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Disease-Focused Panels

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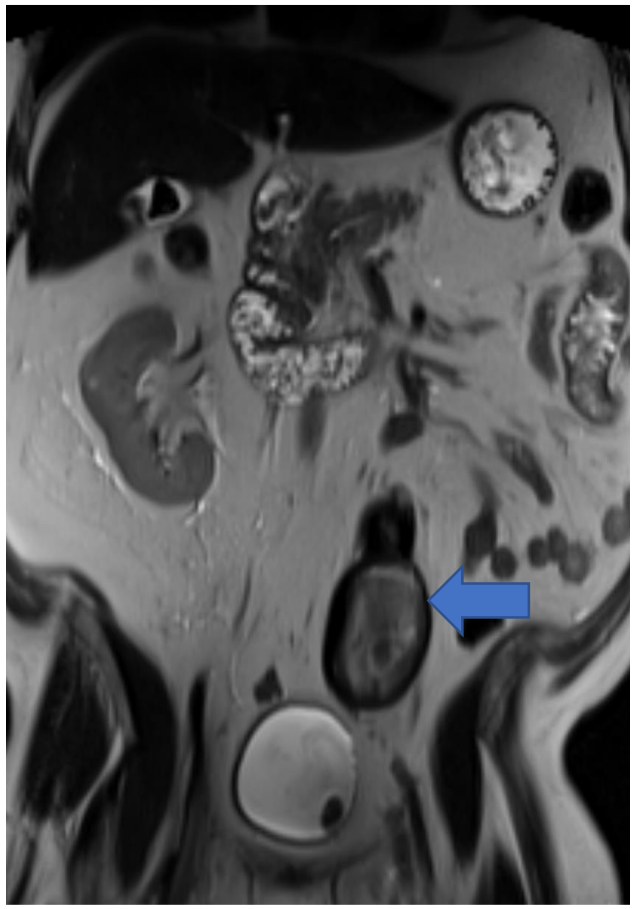
Well Differentiated Neuroendocrine carcinoma of Ureteric stump.

Presented By: A. Singareddy, A. Gopinath, I. Kadambi, M. Virarkar, S. Kumar, D. Gopireddy, C. Lall.

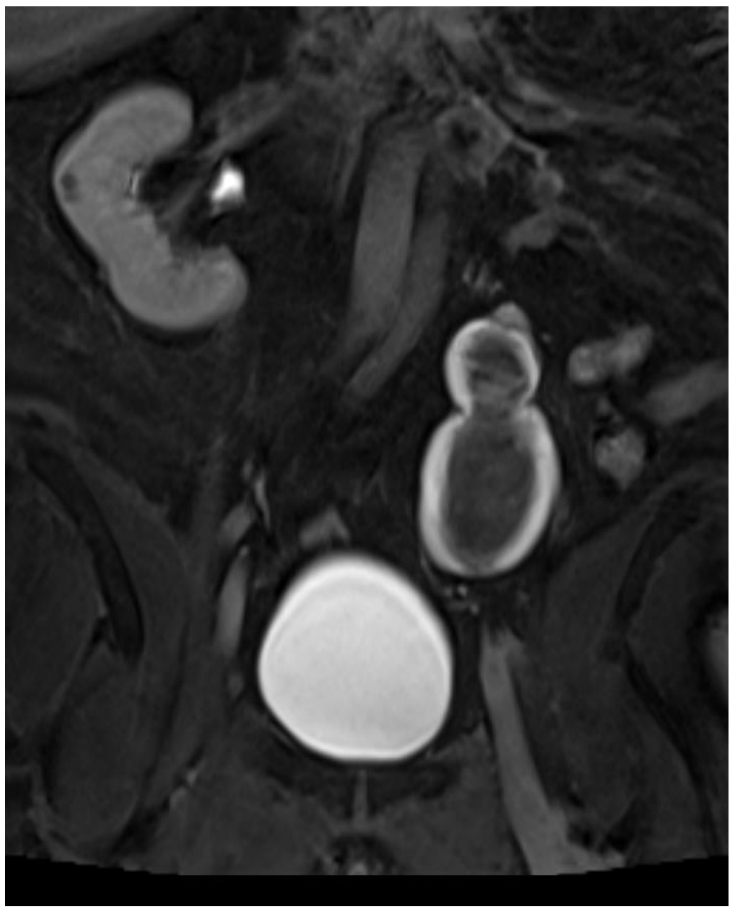
Case history and Lab values:

- 66yr-old-male with painless hematuria.
- PMH: **2004** left radical nephrectomy for pT3b RCC.
  2011 Pulmonary nodule recurrence followed by chemotherapy.
  2020 Painless hematuria, TURBT showed a trigone papillary urothelioma and left ureteric stump mass.
- Labs: Urine cultures 40,000 colonies/ml streptococcus agalactiae.
- Pertinent Imaging: MR Urogram and Retrograde Urogram.

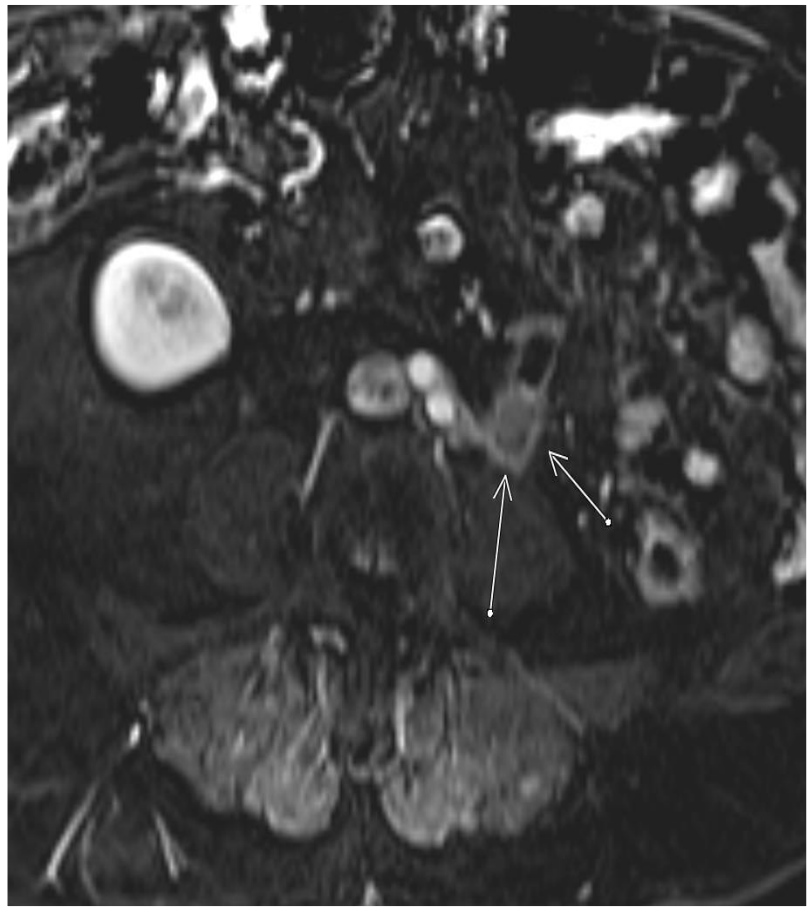
Imaging: MR Urogram



Coronal T2 nonfat sat image: Shows a large expansible hematoma in the ureteric stump (arrows)

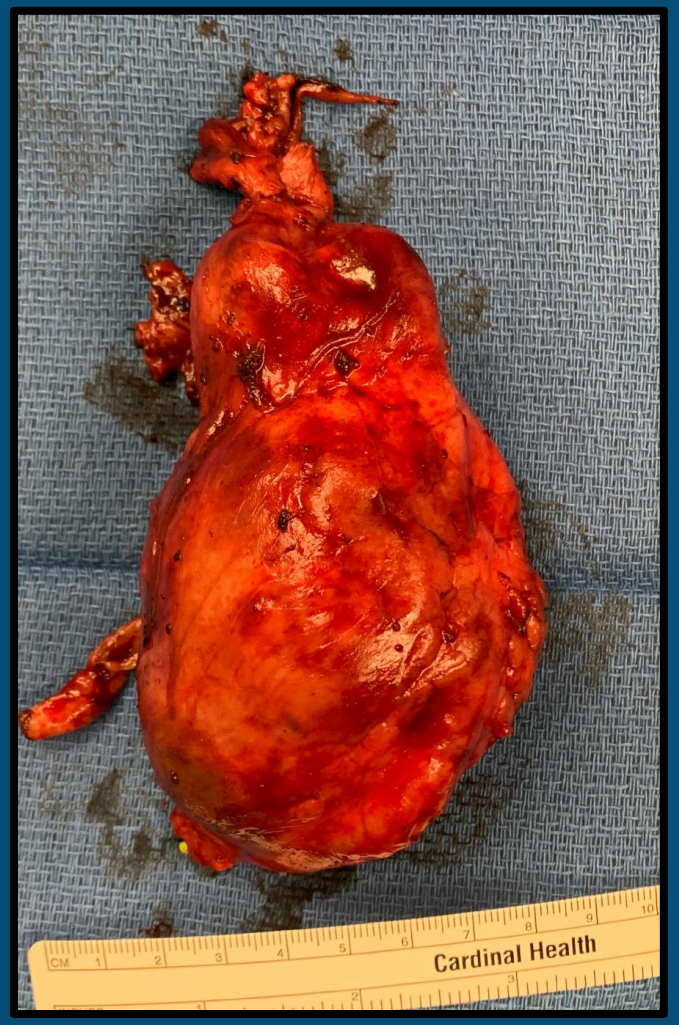


Coronal T1 post contrast delayed fat sat image: Shows a large expansible hematoma with intrinsic high T1 signal



Axial T1 post contrast delayed fat sat subtraction image: Shows a small enhancing nodule along the superior aspect of the stump.

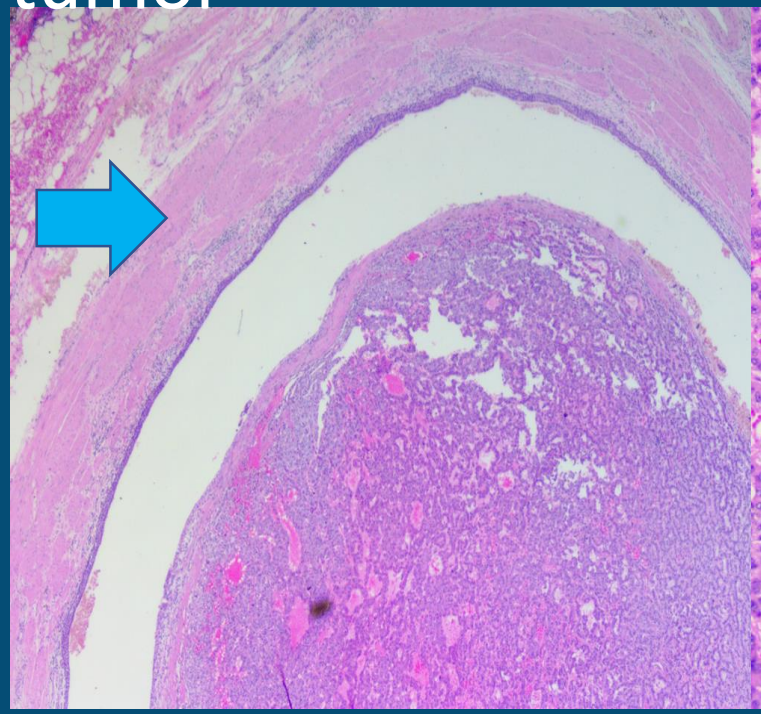
Surgical Specimen and Gross Pathology report



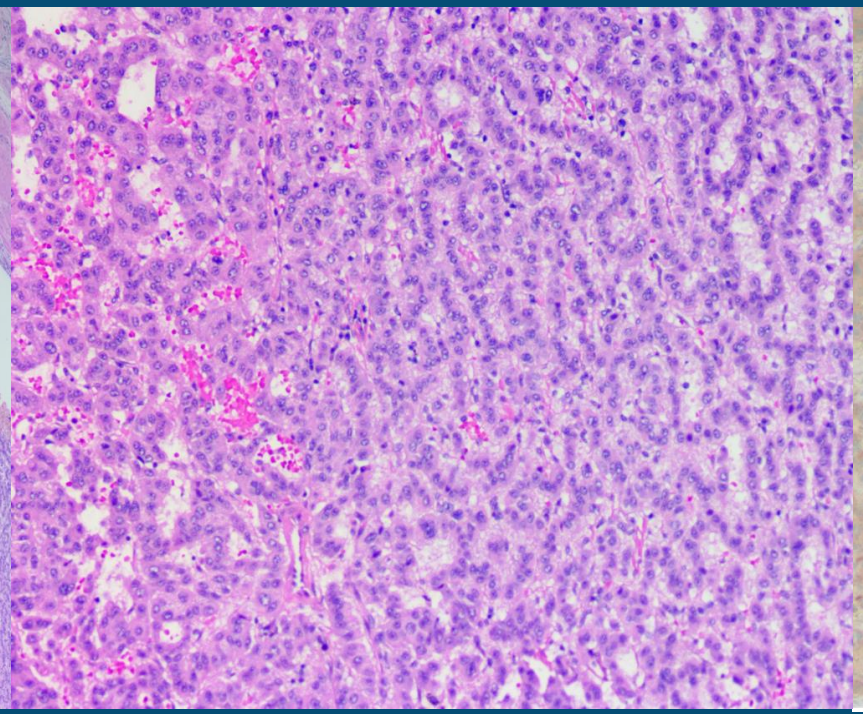
- Left lower ureter mass" and consists of a segment of ureter with attached firm, tan-brown, irregular, mass, measuring 11.5 x 7.0 x 6.0 cm.
- Serial sections of the specimen show a cystic blood-filled mass. No papillary fronds or excrescences identified.

Rad-Path

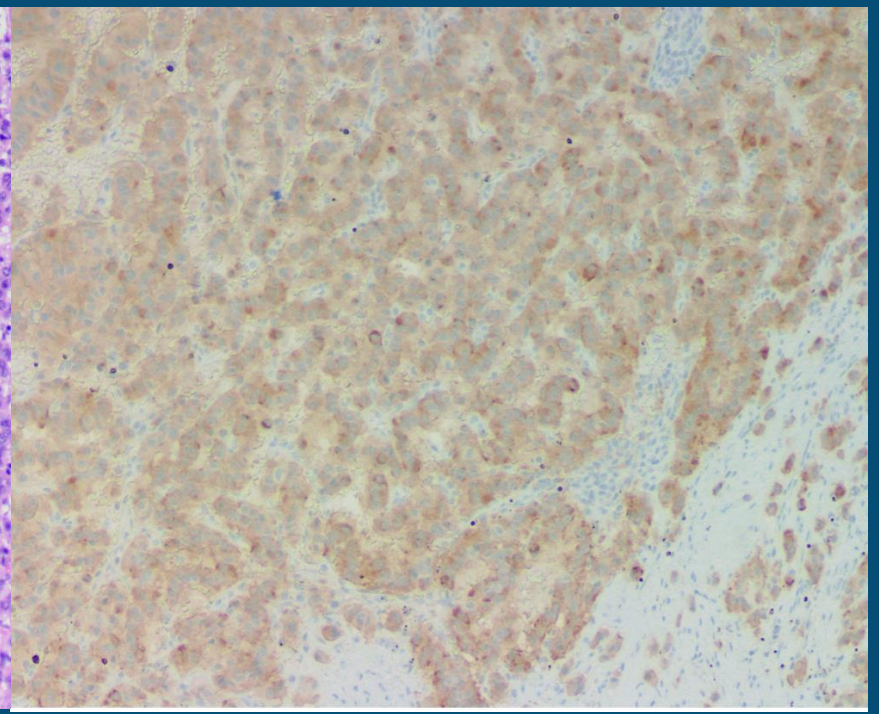
Histology: Well-differentiated Intermediate grade neuroendocrine tumor



H and E straining: 20 X
Shows polypoid tumor bulging into the ureter lumen. Normal urothelial mucosa and muscle layer can be seen on the top half (arrow).



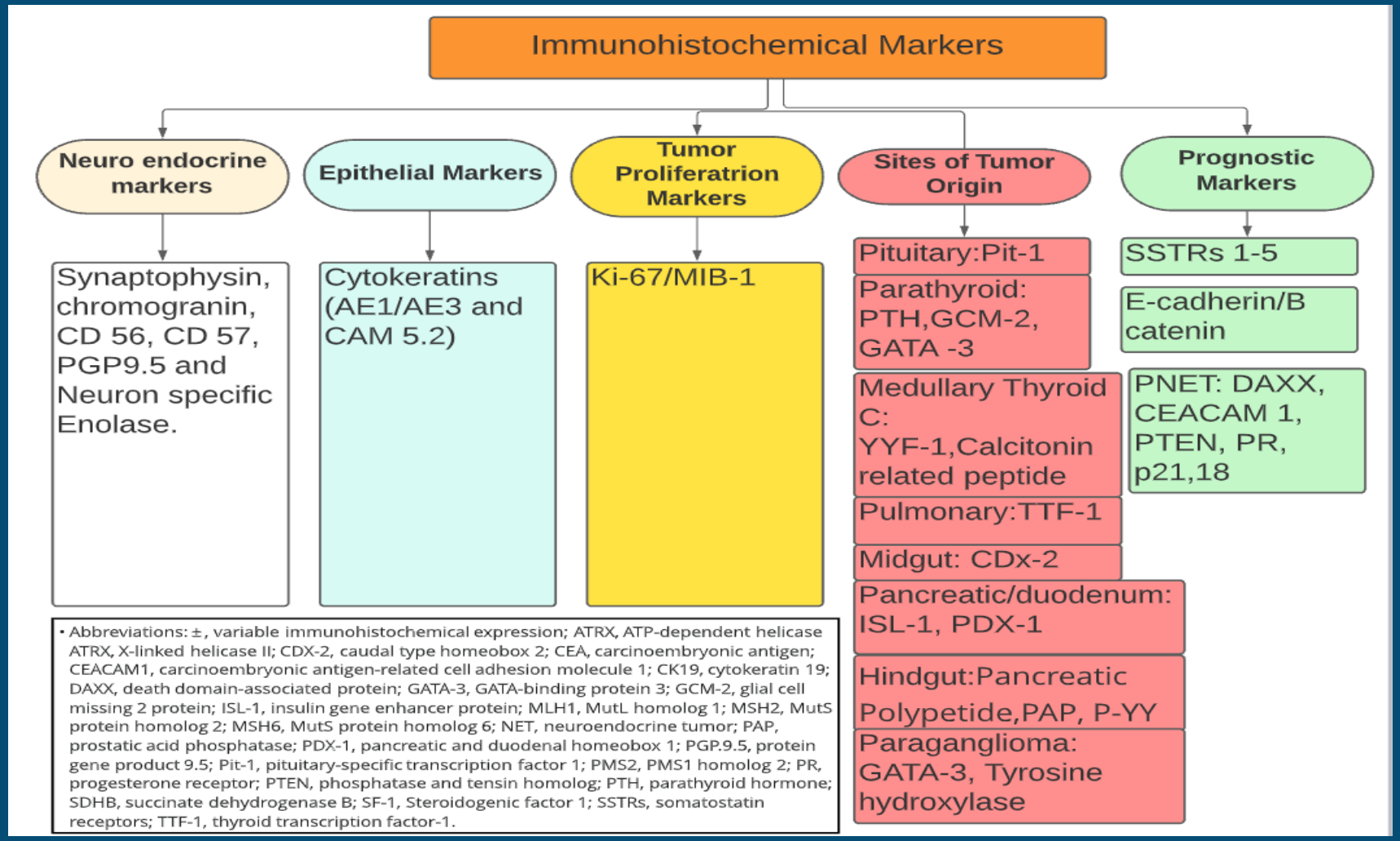
H and E straining: 200 X
Higher power view shows tumor cells arranged in trabecular and tubular pattern.



Synaptophysin staining : 200 X
Tumor cells expressing synaptophysin (brown staining) which is a marker of neuroendocrine differentiation.

ki-67 proliferation index of 7%

Pathology: Immunohistochemical markers Analysis



Current Case:
1:Positive for CK AE1/AE3
2:ki-67 index of 7%
3:CD 56 positive
3: E-cadherin present
4: GATA 3: Negative

Discussion: Immunohistochemical markers

- Suspected neuroendocrine neoplasm typically begins by confirming neuroendocrine differentiation, using a panel of general neuroendocrine immunohistochemical markers.
- Chromogranin A is the most specific marker.
- Synaptophysin is often regarded as the most sensitive marker.
- Weak, or even absent chromogranin A staining may be noted in poorly differentiated neuroendocrine carcinomas.
- L-cell NETs of hindgut origin, may preferentially express chromogranin B instead of chromogranin A.
- Some NETs can be seen in the context of mixed tumors (i.e., mixed adeno-NEC), divergent neuroendocrine differentiation is generally <30% of the tumor volume.
- Epithelial biomarkers (cytokeratins AE1/AE3, CAM5.2, and/or CK18) to exclude paraganglioma.

Discussion: Immunohistochemical markers: Differential Dx

Type of Cancer	Markers	Comments
Urothelial Carcinoma	GATA3 and P53 positive	Negative in this case
Prostate Cancer	PSA/PSAP	Negative in this case
Melanoma	S-100 SOX 10	Melanoma markers negative on this case

Teaching Point: A positive pathogenic mutation in CHEK2-suppressor gene involved in DNA repair, cell cycle arrest, and apoptosis in response to DNA damage was identified on Next generation sequencing analysis. This mutation has been reported in neuroendocrine tumors as well as other carcinomas and may be potential target for therapy.

Discussion: Imaging of NEN; Molecular and Anatomical Paradigm

- Primary NET of Ureter are rare tumors with pain/hematuria as the common symptoms.
- Locally advanced or nodal disease at presentation is common at the time of diagnosis.
- Occur commonly in the 6^{th}-7^{th} decade of life.
- Imaging modalities include molecular and anatomical with cross section imaging
- PET/CT using Gallium-68-labeled octreotide derivatives (DOTATOC, DOTATATE, and DOTANOC), has demonstrated a superior sensitivity for tumor detection (well differentiated tumors).
- Liver MRI has been demonstrated to be superior to CT in detection of NET liver metastases.
- 68Ga-DOTANOC PET/MRI superior diagnostic performance than 68Ga-DOTANOC PET/CT especially for liver metastasis.
- Treatment options include Cisplatin-based neoadjuvant chemotherapy followed by nephroureterectomy.

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