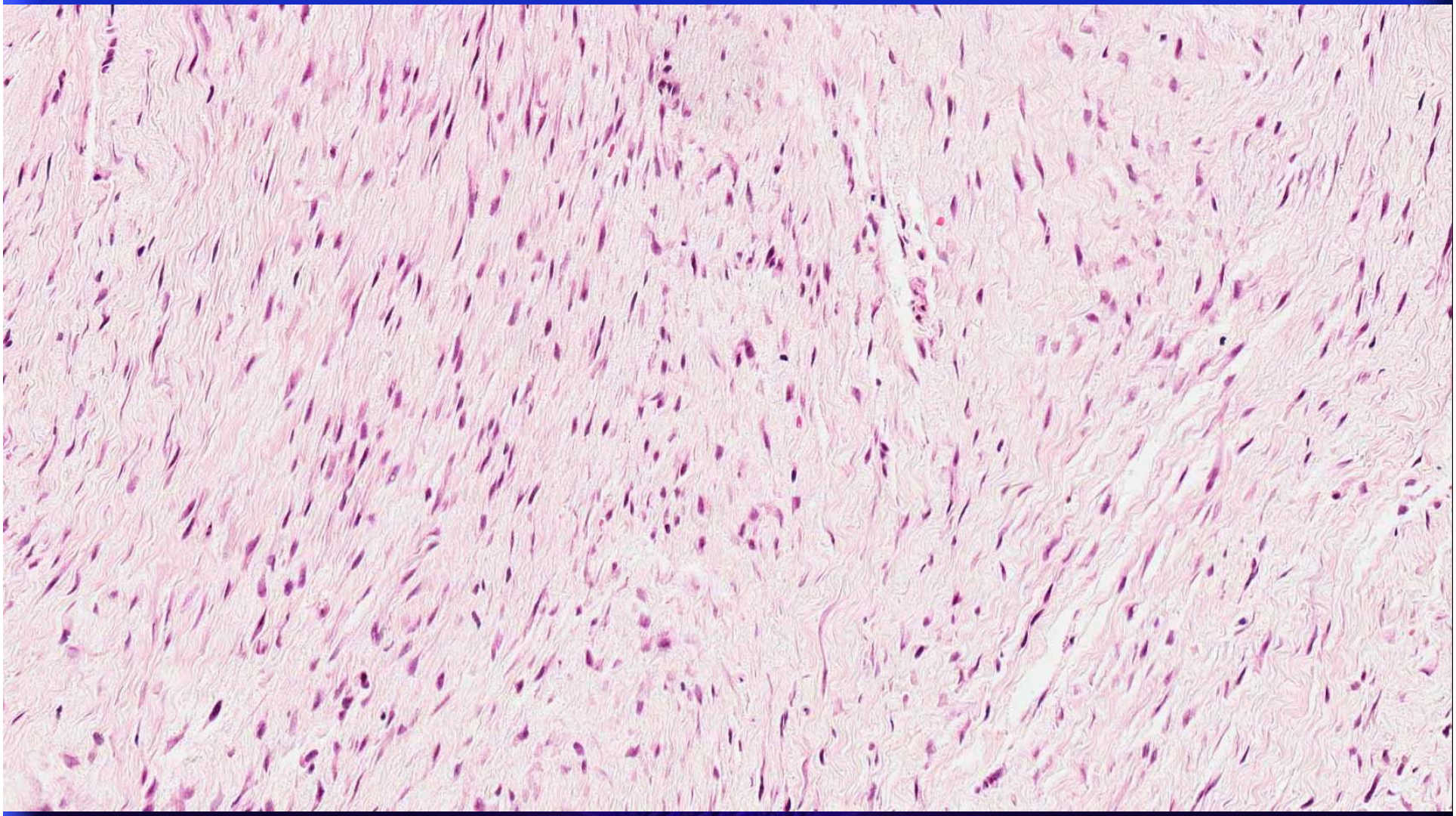
Case 9

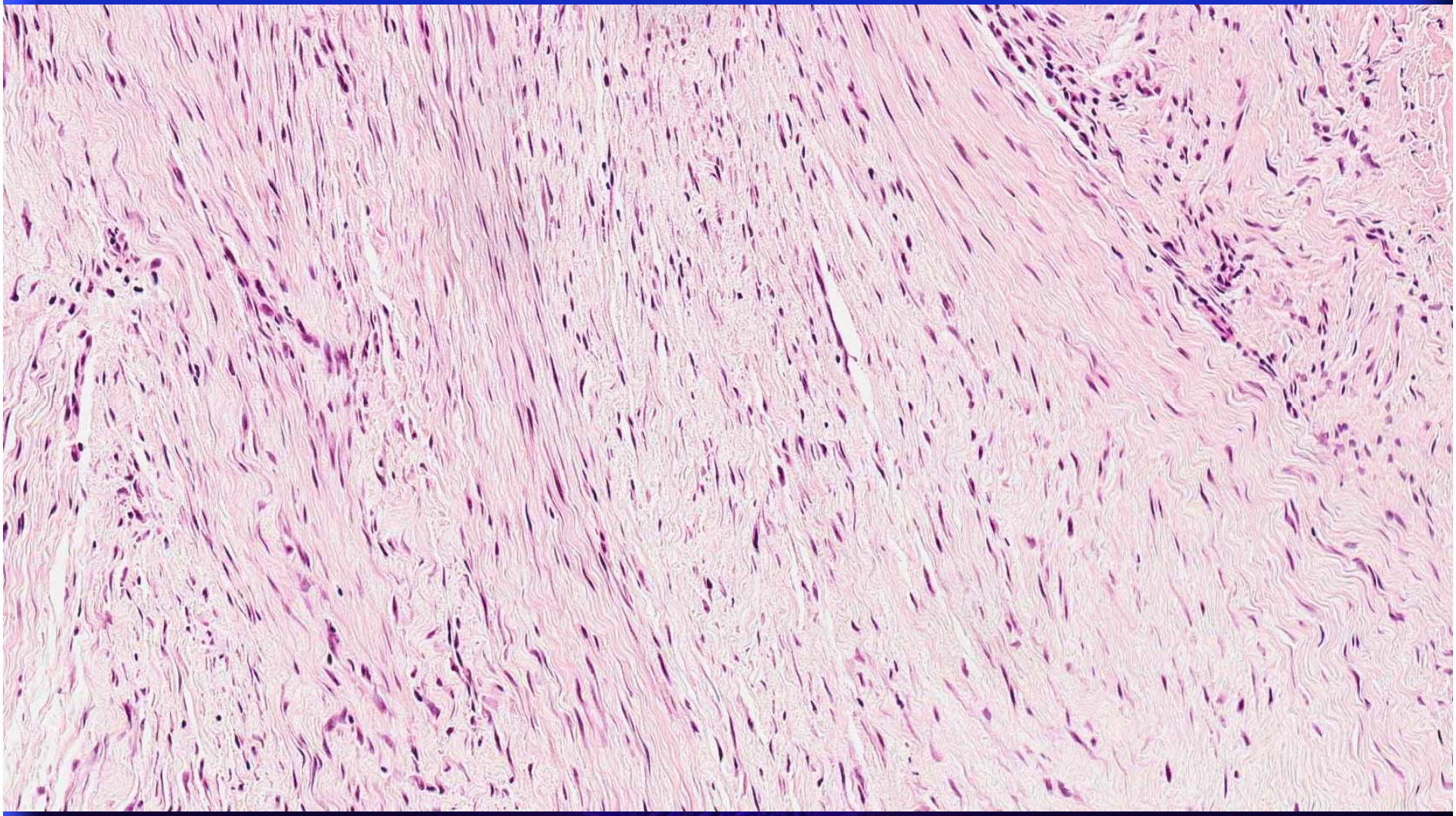
SP12-3292

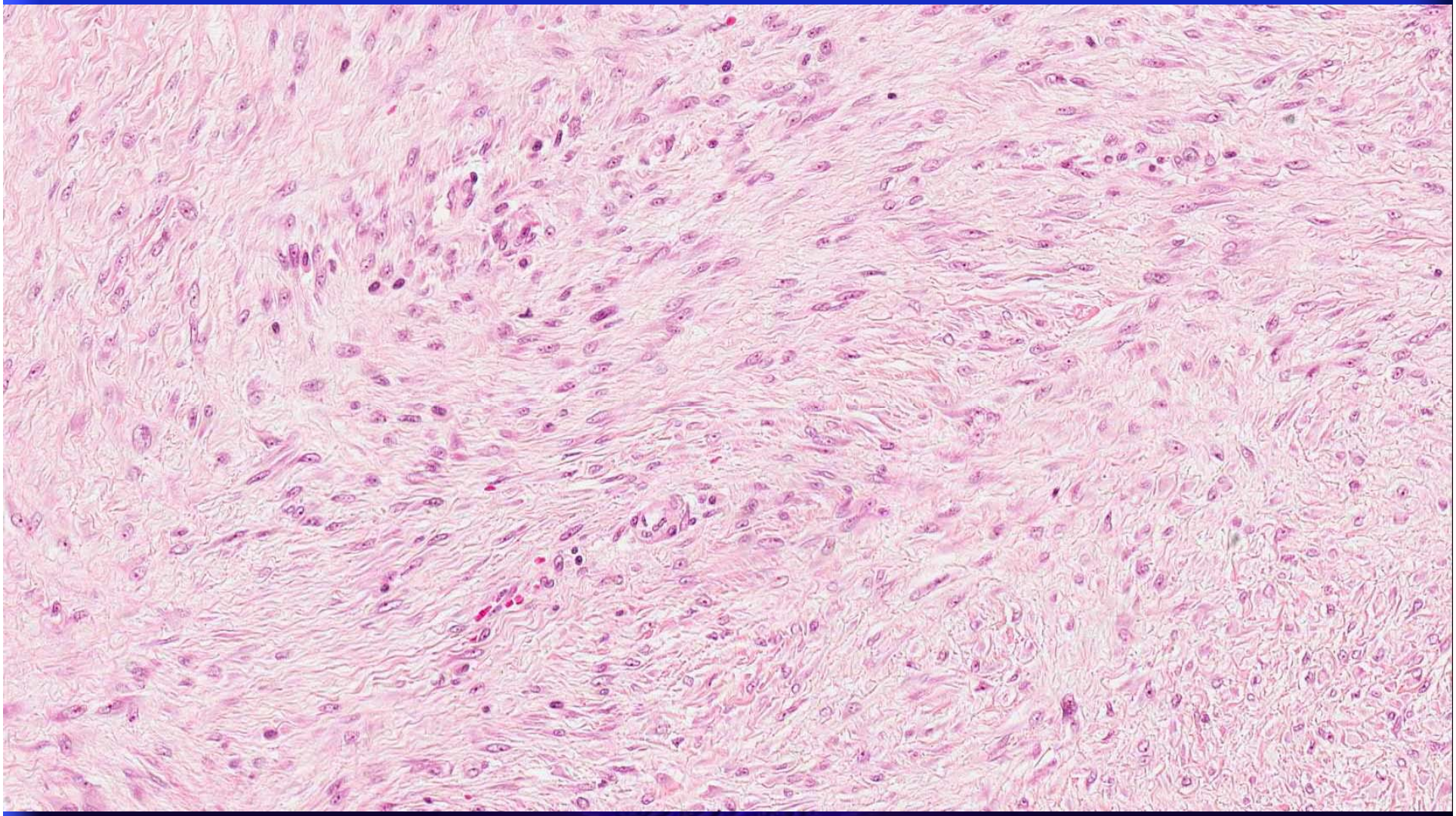
History:

16-year-old with history of wrist pain and swelling for nine months.









SP12-3292

Diagnosis

Desmoplastic fibroma

Desmoplastic fibroma

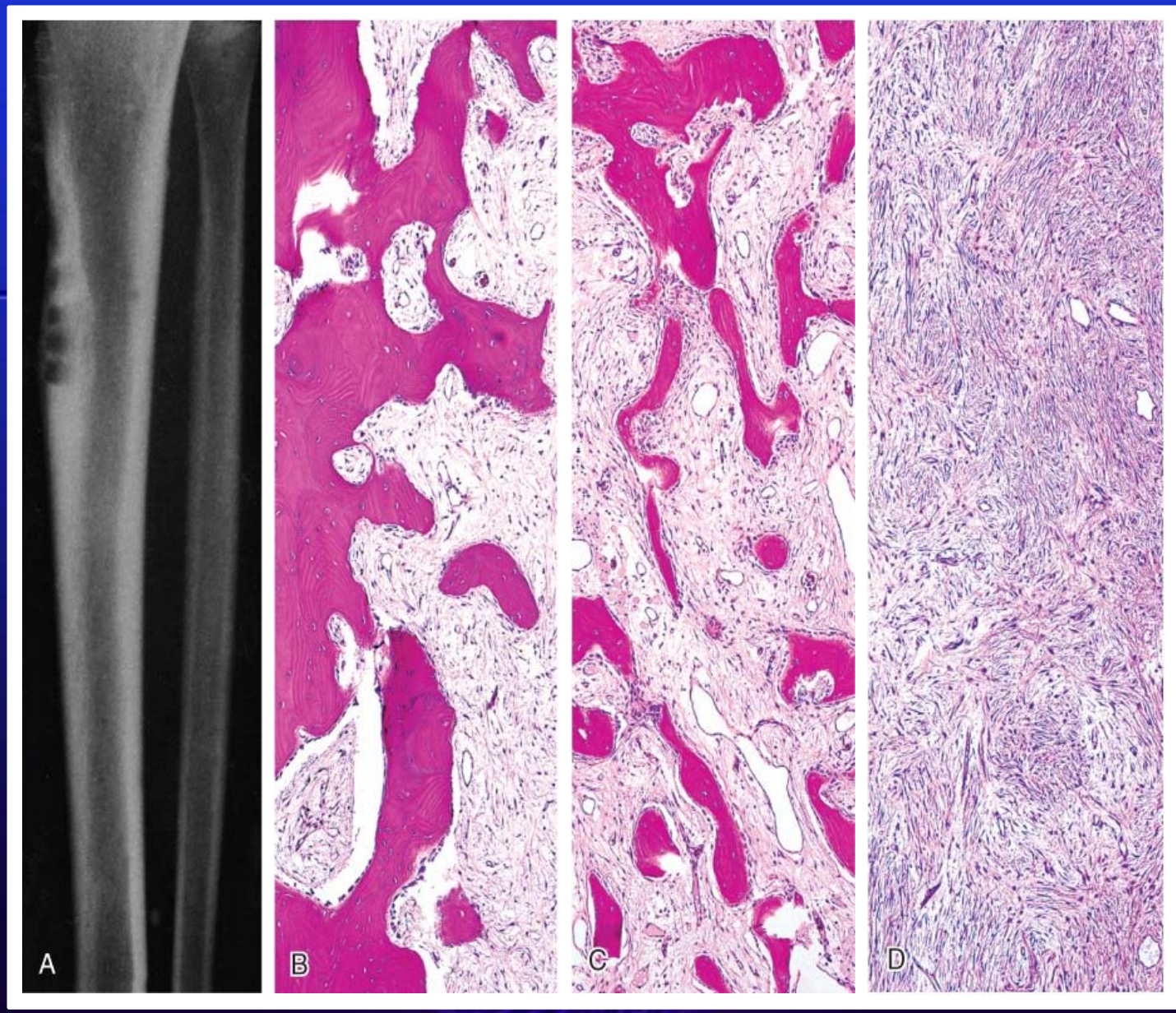
- Resemble fibromatosis
- 1st three decades of life
- Long bones, mandible and pelvic bones
- No β catanin expression or mutation

DD: low grade osteosarcoma: +ve for MDM2 and CDK4
fibrous dysplasia: presence of woven bone

Fibrous and Fibro-esseous Proliferative of the Bone

Corteal osteofibrous dysplasia

- Affects tibia and fibula
- Solitary lesion
- Lucent intracortical mass in diaphysis
- Isolated stromal positivity for keratin can be seen (precursor for adamantinoma)
- DD: Adamantinoma
  - low grade malignant neoplasm
  - anterior surface of tibia, corticol
  - presence of basoloid cells, glandular or tubular structure
  - positive for keratin
  - positive for podoplanin (D2-40)

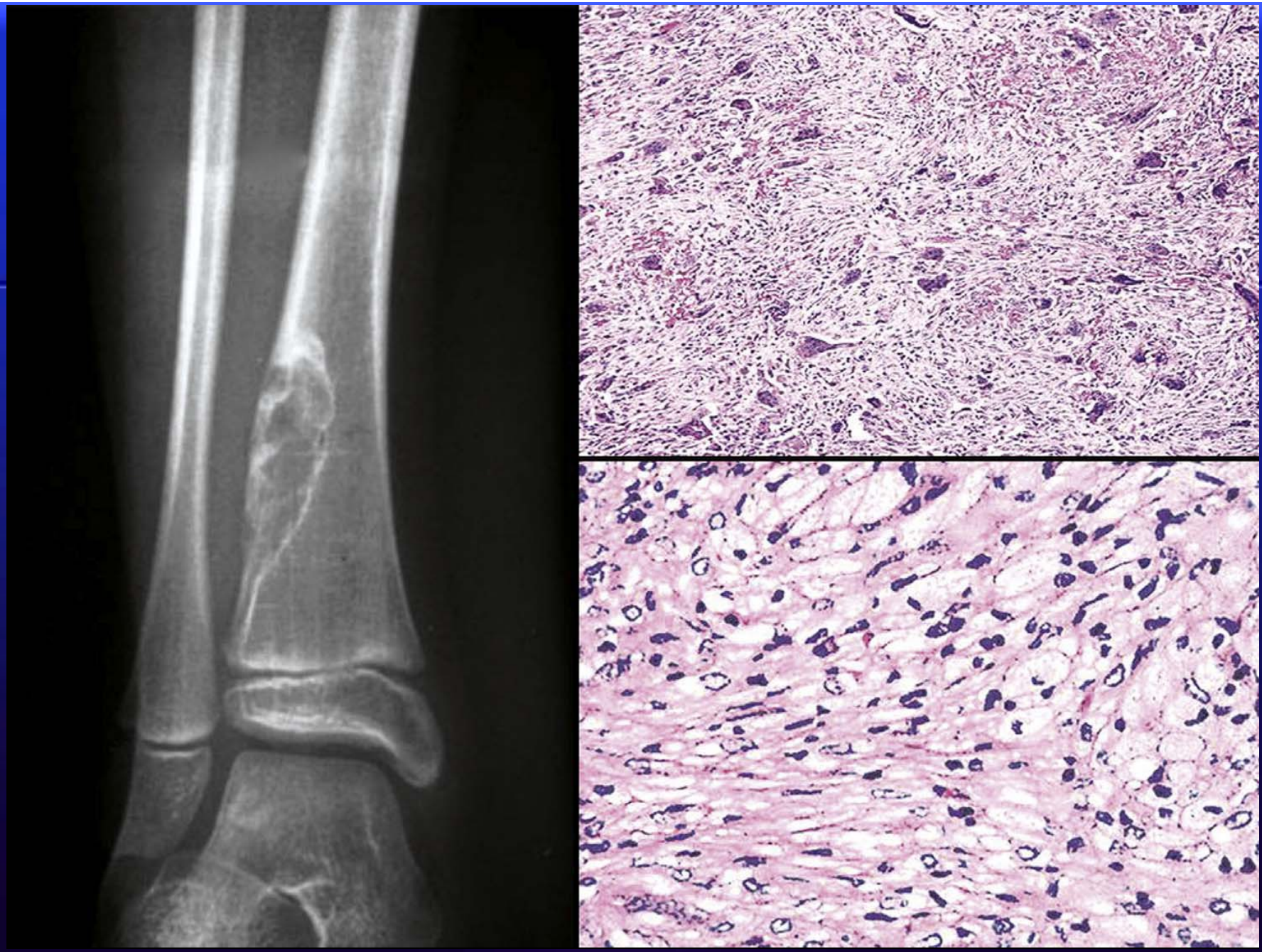


Dorfman and Czerniak's, Bone Tumors, Second Edition

Fibrous and Fibro-esseous Proliferative of the Bone

Metaphyseal fibrous defect (nonossifying fibroma

- Most patients less than 10 years old
- Intracortical, asymptomatic, incidental
- DD: Fibrous histiocytoma of bone
  - diaphyseal
  - axial skeleton
  - painful

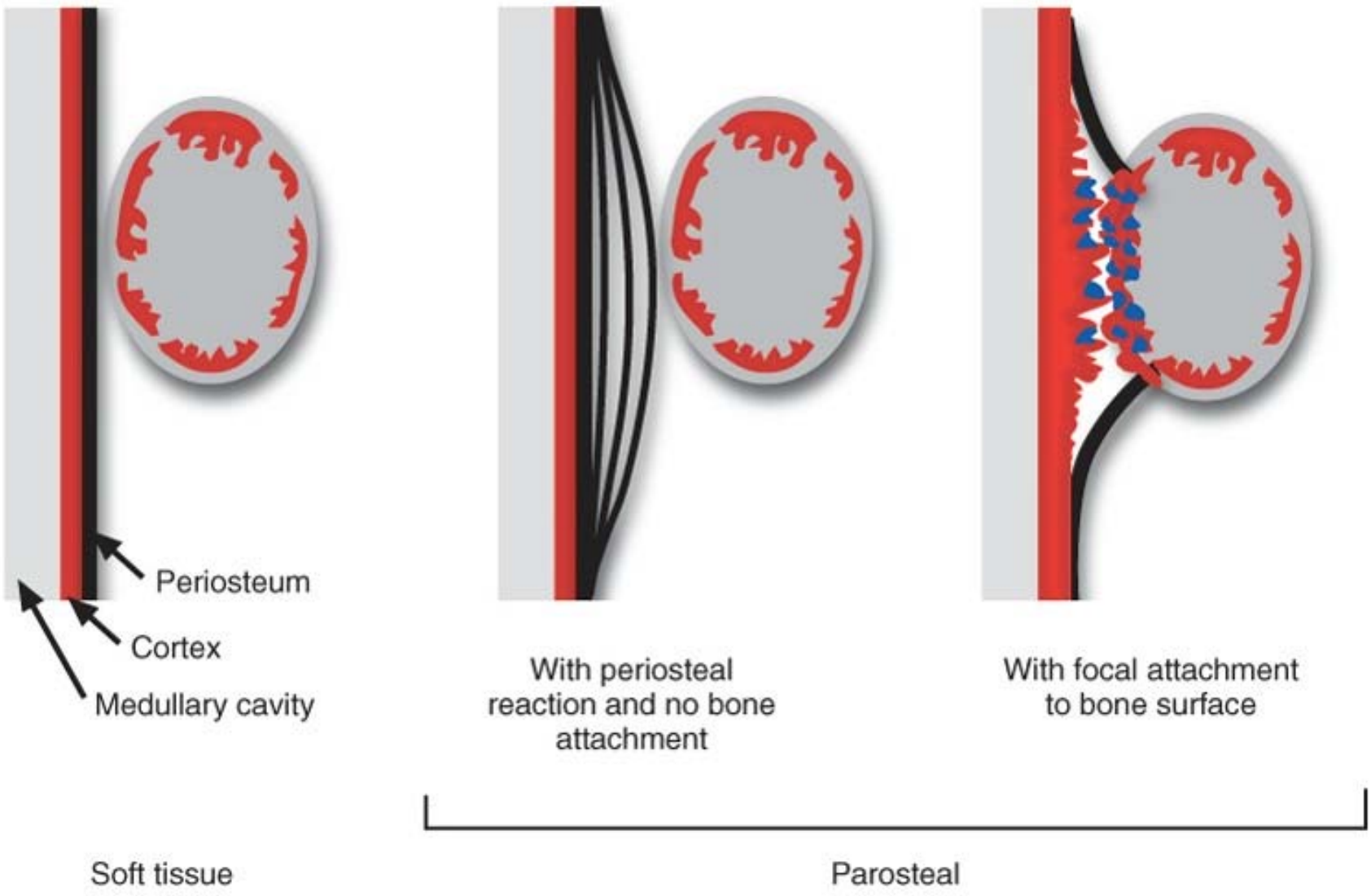


Seminars in Diagnostic Pathology 31 (2014), 53-65

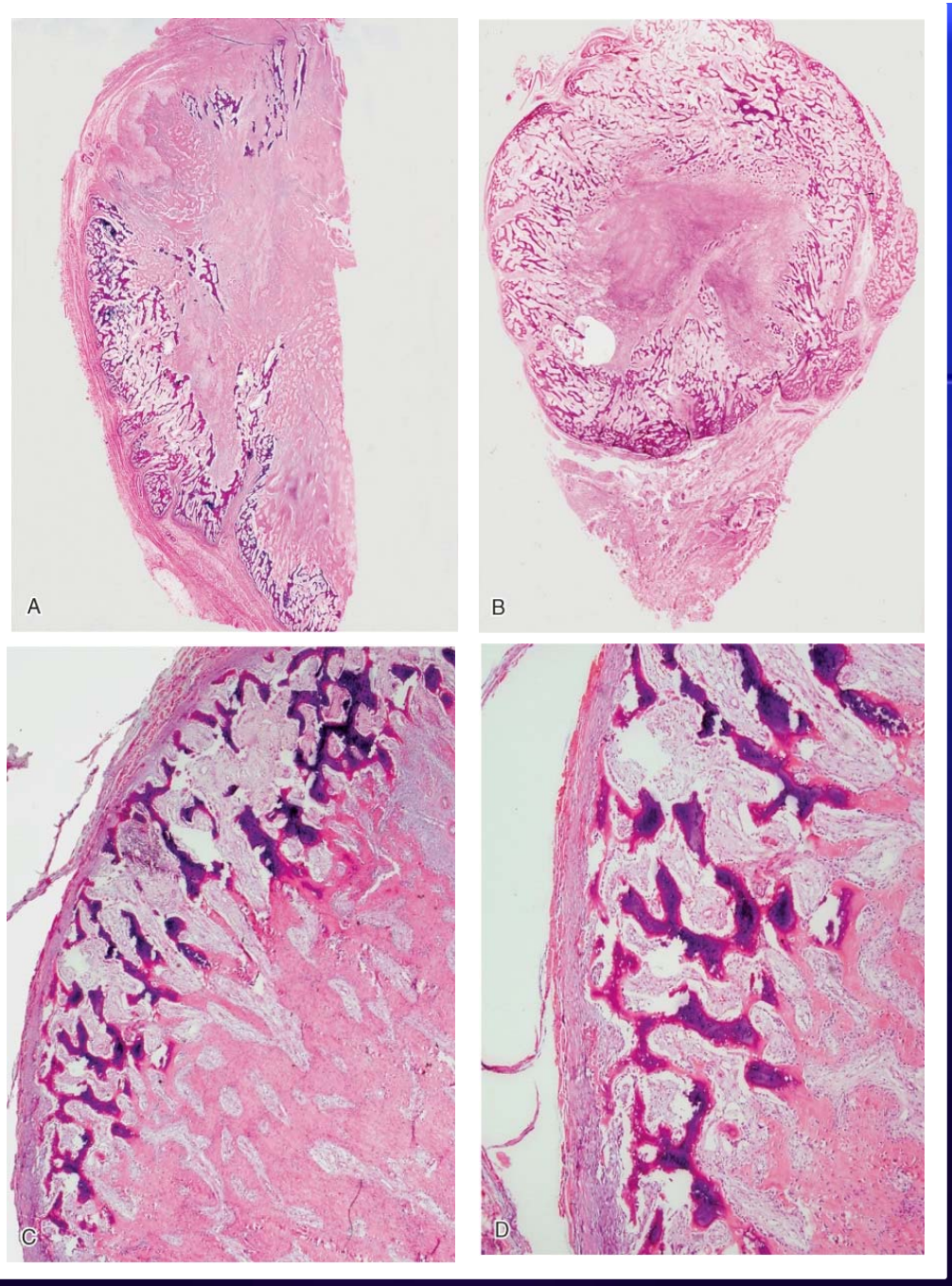
Myositis Ossificans

- Zoning phenomenon
- Functional arrangement
- Maturation
- ± cartilages

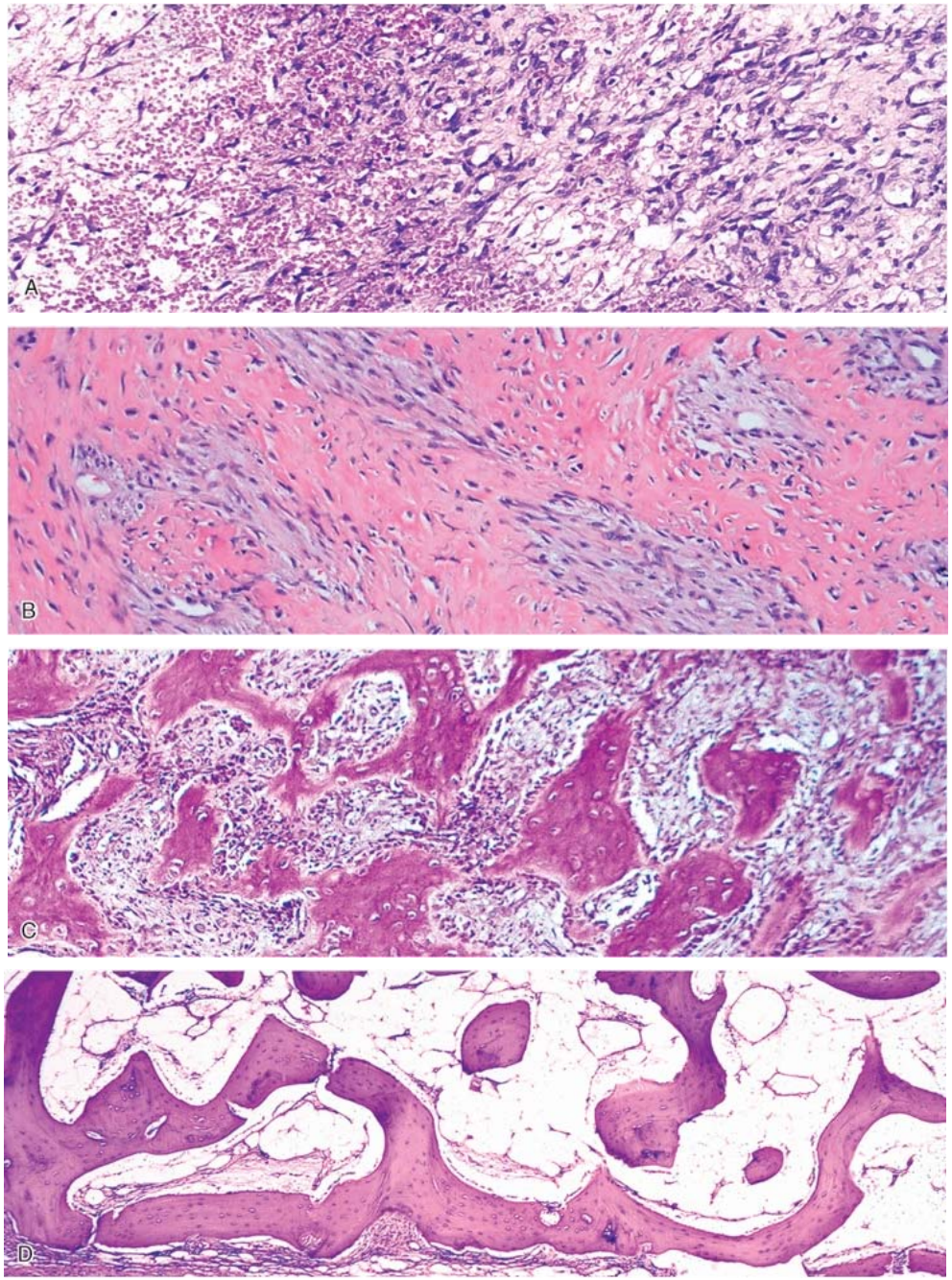
DD: Perosteal osteosarcoma
Soft tissue osteosarcoma
Subungual exostosis
Florid reactive periostitis
Nora disease



Dorfman and Czerniak's, Bone Tumors, Second Edition



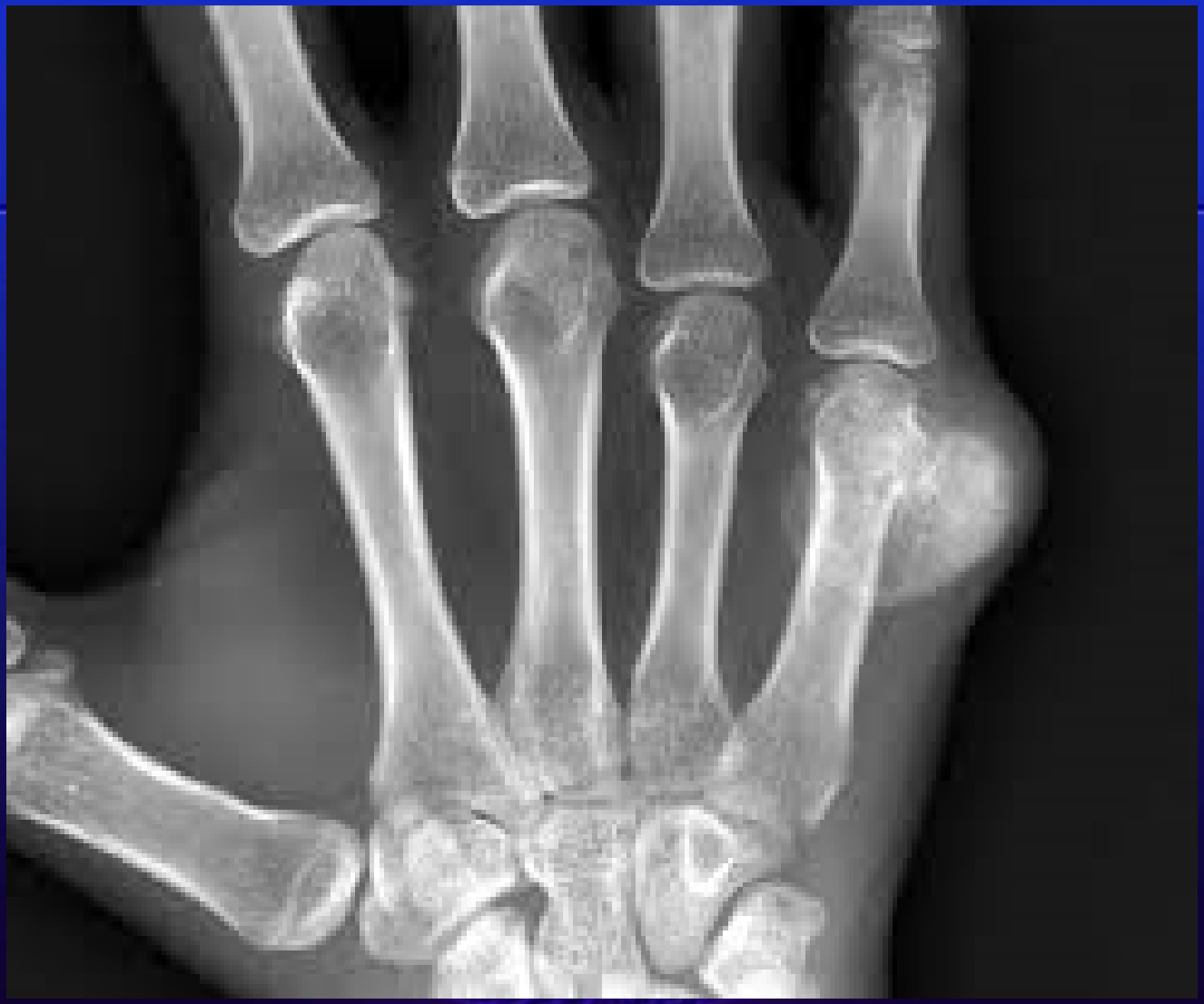
Dorfman and Czerniak's, Bone Tumors, Second Edition

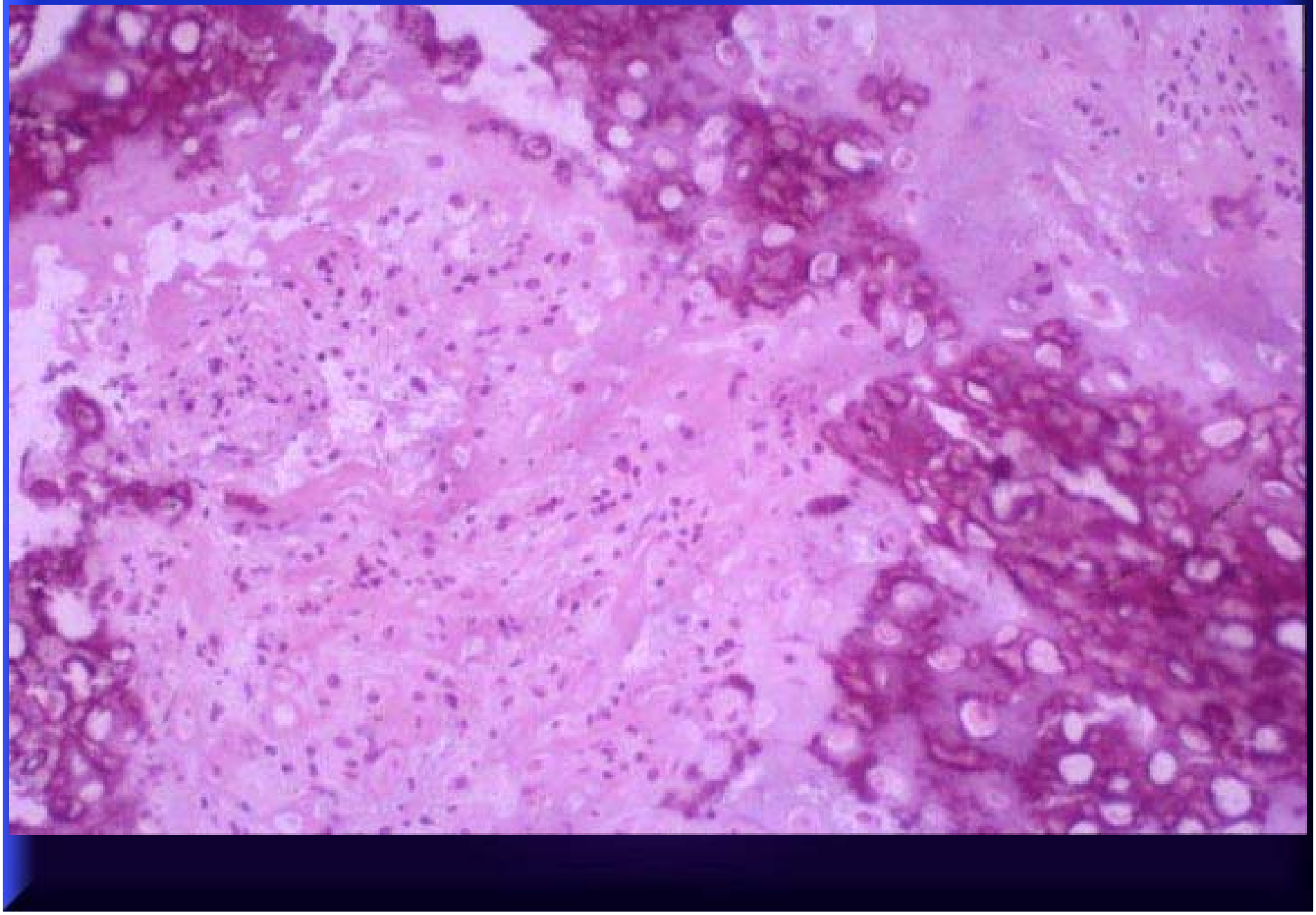


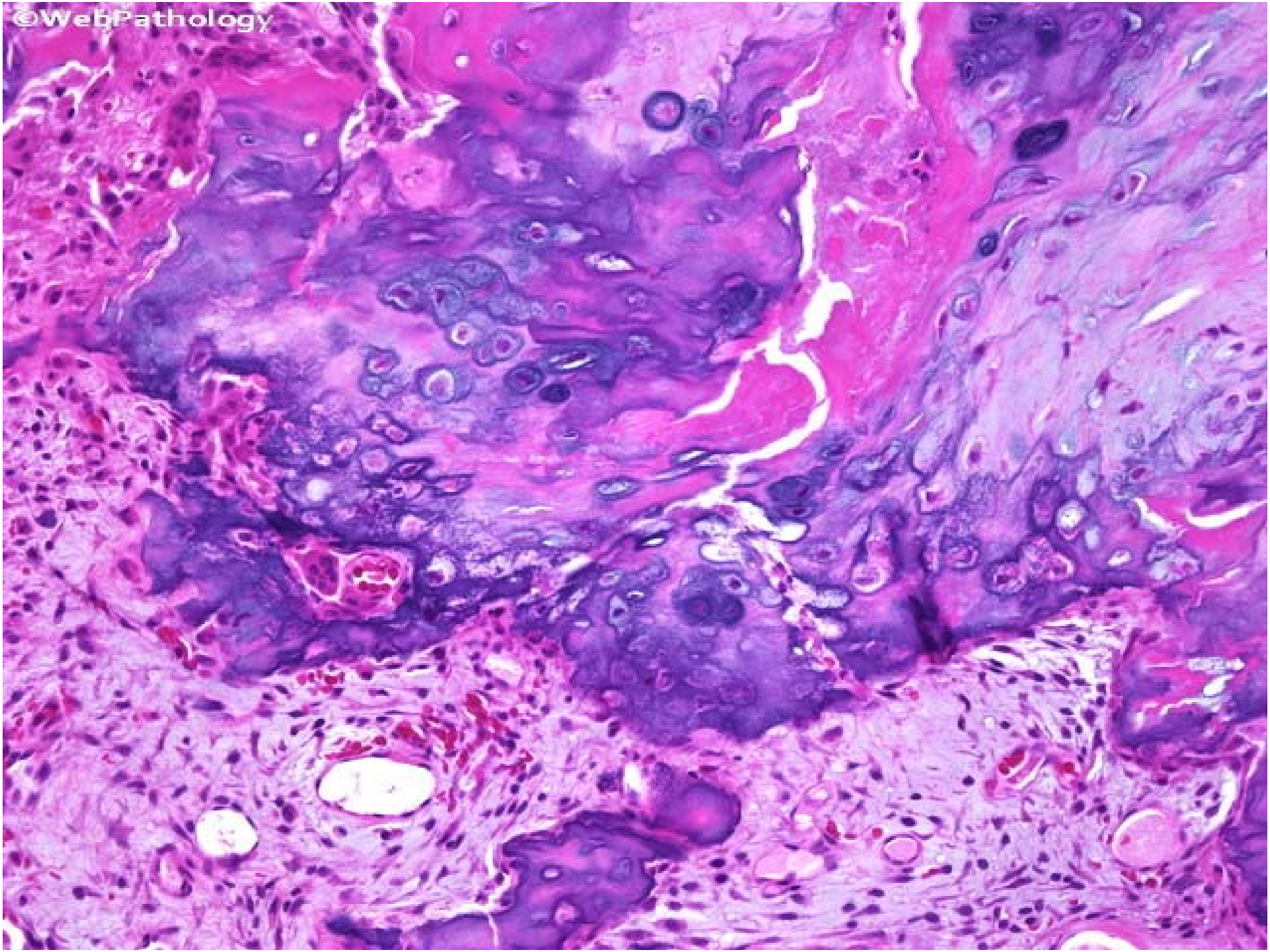
Dorfman and Czerniak's, Bone Tumors, Second Edition

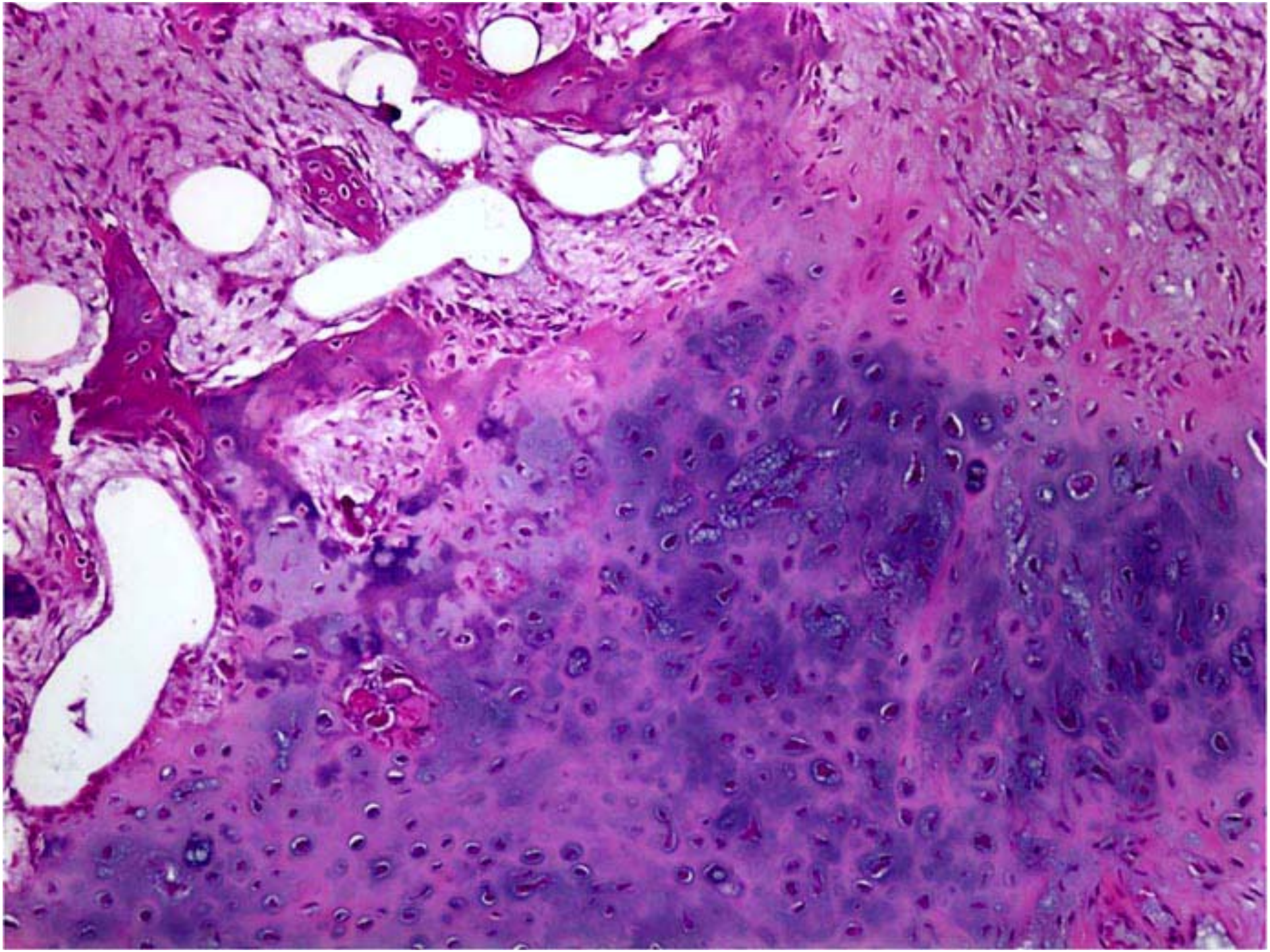
Nora lesion (Bizarre parosteal osteochondromatous proliferation)

- Usually involves the surface of small bones of hands and feet
- Related to subungual exostosis






©WebPathology




Thank you