Beth Israel Deaconess Medical Center
Harvard Medical School

August 2009

Radiologic Evaluation of Pheochromocytoma

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Agenda

- Introduction
  - Adrenal anatomy
  - CT and MR appearances of normal adrenals
  - Common adrenal abnormalities
- Case: Pheochromocytoma
  - Diagnostic imaging modalities
  - Classic radiologic appearances
  - Differential diagnoses
  - Clinical presentation and diagnosis
  - Management
- Summary

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Introduction

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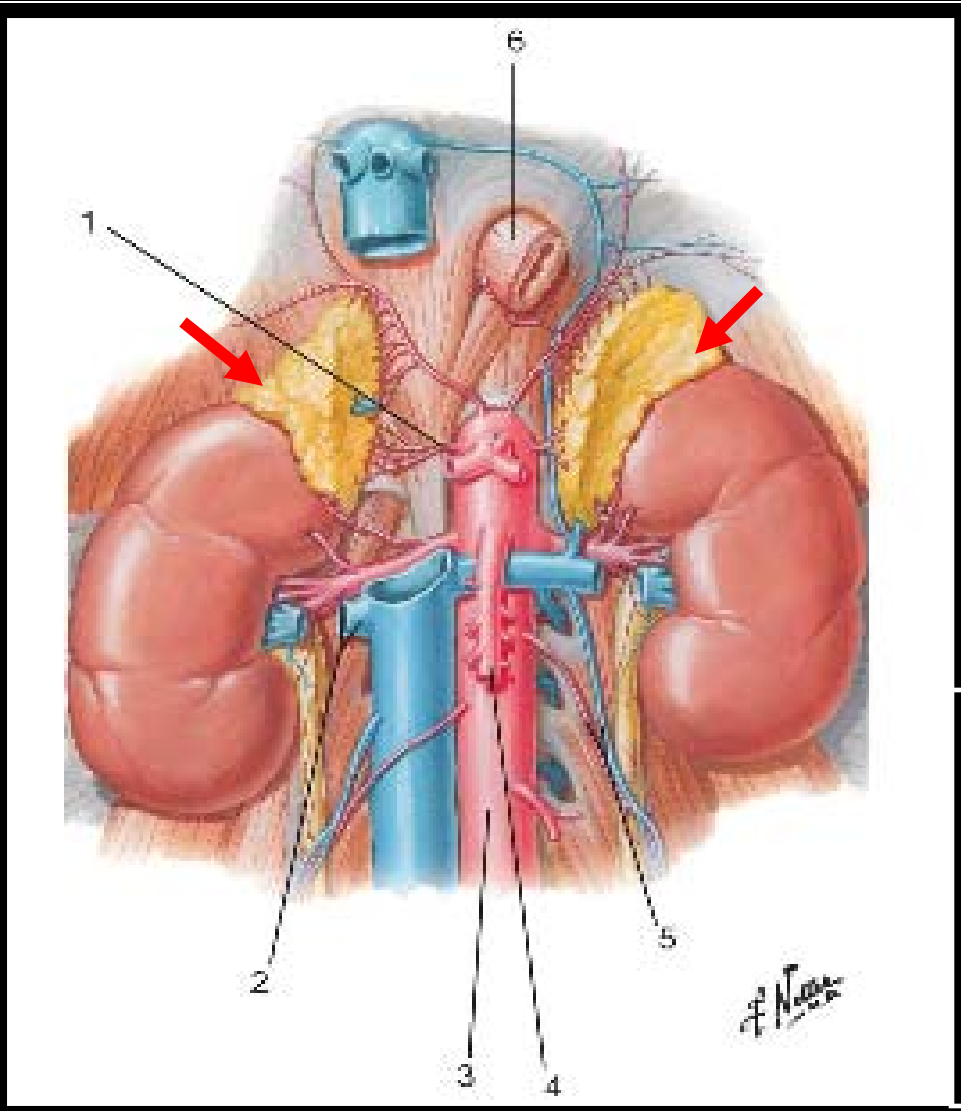
Review of the Adrenal Anatomy



The adrenal receives a rich vascular supply from 3 different vessels: superior, middle and inferior suprarenal arteries.

The adrenal is surrounded by the renal fascia, but is separated from the kidney by the transverse fibrous lemella.

1. Right middle adrenal artery
2. Right renal artery and vein
3. Abdominal aorta
4. Superior mesenteric artery
5. Left gonadal artery and vein
6. Esophagus

Hansen, John T. *Netter's anatomy flash cards.* 2nd ed. Saunder Elsevier: 2007.

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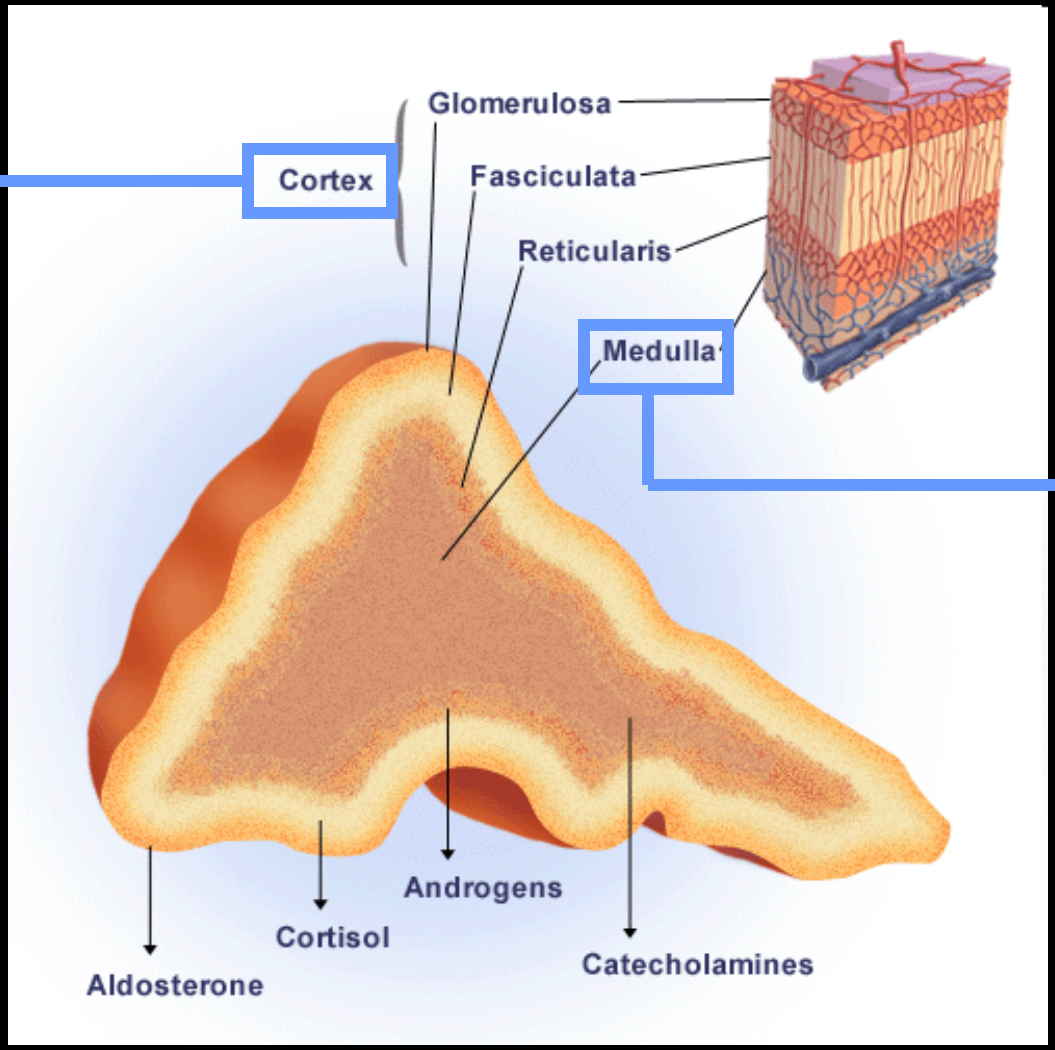
Review of the Adrenal Anatomy

From mesoderm



From ectoderm (neural crest cells)

Chromaffin cells are also found along the paraaortic and paravertebral axes

http://www.mmi.magill.ca/mmimediasampler2002/images/zingg-61no2.gif

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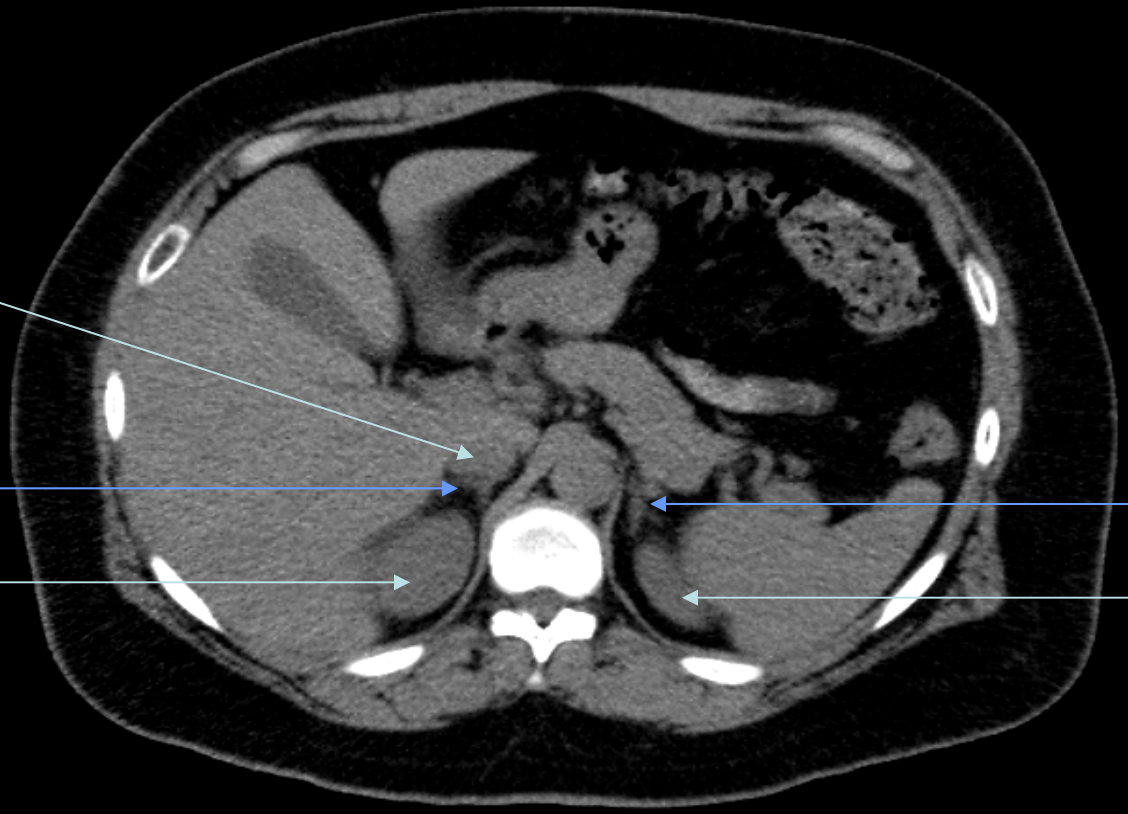
Normal Adrenal Glands on CT



- Inverted Y, V or T shape
- Homogeneous, symmetric
- Density resembles the kidney on non-contrast CT
- Adrenal body measures < 12 mm
- Adrenal limbs measure < 6 mm

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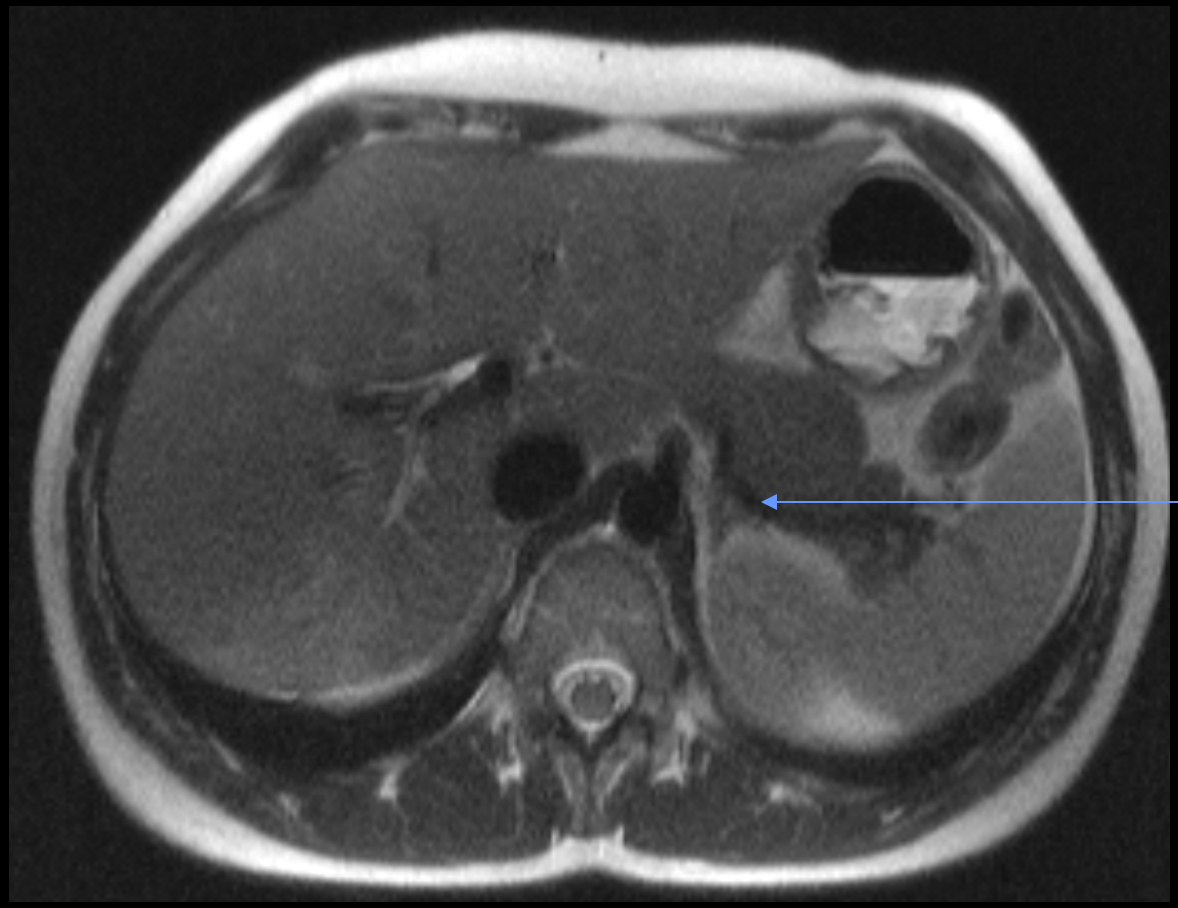
Normal Adrenal Gland on MRI



Axial T2-weighted image

The normal signal on MRI is isointense or slightly hypointense to the liver.

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Common Adrenal Abnormalities

Non-functioning adrenal abnormalities:

Benign

- Non-functioning adenoma (most often found incidentally, "adrenal incidentalomas")
- Myelolipoma
- Hematoma

Malignant

- Metastases (lung, breast, lymphoma, melanoma)
- Non-functioning adrenocortical carcinoma

Hyper-functioning adrenal abnormalities:

- Adrenal cortical hyperplasia (primary or secondary)
- Pheochromocytoma
- Adrenocortical carcinoma (40-50% are hyper-functioning)

Let's move on to discuss our patient's presentation

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Meet the Patient, JC

- 43 year-old male
- Three months history of episodic palpitations and chest burning, radiating to his back
- Past medical history: hypertension, dyslipidemia
- Social history: Alcohol abuse, non-smoker
- Review of system: No fever, no chills, no changes in his weight, no temperature intolerance, no visual difficulties, no headaches, no difficulty swallowing, no cough, no shortness of breath, no leg edema, no GI or GU symptoms, no skin rashes.
- Physical Exam: Regular apical pulse of 110
- A portable AP chest radiograph was obtained in the ED to rule out any acute cardiopulmonary processes.

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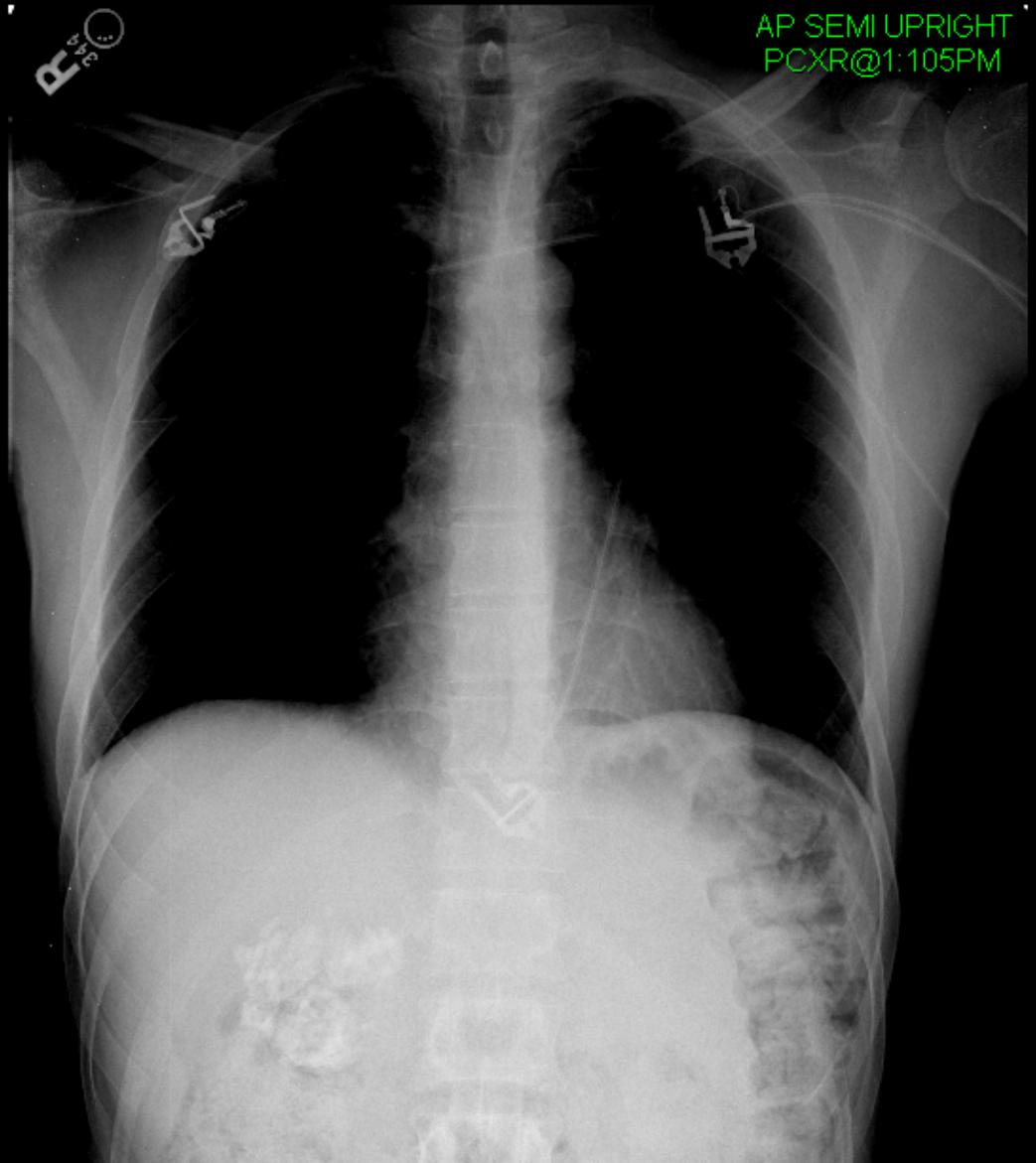
Our Patient: Frontal Chest Radiograph



What are the findings?

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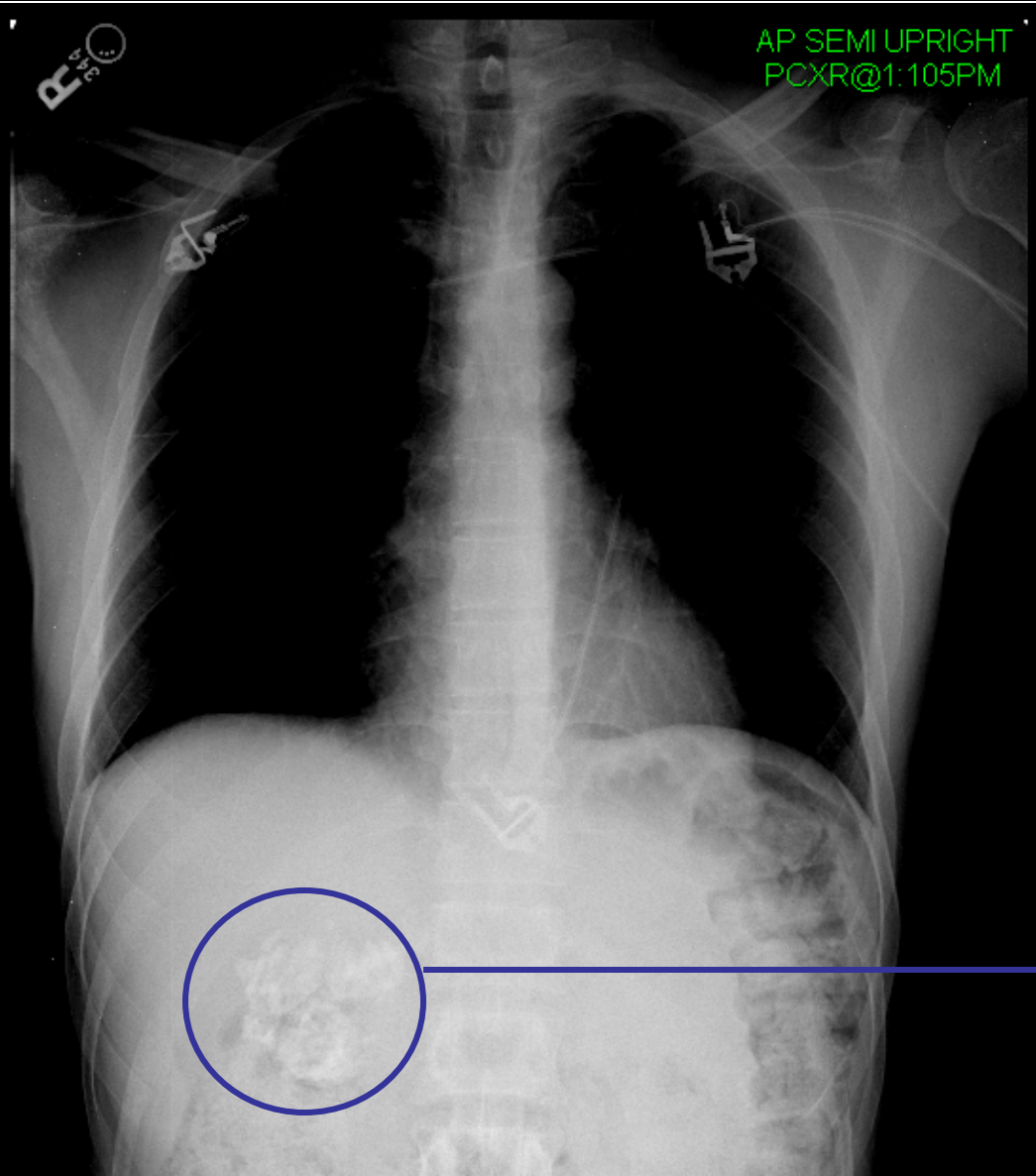
Our Patient: Frontal Chest Radiograph



- Cardiomediastinal and hilar contours are normal.
- Lungs are clear with out consolidation or pulmonary edema. No pleural effusion.
- Osseous structures are unremarkable.

Heavy metal/calcific opacity superimposed the RUQ

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Meet the Patient…cont'd

- EKG shows sinus tachycardia
- Mild hypertension was also noted
- Comprehensive workup for cardiac problems including:
  - Echocardiogram
    - Mild right ventricular hypertrophy with hyperdynamic LV function
    - No valvular abnormality
  - Stress test & exercise MIBI scan
    - Normal myocardial perfusion
    - Calculated LV ejection fraction of 65%
- Diagnosed with "high output heart failure" secondary to beriberi

Patient Presentation: 5 Months Later

- More frequent palpitations with chest pain
- Episodic hypertension
- Complaint of night sweats and headache
- EKG unchanged
- Due to complaints of upper abdominal/lower chest pain, chest radiographs were obtained to rule out any acute cardiopulmonary processes.

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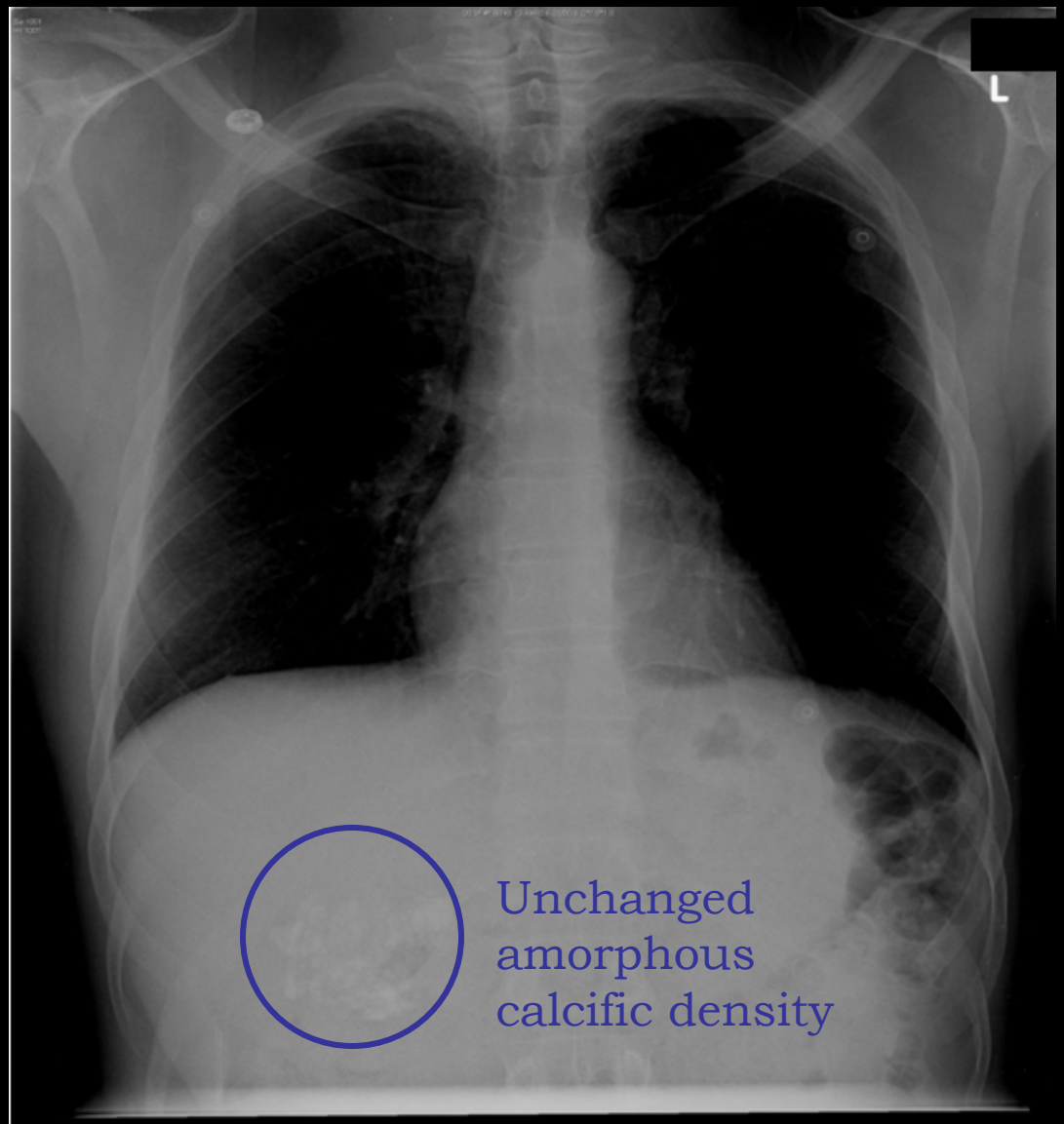
Our Patient: 5-month Follow-up Chest Radiograph



Where is this lesion?

- In the liver?
- In the gallbladder?
- In the bowel?
- In the kidney?
- In the adrenal?
- In the connective tissue?

Let's look at the lateral chest radiograph.

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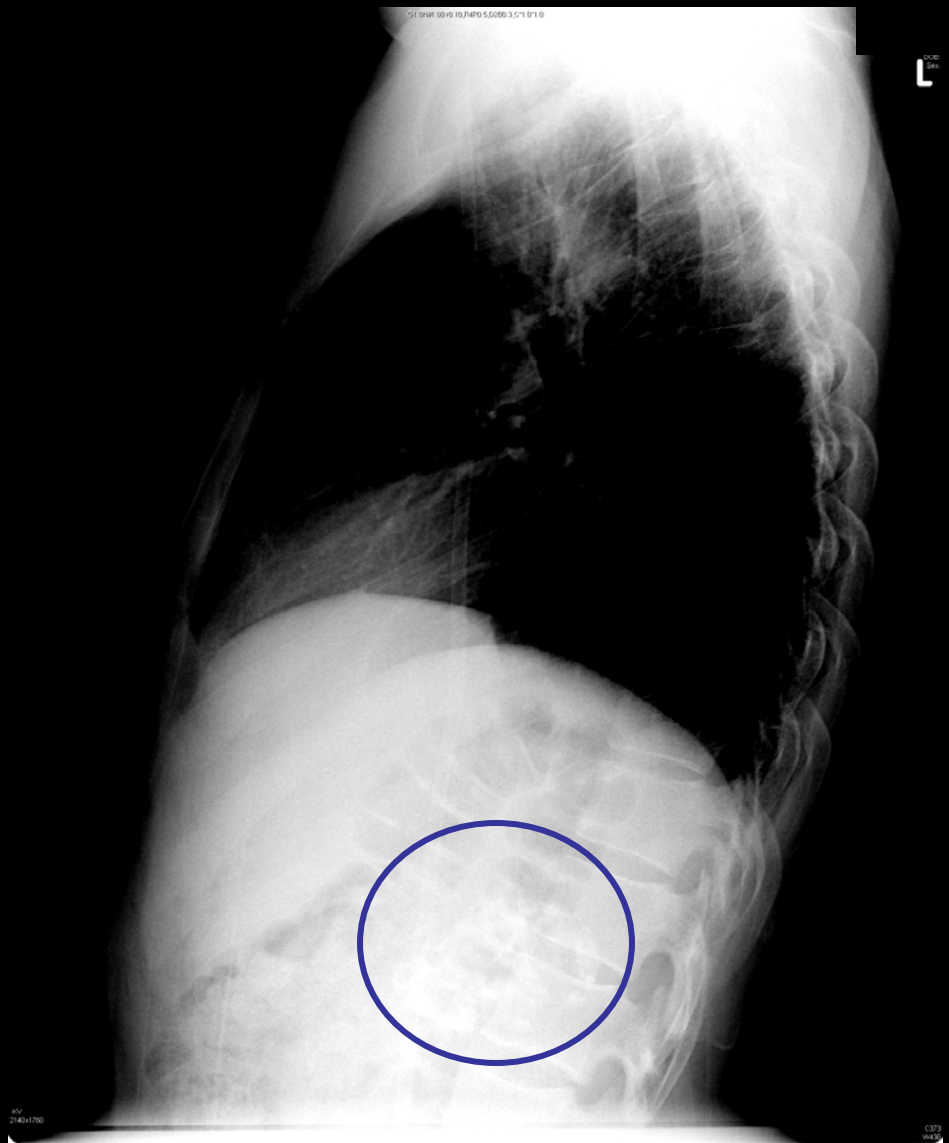
Our Patient: 5-month Follow-up Chest Radiograph

The lesion is posterior, possibly retroperitoneal.

It does not seem to involve the liver or gallbladder

The lesion may be in the right adrenal, right kidney, bowel, or connective tissue



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Differential Diagnoses for the Patient's Posterior Calcific Lesion

Based on Organs:

- Right Adrenal gland
  - Pheochromocytoma
  - Adrenocortical carcinoma
  - Myelolipoma
  - Prior hemorrhage, trauma, infection
  - Metastases (calcifications rare)
- Right Kidney
  - Renal cell carcinoma
  - Hemorrhagic cyst
  - Prior infarction, laceration
- Bowel
  - Gastrointestinal stromal tumor

Not Organ-related: Liposarcoma

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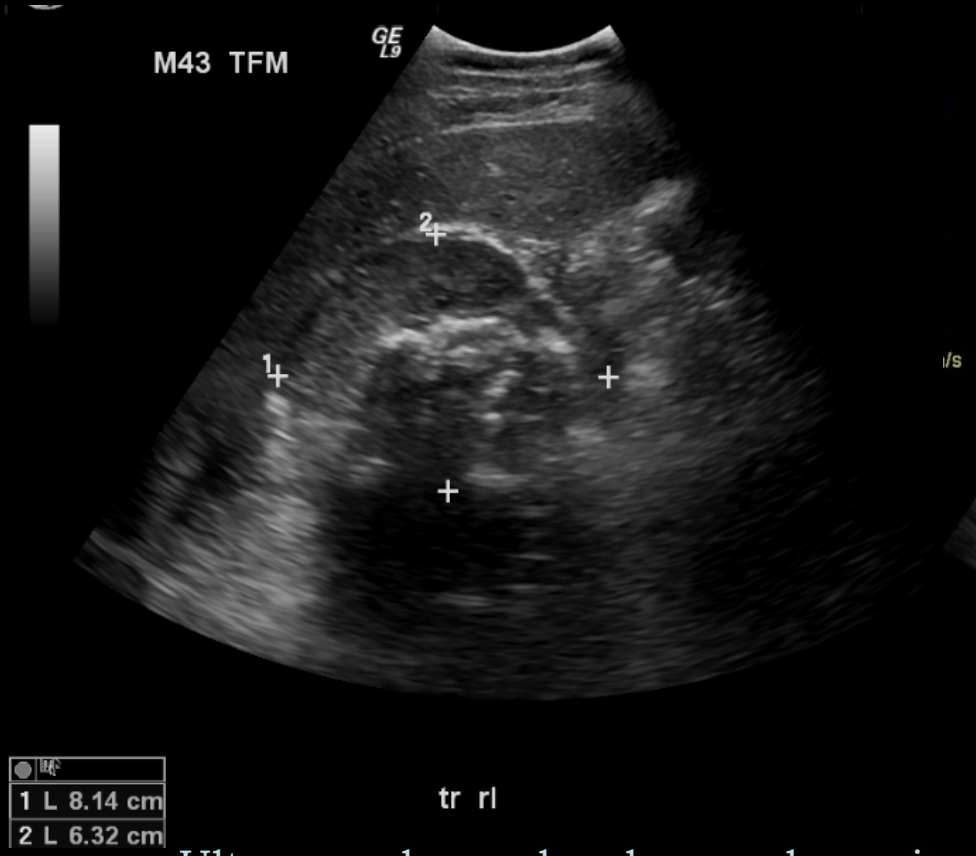
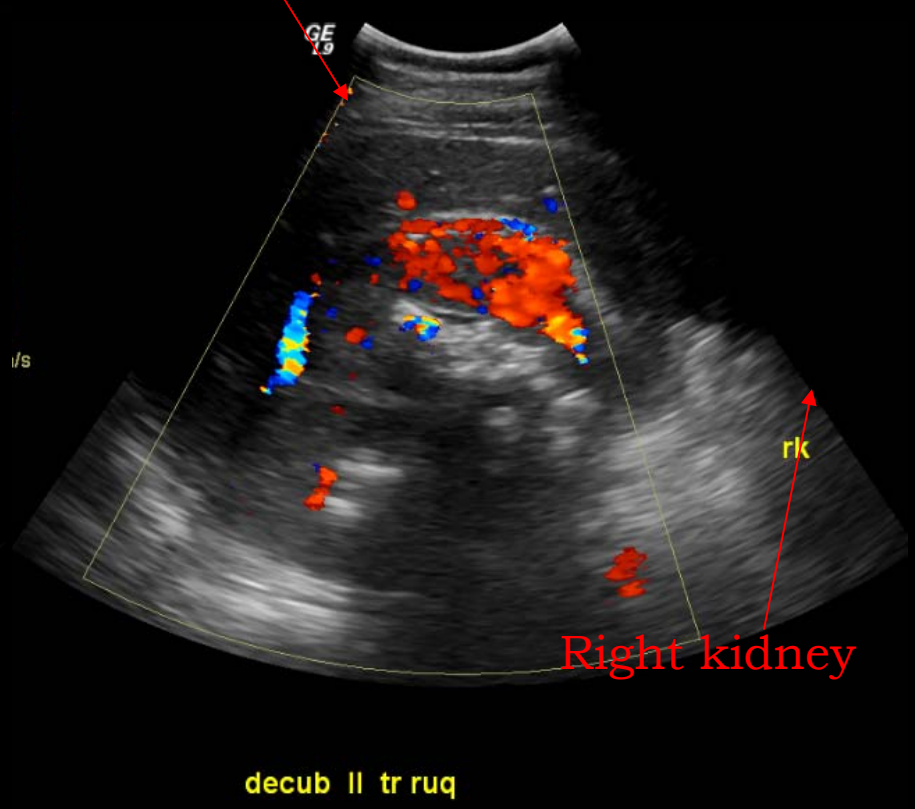
Our Patient: RUQ ultrasound



Ultrasound reveals a large echogenic mass with calcifications that cause distal shadowing. The mass is adjacent to the liver but does not seem to arise from or invade into the liver. It however creates a mass effect on the liver.



Doppler ultrasound demonstrates blood flow within the lesion. The mass is seen here separated from the right kidney

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Preliminary Diagnosis

The patient's history of episodic tachycardia, diaphoresis, headache and hypertension combined with findings on chest radiographs and ultrasound suggest pheochromocytoma and further workup is indicated.

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Pheochromocytoma

- A rare tumor (~1-4/10^6) arising from chromaffin cells that produces, stores and secretes catecholamines
- Most arise from adrenal medulla; 10% from extra-adrenal paraganglionic tissue (paraganglioma)
- Typically solitary and benign, but may be bilateral and malignant (10%)
- Most are sporadic, but may be part of familial syndromes e.g. MEN 2, VHL syndrome, NF-1, tuberous sclerosis

Common clinical presentation

- Triad of tachycardia, diaphoresis and headache is seen in 40-80% of patients
- Hypertension, most often paroxysmal, seen in over 90% of patients

Epidemiology

- Peak age: 40-50 yr
- Equal female/male ratio

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Clinical Diagnosis of Pheochromocytoma

Biochemical Diagnosis

- Plasma catecholamine levels
- 24-hour urine vanillylmandelic acid and metanephrine levels

Sensitivity range from 89% to 100%

Reasons for false negatives:

- Exogenous medications
- Episodic catecholamine production

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Imaging Modalities for Pheochromocytoma

Incidentally identified:

- Plain radiograph
  - Calcifications occur in approximately 12% of pheochromocytoma
- Ultrasound

Anatomical imaging modalities:

- MRI
- CT

MRI, CT and MIBG scan are commonly used modalities

Functional imaging modalities:

- [^{123}I] and [^{131}I] Meta-iodobenzylguanidine (MIBG) scintigraphy
- PET imaging
  - Specific: [^{11}C]Hydroxyephedrine, [^{18}F]Dopamine, [^{18}F]DOPA
  - Non-specific: [18F]Deoxyglucose

    If specific functional modalities are negative, tumor is recurrent, potentially malignant or metastatic

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MR Imaging of Pheochromocytoma

Typical Appearance

- T2 hyperintense (classic "light-bulb bright"), unless there is hemorrhage or intratumoral necrosis
- T1 hypointense or isointense relative to the liver
- Bright enhancement, usually rapid and intense
- Central necrosis may be present
- No signal loss on chemical-shift imaging

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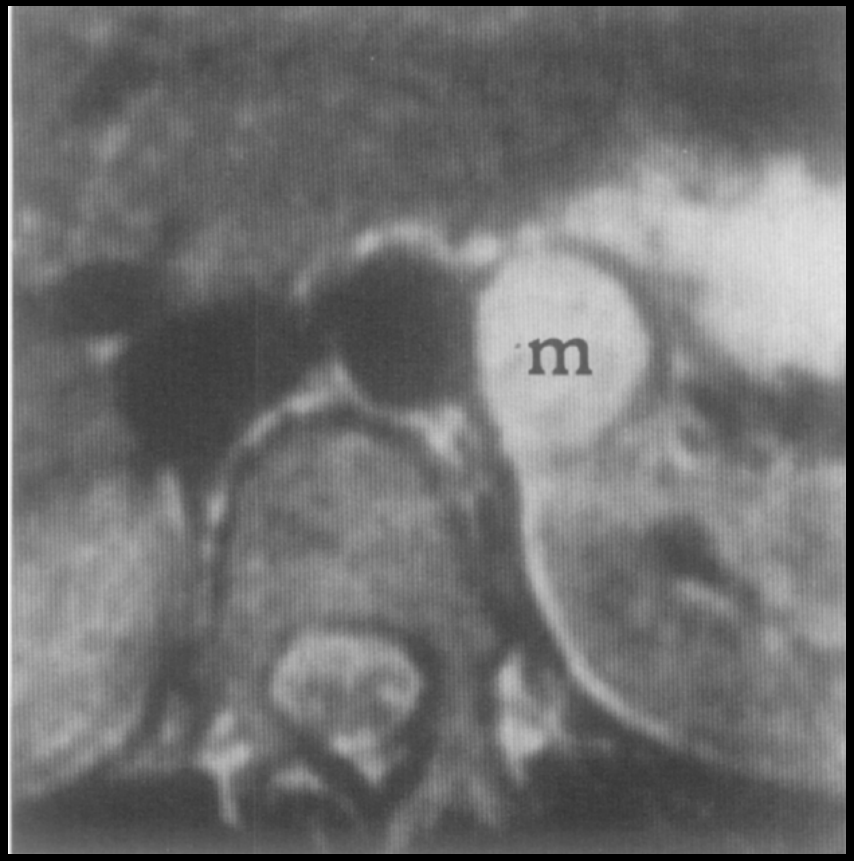
Companion Patient #1: Pheochromocytoma

Typical Appearance

- T2 hyperintense (classic "light-bulb bright"), unless there is hemorrhage or intratumoral necrosis



T2-weighted MR image of another patient with left adrenal pheochromocytoma (m)

Image Source: Korobkin M, Francis IR. Adrenal Imaging. *Seminars of Ultrasound, CT, and MRI.* 1995; 16(4): 317-30.

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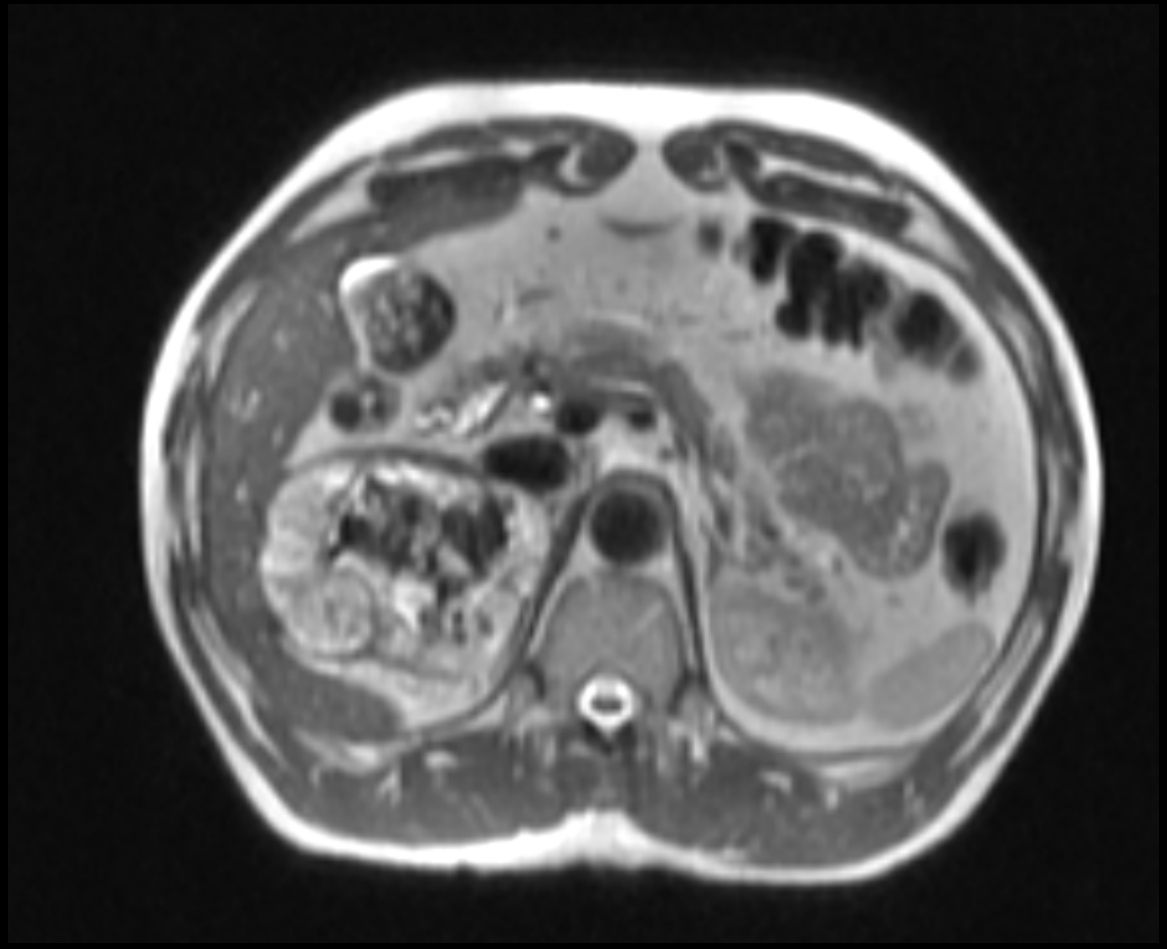
Our Patient: T2-weighted axial MRI



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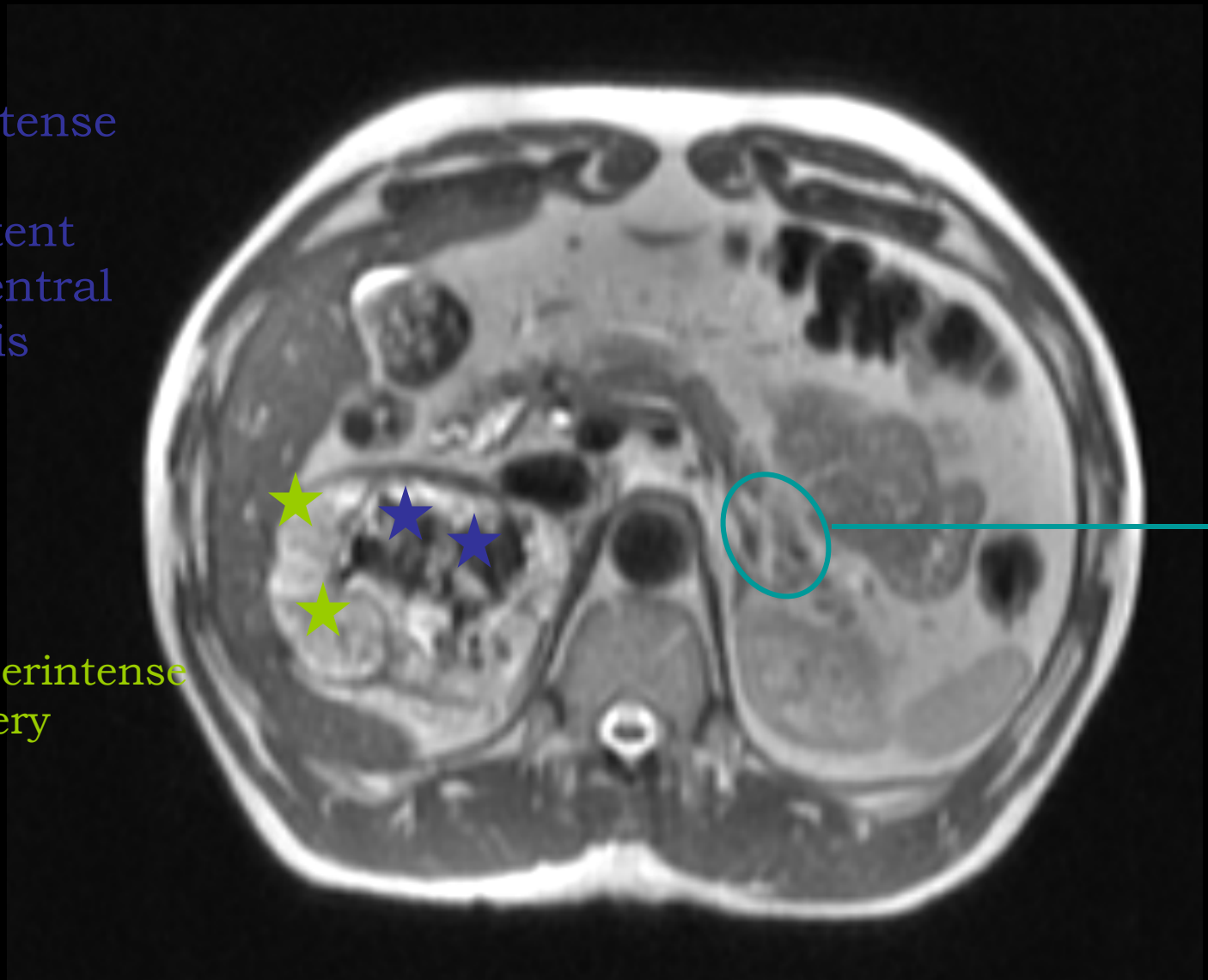
Our Patient: T2-weighted axial MRI

★ T2-hypointense center consistent with central necrosis

★ T2-hyperintense periphery



Normal left adrenal

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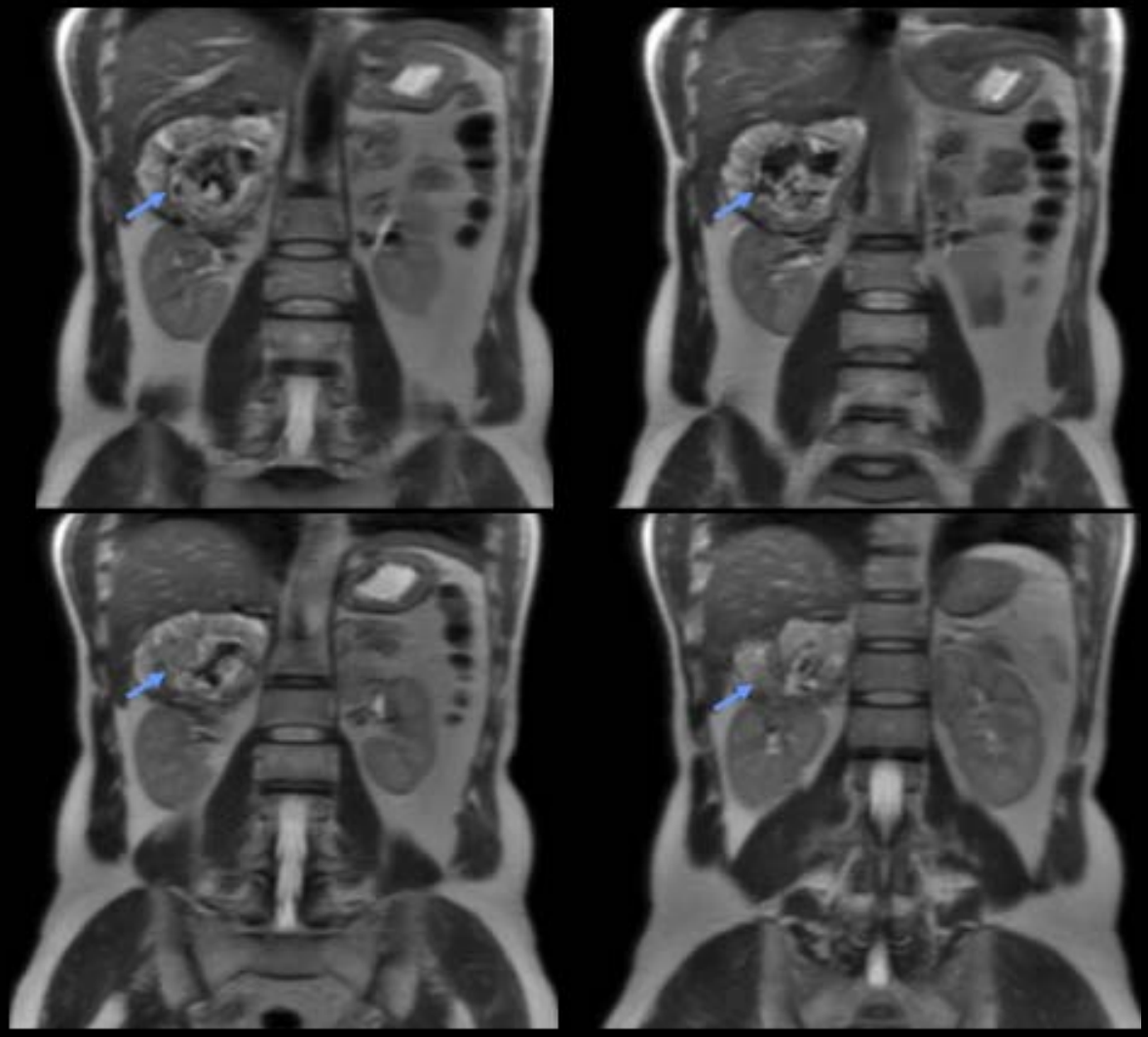
Our Patient: Pheochromocytoma on Coronal T2-weighted MRI



- A large (6.3 x 8.9 x 7.9 cm) heterogeneous mass with T2 hyperintensity relative to the liver
- The central region is hypointense consistent with a necrotic center.
- Normal right adrenal is NOT seen.
- The mass appears separated from the right kidney
- No definite invasion of the liver

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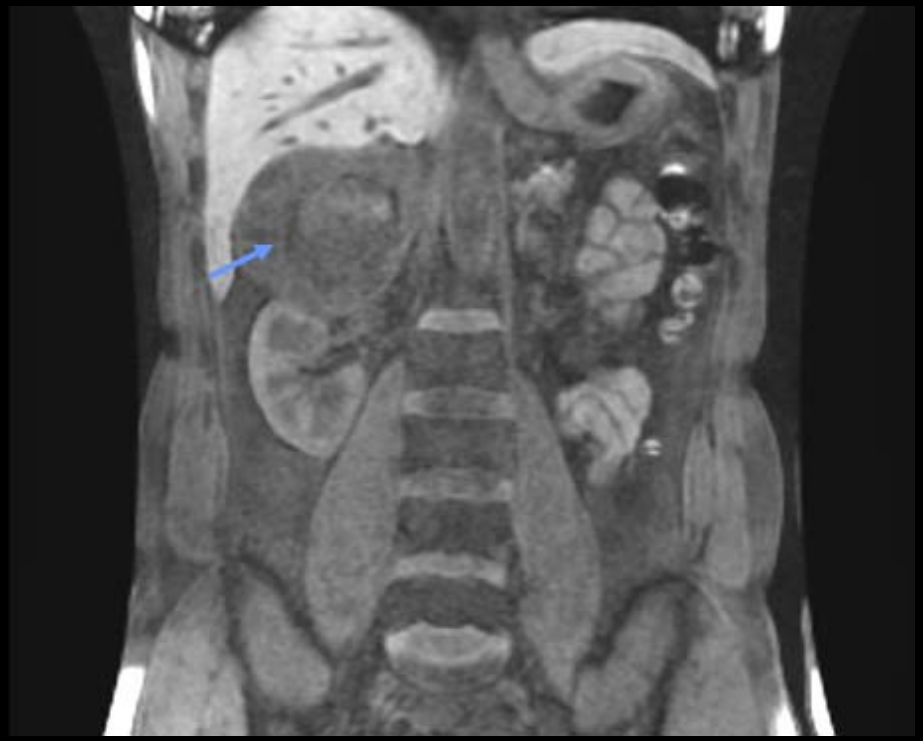
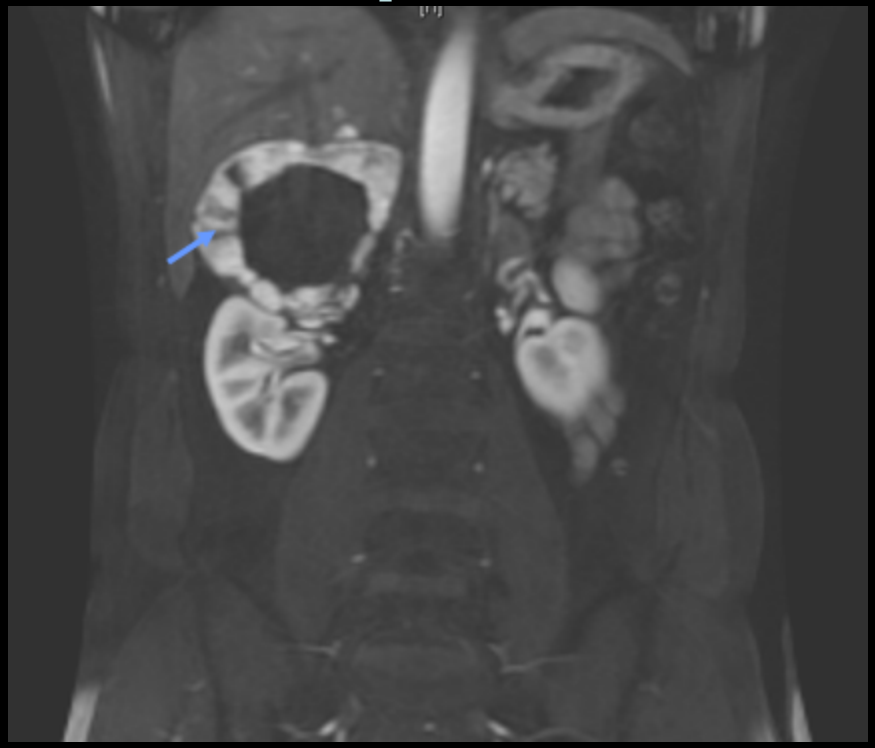
Our Patient: Pheochromocytoma on Contrast-enhanced MRI

T1 weighted, pre-contrast



T1 hypointense relative to skeletal muscle

T1 weighted, post-contrast, arterial phase



The periphery avidly enhances.

The central area of necrosis demonstrates no uptake.

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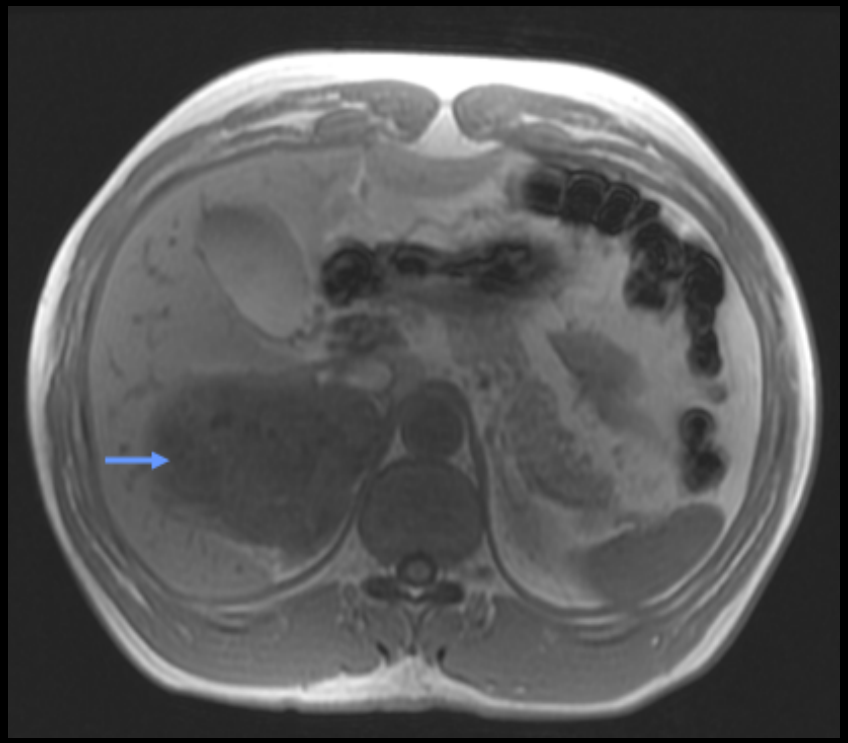
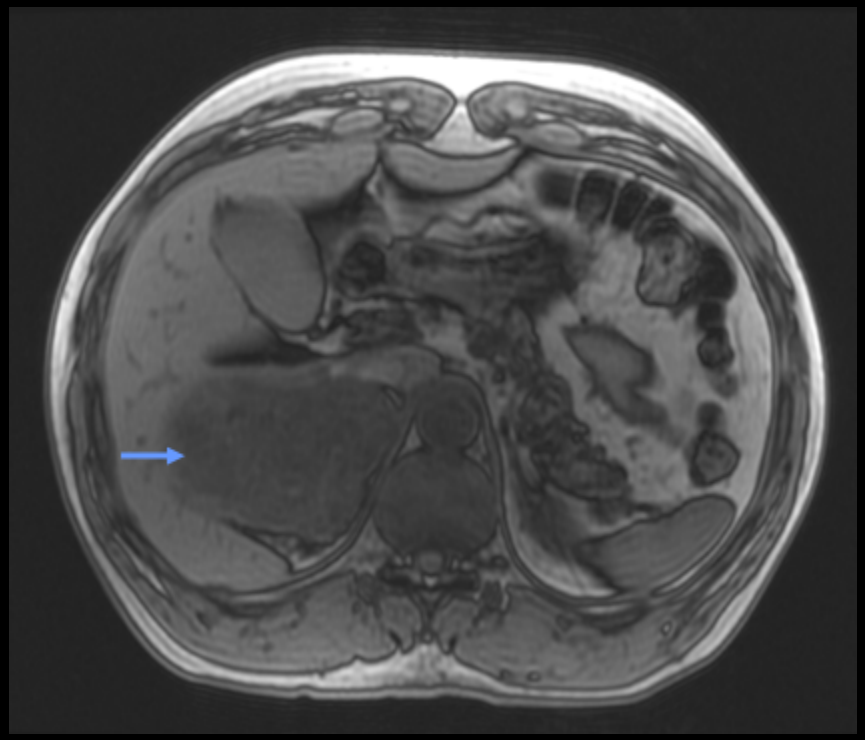
Our Patient: Pheochromocytoma on Chemical-shift Imaging



In phase



Opposed phase

No phase cancellation

↓

The mass does not contain lipid

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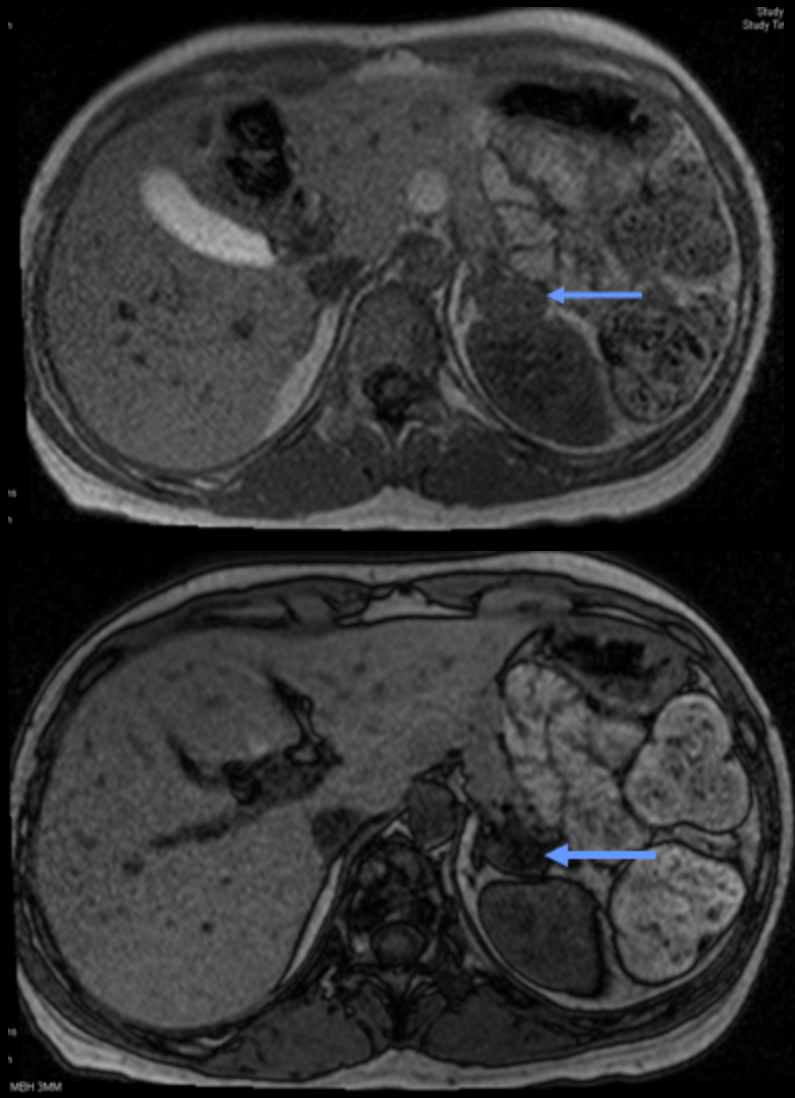
Companion Patient #2: Adrenal Adenoma on Chemical-shift MR imaging

Illustration of signal drop-off from in-phase (top) to out-of-phase (bottom) sequences

Adrenal Adenoma:

- Most common adrenal mass
- Arises from adrenal cortex
- Contains high levels of intracellular lipids



In phase

Out of phase

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MR Imaging of Pheochromocytoma, cont'd

Advantages

- Best contrast resolution
- Highly sensitive in detecting primary adrenal pheochromocytoma (91-100% sensitive)
- MRI is more sensitive than CT in detecting extra-adrenal paragangliomas
- MRI delineates the relationship of pheochromocytomas with blood vessels; this feature is appreciated when surgery is envisaged
- Multi-planar imaging helps detect extension of adrenal masses into adjacent structures

Disadvantage

- MRI is less specific (50-90%) than MIBG scintigraphy

Update on the patient

- The patient's serum catecholamines and urine metanephrine levels are markedly elevated → Biochemical diagnosis of pheochromocytoma
- MR findings are most consistent with a pheochromocytoma arising from the right adrenal.

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10% of Pheochromocytomas are identified outside of the adrenals. Therefore, one needs to thoroughly evaluate outside of the adrenals as well.

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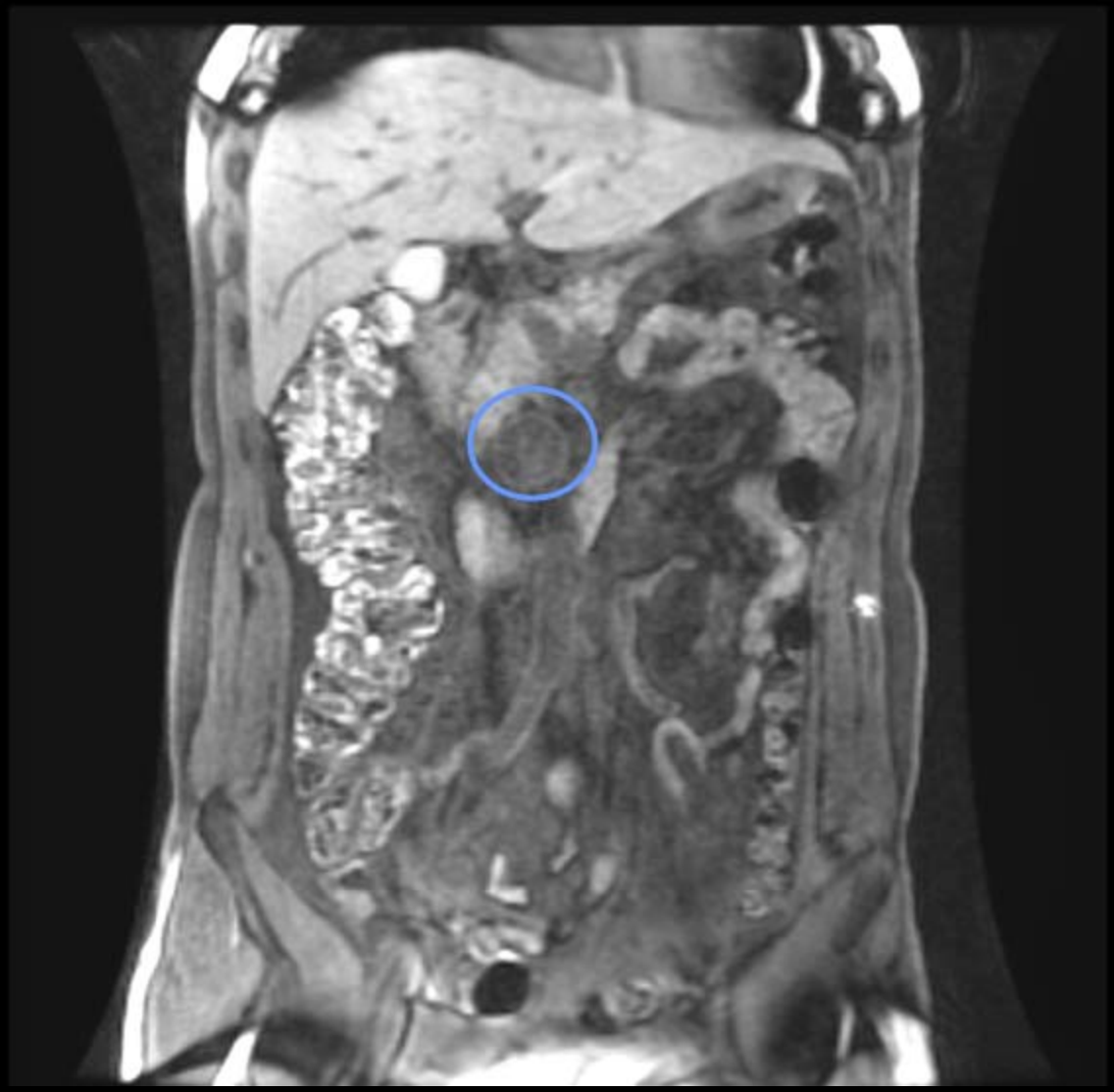
Our Patient: Second Lesion on Coronal T1-weighted Image



- There is a well-defined, round, heterogeneous mass with T1 hypointense signal relative to skeletal muscle
- The mass measures 2.4 x 2.6 x 2.8 cm

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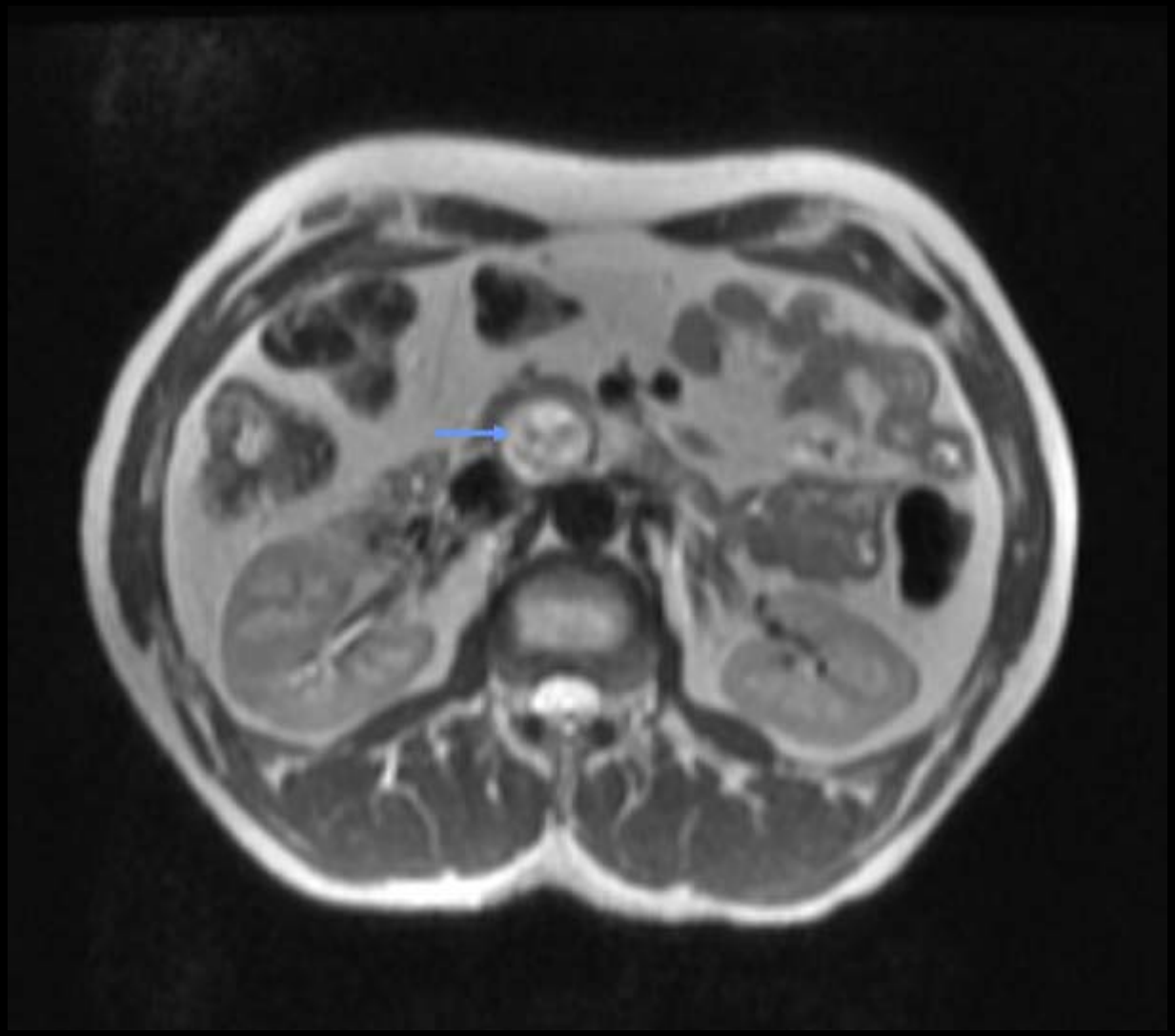
Our Patient: Second Lesion on Axial T2-weighted Image



- The mass is heterogeneous with signal hyperintensity on T2
- The mass is located anterior to the aorta and medial to the IVC

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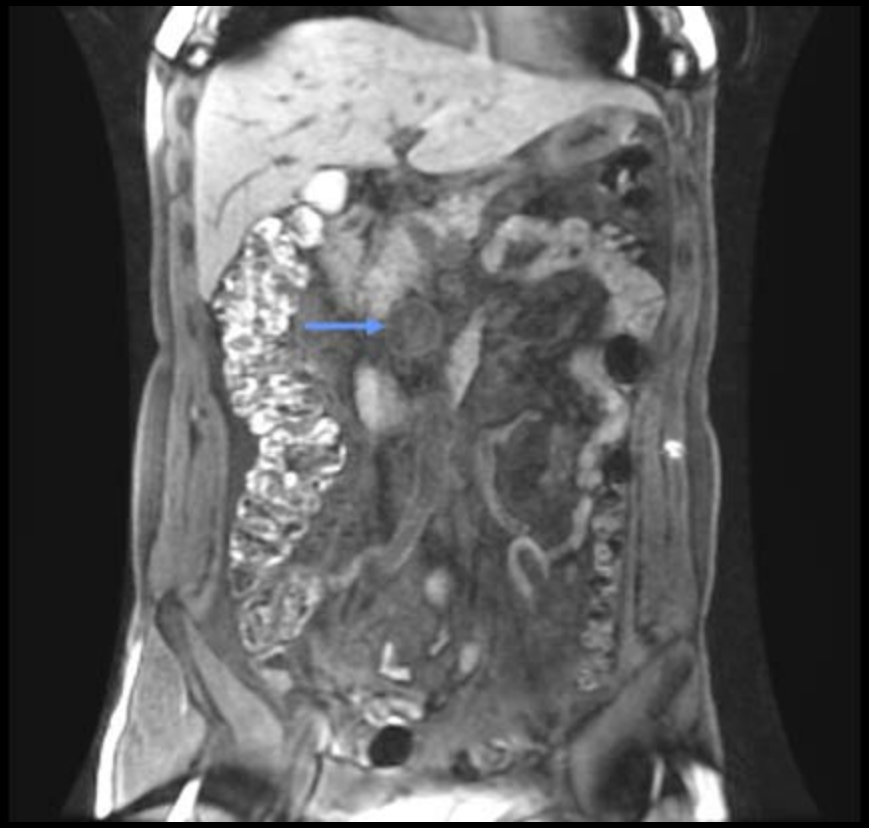
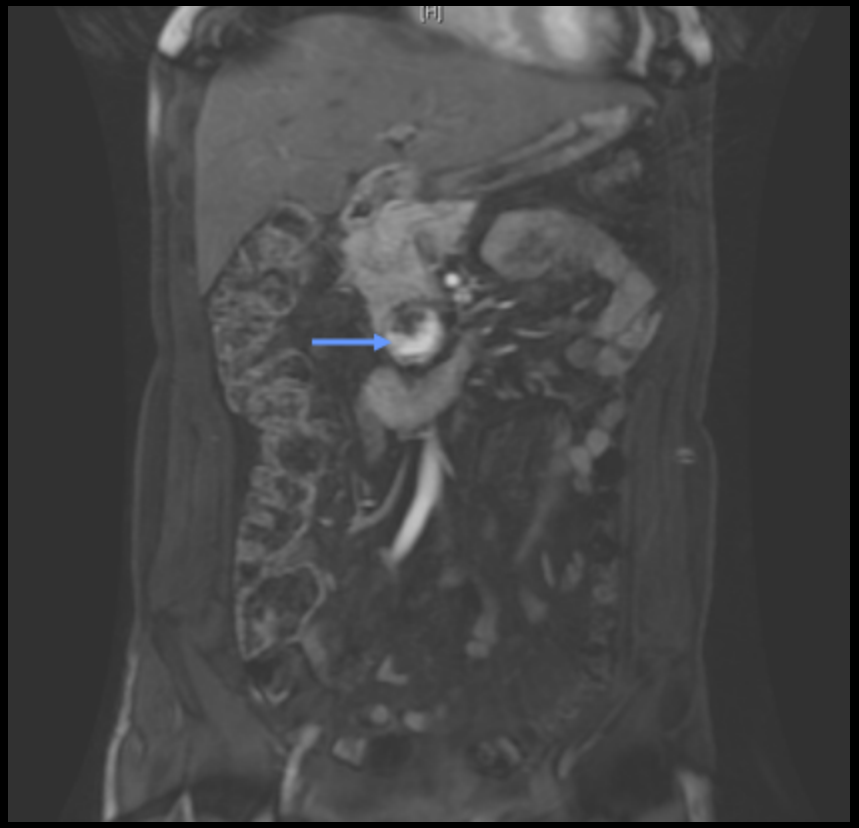
Our Patient: Second Lesion on Contrast-enhanced MRI



T1 weighted, pre-contrast



T1 weighted, post-contrast arterial phase

The mass is heterogeneously, avidly enhancing after contrast administration.

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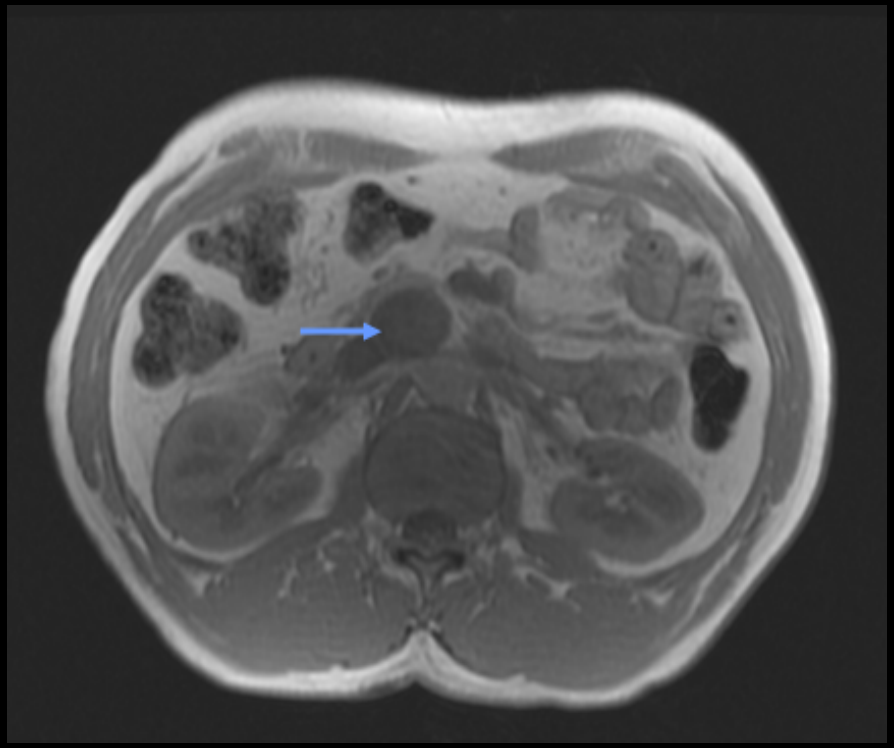
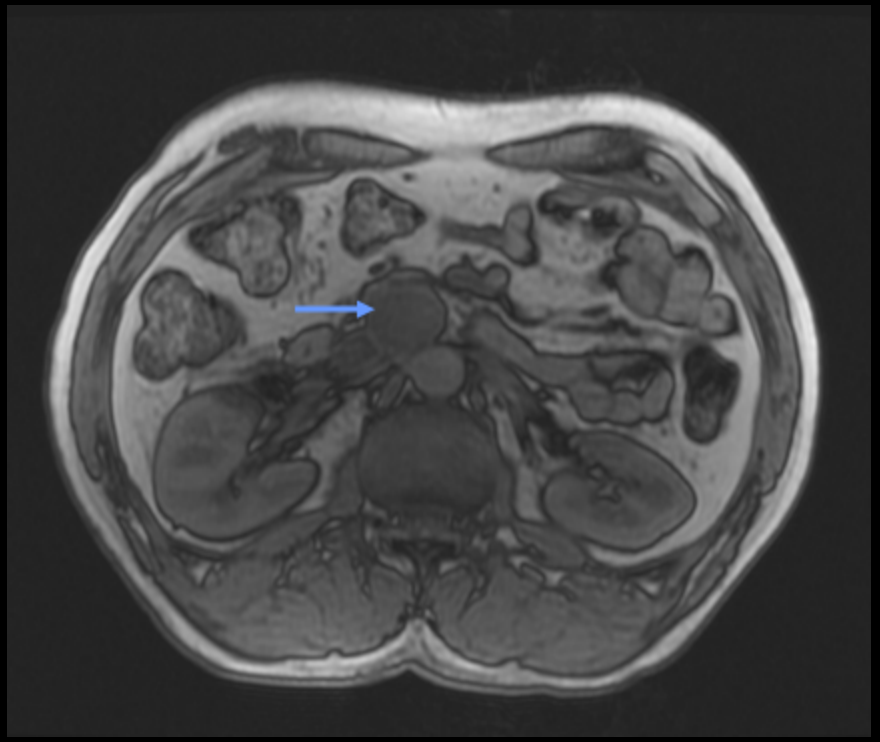
Our Patient: Second Lesion on Chemical-shift MRI





In phase

Opposed phase

No loss of signal from in phase to out of phase

All of the MR features are similar to those of the larger right adrenal mass.

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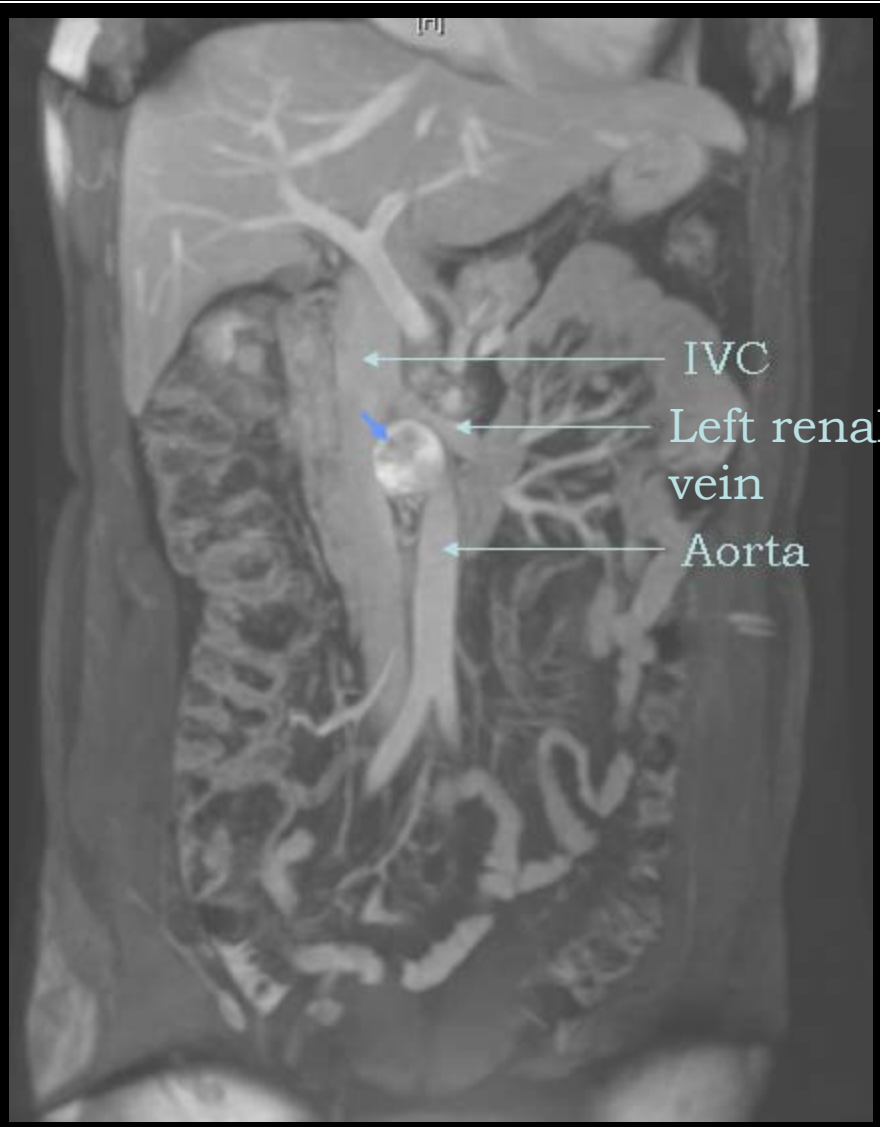
Our Patient: Second Lesion on Reformatted Contrast-enhanced MRI



- The lesion is located in the retroperitoneum, just inferior to the left renal vein, medial to the IVC and alongside the aorta (paraaortic)
- Recall that extra-adrenal chromaffin cells can be found along the paravertebral and paraaortic axes
- MR findings suggest that this mass is most likely a synchronous paraganglioma or a lymph node metastasis

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CT Imaging of Pheochromocytoma

Appearance

- Small pheochromocytomas are often homogeneous, solid masses that typically measure above 10 HU on non-contrast CT
- More commonly, they are large with central necrosis
- Scattered parenchymal calcifications can be observed in ~10% of the tumors
- Most pheochromocytomas enhances markedly

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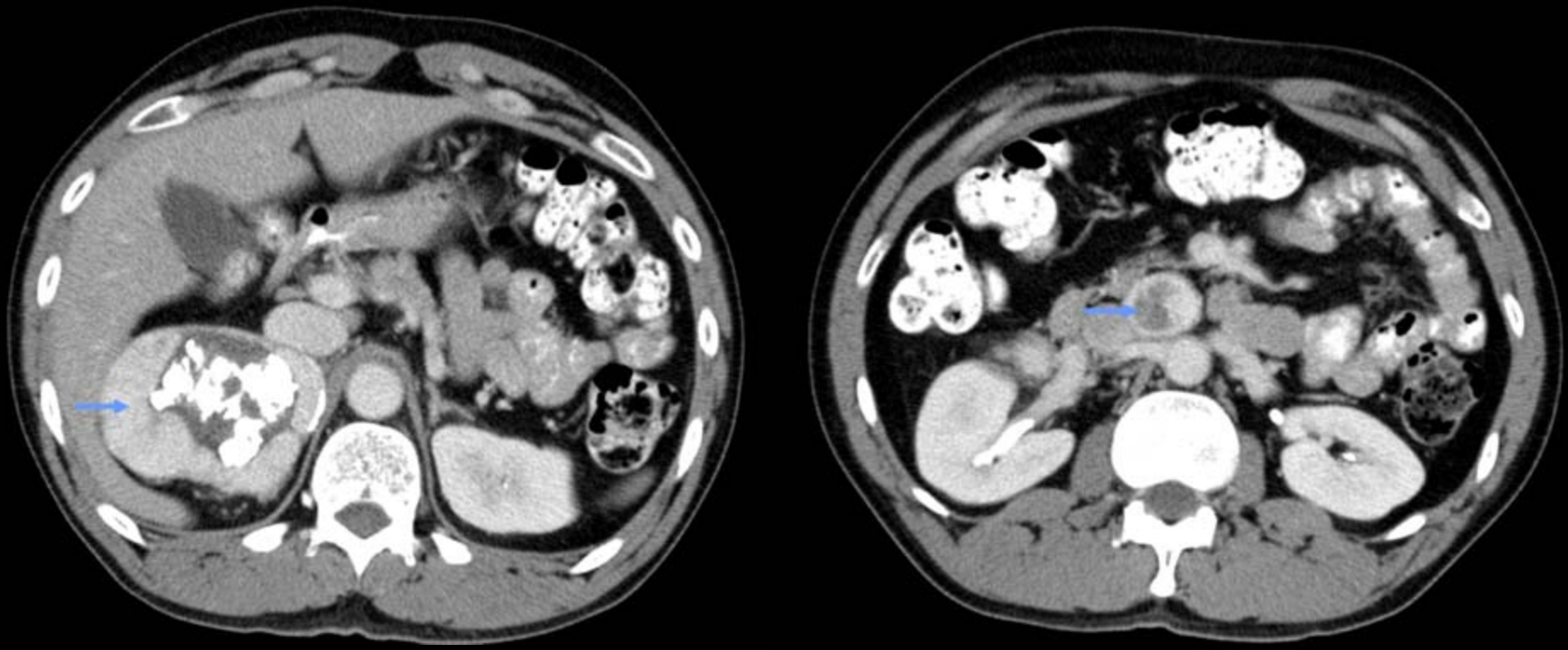
Our Patient: Contrast-enhanced Axial CT Images



(These Images were obtained for a reason unrelated to the patient's pheochromocytoma)

Both lesions demonstrate avid peripheral enhancement. Both appear heterogeneous. The larger mass (left) shows central calcifications.

CT Imaging of Pheochromocytoma, cont'd

Advantage

- Fast, readily available, highest spatial resolution
- Very high sensitivity in detecting primary adrenal pheochromocytomas (93-100%), equivalent to MRI

Disadvantages

- CT is slightly less sensitive (90%) than MRI in detection of extra-adrenal paragangliomas
- Like MRI, CT is less specific than MIBG scintigraphy

Common anecdotal concern

- IV contrast administration is thought to be associated with release of catecholamines, resulting in hypertensive crisis

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MIBG Scintigraphy

How it works

- Meta-iodobenzylguanidine (MIBG) is a catecholamine precursor that is taken into chromaffin cells via the human norepinephrine transporter (hNET).
- Following IV administration of [^{123}I] or [^{131}I]MIBG, planar images of the whole body are obtained in anterior and posterior projections

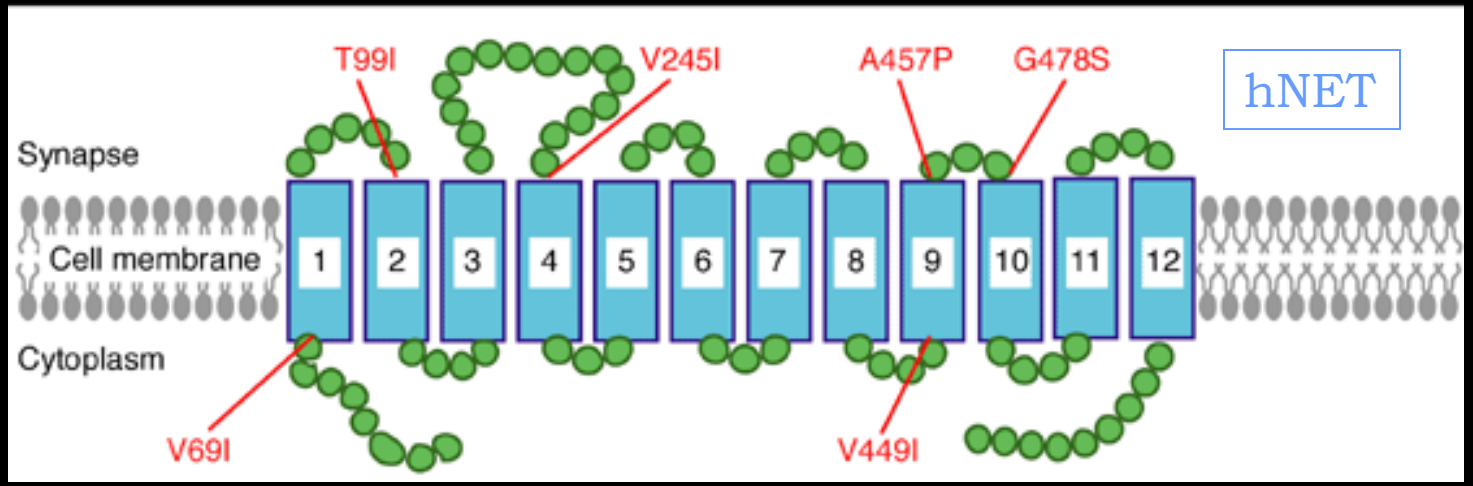

Image Source: Expert Reviews in Molecular Medicine: http://www-ermm.cbcu.cam.ac.uk

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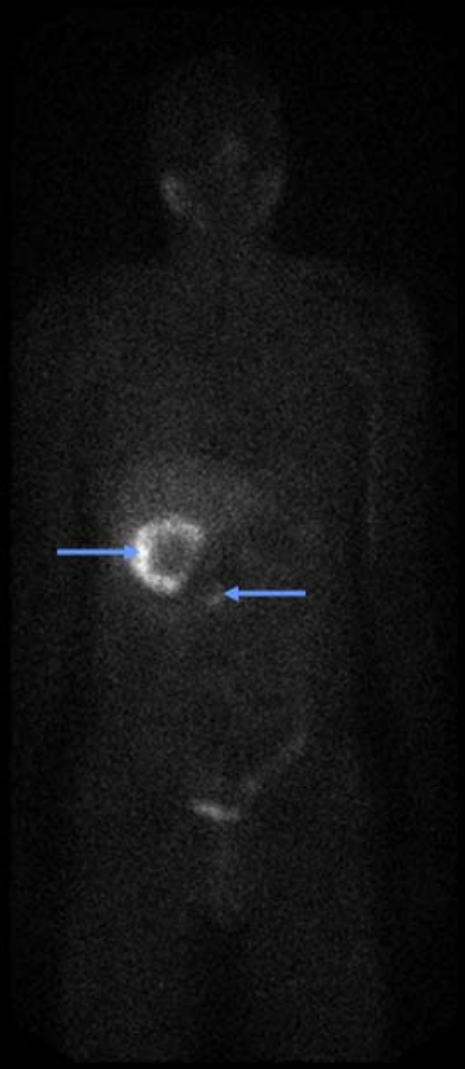
Our Patient: MIBG Scintigraphy



[^{131}I] MIBG scan, anterior projection

- MIBG was performed in order to rule out other paragangliomas or metastatic lesions.
- There is circumferential uptake in the region of the right adrenal gland consistent with uptake in the periphery of the known right adrenal pheochromocytoma. Centrally necrotic areas are not MIBG-avid.
- The second focus of tracer uptake seen in the midline paraaortic region.
- No other areas of abnormal tracer uptake

PACS, BIDMC

MIBG Scintigraphy, cont'd

Advantages

- Very high specificity (95-100%)
- High sensitivity (83-100%) for [^{123}I] MIBG scan
- Superior to other studies in the detection of extra-adrenal lesions
- Routinely performed whole-body scanning
- Particularly useful in evaluation of metastases in patients with malignant pheochromocytoma or rare tumors in the chest

Disadvantages

- The technique is expensive, time-consuming, not readily available
- Low sensitivity for lesions smaller than 2 cm

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Management of Non-malignant Pheochromocytoma

Treatment

- Definitive treatment is surgical (laparoscopic or transabdominal)
- Preoperative selective alpha-1 blockers (e.g. prazosin, doxazosin) or nonselective noncompetitive alpha blockers (e.g. phenoxybenzamine) are mainstay
- Phenoxybenzamine is preferred for inoperable disease

Follow-up

- Biochemical evaluation 2-6 wks post surgery
- Annual biochemical work-up for the first 5 years and once every 2 years thereafter

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Summary

- Pheochromocytoma is a rare tumor, but should be considered in a young patient with a new onset of “the triad” of symptoms (tachycardia, diaphoresis and headache) and/or paroxysmal hypertension.
- Imaging modalities are used in conjunction with biochemical evaluations in the diagnosis of pheochromocytomas and paragangliomas.
- MR and CT are highly sensitive modalities in detecting of pheochromocytomas and paragangliomas. However, these methods are less specific than MIBG scintigraphy.
- The typical MR appearance of pheochromocytoma is T2 hyperintense, avid contrast uptake and absence of signal loss on chemical-shift MR imaging. Central necrosis may be present.
- The definitive treatment for pheochromocytoma is surgical resection.

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