AANP 2020 Diagnostic Slide Session

Case 5

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Case 6

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Case 5

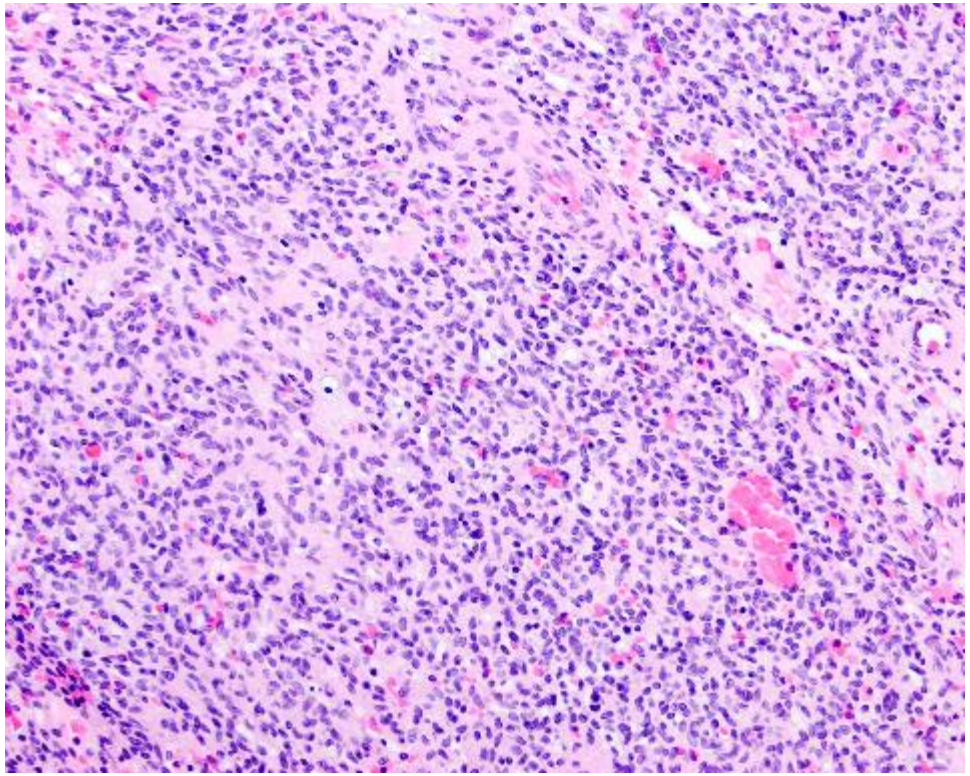
Clinical Presentation and Histology Presented by Cathryn Cadwell

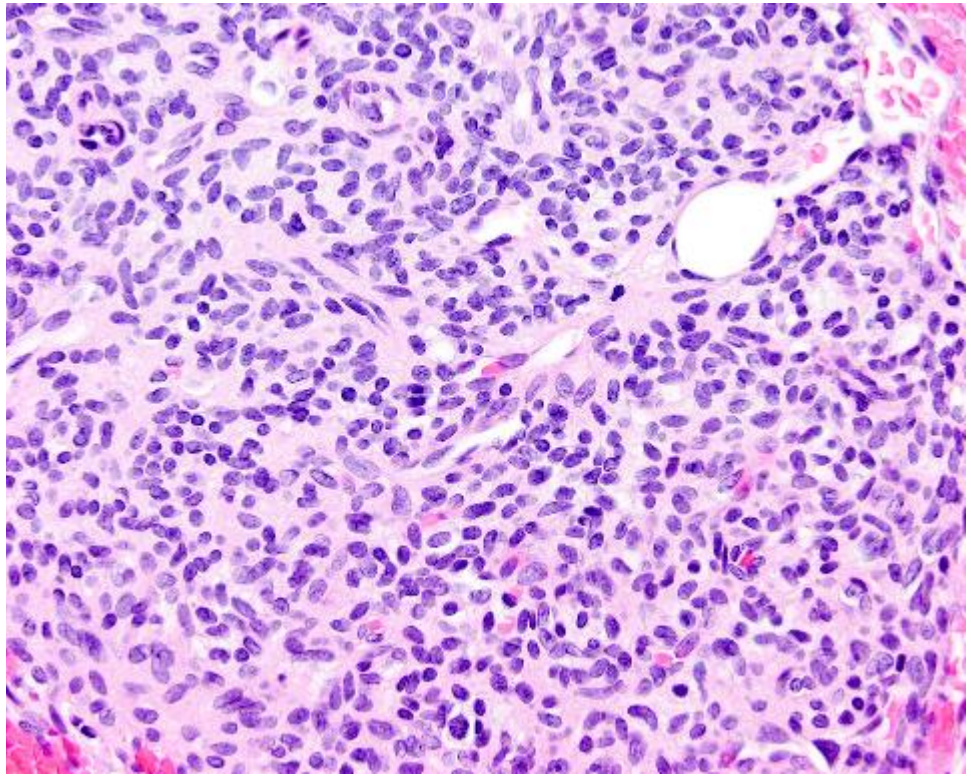
Case 5 – Clinical Presentation

- 45-year-old man who presented with generalized weakness, multiple fractures and hypophosphatemic osteomalacia.

- Imaging revealed an osteolytic, hypervascular mass in the left skull base, extending into the left middle ear, several skull base foramina, and encasing the internal carotid artery.

H&E





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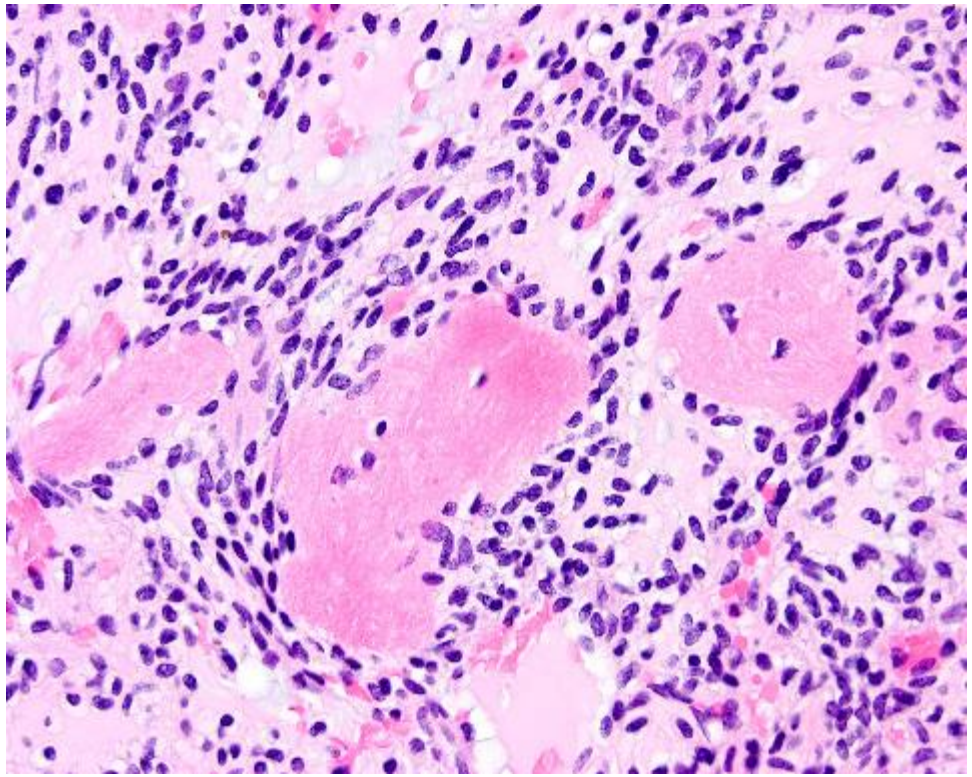
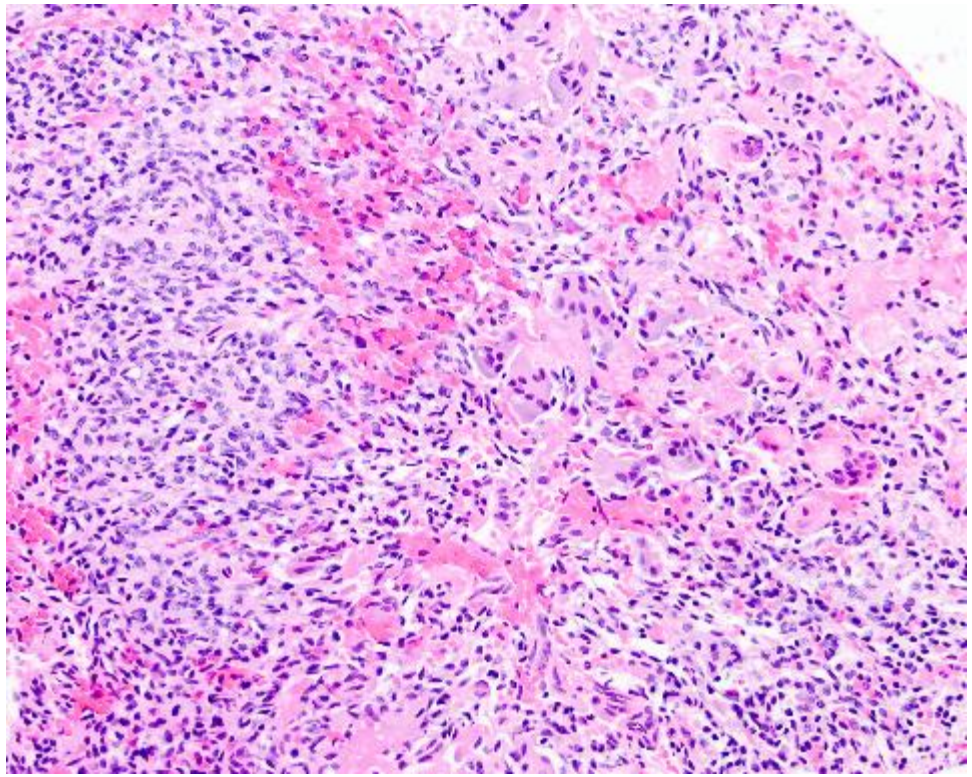


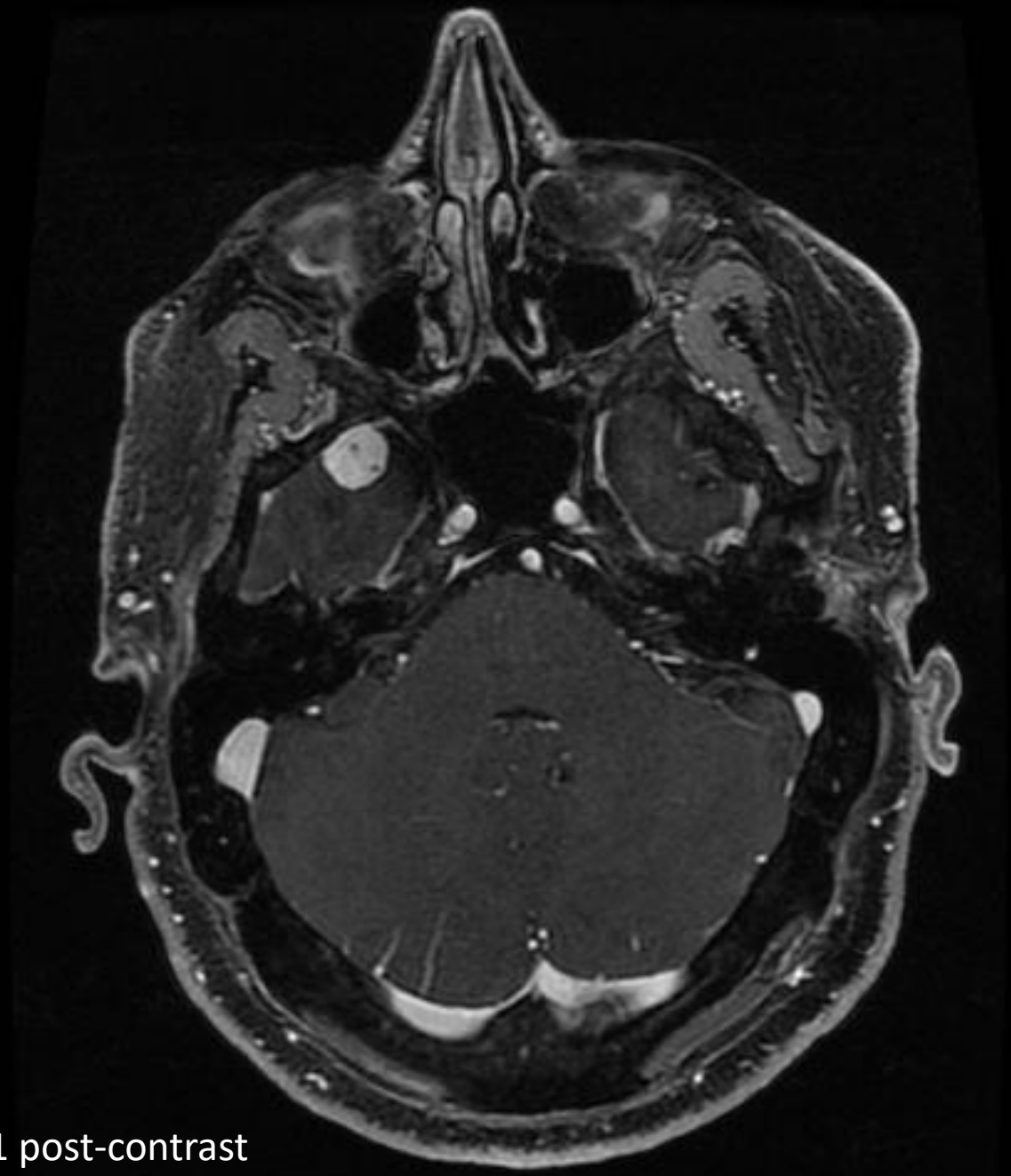


Case 6

Clinical Presentation and Histology Presented by Hannah Harmsen

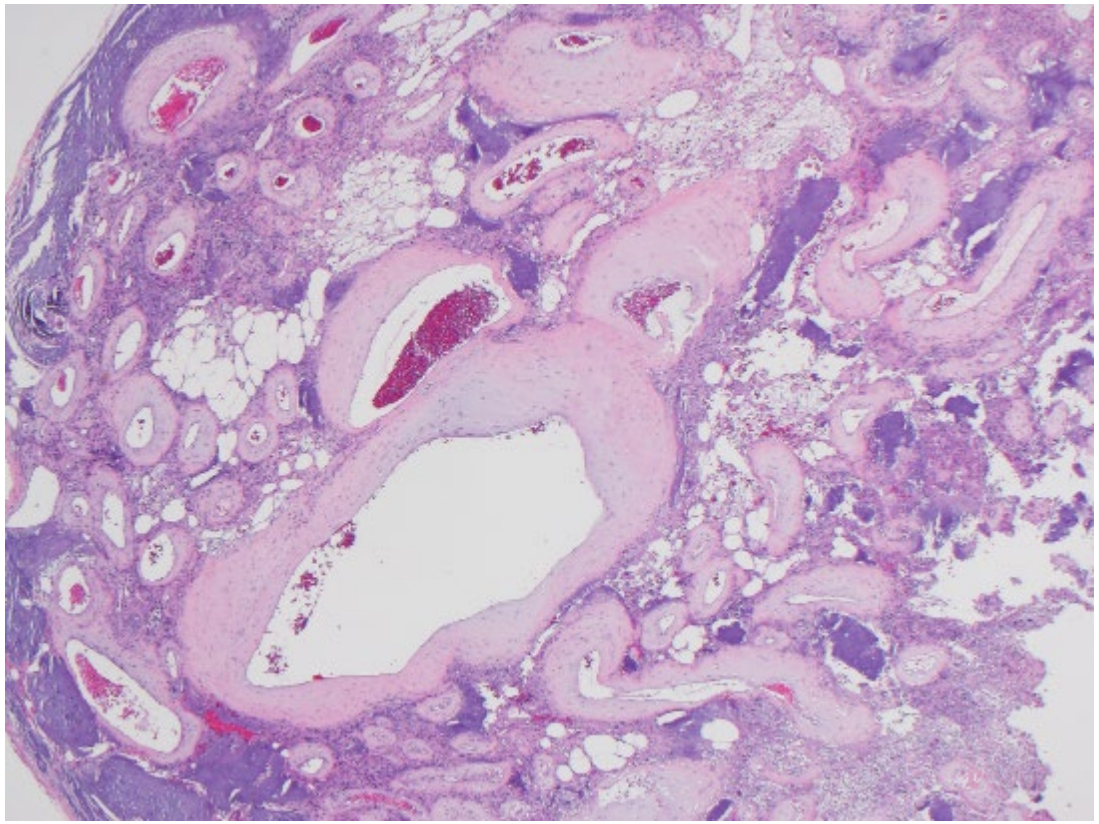
Case 6 – Clinical Presentation

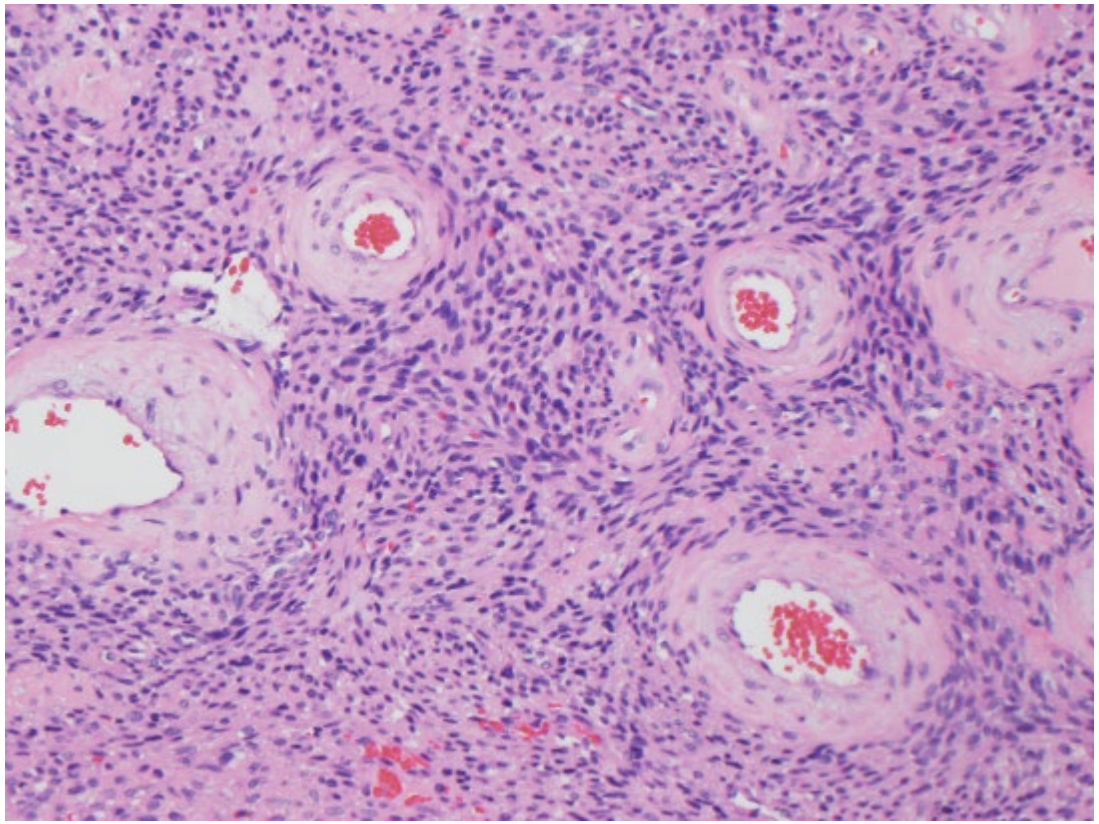
- 29-year-old man who presented with back and hip pain, multiple fractures, and generalized weakness
- Laboratory studies: hypophosphatemia, hyperphosphaturia, low Vitamin D and 1,25-dihydroxyvitamin D
- PET scan: single avid lesion in middle cranial fossa



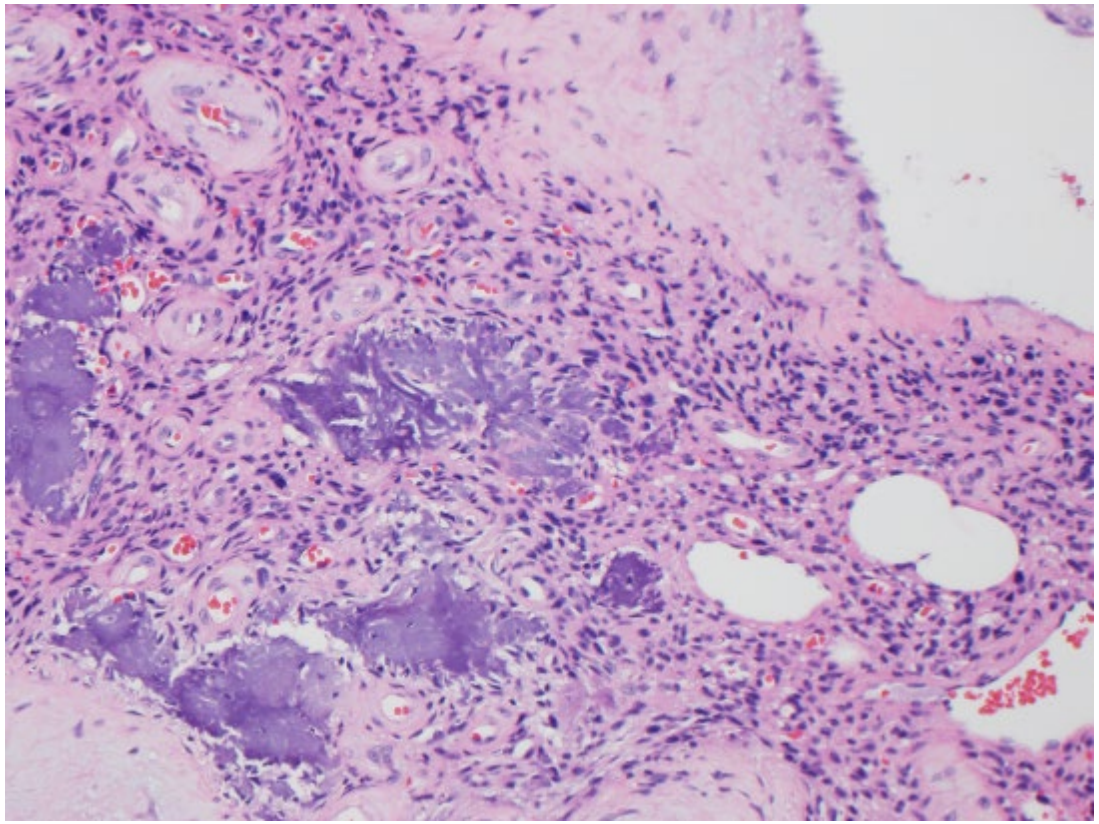
T1 post-contrast

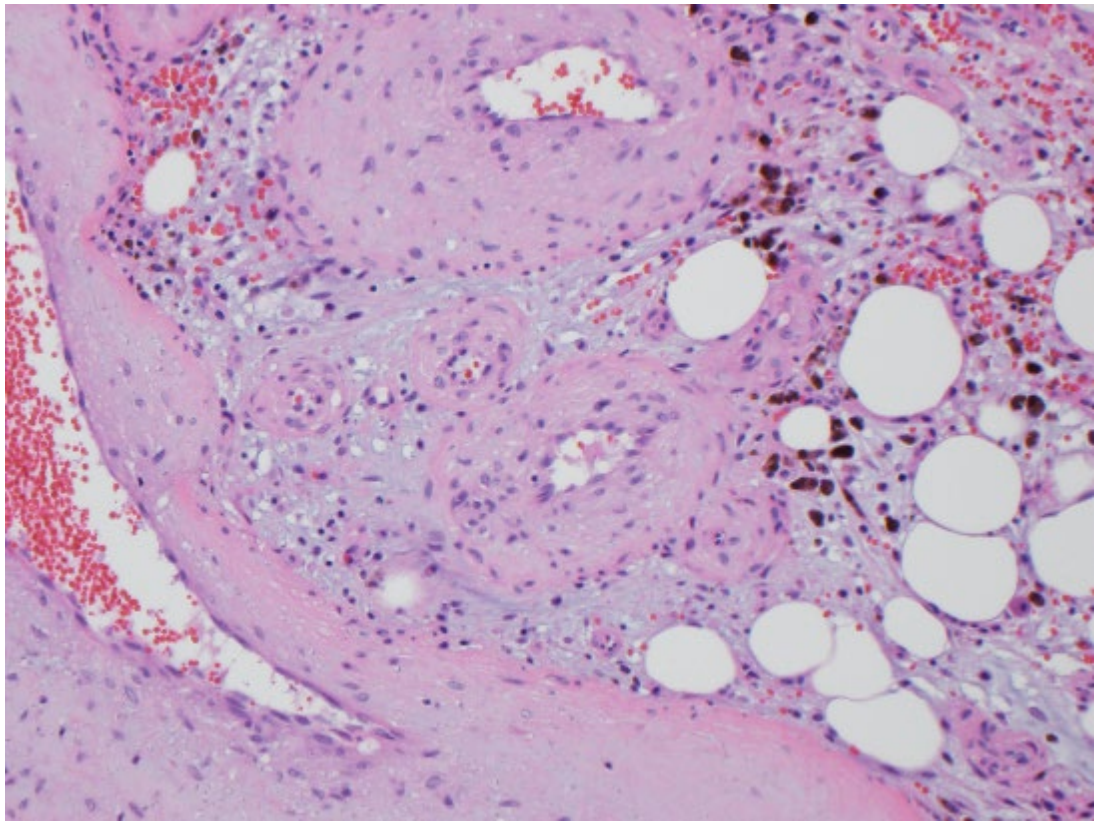
H&E





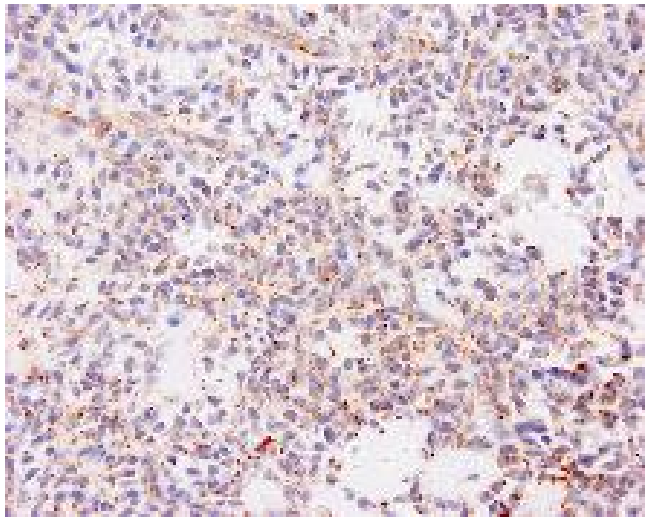
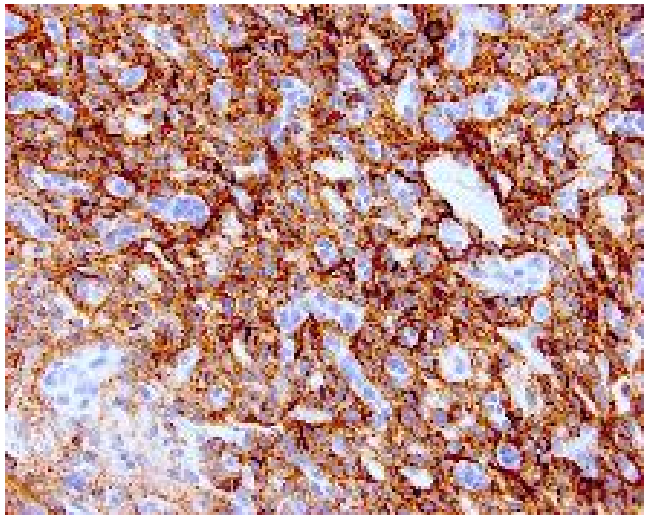
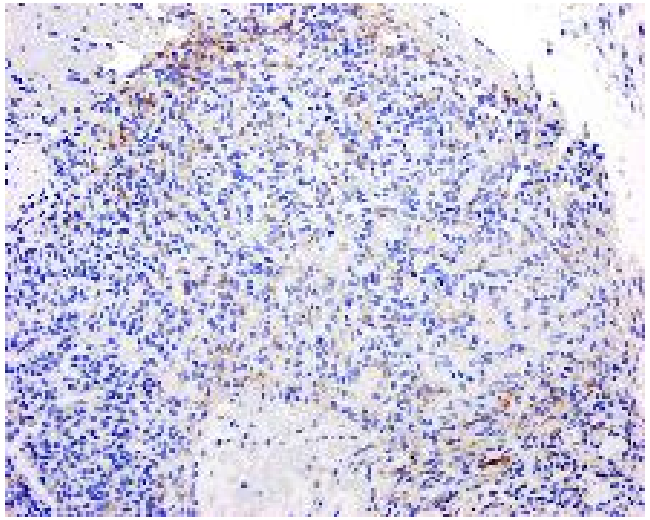
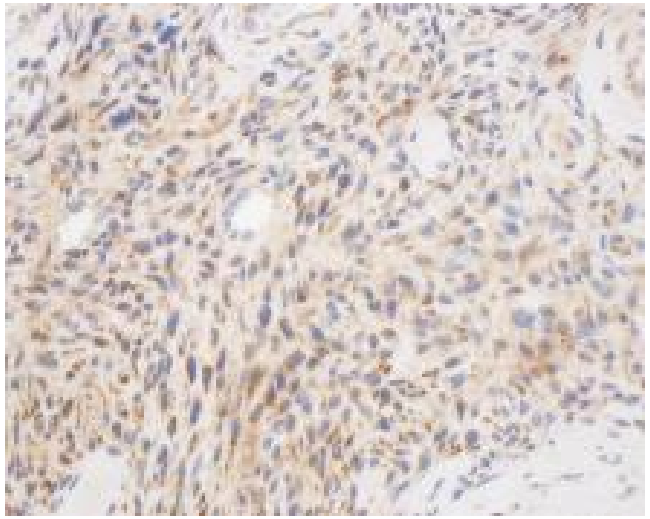
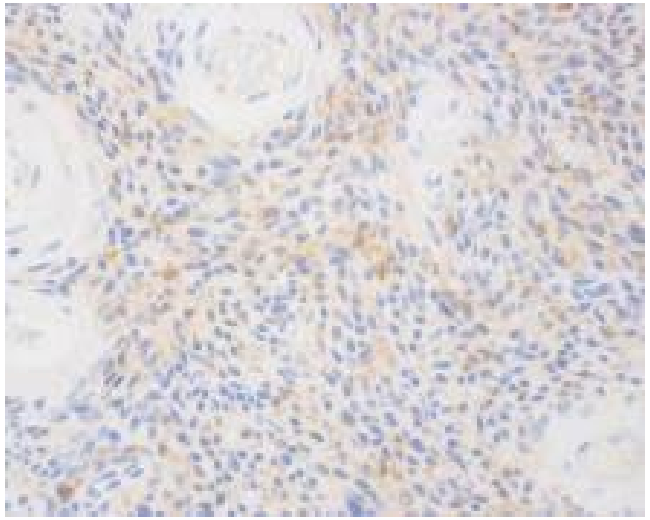
H&E



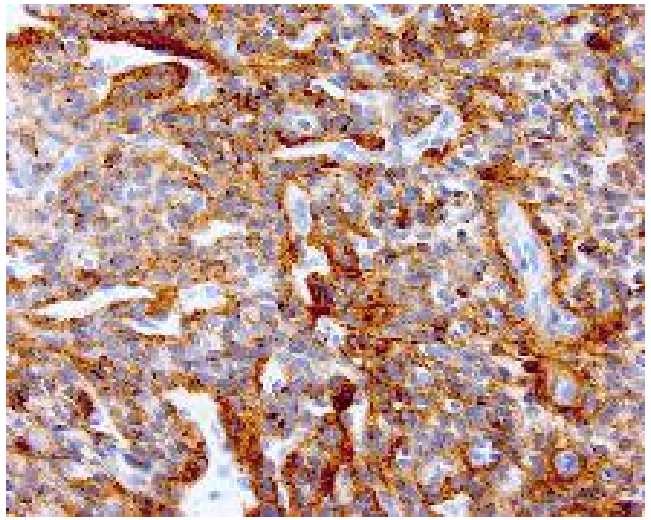
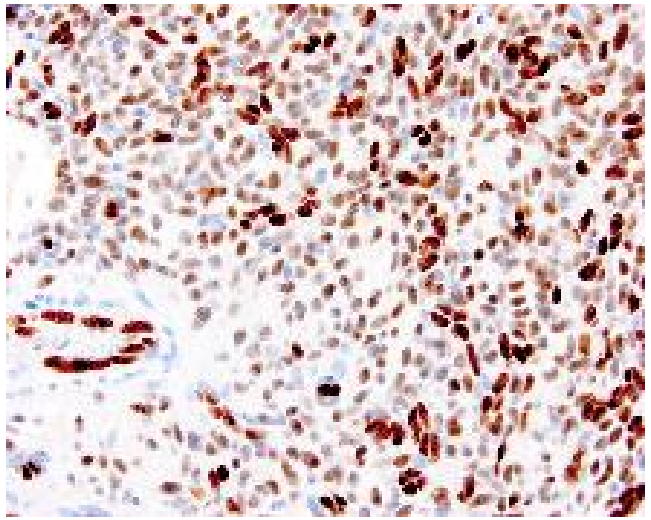
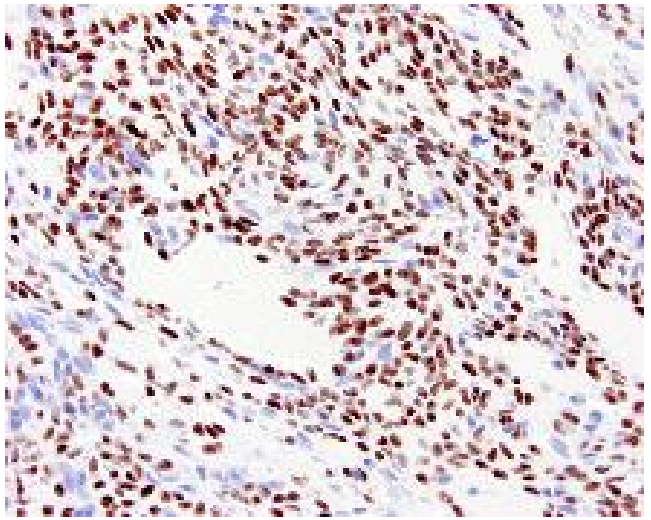
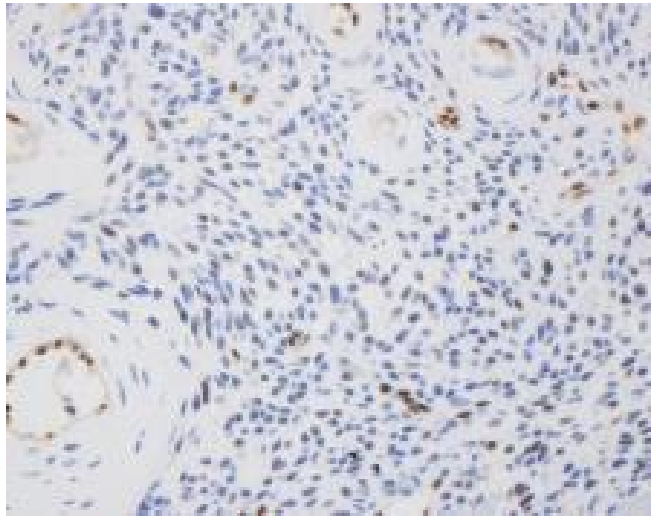


Audience Discussion

Immunohistochemistry

	STAT6	CD56	EMA
Case 5			
Case 6			

Immunohistochemistry

	SSTR2	ERG	SATB2
Case 5			
Case 6			

Final Diagnosis:
Phosphaturic Mesenchymal Tumor

Phosphaturic Mesenchymal Tumor: Key Diagnostic Points

- Clinicopathologically and genetically distinct neoplasm that causes the vast majority of mesenchymal tumor-associated osteomalacia

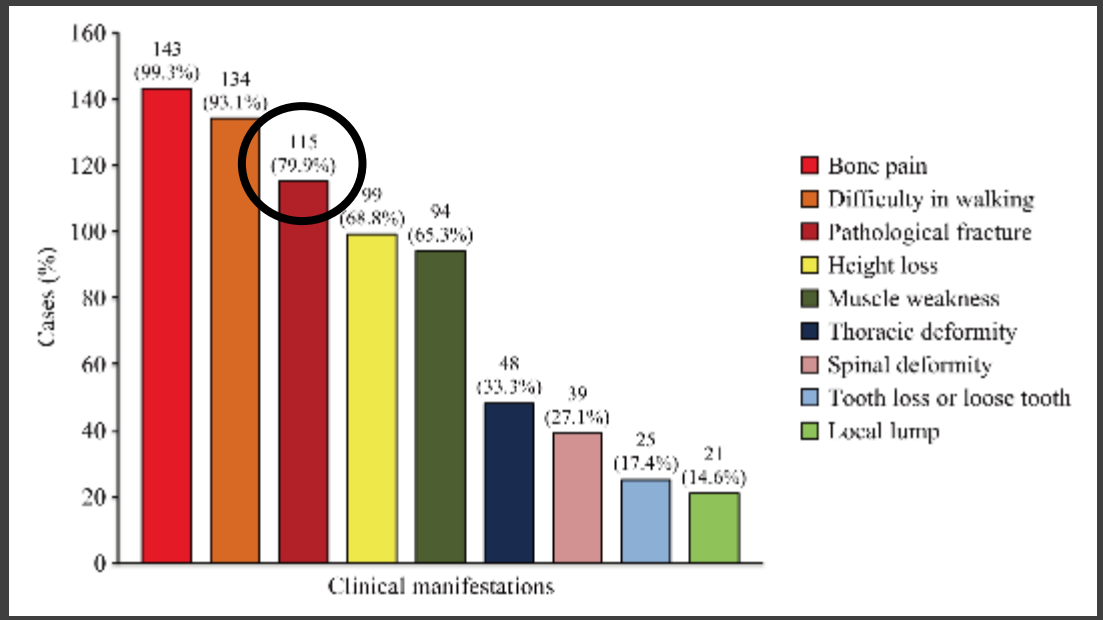
- Microscopic findings:
  - Hypocellular to moderately cellular proliferation of bland spindled to stellate cells with richly vascularized stroma
  - Unusual “smudgy” basophilic matrix, may produce “grungy” calcifications or resemble primitive osteoid or cartilage
  - Osteoclast-like giant cells and “fibrohistiocytic” spindled cells

Phosphaturic Mesenchymal Tumor: Differential Diagnosis and Ancillary Testing

- Diagnostic pitfalls when occurring intracranially:
  - Morphologically, can resemble solitary fibrous tumor/hemangiopericytoma
  - Immunohistochemically, overlaps with meningioma (SSTR2A, EMA and CD56 positive)
    - Also expresses SATB2 and ERG
    - May have limited CD34, SMA, S100, synaptophysin
- FGF23 overexpression by CISH or FISH for FN1-FGFR1/FGF1 fusions can confirm the diagnosis

Phosphaturic Mesenchymal Tumor: Clinical Presentation

- Often presents with fractures/severe osteomalacia rather than symptoms from the mass itself, ***but not always***
- Often misdiagnosed as lumbar disc herniation, spondyloarthritis, osteoporosis, etc.
- Average time from symptom onset to tumor resection is greater than 5 years

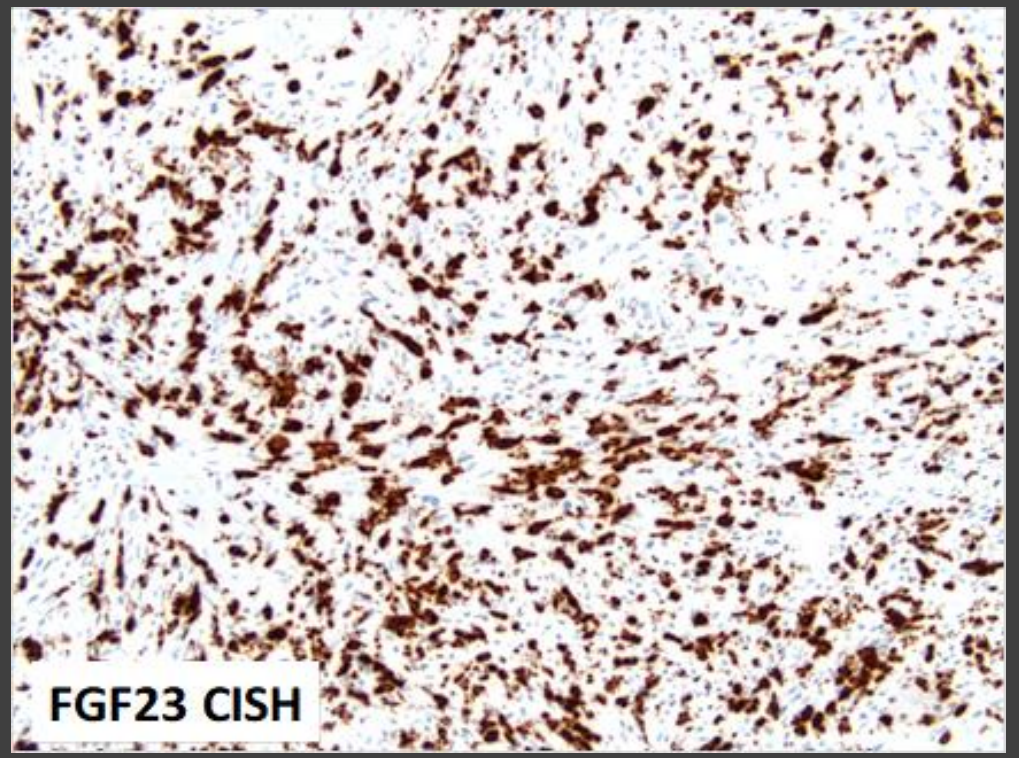


Feng et al., 2017

Phosphaturic Mesenchymal Tumor: Molecular Characteristics

- FN1-FGFR1 fusion
  - Fibronectin (chr 2) to FGFR1 (chr 8)
  - Overexpression of FGFR1
  - Increased FGFR1 signaling
  - FGF23 expression

- FN1-FGF1 fusion (6%)



Phosphaturic Mesenchymal Tumor: Tumor Induced Osteomalacia

- Paraneoplastic syndrome - tumoral production of FGF23
- FGF23
  - Normal function
  - Hypophosphatemia
  - Hypovitaminosis D
- Hypophosphatemic osteomalacia

Phosphaturic Mesenchymal Tumor: Behavior

- Most benign
- Local recurrence
- Rare malignant behavior with metastasis
- Histologic features associated with aggressive behavior
  - Hypercellularity
  - Marked nuclear atypia
  - Increased mitotic activity (>5 per 10 high power fields)
  - Necrosis

Acknowledgements

- Drs. Arie Perry and Nancy Kois (Case 5)
- Drs. Reid Thompson and Ty Abel (Case 6)
- Dr. Caterina Giannini, Dr. Rebecca Folkerth, Sarah Porter and Renea Marin (DSS Organizers)

References

1. Feng J, et al. (2017) The diagnostic dilemma of tumor induced osteomalacia: a retrospective study of 144 cases. *Endocr J*, 64(7), 675-683.

2. Folpe AL. (2019) Phosphaturic mesenchymal tumors: A review and update. *Seminars in Diagnostic Pathology*, 36, 260-268.

3. Florenzano P, et al. (2017) Tumor-induced osteomalacia. *Bone Reports*, 7:90-97.

Questions???