AMSER Rad Path Case of the Month:

MEN1 Associated Pancreatic Neuroendocrine Tumor

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Patient Presentation

Clinical History:

19 y/o pt newly diagnosed with MEN1 presents for screening

Family History:

Father - MEN1 - multiple pancreatic neuroendocrine and parathyroid tumors

Sister - MEN1 – pulmonary carcinoid tumor

Physical Exam:

Unremarkable

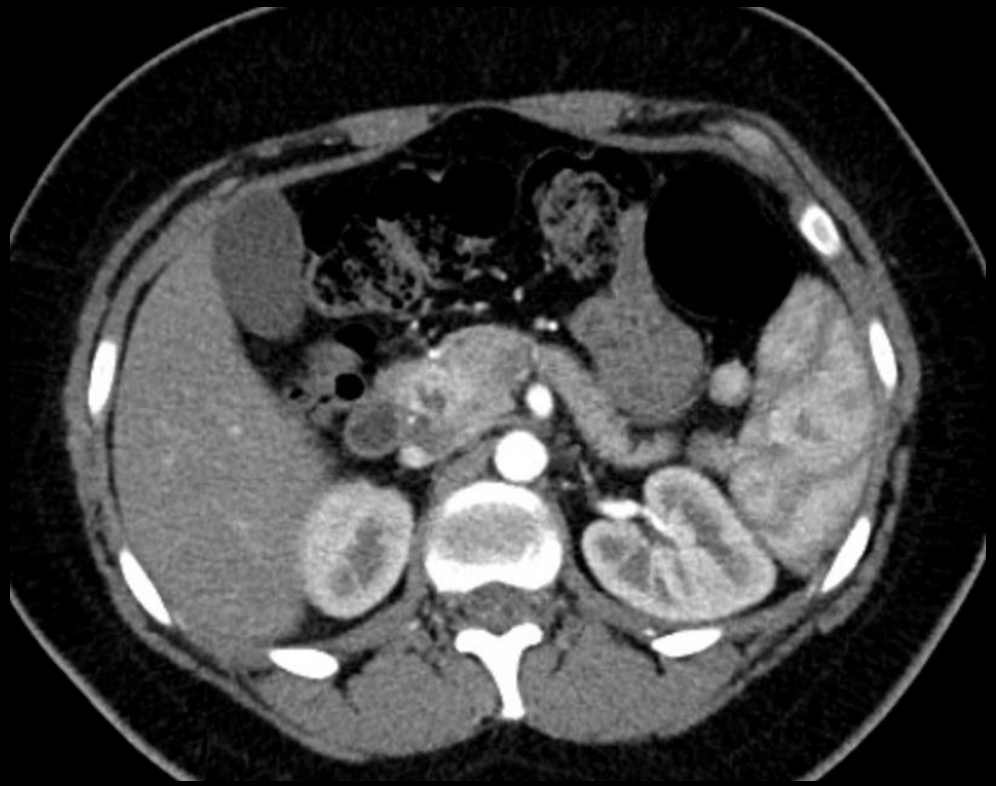
Pertinent Labs

- Glucose elevated at 113
- Calcium elevated at 10.8
- 24 hour urinary calcium elevated at 578.9 mg (N 100-250 mg/24hr)

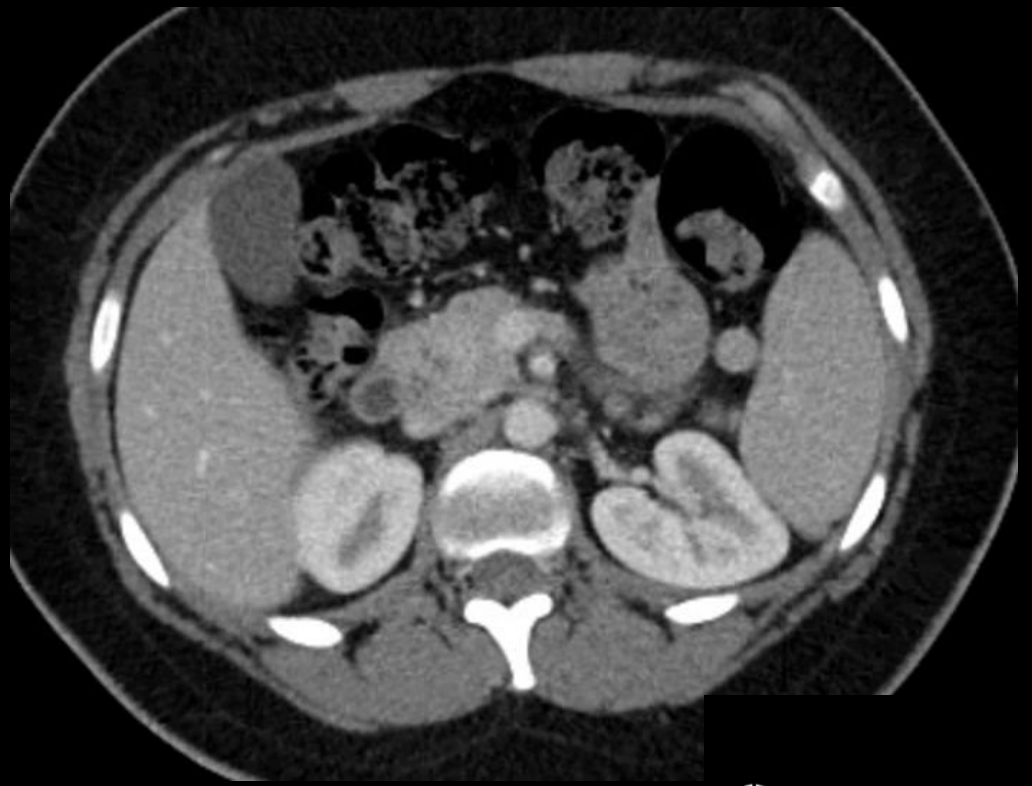
- Remainder of workup within normal range
  - CBC
  - CMP
  - TSH/T4
  - Cortisol
  - ACTH
  - PTH
  - Chromogranin A
  - 5-HIAA
  - Vitamin B12 and 25-hydroxy D
  - Prolactin

Screening CT W/ Contrast

Arterial Phase

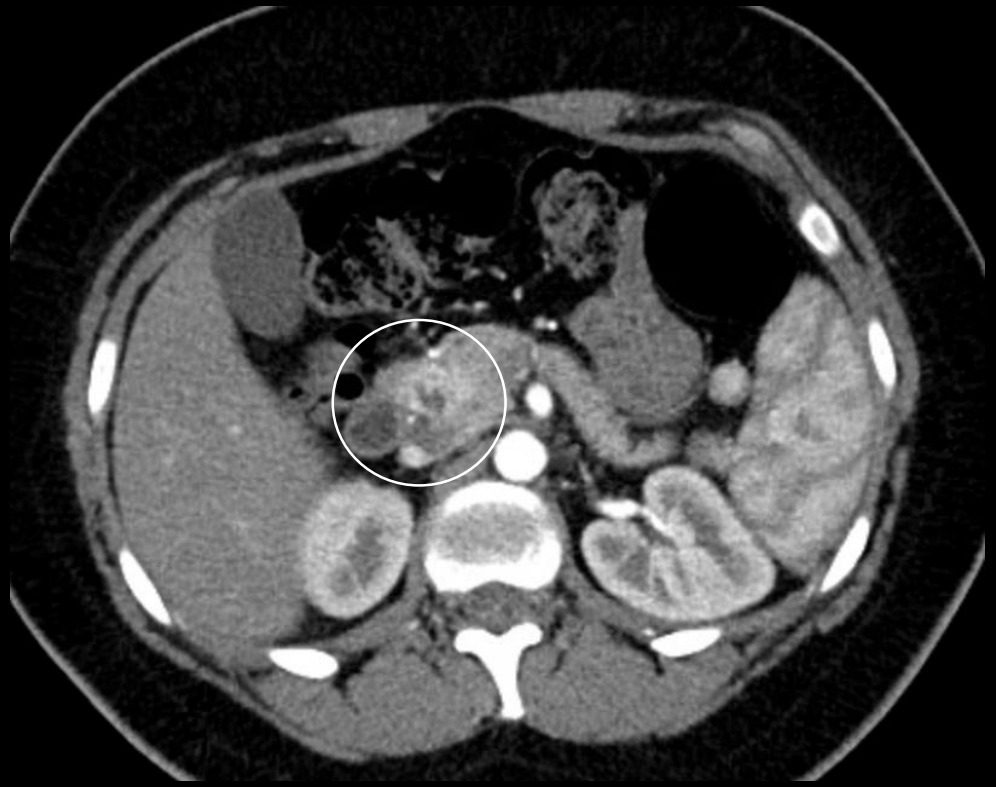


Venous Phase

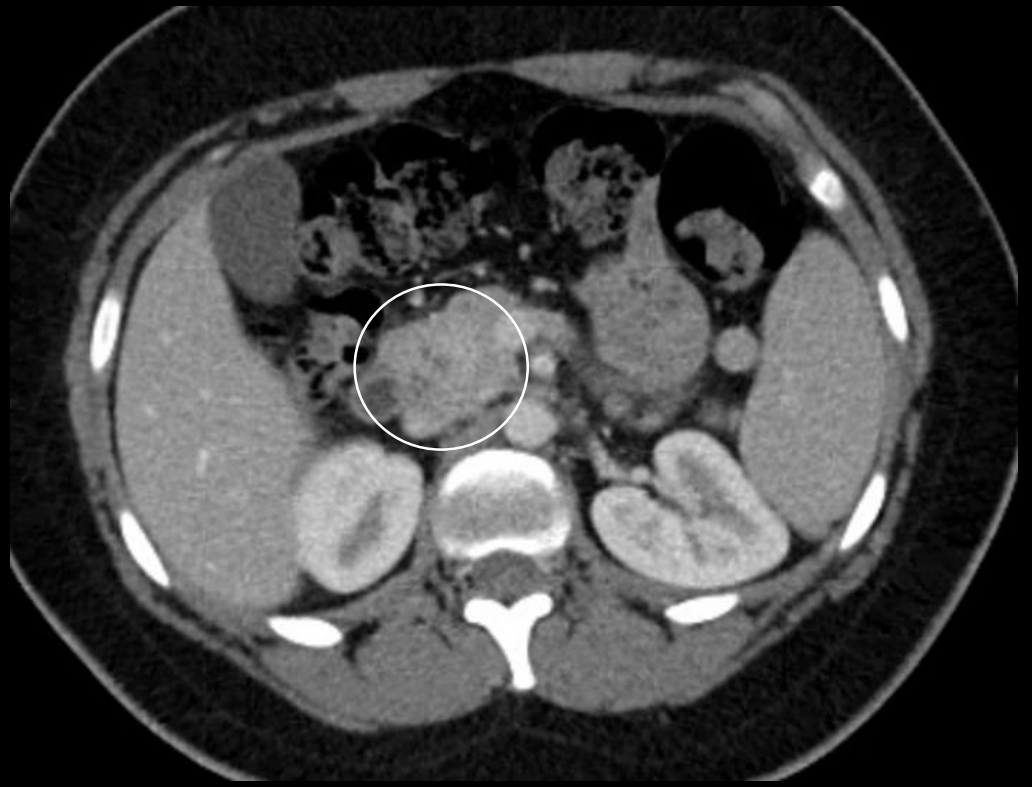


Screening CT W/ Contrast

Arterial Phase



Venous Phase

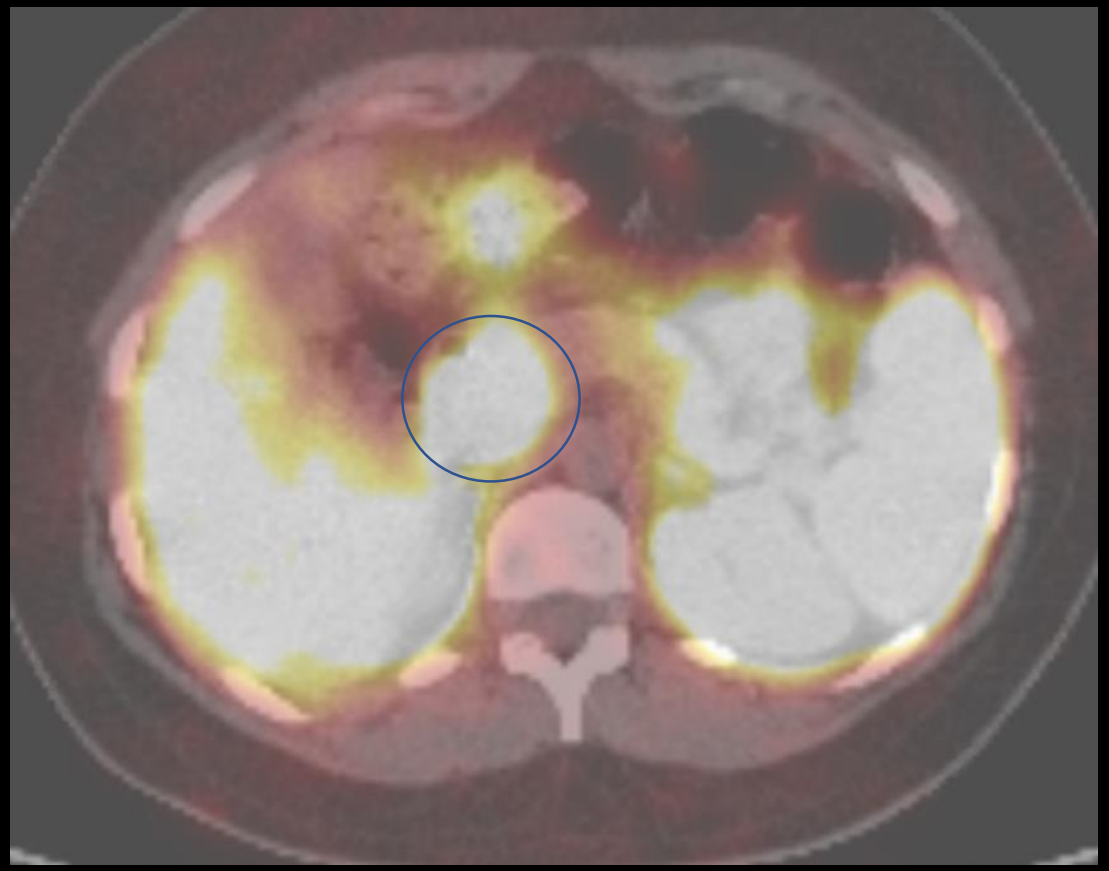


1.8cm heterogenous lesion in the head of the pancreas enhances peripherally in the arterial phase and nearly isodense in the venous phase

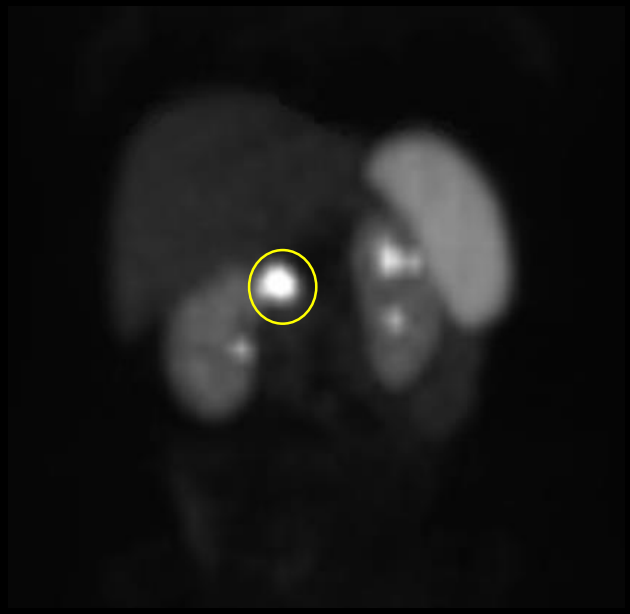
DDX (based on imaging)

- Pancreatic neuroendocrine tumor
- Adenocarcinoma
- Primary pancreatic lymphoma
- Metastasis

GA68 PET-CT

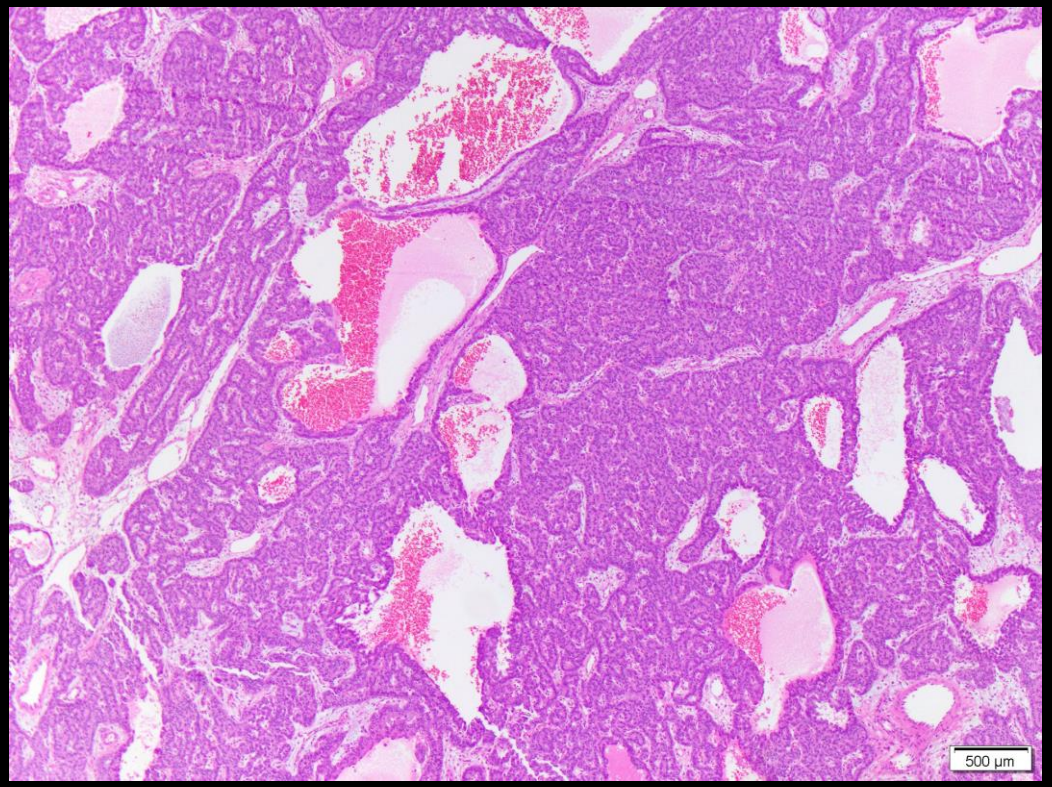


- Markedly gallium-68 avid indistinct pancreatic head lesion
- Consistent with somatostatin receptor positive PNET

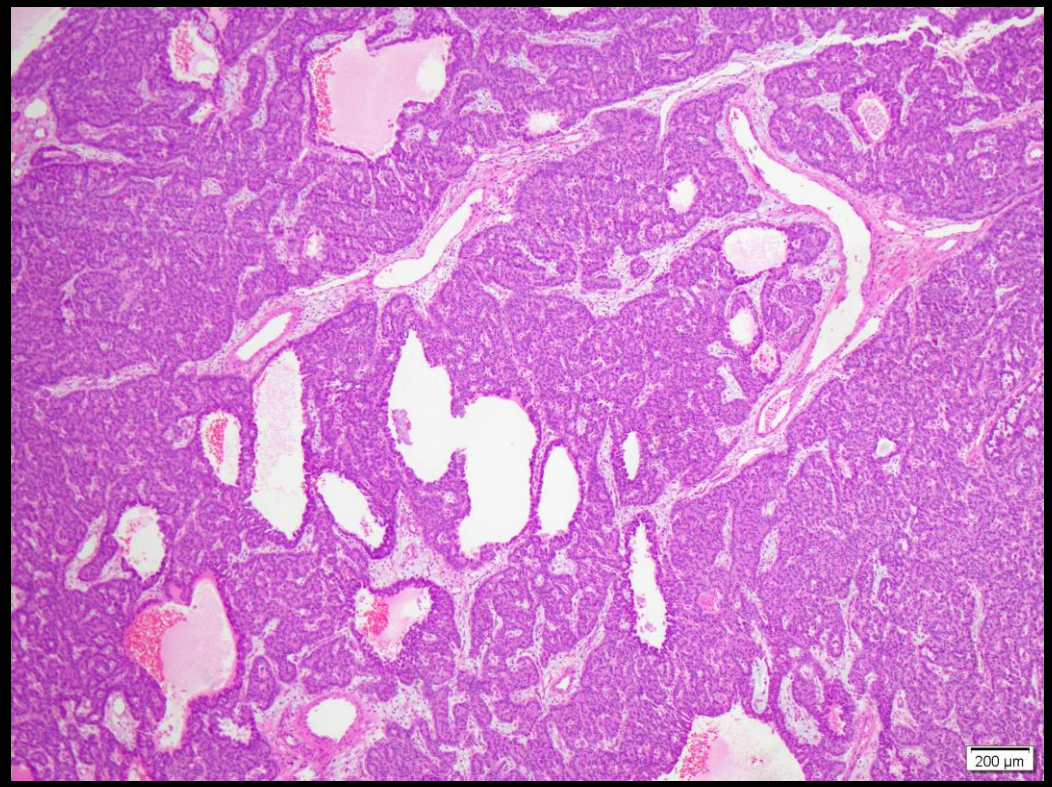


Micro Path (Low Power)

4x

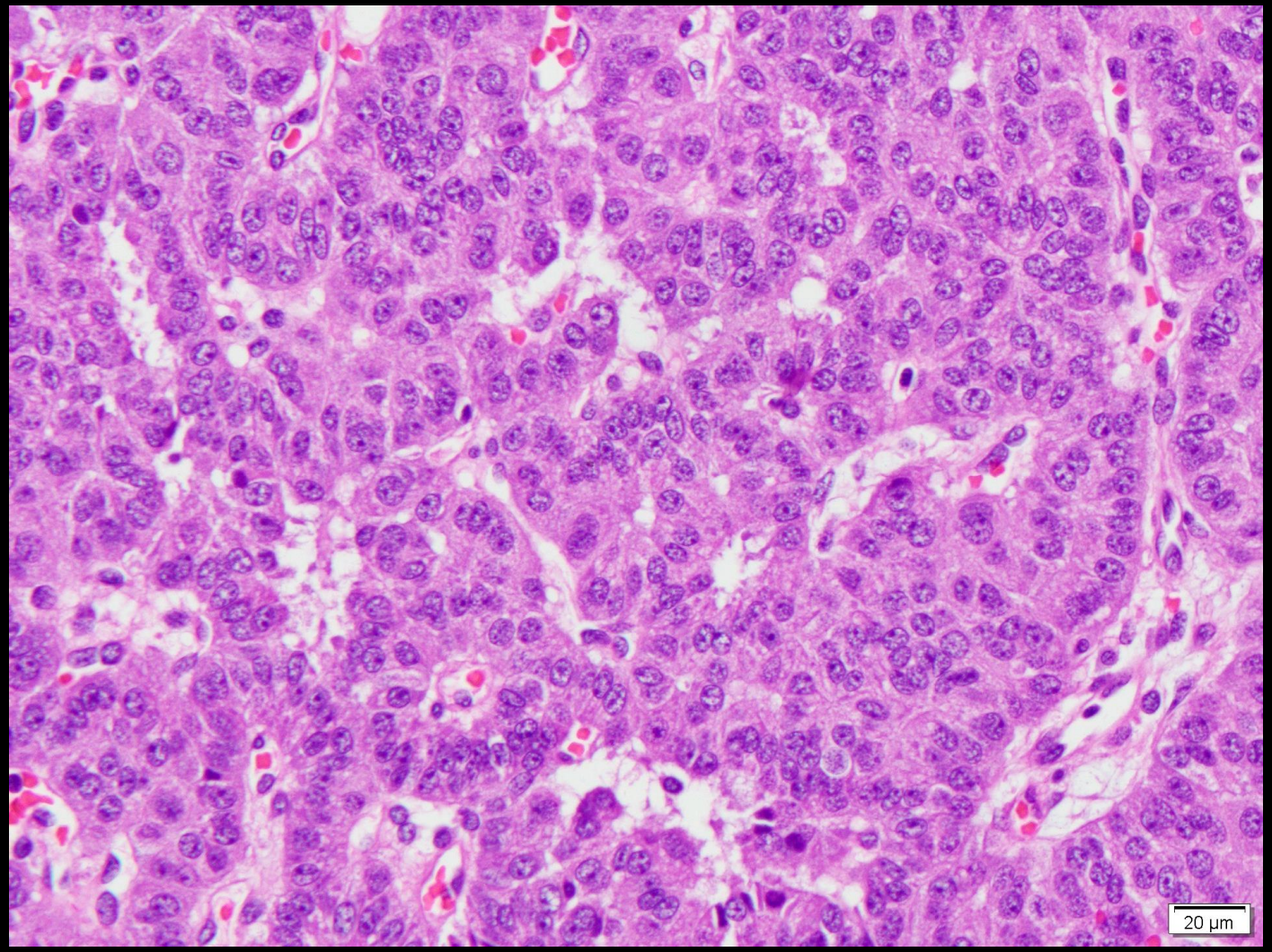


10x



Sheets of uniform tumor cells arranged in solid nests. Microcysts and fibrovascular stroma

Micro Path (High Power) 40x



- Small monomorphic cells, roughly uniform in size, arranged in nests and rosettes
- Round to oval uniform nucleoli
- “salt and pepper appearance” of coarsely clumped chromatin

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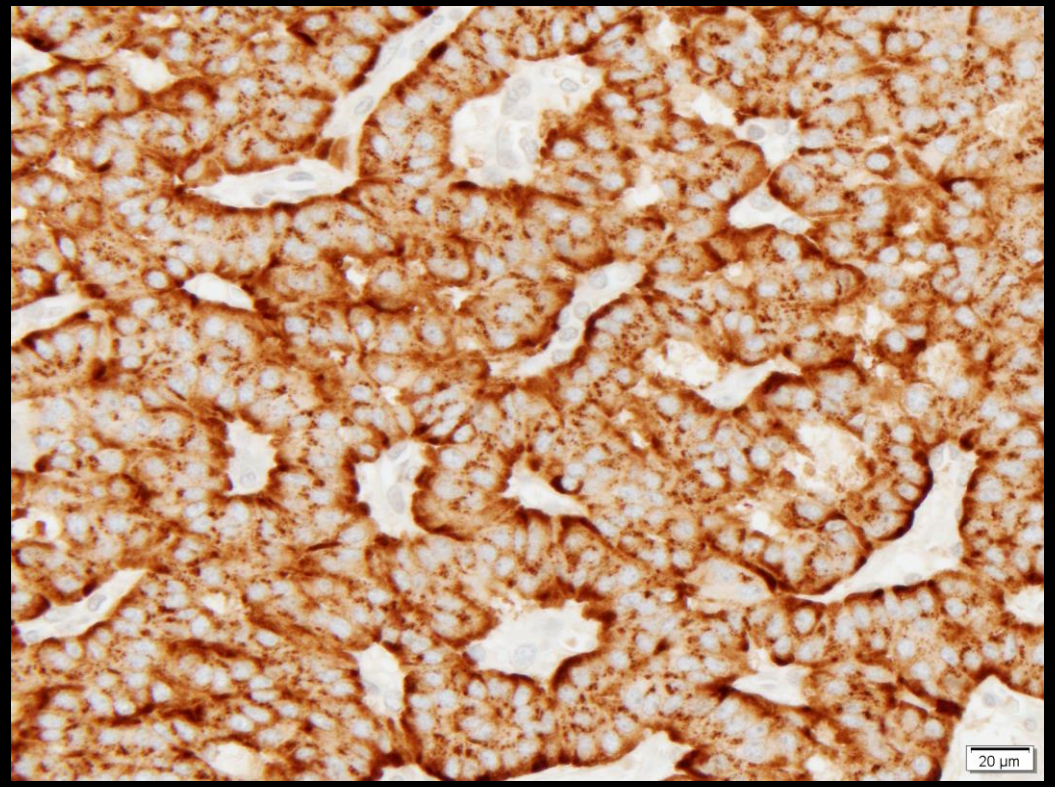
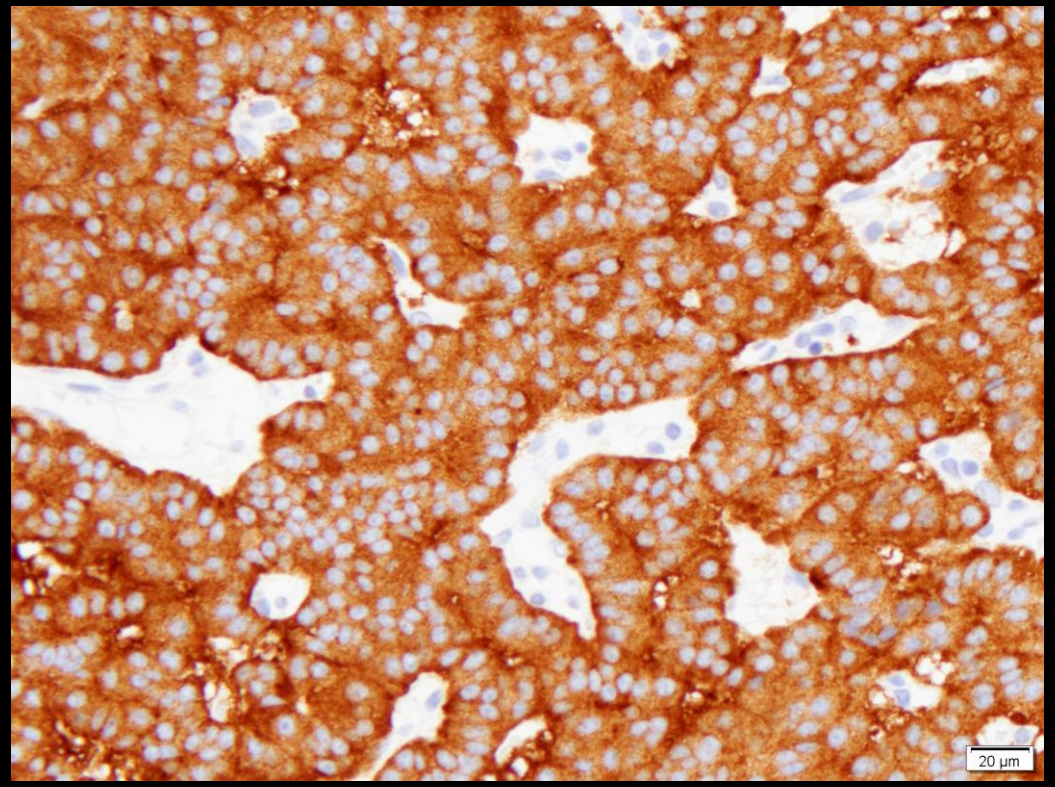
Immunohistochemical Staining for NET Markers

Chromogranin +



Synaptophysin +



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Final Dx:

Nonfunctional Pancreatic Neuroendocrine Tumor

Multiple Endocrine Neoplasia Type 1

- Autosomal dominant disorder with near-complete penetrance
- Most common mutation is in the MEN1 tumor suppressor gene on chromosome 11
- Multiple tumors of the parathyroid, pancreas, pituitary
  - Other associated tumors include lipomas, angiofibromas, meningiomas, adrenal cortical tumors, and pheochromocytomas
- Screening recommendations for pancreatic NET in MEN1 include annual fasting GI tract hormone panel; imaging of the pancreas and duodenum by MRI, CT, or endoscopic ultrasound

Pancreatic Neuroendocrine Tumors

- Islet cell tumors
- 2% of all pancreatic neoplasms, 50% present as metastasis
- Varied radiographic, gross, and histologic appearance
  - Solid and cystic
  - Nests, trabecular, gyriform, rosette, glandular patterns
- Hormone secreting or nonfunctional
  - Insulin (80%), somatostatin, gastrin, VIP
  - Malignant nonfunctioning PNET is one of the most common causes of death in individuals with MEN1

Radiographic Findings in PanNET

- Typically can be differentiated from adenocarcinoma by hypervascularity
- MRI and CT are the most common modalities
  - Nonfunctional tumors are often incidental findings
- Varied radiographic appearance depending on size
  - Smaller tumors
    - Solid and hypervascular
    - Usually homogenous and well-circumscribed
  - Larger tumors
    - Often heterogeneous and contain areas of cystic or necrotic change
    - Can manifest as primarily cystic lesions, distinguished by their hypervascular rim

- Gallium-68 DOTATATE
  - PET radiotracer
  - Somatostatin receptor (SSTR) functional imaging
    - Affinity for SSTR subtypes 3 and 5
  - Normal uptake
    - Pituitary, spleen, liver, adrenal, urinary tract, salivary glands, and thyroid
  - Useful for evaluating primary and metastatic well-differentiated neuroendocrine tumors
    - Superior to previously used octreotide indium 111 SPECT/CT
      - Lower radiation dose for patient
      - More detailed anatomic correlation

This Patient

- After extensive imaging and laboratory evaluation, tumor in the head of the pancreas was determined to be solitary and resectable
- Pt underwent pancreaticoduodenectomy (Whipple procedure)
  - Final pathology determined tumor to have multiple foci with benign margins
  - Two additional neuroendocrine microadenomas identified
  - Well-differentiated tumor grade 1, mpT2 pN0 pMX
- Pt discharged on post-op day 6
- Pt will continue lifelong screening for additional tumors

References:

- Hofman, M., Lau, W. and Hicks, R., 2015. Somatostatin Receptor Imaging with68Ga DOTATATE PET/CT: Clinical Utility, Normal Patterns, Pearls, and Pitfalls in Interpretation. *RadioGraphics*, 35(2), pp.500-516.
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