AMSER Rad Path Case of the Month:

66-year-old female presents with an incidental 4.2 cm left renal mass

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Patient Presentation

HPI: 66-year-old female with past medical history of hypertension initially presented to the emergency room with abdominal pain. During her workup, CT scan incidentally revealed a 4.2 cm left renal mass. No dysuria, urinary frequency, gross hematuria, or weak urinary stream.

PMHx: Hypertension

PSHx: Appendectomy, hysterectomy

Family Hx: Prostate cancer (father), lung cancer (father), throat cancer (mother)

Social Hx: No smoking history

Pertinent Labs

- BUN, creatinine, eGFR all within normal limits
- Urinalysis unremarkable

What Imaging Should We Order?

Select the applicable ACR Appropriateness Criteria

Variant 1: **Indeterminate renal mass. No contraindication to either iodinated CT contrast or gadolinium-based MR intravenous contrast. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
US abdomen with IV contrast	Usually Appropriate	O
MRI abdomen without and with IV contrast	Usually Appropriate	O
CT abdomen without and with IV contrast	Usually Appropriate	☢☢☢☢
US kidneys retroperitoneal	May Be Appropriate	O
MRI abdomen without IV contrast	May Be Appropriate	O
CT abdomen with IV contrast	May Be Appropriate	☢☢☢
CT abdomen without IV contrast	May Be Appropriate	☢☢☢
CTU without and with IV contrast	May Be Appropriate	☢☢☢☢

Ordered by urologist during renal mass workup

Ordered initially by ER during abdominal pain workup

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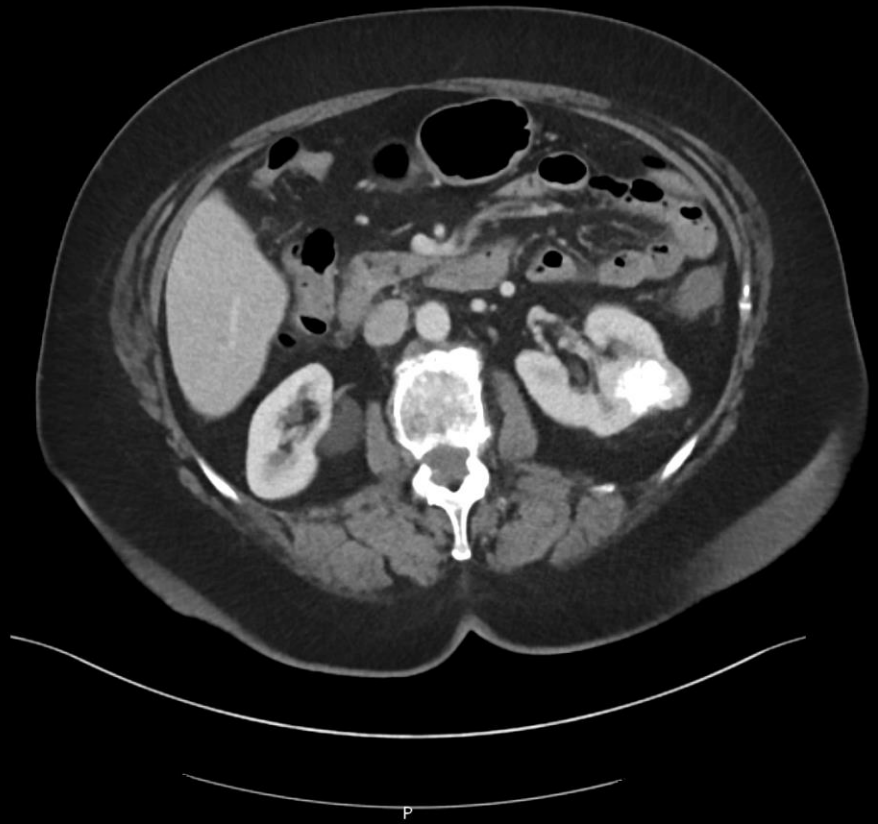
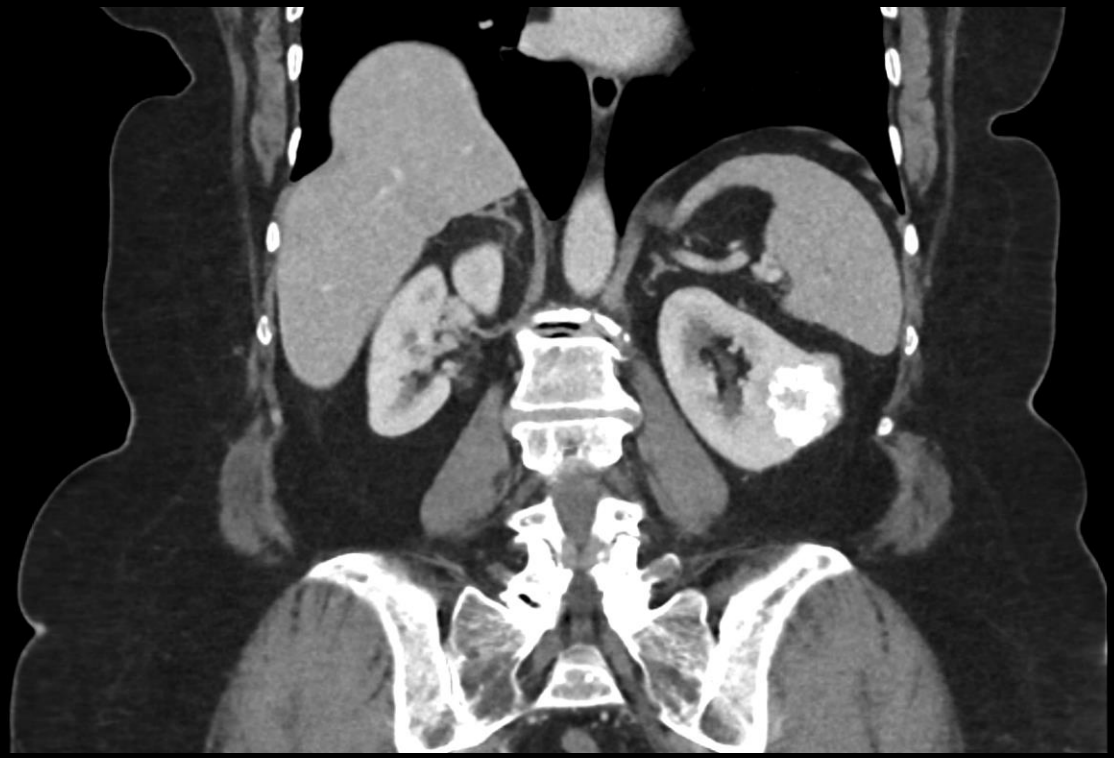
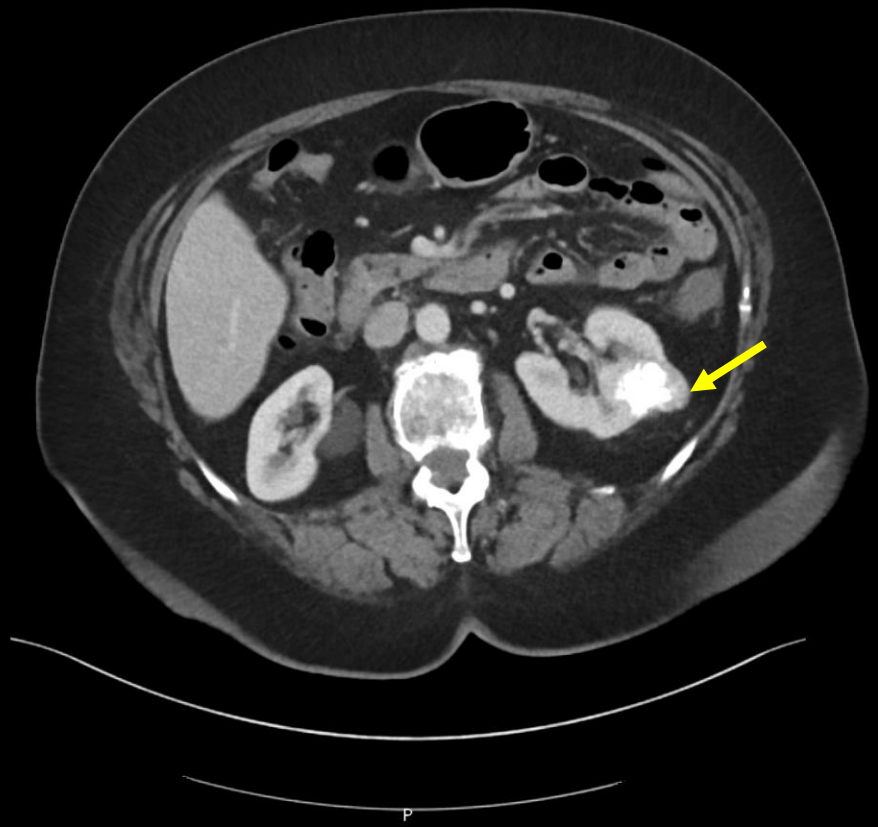
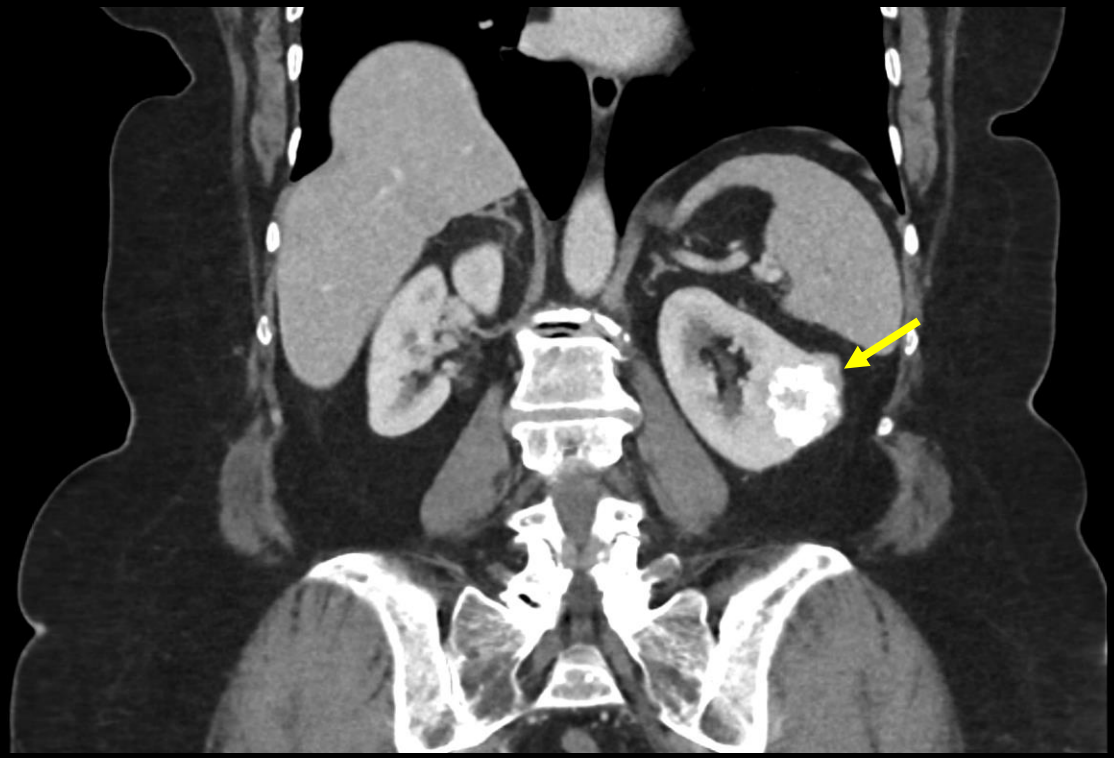
CT without Contrast (not labeled)





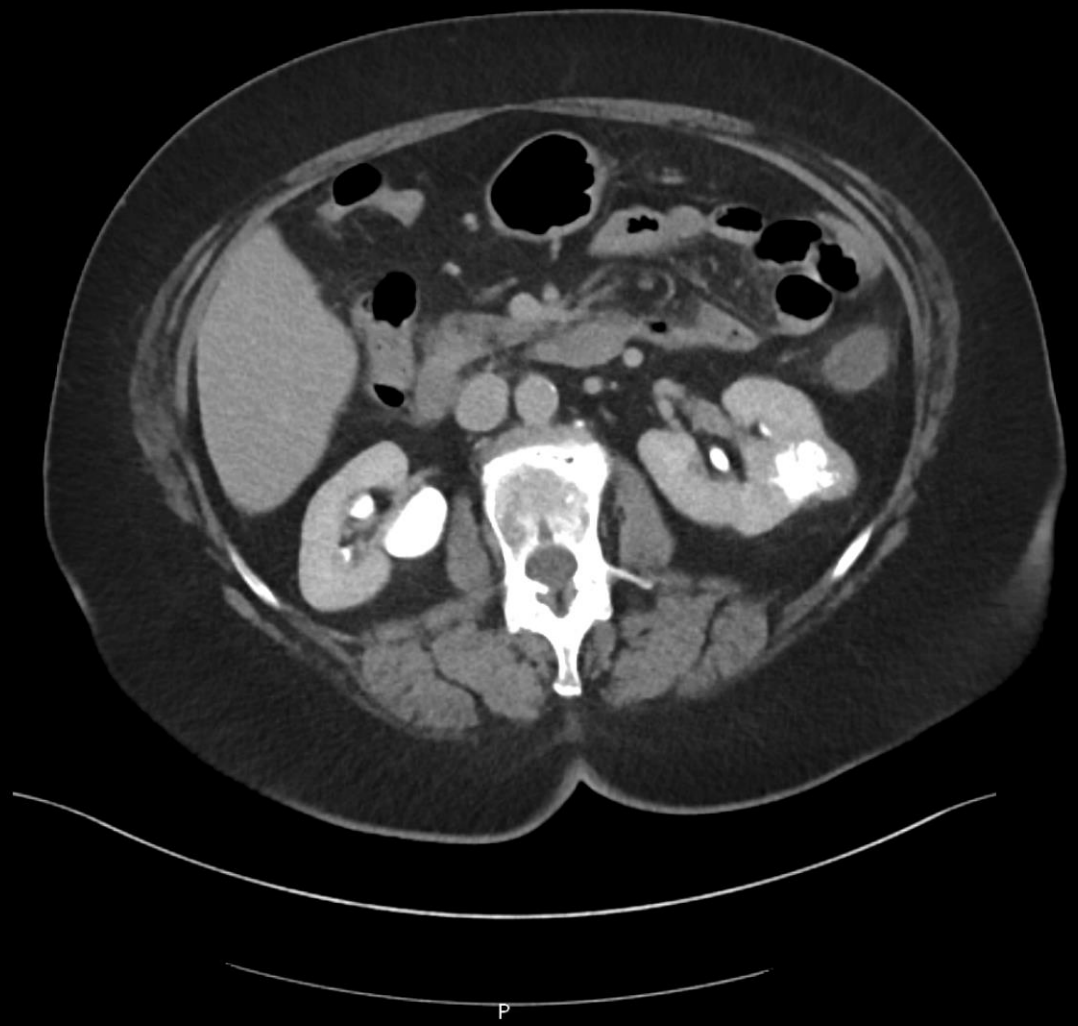
CT without Contrast (labeled)



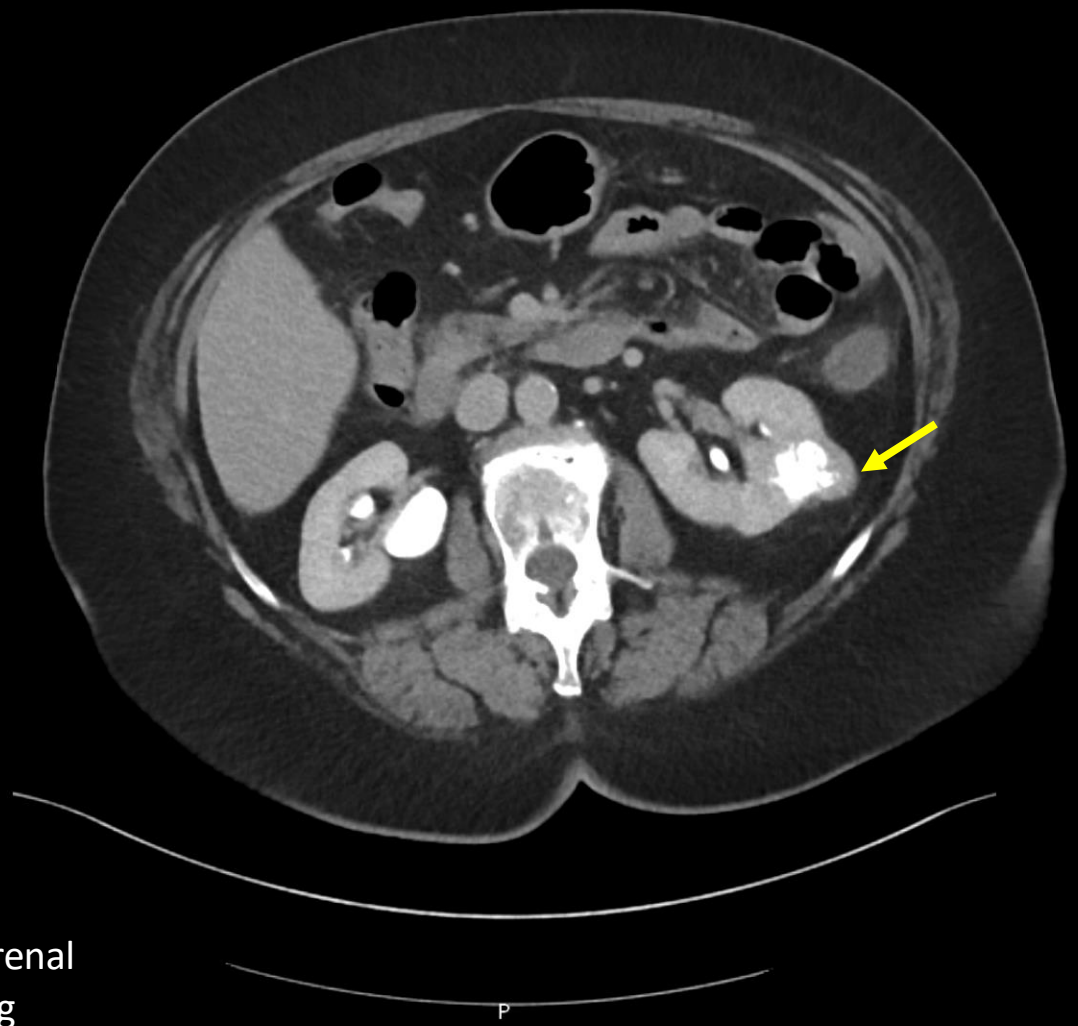


3.6 cm complex, heavily calcified left renal lesion with small amount of enhancing tissue (arrow).

CT with Contrast (not labeled)

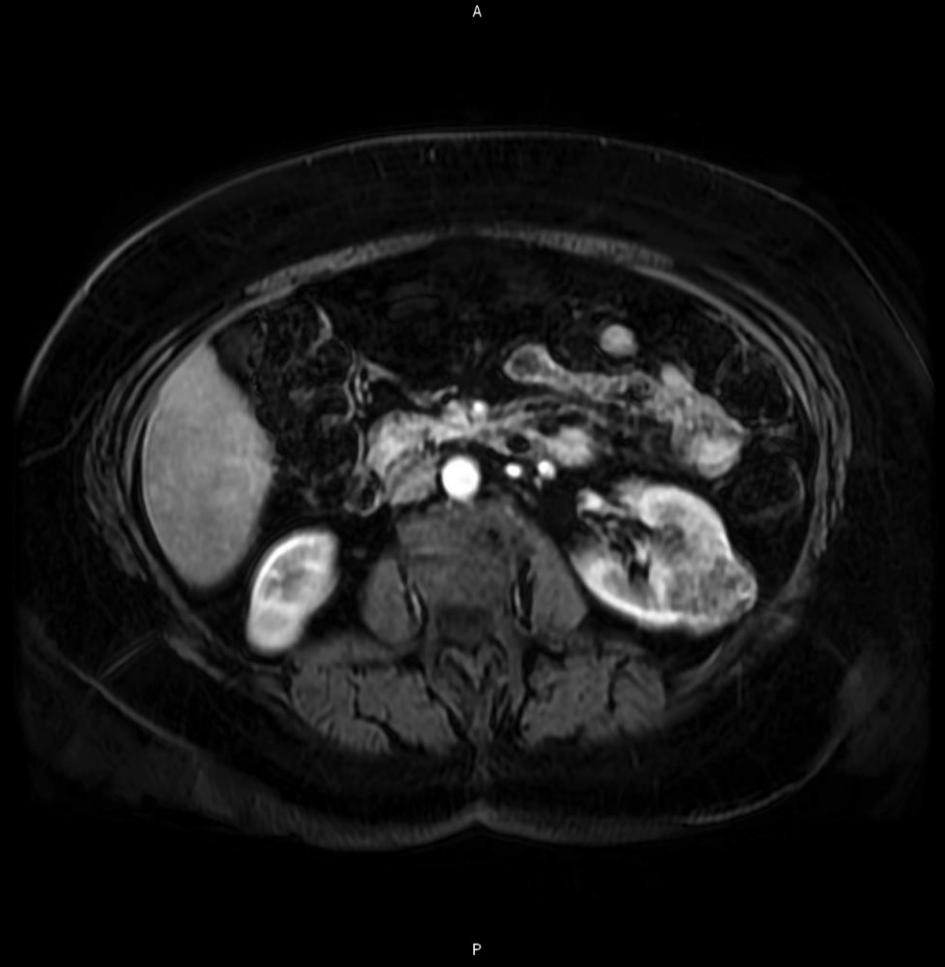


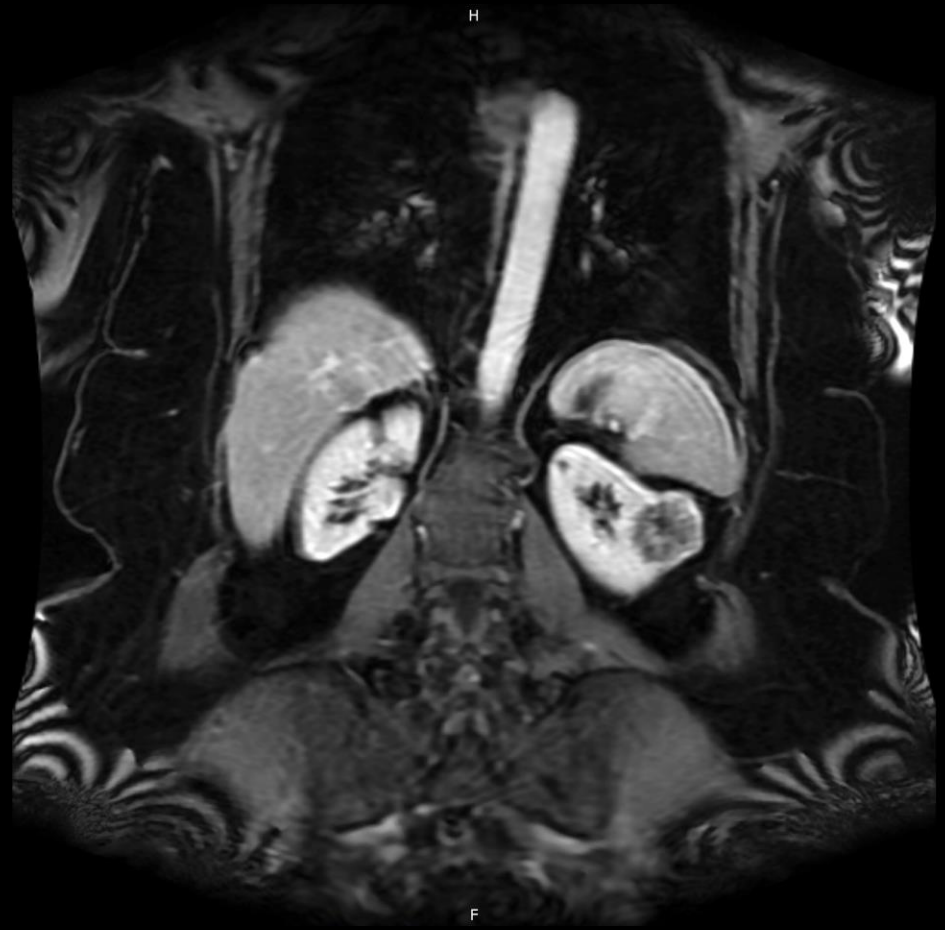
CT with Contrast (labeled)



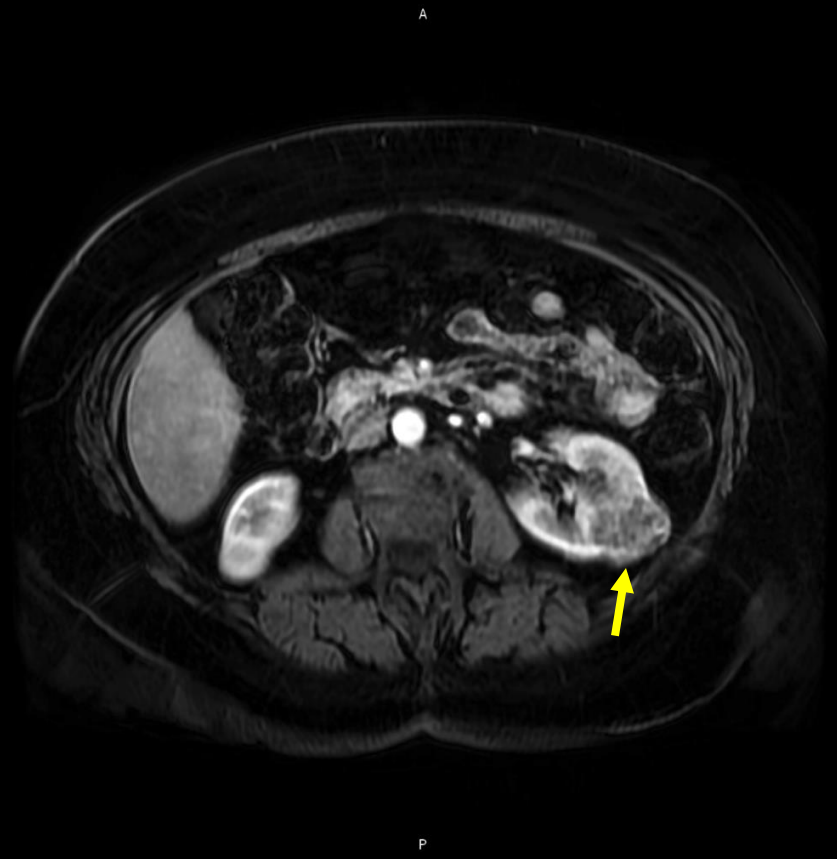
3.6 cm complex, heavily calcified left renal lesion with small amount of enhancing tissue (arrow).

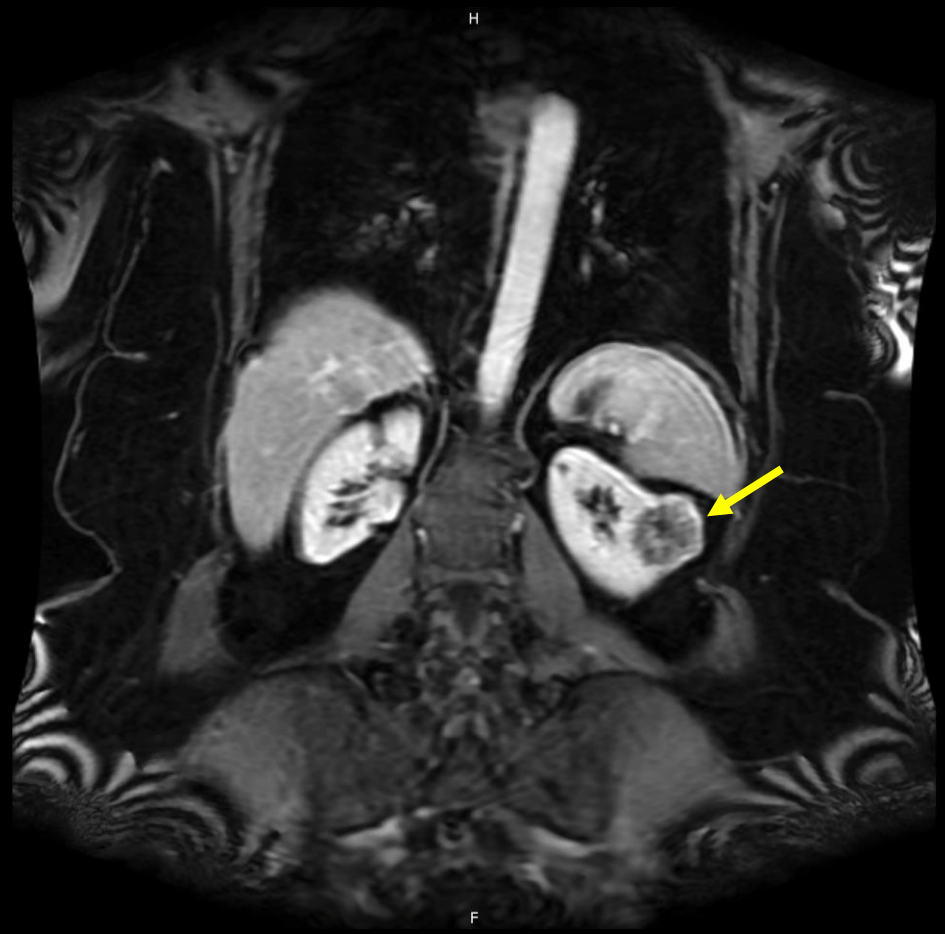
T1-weighted MRI with Contrast (not labeled)





T1-weighted MRI with Contrast (labeled)





4.2 cm heterogeneous mass with innumerable enhancing septa in the lateral mid to lower pole of the left kidney with small amount of enhancing tissue (arrow). Calcifications not well-appreciated on T1-weighted MRI.

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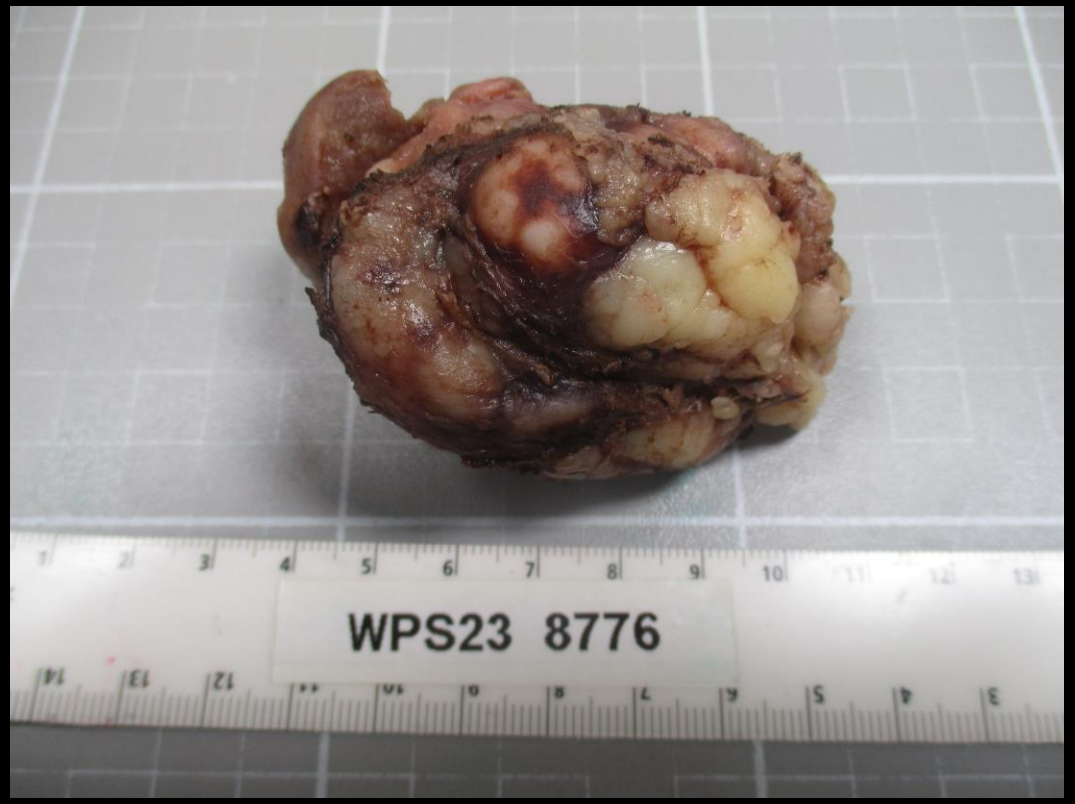
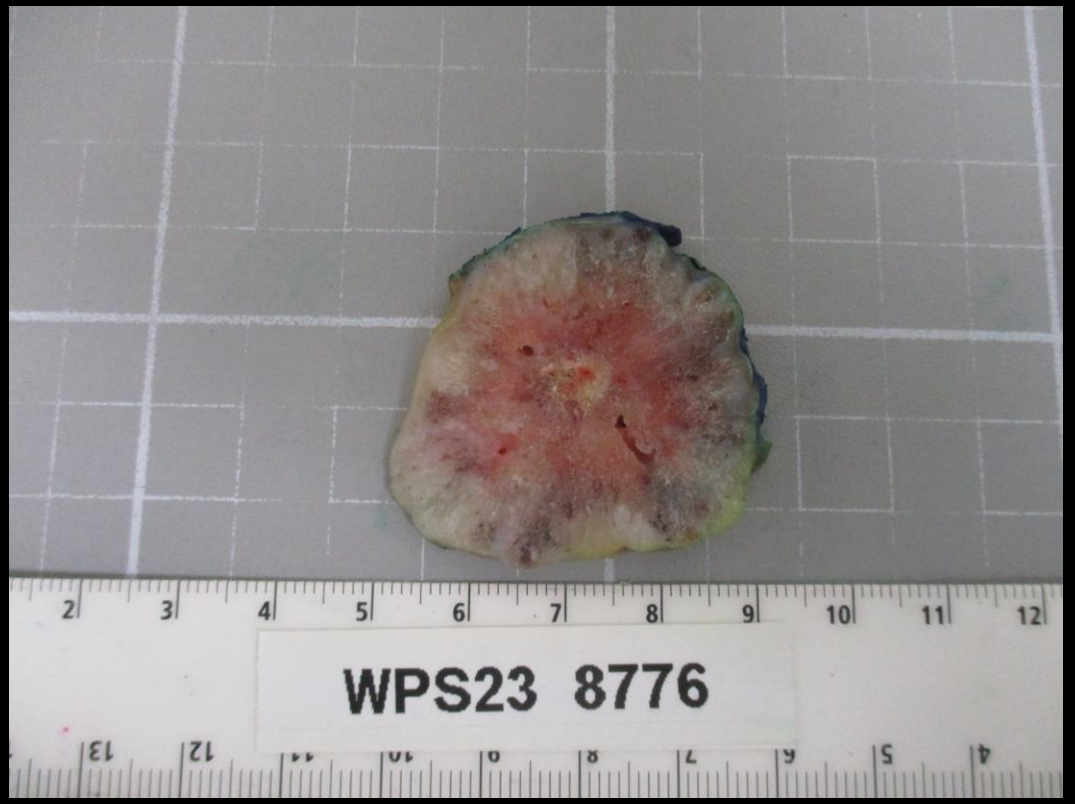
DDX (based on imaging): Calcified Renal Mass

- Renal cell carcinoma (heavily calcified)
  - Clear cell (most common)
  - Chromophobe
  - Papillary
  - Collecting duct (<1%)
- Calcified renal cyst
- Other calcified renal mass
  - Leiomyoma
    - Well-defined, capsular lesions with hyperattenuation on noncontrast CT
  - Oncocytoma
    - Sharply demarcated lesions with uniform enhancement on CT and central scar

Gross Path



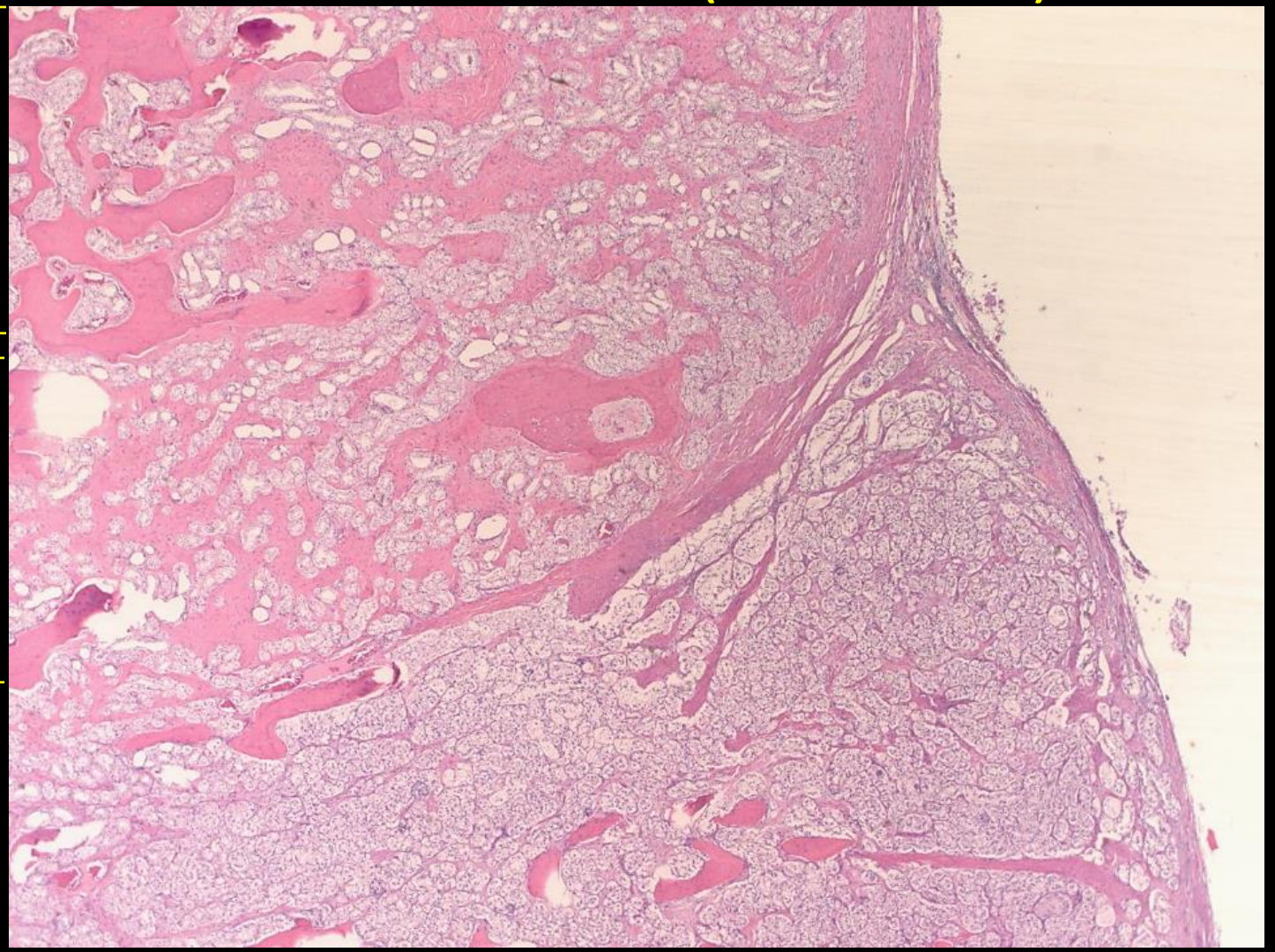
Hardened, heavily calcified mass removed during partial nephrectomy.



Cross-section of hardened, heavily calcified mass removed during partial nephrectomy.

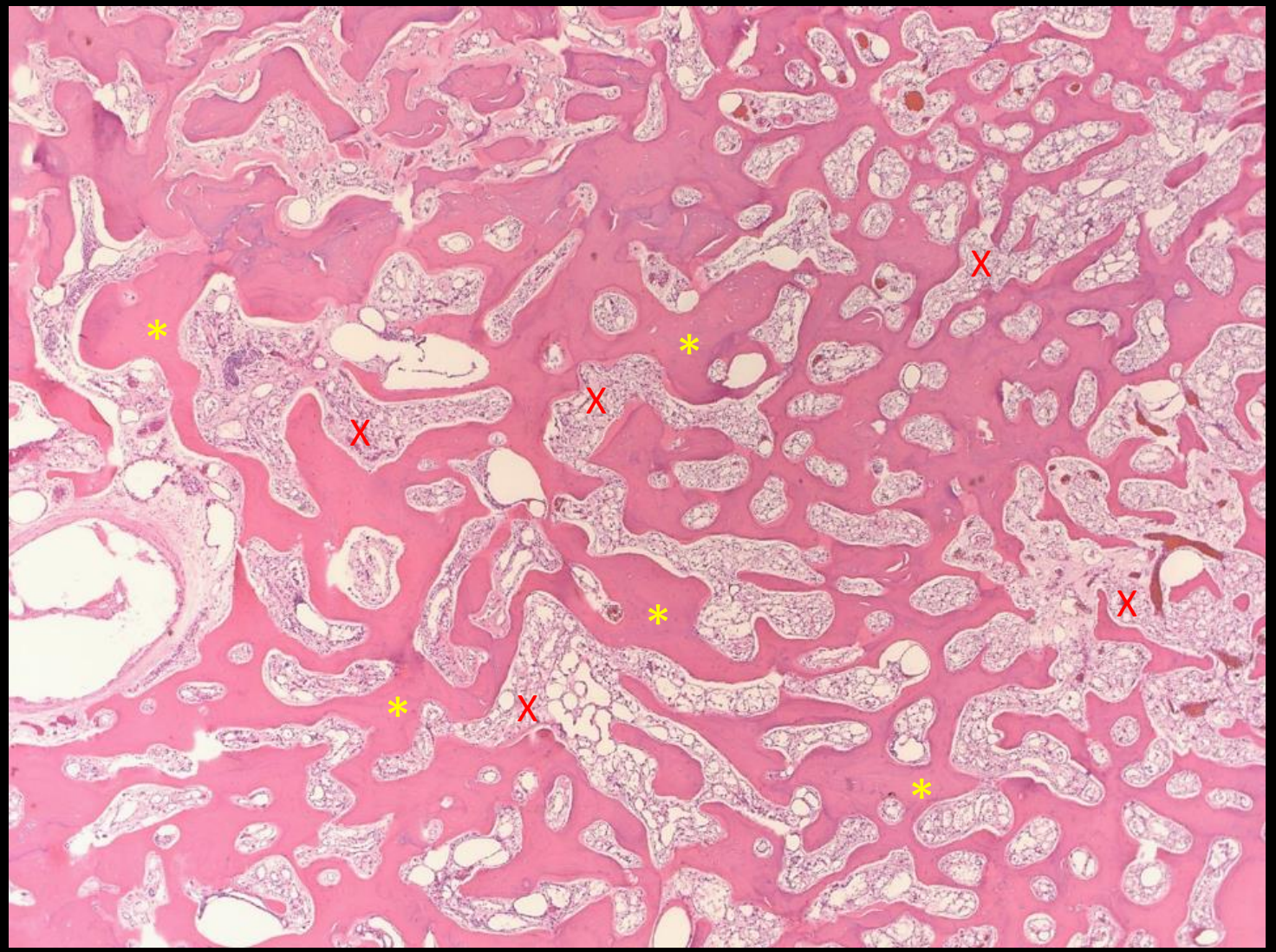
Credit: Thank you to Mark Blackburn for obtaining the gross images.

Micro Path (labeled)



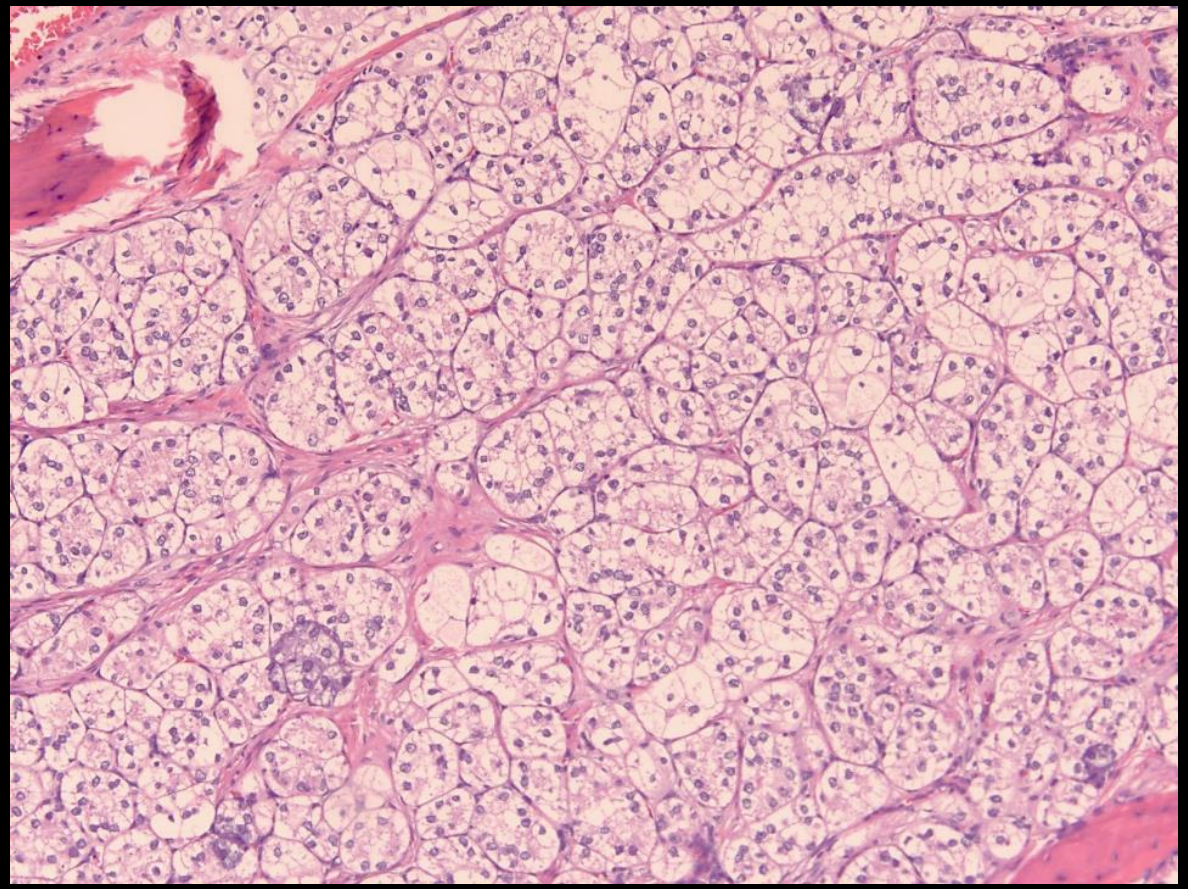
Interface of clear cell component of tumor, eosinophilic tubular component of tumor, and osseous metaplasia.

Micro Path (labeled)

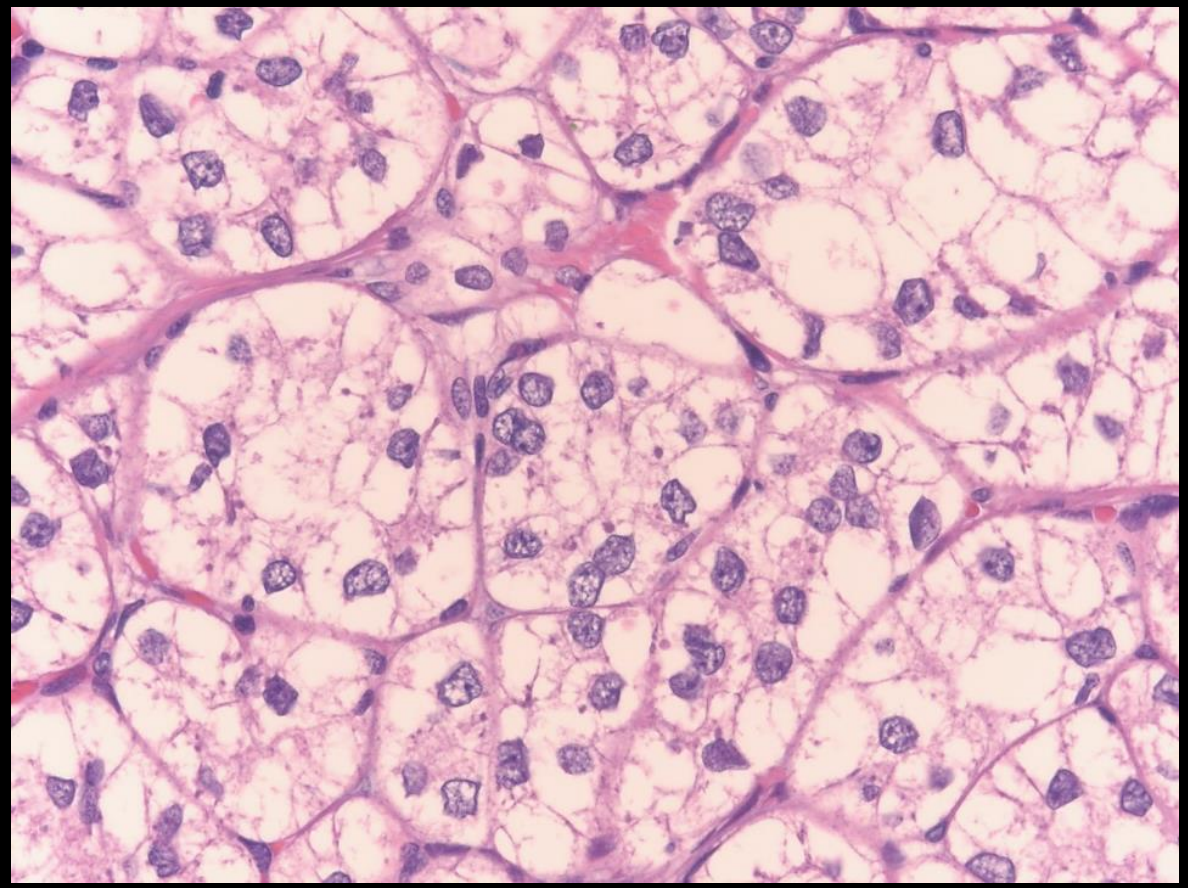


Further extent of osseous metaplasia. Thick segments of metaplastic cortical bone (*) interdigitate with tumor (X).

Micro Path (labeled)

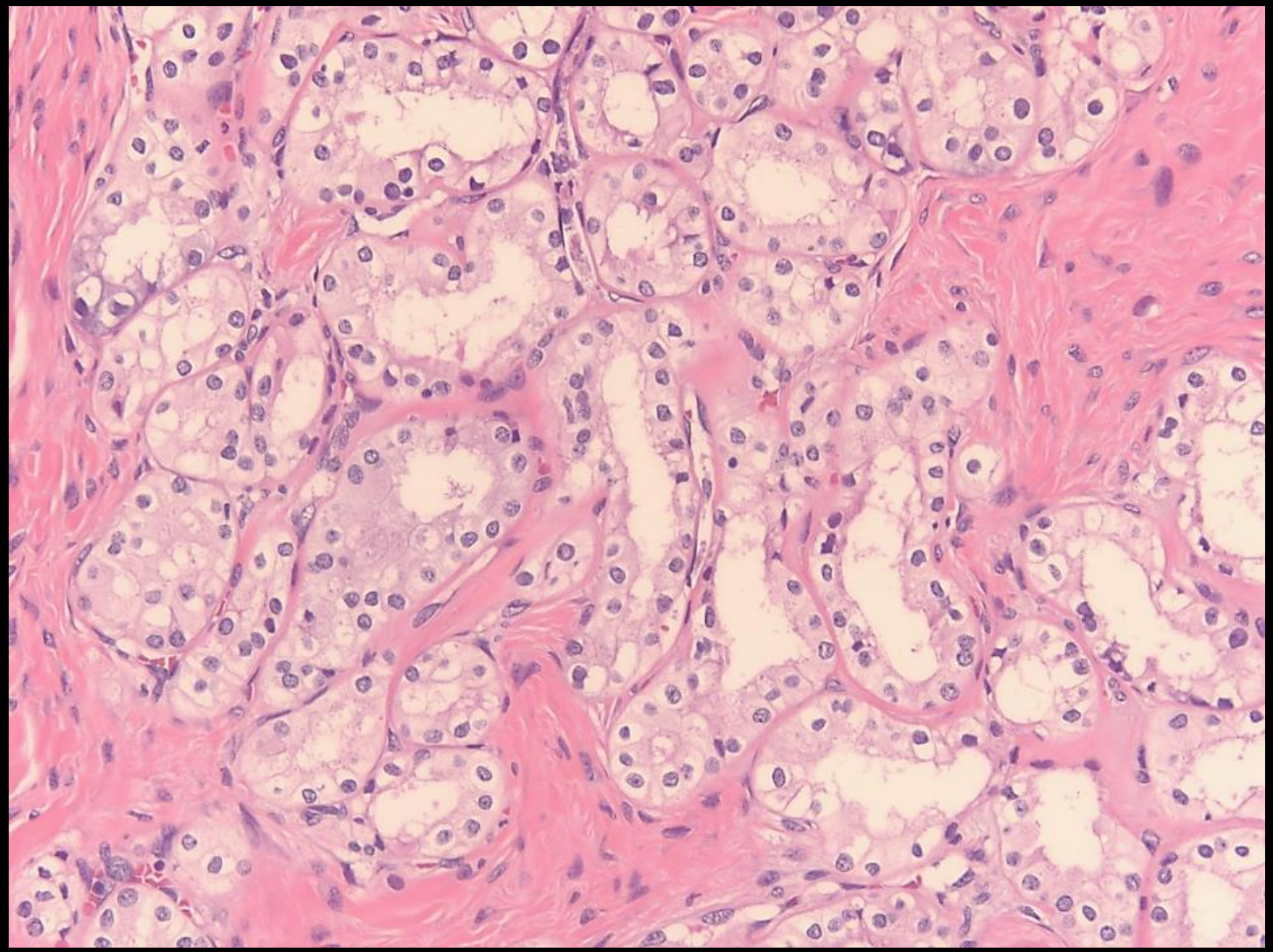


Higher-power (10X) view of the clear cell component of the tumor. Solid nests containing cells with small, round to oval nuclei and abundant clear cytoplasm.



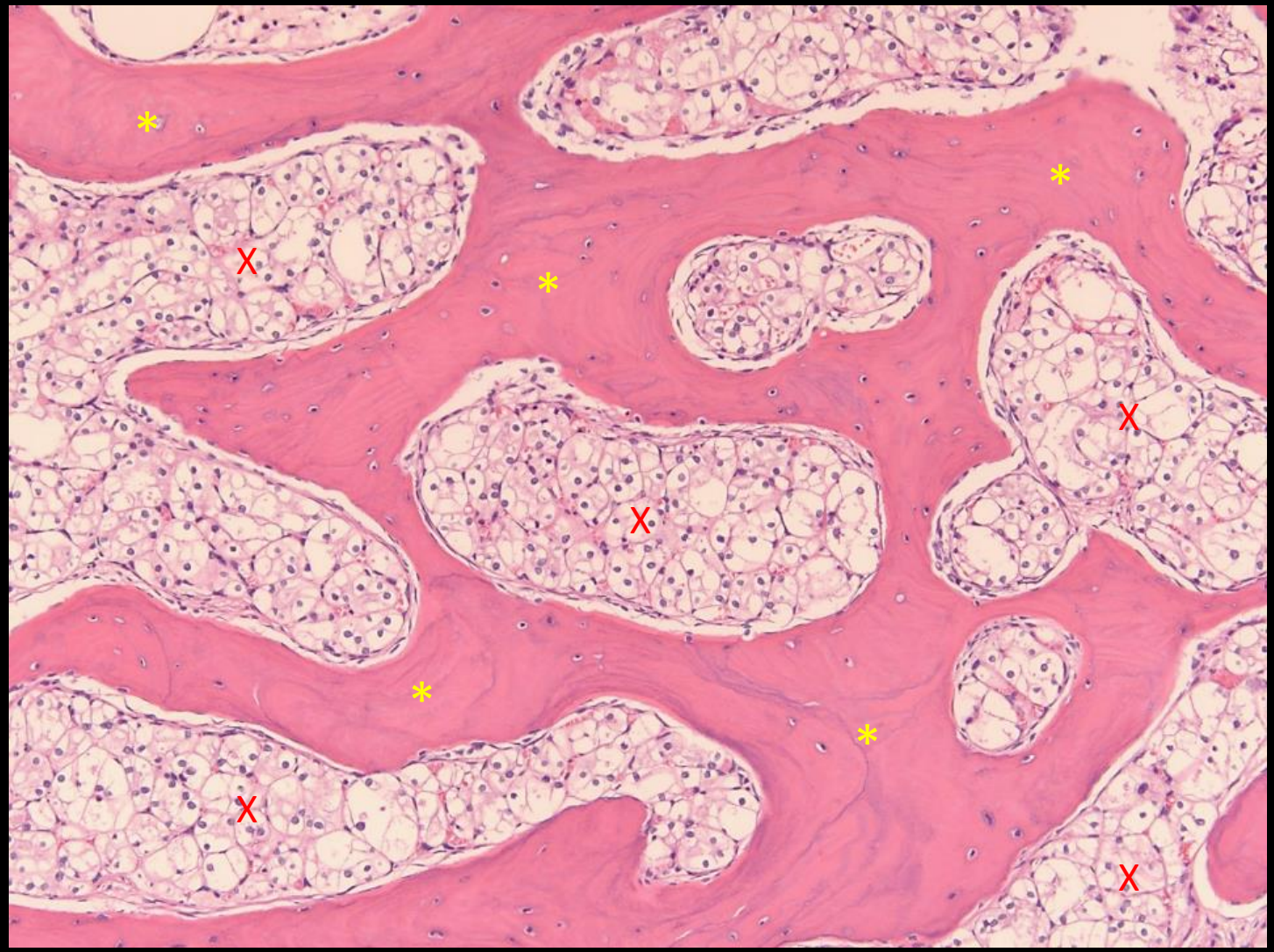
At 40X magnification of the clear cell areas, the nuclei are conspicuous and eosinophilic.

Micro Path (labeled)



Histomorphology of the tubular areas. These areas are composed of tubules with central lumina, lined by cells with abundant, pale pink cytoplasm.

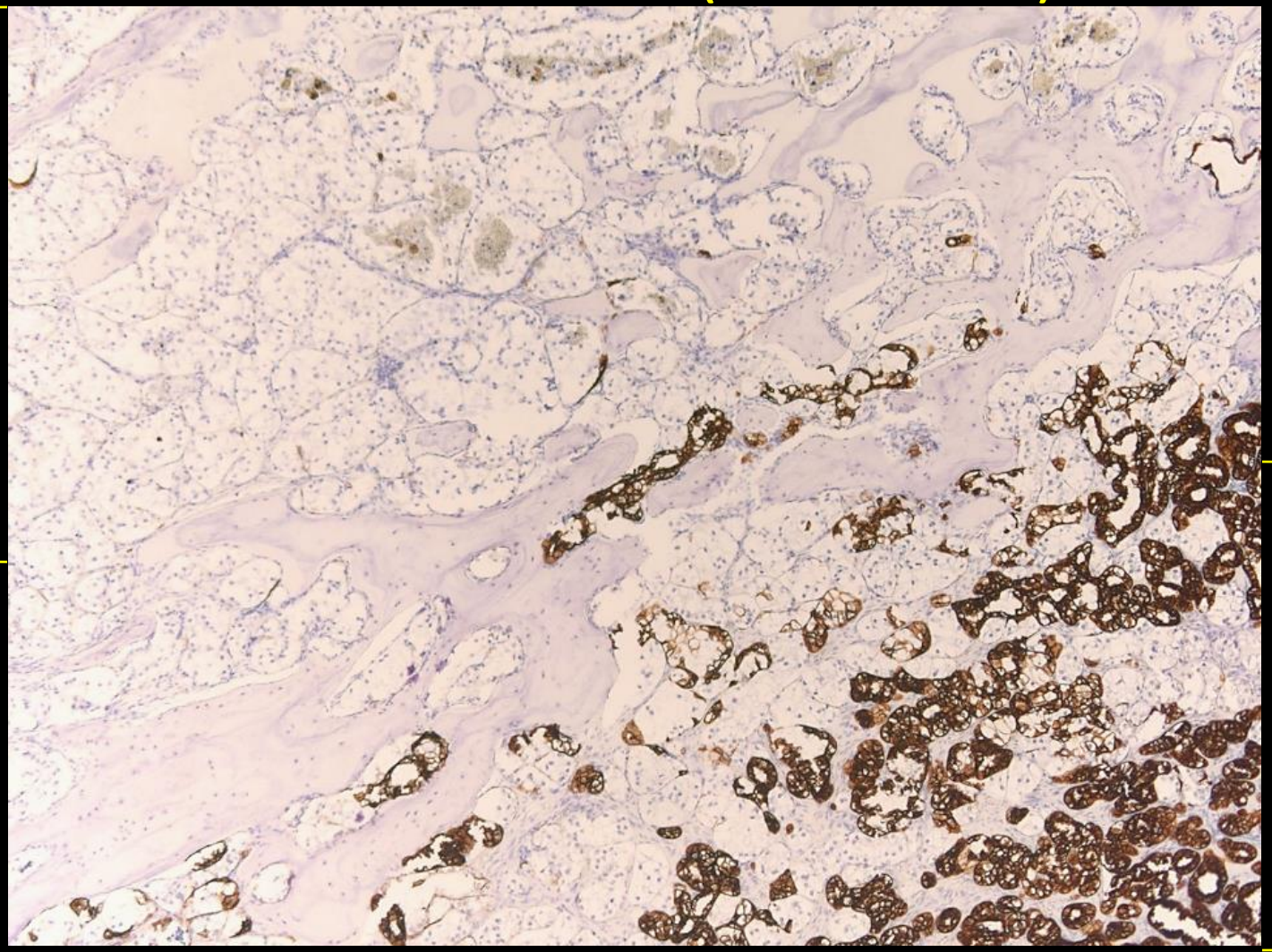
Micro Path (labeled)



Higher-power (10X) view of interface between clear cell component (X) and metaplastic bone (*).

Micro Path (labeled)

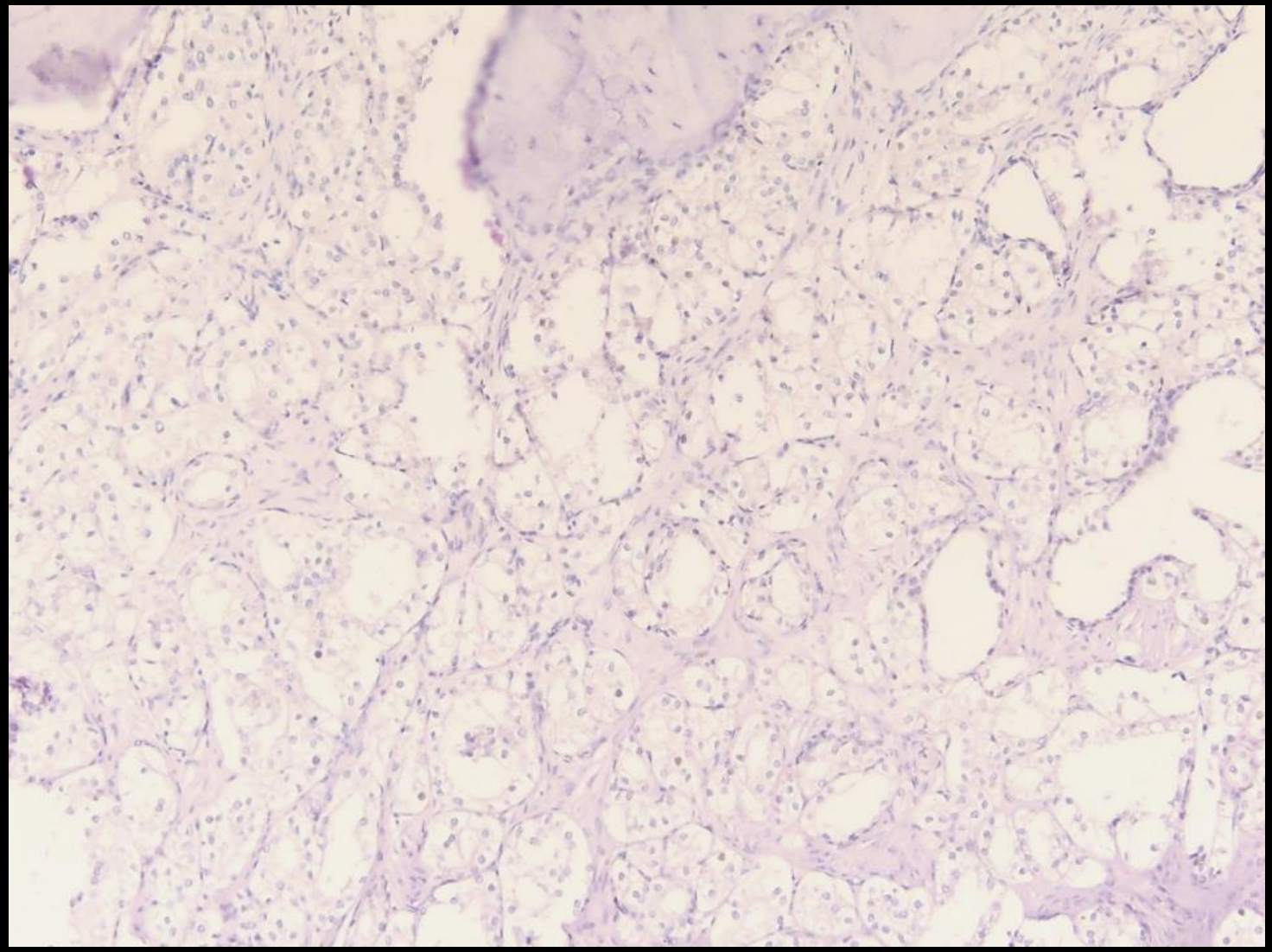
CK7 negative clear cell component



CK7 positive tubular component

The tubular component of the tumor was strongly positive for Cytokeratin 7 (CK7), while the clear cell component was negative.

Micro Path (labeled)



Immunohistochemistry for Carbonic Anhydrase IX (CA IX) was negative in both the clear cell and tubular components of the tumor.

Final Dx:

Renal Cell Carcinoma, unclassified, with extensive osseous metaplasia
pT1a NX

Case Discussion

- Epidemiology
  - Renal malignancies account for 2% of all cancer diagnoses and cancer deaths worldwide
    - Renal Cell Carcinoma (RCC) accounts for >90% of renal malignancies, with the clear cell histologic subtype (ccRCC) being most common
  - Median age at diagnosis: 64 years
  - Higher incidence in males (2:1)
  - Major risk factors: smoking, hypertension, excess body weight
    - Genetic risk factors: Von Hippel Lindau and Tuberous sclerosis

Case Discussion

- Radiologic Features of ccRCC
  - Hypervascular, heterogenous lesions on contrast-enhanced studies
    - Heterogenous due to presence of hemorrhage, necrosis, cysts, or calcifications
  - Iso- to hypointense lesions on T1-weighted MRI and hyperintense on T2-weighted MRI
- Histopathology of ccRCC
  - Nests of tumor cells with lipid-rich, optically clear cytoplasm surrounded by a delicate branching fibrovascular network
    - This patient's tumor had nests of clear cells with interspersed areas of osseous metaplasia
  - Immunohistochemistry generally CK7 negative, CA IX positive in ccRCC
    - The clear cell component of this patient's tumor was both CK7 and CA IX **negative**
- **Of note, this patient's tumor morphology and immunohistochemical profile did not fit any of the WHO renal tumor categories**

Case Discussion

- RCC with osseous metaplasia is extremely rare with approximately 30 cases reported in the current literature
  - Seen in multiple RCC subtypes, but predominantly clear cell and chromophobe
- Osseous metaplasia in RCC is thought to be a secondary change to ischemia, hemorrhage, necrosis, fibrosis, and/or hyalinization
  - Recent reports suggest a possible correlation with Bone Morphogenetic Protein 2 (BMP2)
- Prognostic Value: RCC with osseous metaplasia was found during early stages of disease with no evidence of metastasis in previous cases, suggesting that its presence may imply favorable outcomes in RCC patients

Case Discussion

- Treatment
  - Radical or partial nephrectomy is curative in most patients without metastasis
  - Inoperable or metastatic RCC requires systemic therapies
    - Antiangiogenic tyrosine kinase inhibitors targeting the VEGF signaling axis:
      - First-line: Sunitinib, Pazopanib, and Bevacizumab + interferon-α combination therapy
      - Second-line: Axitinib and Cabozantinib
    - mTOR inhibitors:
      - Everolimus and Temsirolimus
    - PDL1 immune checkpoint inhibitors:
      - Nivolumab and Pembrolizumab

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