AMSER Case of the Month July 2023

89 yo M presents with an indeterminate left adrenal mass

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Supervising Physician: Dr. Brahee

Cleveland Clinic Foundation

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Patient Presentation

HPI: 89 yo M presents to the Cleveland Clinic with an indeterminate adrenal mass measuring up to 7 cm found incidentally at outside institution for further evaluation

Past Medical Hx: Dementia, Type 2 Diabetes Mellitus, GERD, Hypertension

Past Surgical Hx: Pilonidal cyst removal, no abdominal surgeries

Social Hx: Former smoker, 15 pack years

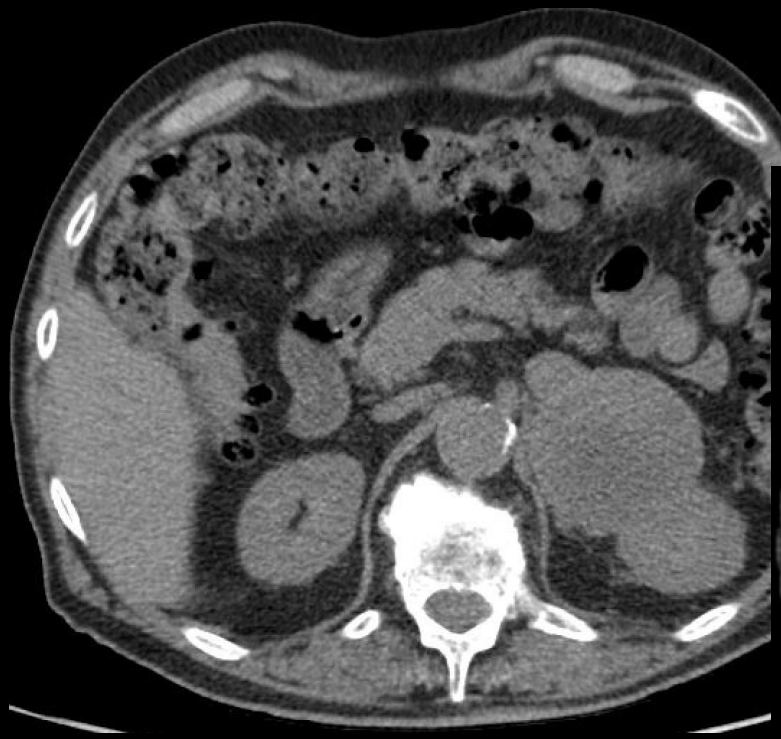
Family Hx: Mother: Coronary artery disease | Father: Type 2 Diabetes Mellitus

Vitals: BP: 116/52 (on anti-hypertensive medication), HR 62

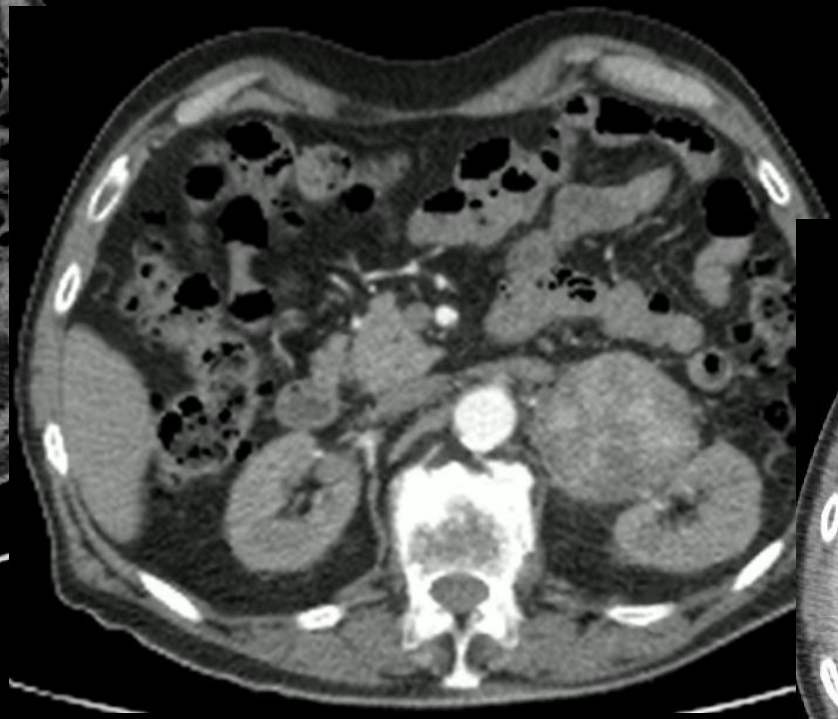
Physical Exam: No significant findings

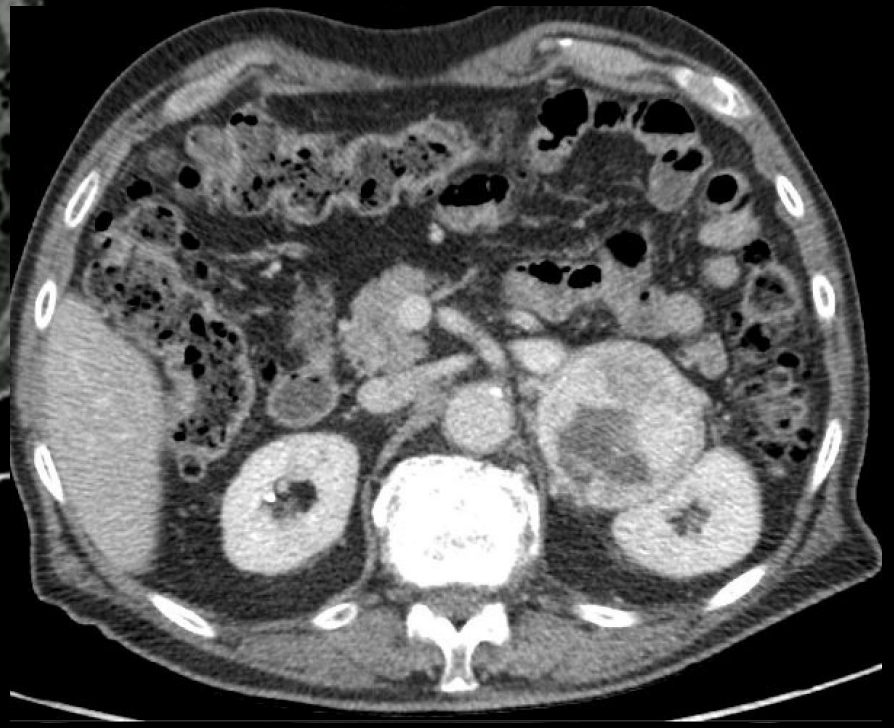
Labs: CBC, CMP were within normal limits. Additional relevant lab work that was performed is discussed later.

Initial CT with contrast (unlabeled)



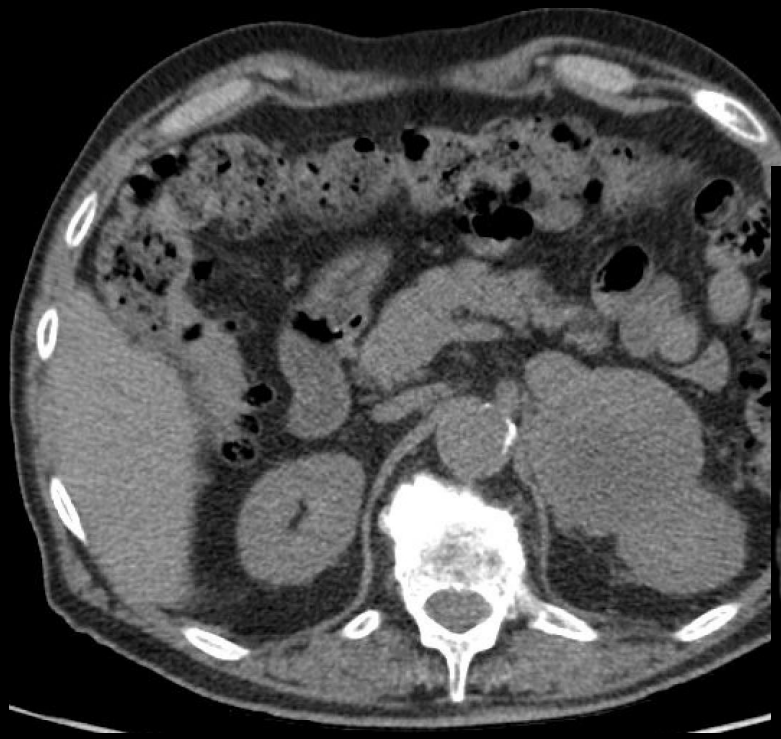
Pre-contrast



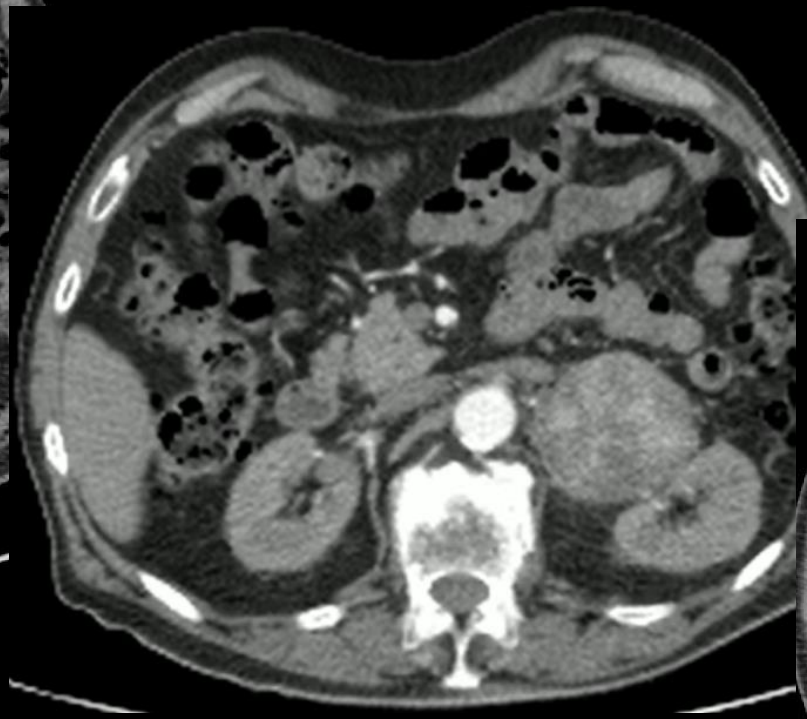


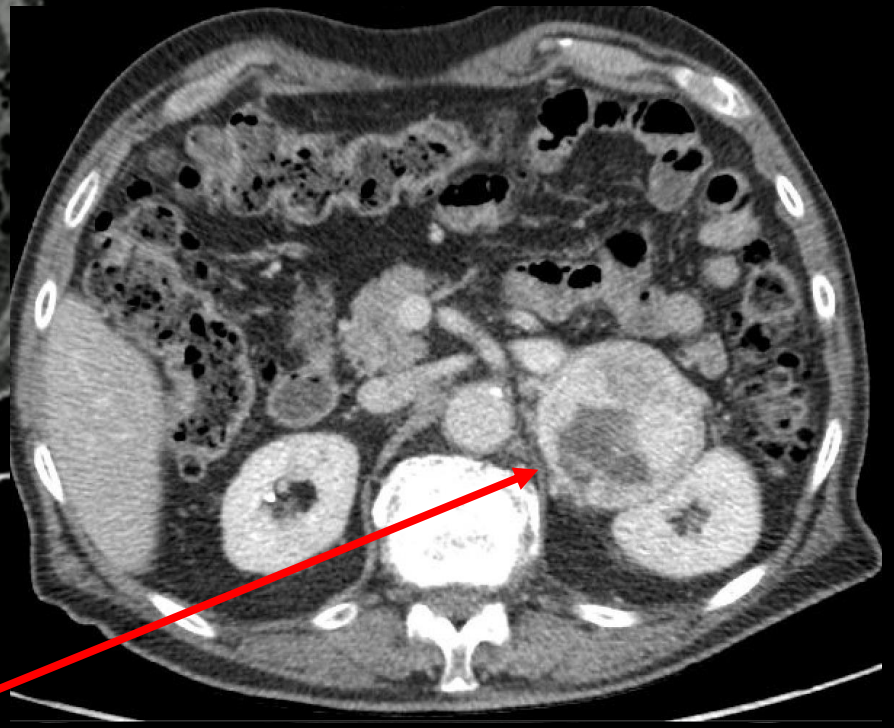
Post-contrast

Initial CT with contrast (labeled)



Pre-contrast





Post-contrast

Large, heterogeneous adrenal mass anterior to the left kidney along the upper/mid pole with central areas of non-enhancement, possibly representing necrosis

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What Imaging Should We Order?

ACR Appropriateness Criteria

Variant 4: **Indeterminate adrenal mass, greater than or equal to 4 cm on initial imaging. No diagnostic benign imaging features. No history of malignancy. Adrenal specific imaging.**

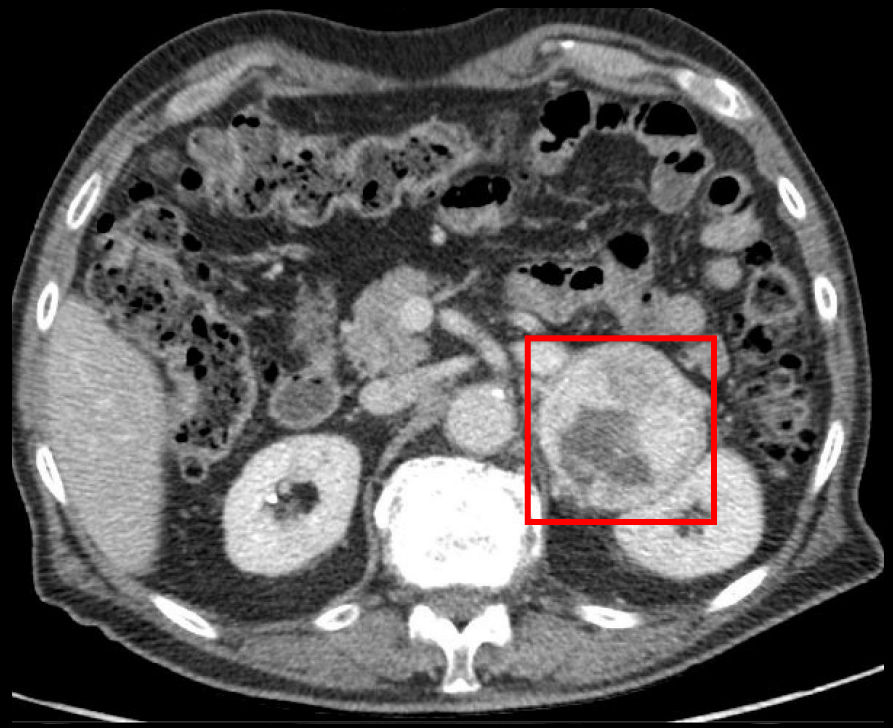
Procedure	Appropriateness Category	Relative Radiation Level
Image-guided biopsy adrenal gland	Usually Not Appropriate	Varies
MRI abdomen without and with IV contrast	Usually Not Appropriate	O
MRI abdomen without IV contrast	Usually Not Appropriate	O
CT abdomen with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen without IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen without and with IV contrast	Usually Not Appropriate	☢☢☢☢
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☢☢☢☢

ACR Appropriateness Criteria (continued)

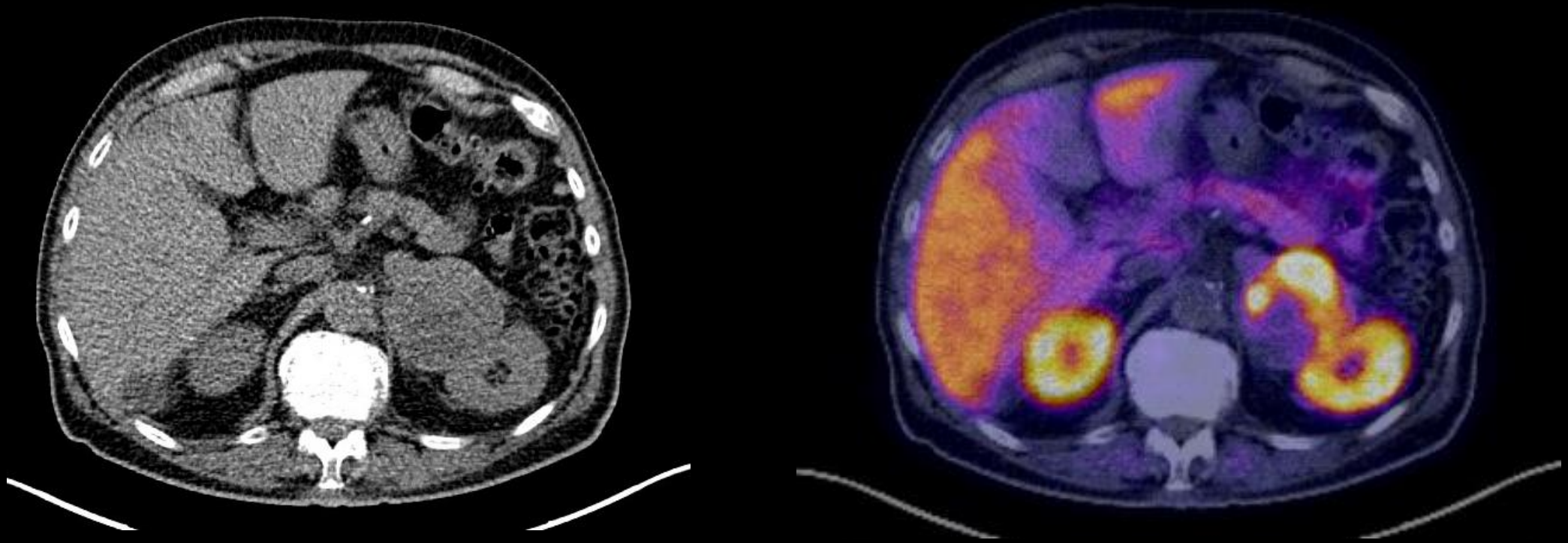
- Typically, for a lesion of this size, surgical resection (without biopsy) is recommended because of the increased likelihood of adrenocortical carcinoma.
  - However, overall, size is considered too *unreliable* to be used alone as a criterion for malignancy, although a 4 cm cutoff is generally used to make decisions regarding surgery for lesions that do not have diagnostic benign imaging features.

- Although only approximately 6% of lesions between 4 and 6 cm are malignant, adrenalectomy is often recommended for individuals who are at acceptable risk for surgery.
  - Masses ≥6 cm are resected, as the malignancy rate in this patient group is reported to exceed 25%.

- **Given the indeterminate large adrenal mass, no access to outside imaging, and the patients age and comorbidities, this was a unique case where additional imaging was ordered for further characterization and staging.**

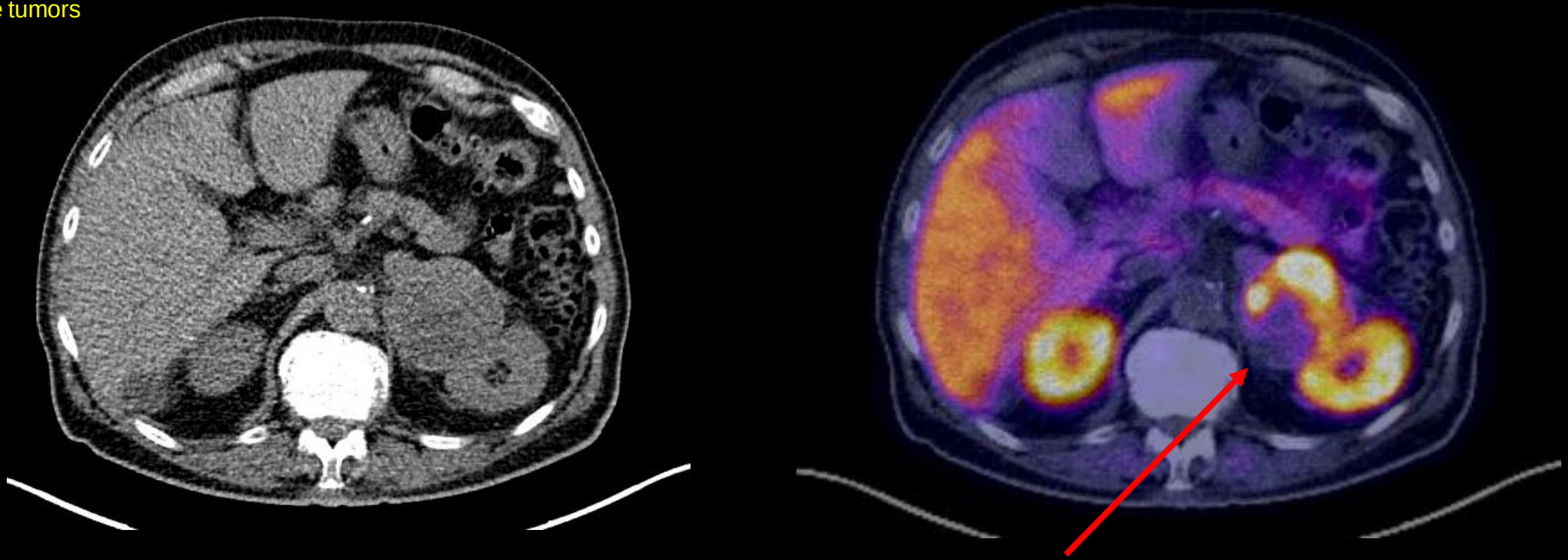


^{68}Ga-DOTATATE PET/CT (unlabeled)



Gallium 68, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA)–octreotate is a somatostatin analog radiotracer that allows for whole-body detection of somatostatin receptors, commonly found in neuroendocrine tumors

^{68}Ga-DOTATATE PET/CT (labeled)



Left adrenal mass displaying avid, heterogeneous ^{68}Ga-DOTATATE uptake with maximum SUV of 45.9
No other suspicious ^{68}Ga-DOTATATE avid masses or lesions were seen.

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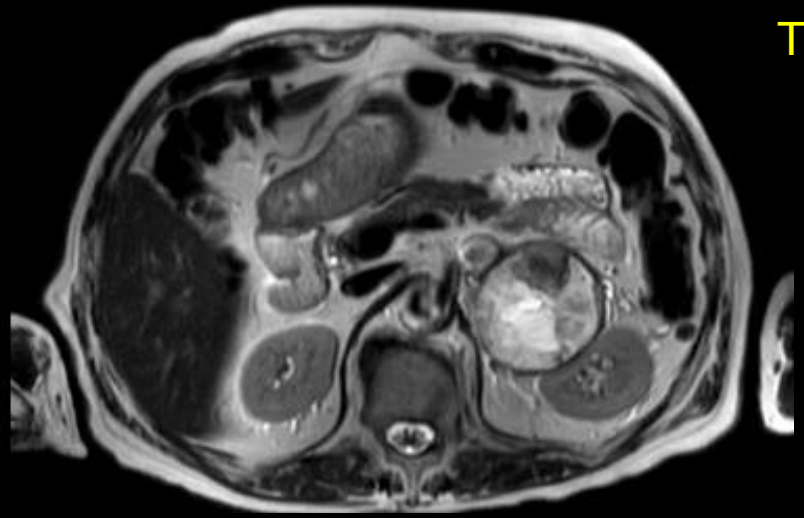
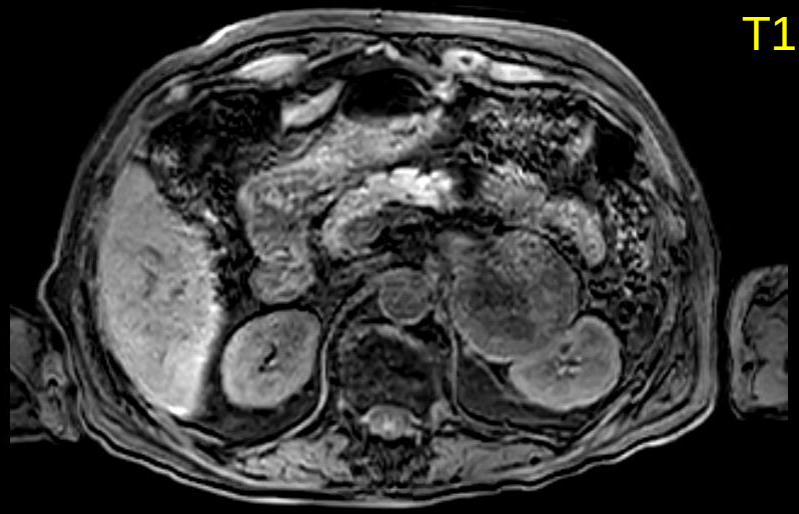
MR Abdomen with/without contrast (unlabeled)

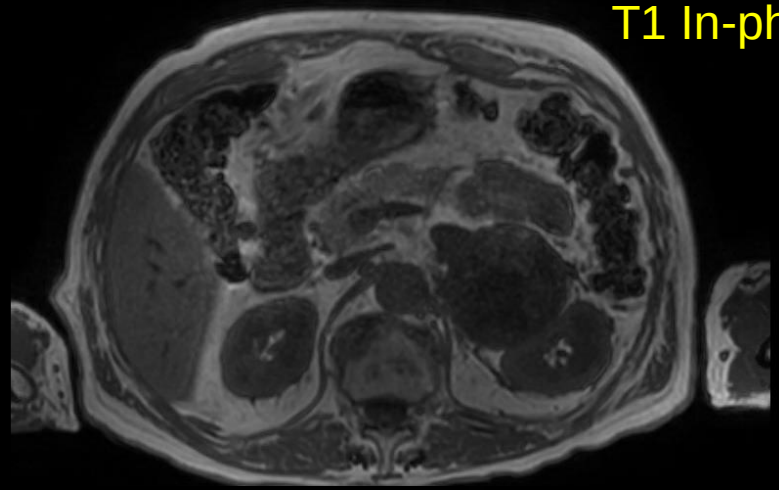
T2



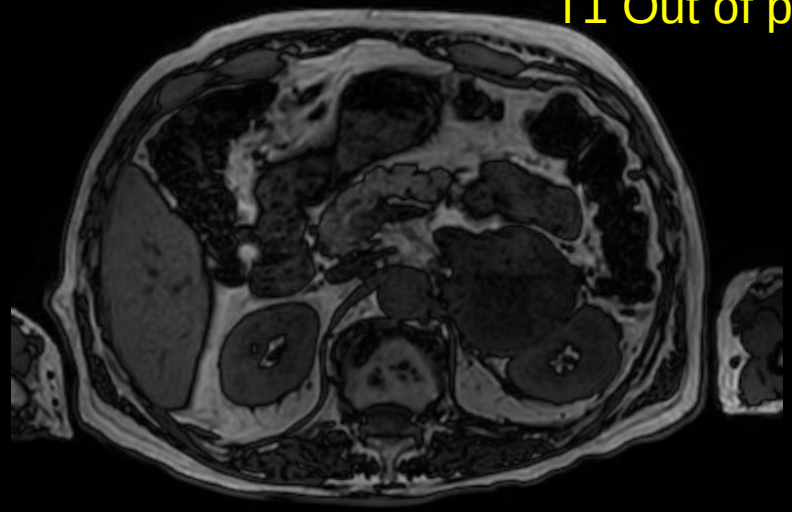
T1



T1 In-phase



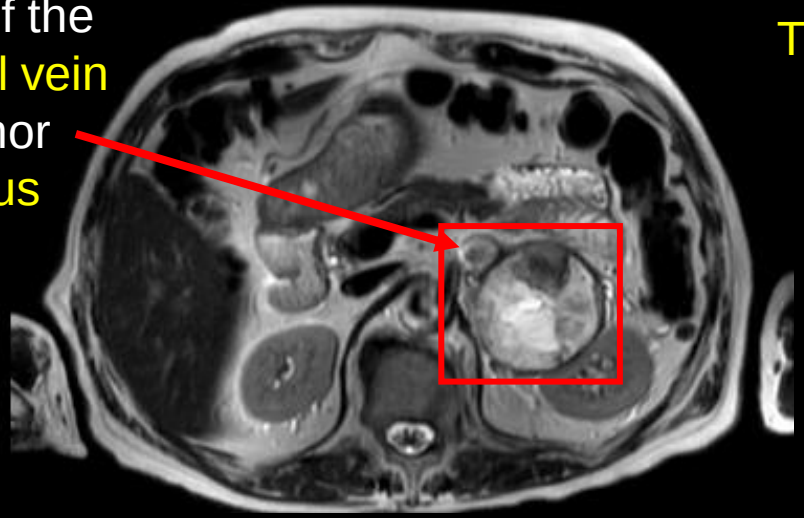
T1 Out of phase



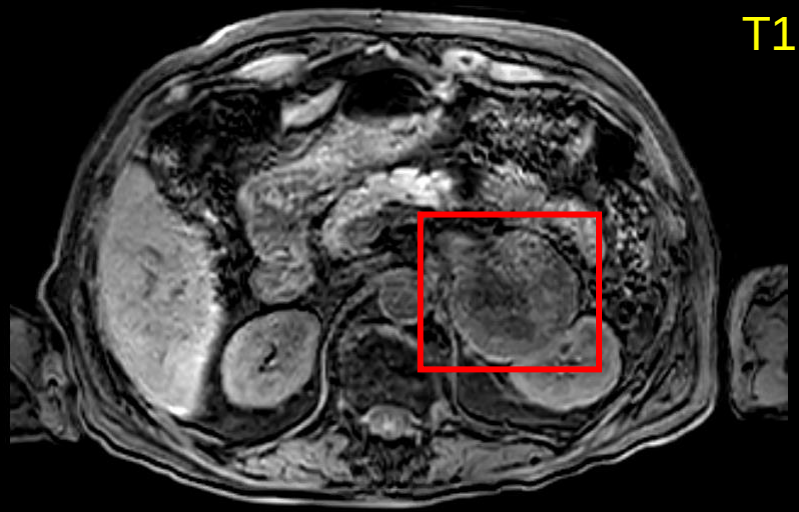
MR Abdomen with/without contrast (labeled)

invasion of the left adrenal vein with tumor thrombus

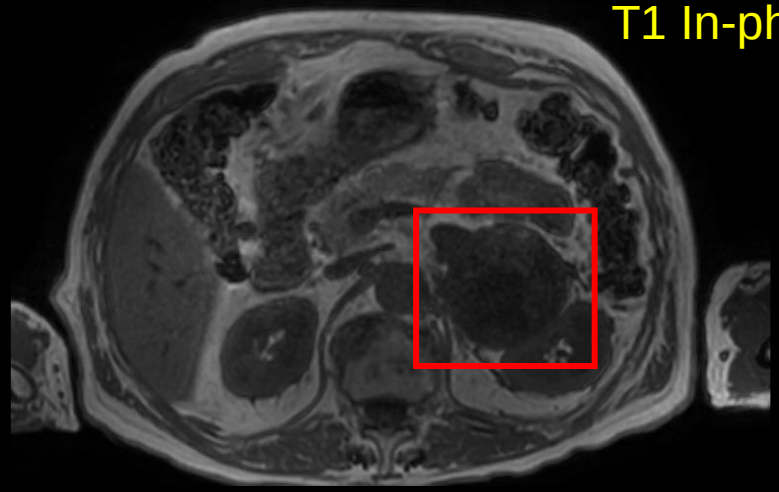
T2



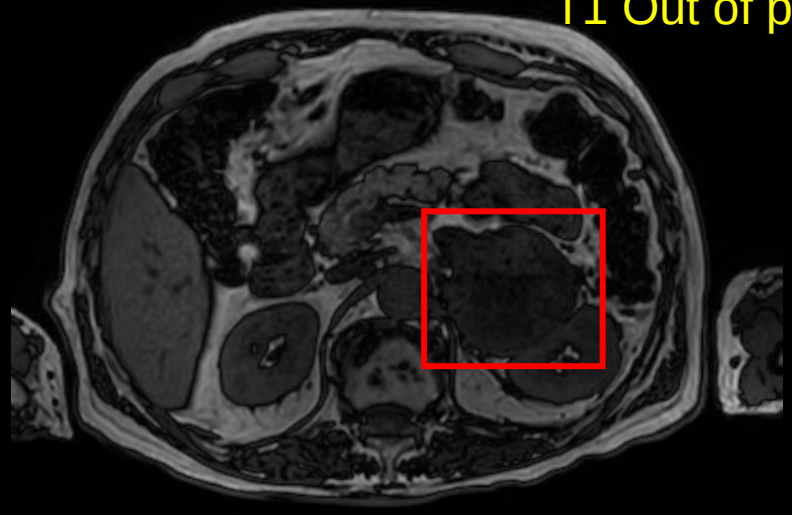
T1



T1 In-phase



T1 Out of phase



Left adrenal mass with heterogeneous T2 hyperintensity and T1 iso/hyperintense signal likely due to necrosis and hemorrhage

No drop in signal in T1 Out of phase sequence compared to In-phase (no microscopic fat content)

Other Relevant Labs

Labs showed elevated levels of urine and plasma normetanephrines and urine norepinephrine

Plasma-free metanephrines and normetanephrines

Ref Range & Units	
Metanephrine, Plasma 12 - 67 pg/mL	55
Comment: Reference Ranges: Hypertensive adult > or = 18 yrs old: 12-72 pg/mL Normotensive adult > or = 18 yrs old: 12-67 pg/mL Normotensive children < 18 yrs old: 10-95 pg/mL	
Normetanephrine, Plasma 18 - 101 pg/mL	1,510 ^
Comment: Reference Ranges: Hypertensive adult > or = 18 yrs old: 24-145 pg/mL Normotensive adult > or = 18 yrs old: 18-101 pg/mL Normotensive children < 18 yrs old: 22-83 pg/mL	

Urine fractionated metanephrines and catacholamines

Total Volume mL	1650
Epinephrine, Ur per vol ug/L	2
Norepinephrine, Ur per vol ug/L	109
Dopamine, Ur per vol ug/L	71
Epinephrine, Ur ratio to CRT 0 - 20 ug/g CRT	4
Epinephrine, Ur 24hr 1 - 14 ug/d	3
Comment: REFERENCE INTERVAL: Epinephrine, Urine - ug/d Access complete set of age- and/or gender-specific reference intervals for this test in the ARUP Laboratory Test Directory (aruplab.com).	
Norepinephrine, Ur ratio to CRT 0 - 45 ug/g CRT	210 ^
Norepinephrine, Ur 24hr 14 - 120 ug/d	180 ^
Comment: REFERENCE INTERVAL: Norepinephrine, Urine - ug/d	
Ref Range & Units	(9/28/22)
Metanephrine, Urine 24 Hour 52 - 341 ug/24 hr	132
Normetanephrine, Urine Random 24 Hour 88 - 444 ug/24 hr	1,968 ^
Metanephrine Total, Urine 24 Hour 140 - 785 ug/24 hr	2,100 ^

Final Dx:

Pheochromocytoma

Pheochromocytoma

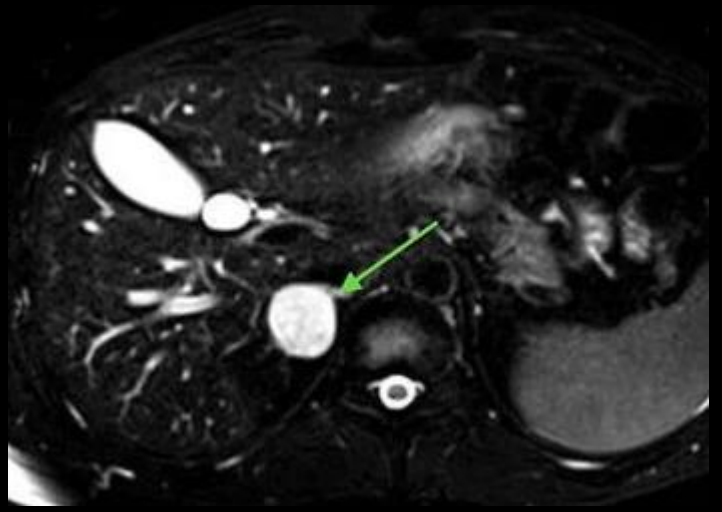
- Rare, catecholamine-producing tumor, typically found in the adrenal gland
  - If extra-adrenal, termed "paraganglioma"
  - Incidence is 0.8 per 100,000, rare cause of hypertension (<0.2% of patients)
- Classically presents with symptoms of catecholamine excess:
  - However, classic triad of sweating, headache, palpitations is rare
  - "The great masquerader" – can present with a range of symptoms
  - Majority of cases are actually incidental in asymptomatic patients due to more widespread use of imaging
- Only reliable criterion for malignancy is metastasis

Work-up: Check urine/plasma metanephrines before imaging, genetic testing

- Diagnosis requires proof of excessive catecholamine release (discontinue any interfering medications) and anatomic documentation of tumor
- If adrenal incidentaloma > 10 HU, get biochemical testing
- More than 40% carry germline mutations (*VHL, RET, NF1*, etc.)

Pheochromocytoma

- Imaging characteristics vary greatly
  - Persistent, avid enhancement
  - CT: Most have attenuation > 10 HU, think adenoma if less
  - MR: Low T1 signal (dark), High T2 signal (bright), hypervascular appearance
  - Large tumors are often heterogeneous; may be calcified, necrotic, hemorrhagic
  - Increased uptake on molecular imaging, E.G., ^{68}Ga-DOTATATE PET/CT
- Differential for suspected pheochromocytoma:
  - Lipid-poor adrenal adenoma
  - Adrenal cortical carcinoma
  - Adrenal metastasis
  - Renal cell carcinoma (often indistinguishable from renal mass)



Lightbulb sign due to homogeneous, marked T2 hyperintensity
Fonseca et al. (2017)

Pheochromocytoma

- Main treatment is resection of the entire adrenal gland with tumor
  - Preoperative adrenal blockade with α/β blockers to prevent hypertensive crisis
  - Presence of mutations guides post-operative care and screening

Adapted from Neumann et al. (2019)

Clinical Scenario	Initial Biochemical Testing and Imaging	Follow-up Biochemical Testing and Imaging
RET mutation	Measure metanephrines and perform abdominal MRI; measure serum calcitonin and calcium; seek endocrine surgery consultation if thyroid gland not previously resected	Measure serum calcitonin, metanephrines, and serum calcium annually
VHL mutation	Measure metanephrines; perform MRI of the brain, spinal cord, and abdomen; perform ophthalmoscopy	Measure metanephrines yearly; perform MRI of the brain, spinal cord, and abdomen; perform ophthalmoscopy; if no tumor found, monitor every 2 or 3 years
SDHA, *SDHB*, or *SDHD* mutation	Perform MRI of skull base and neck, thorax, retroperitoneum, and pelvis; alternatively, perform ^{68}Ga-DOTATATE–PET–CT; also measure metanephrines	Measure metanephrines yearly; if a pheochromocytoma or paraganglioma was removed, perform MRI of the surgical region annually for yr 1–3; for body areas that had no tumors, perform MRI every 3 yr
SDHC or *SDHAF2* mutation	Measure metanephrines; perform MRI of skull base and neck or ^{68}Ga-DOTATATE–PET–CT	If a paraganglioma or pheochromocytoma was removed, perform MRI of the surgical region annually for yr 1–3; for body areas that had no tumors, perform MRI every 3 to 5 yr
MAX or *TMEM127* mutation	Measure metanephrines; perform MRI of the abdomen or ^{68}Ga-DOTATATE–PET–CT	Measure metanephrines yearly; if a pheochromocytoma or paraganglioma was removed, perform MRI of the surgical region annually for yr 1–3; perform MRI of the abdomen every 3 yr
Neurofibromatosis type 1	Measure metanephrines	If hypertension or clinical symptoms develop, measure metanephrines

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Patient Outcome

- Patient successfully underwent left robotic adrenalectomy
  - Surgery notes described a challenging operation as the tumor was found to be adherent to L. kidney and adrenal vein, with multiple feeding vessels into tumor that needed to be meticulously dissected
  - No extra-adrenal disease was seen

References:

American College of Radiology ACR appropriateness criteria: Incidental adrenal mass. https://acsearch.acr.org/docs/69366/Narrative/

Arnold DT, Reed JB, Burt K. Evaluation and management of the incidental adrenal mass. Proc (Bayl Univ Med Cent). 2003;16(1):7-12. doi:10.1080/08998280.2003.11927882

Blake MA, Kalra MK, Maher MM, et al. Pheochromocytoma: an imaging chameleon. Radiographics. 2004;24 Suppl 1:S87-S99. doi:10.1148/rg.24si045506

Fonseca, E.K.U.N., Ponte, M.P.T.R., Yamauchi, F.I. et al. The light bulb sign in pheochromocytoma. Abdom Radiol 42, 2779 (2017). https://doi.org/10.1007/s00261-017-1198-0

Neumann HPH, Young WF Jr, Eng C. Pheochromocytoma and Paraganglioma. *N Engl J Med*. 2019;381(6):552-565. doi:10.1056/NEJMra1806651

Young, WF. Clinical presentation and diagnosis of pheochromocytoma. In: Nieman LK, ed. UpToDate. UpToDate; 2022. Accessed Nov 9, 2022. https://www.uptodate.com/contents/clinical-presentation-and-diagnosis-of-pheochromocytoma#H4050401766

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