Radiologic evaluation of adrenal masses and an atypical radiologic presentation of adrenocortical carcinoma in a patient with primary aldosteronism

Odise Cenaj, Harvard Medical School Year III
Gillian Lieberman, MD

Odise Cenaj, MSIII
Gillian Lieberman, MD

Objectives

- Index Patient Presentation
- Primary aldosteronism
- Initial radiologic evaluation
- Differential diagnosis of adrenal masses
- Radiologic workup of adrenal masses
- Index Patient diagnosis
- Adrenocortical carcinoma
- Conclusions

Odise Cenaj, MSIII
Gillian Lieberman, MD

Index Patient Presentation

- Middle-aged woman with 10-month history of uncontrolled hypertension, persistent hypokalemia and worsening peripheral edema.

- WBC 6.5, hematocrit 42.7, platelets 240,000
- Sodium 142, potassium 3.1, chloride 101, bicarbonate 27, BUN 13, creatinine 0.8
- LFT, plasma cortisol and urine catecholamines normal.
- Aldosterone 40 ng/dL, elevated.
- Plasma renin activity 0.3 ng/mL/h, suppressed.

- The clinical presentation and laboratory findings raise the suspicion for primary aldosteronism or Conn's syndrome.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Objectives

- Index Patient Presentation
- Primary aldosteronism
- Initial radiologic evaluation
- Differential diagnosis of adrenal masses
- Radiologic workup of adrenal masses
- Index Patient diagnosis
- Adrenocortical carcinoma
- Conclusions

Odise Cenaj, MSIII
Gillian Lieberman, MD

Primary Aldosteronism

Causes of primary aldosteronism:

- aldosterone-producing adenomas (35% of cases)
- bilateral adrenal hyperplasia (60% of cases)
- aldosterone producing adrenocortical carcinomas
- ectopic aldosterone-producing tumors

Primary aldosteronism may be more common that once thought and might account for up to 10% of hypertension.

According to the 2008 Endocrine Society Guidelines, once the diagnosis of primary aldosteronism has been confirmed, adrenal CT should be the initial study to determine subtype (adenoma versus hyperplasia) and exclude adrenal carcinoma.

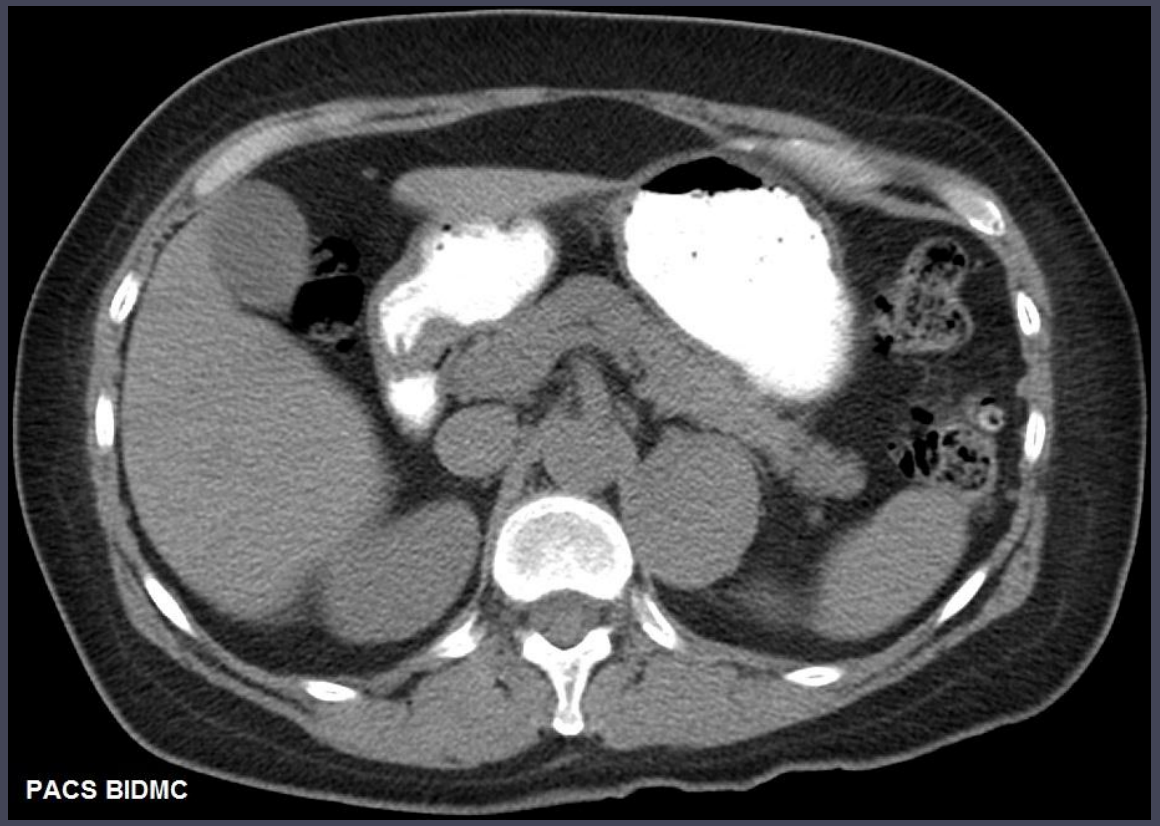
Odise Cenaj, MSIII
Gillian Lieberman, MD

Objectives

- Index Patient Presentation
- Primary aldosteronism
- Initial radiologic evaluation
- Differential diagnosis of adrenal masses
- Radiologic workup of adrenal masses
- Index Patient diagnosis
- Adrenocortical carcinoma
- Conclusions

Beth Israel Deaconess Medical Center
Odise Cenaj, MSIII
Gillian Lieberman, MD

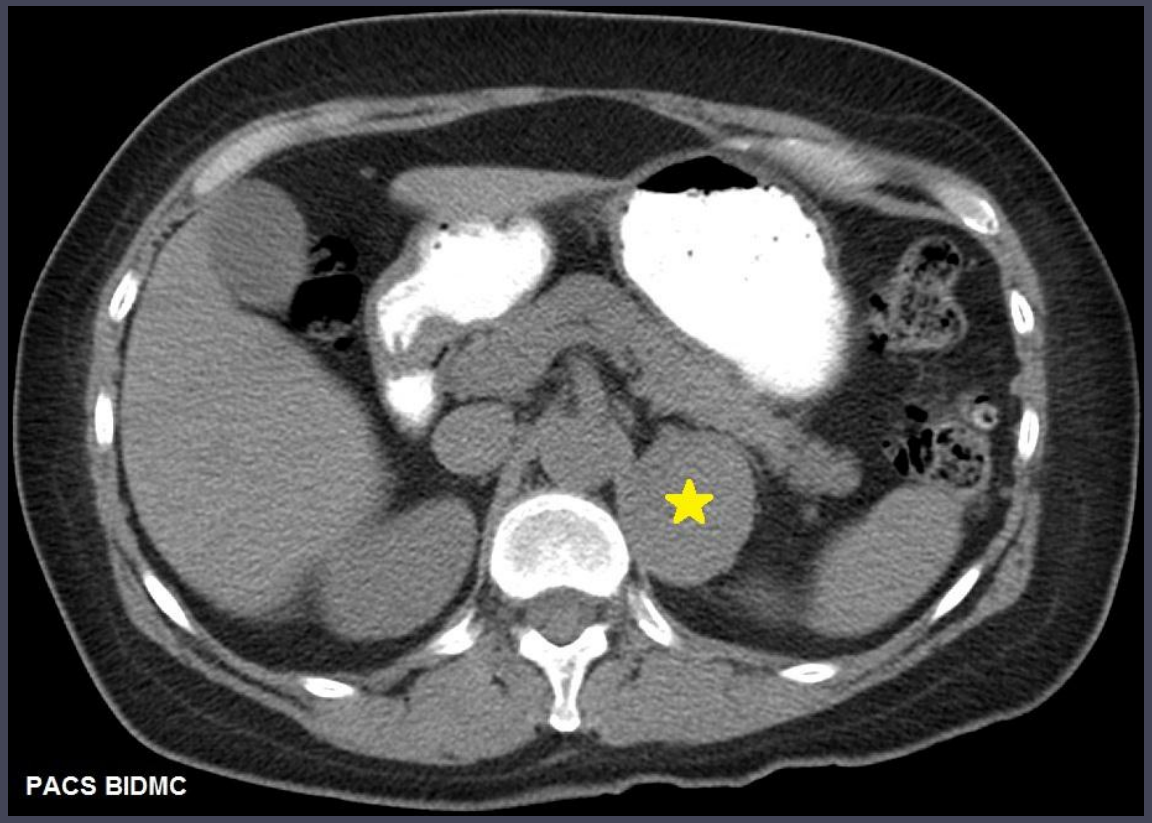
Index Patient: Initial Radiologic Evaluation #1



Please find the abnormality on this imaging modality and compare your findings with the labeled results on the next slide.

Beth Israel Deaconess Medical Center
Odise Cenaj, MSIII
Gillian Lieberman, MD

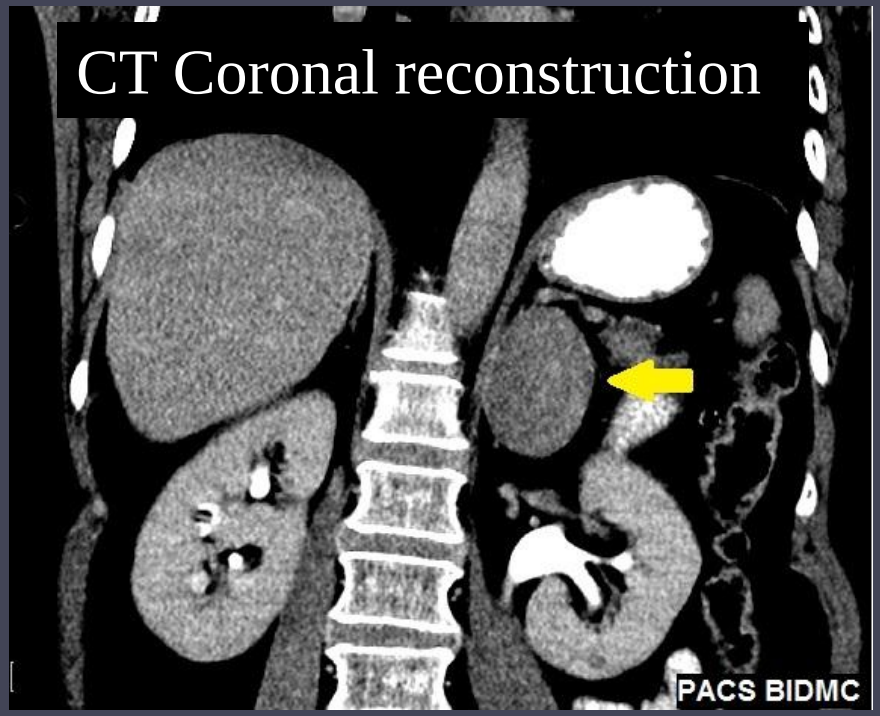
Index Patient: Initial Radiologic Evaluation #2

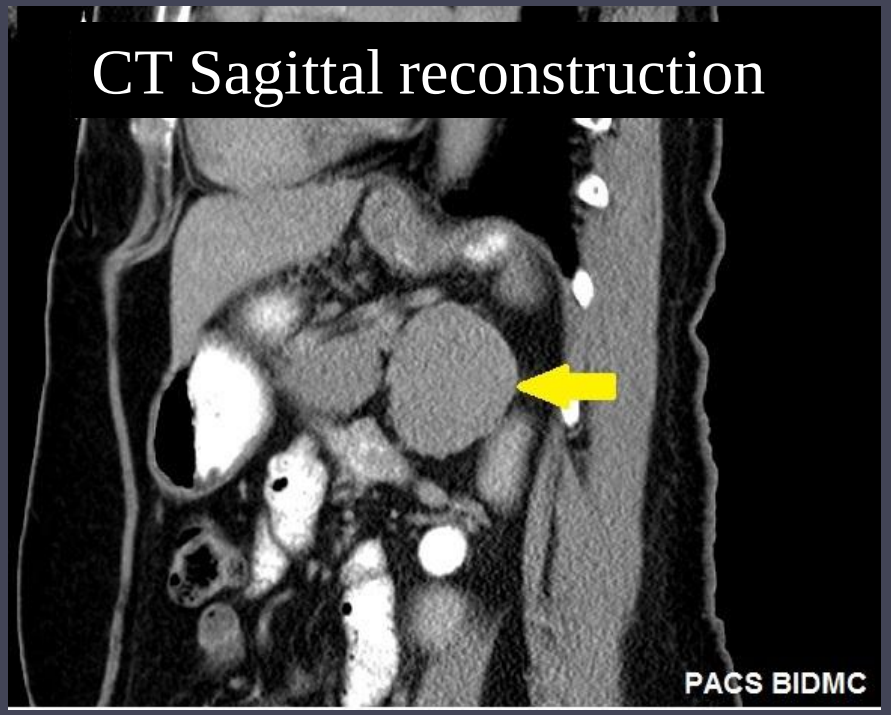


Abdominal CT w/ oral contrast at tbe level of the adrenals: 40 x 48 mm well-circumscribed soft tissue density in the left adrenal gland without invasion of adjacent structures and a well-maintained surrounding fat plane.

Beth Israel Deaconess Medical Center
Odise Cenaj, MSIII
Gillian Lieberman, MD

Index Patient: Initial Radiologic Evaluation #3





These are coronal and sagittal reconstructions of the initial CT of the abdomen with oral contrast only. Please note the oval-shaped adrenal mass labeled with the yellow arrow.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Objectives

- Index Patient Presentation
- Primary aldosteronism
- Initial radiologic evaluation
- Differential diagnosis of adrenal masses
- Radiologic workup of adrenal masses
- Index Patient diagnosis
- Adrenocortical carcinoma
- Conclusions

Odise Cenaj, MSIII
Gillian Lieberman, MD

Classification of Adrenal Masses

Adrenal masses can be classified in the following simple approach:

	Benign	Malignant
Nonfunctioning	common	rare
Hyperfunctioning	less common	very rare

5-10% of all identified adrenal masses are hyperfunctioning adrenal tumors, most of which are benign.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Differential Diagnosis of Benign Adrenal Masses

Type, frequency, and growth rate of benign adrenal masses

Type	Frequency Amongst All Adrenal Masses	Growth Rate
Adenoma	Common, approximately 50%–80% Nonfunctioning in the majority	Stable or very slow
Myelolipoma	5%–10%	Stable to slow
Pheochromocytoma (90% benign)	5% (figure likely less in clinical practice)	Slow
Hematoma	1%	Rapid
Cyst	1%	Usually stable
Ganglioneuroma	Very rare	Variable, slow to rapid
Hemangioma	Very rare	Usually slow
Granulomatous	Rare outside Asia	Variable, slow to intermediate

From Boland GW. Adrenal imaging: from Addison to algorithms. *Radiologic clinics of North America*. 2011 May;49(3):511-28, vii.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Differential Diagnosis of Malignant Adrenal Masses

Type, frequency, and growth rate of malignant adrenal masses

Type	Frequency	Growth Rate
Metastasis	No Cancer: uncommon; known cancer: common (up to 50%)	Variable, slow to rapid
Lymphoma	Primary rare, metastatic more common	Variable, slow to rapid
Carcinoma	Rare, <5%	Variable, usually slow
Pheochromocytoma (10% malignant)	5% (figure likely less in clinical practice)	Slow
Neuroblastoma	Very rare, more common in children	Variable, slow to rapid

From Boland GW. Adrenal imaging: from Addison to algorithms. *Radiologic clinics of North America*. 2011 May;49(3):511-28, vii.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Importance of Adrenal Pathology

Despite their small anatomic size, the pathological condition of the adrenal glands is significant.

- Hyperfunctioning disease with excessive hormonal function – associated with increased morbidity
- Metastatic disease – determines staging and prognosis of primary cancer
- Infiltrative or infectious disease – associated with increased morbidity
- Primary malignancy – can be rapidly fatal if left untreated

The role of radiology is absolutely crucial in detecting and characterizing adrenal masses.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Objectives

- Index Patient Presentation
- Primary aldosteronism
- Initial radiologic evaluation
- Differential diagnosis of adrenal masses
- Radiologic workup of adrenal masses
- Index Patient diagnosis
- Adrenocortical carcinoma
- Conclusions

Odise Cenaj, MSIII
Gillian Lieberman, MD

Radiologic Workup of Adrenal Masses

- Macroscopic characterization
- Serial imaging
- Lipid-sensitive imaging
  - non-contrast CT
  - chemical shift MRI
- Physiologic CT washout test
- Metabolic imaging

Odise Cenaj, MSIII
Gillian Lieberman, MD

Macroscopic Characterization

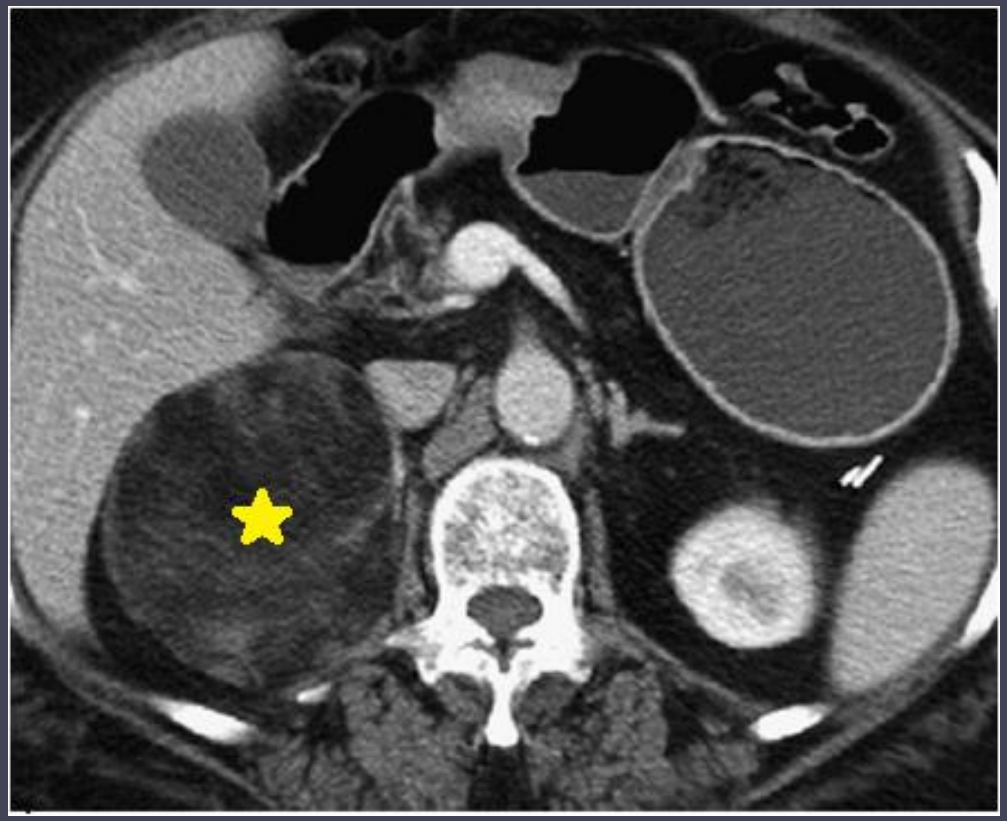
- Diagnosis should not be based on macroscopic features alone.
- Few lesions can be diagnosed by macroscopic features alone.

- The next three slides provide examples where macroscopic characterization is sufficient for accurate diagnosis:

- Myelolipoma: macroscopic fat on CT
- Benign adrenal cysts: smooth-walled water density lesions with rim calcification
- Malignancy: large (70% of >4cm lesions are malignant), irregular lesions, necrosis

Odise Cenaj, MSIII
Gillian Lieberman, MD

Companion Patient #1: Myelolipoma



Axial contrast CT shows a 9cm right adrenal mass containing large amounts of fat, diagnostic of myelolipoma.

From Song JH, Mayo-Smith WW. Incidentally discovered adrenal mass. *Radiologic clinics of North America*. 2011 Mar;49(2):361-8.

Beth Israel Deaconess Medical Center
Odise Cenaj, MSIII
Gillian Lieberman, MD

Companion Patient #2: Benign Adrenal Cyst

Non-contrast CT shows a 1.7cm left adrenal mass (long arrow) with rim calcification (short arrow) and water density values, consistent with adrenal cyst.

From Boland GW. Adrenal imaging: from Addison to algorithms. *Radiologic clinics of North America*. 2011 May;49(3):511-28, vii.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Companion Patient #3: Metastasis

Contrast-enhanced CT shows a 7cm heterogeneous and necrotic right adrenal confirmed to be metastatic when compared with prior imaging. From Boland GW. Adrenal imaging: from Addison to algorithms. *Radiologic clinics of North America*. 2011 May;49(3):511-28, vii.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Serial Imaging

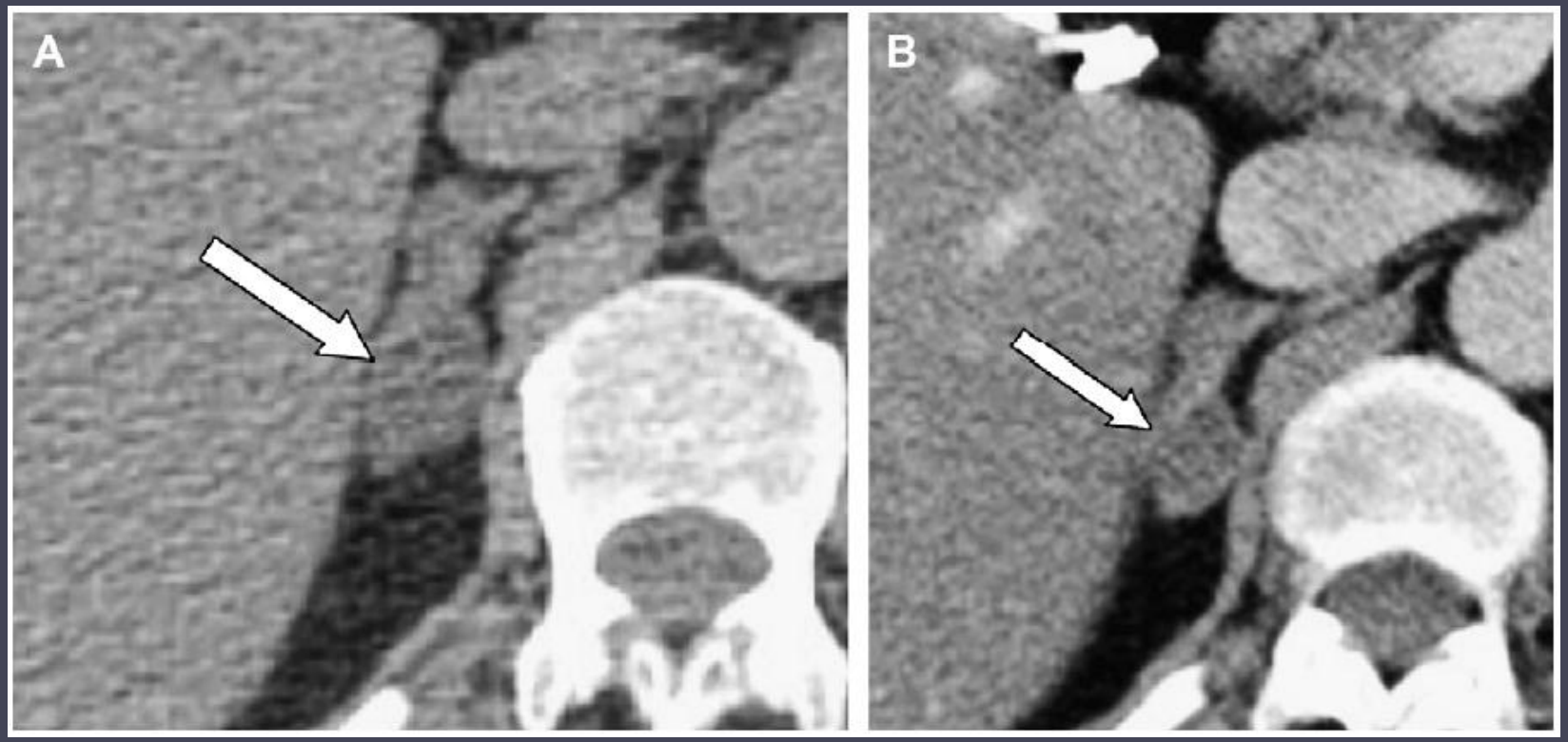
Benign adrenal lesions rarely enlarge in serial imaging, and if they do, the process is very slow.

If lesions have been stable for six months, they are confidently assumed to be benign.

If they grow rapidly, they are almost always malignant (with the exception of adrenal hemorrhage).

Odise Cenaj, MSIII
Gillian Lieberman, MD

Companion Patient #4: Serial Imaging



Non-contrast CT taken 4 years apart of a 1.8cm adrenal lesion, consistent with benign adenoma.

From Boland GW. Adrenal imaging: from Addison to algorithms. *Radiologic clinics of North America*. 2011 May;49(3):511-28, vii.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Lipid-sensitive imaging: non-contrast CT

Adenomas	Non-adenomas
Lipid-rich	Lipid-poor
Low density	High density
<10 Hounsfield units	>10 Hounsfield units

- 71% sensitivity – 1/3 of adenomas not lipid-rich enough
- 98% specificity – rare malignant lesions <10 HU
- Error is introduced when the region of interest (i.e. the area selected to measure the average attenuation index on a specific lesion) is chosen incorrectly, either too small to be representative of the entire lesion or including retroperitoneal fat in the ROI.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Lipid-sensitive imaging: chemical shift MRI

Adenomas	Non-adenomas
Lipid-rich	Lipid-poor
>16.5% signal drop-off	<16.5% signal drop-off

- Lipid-sensitive chemical shift MR imaging is more sensitive than NCCT in detecting intracellular fat. 1/3 of benign adenomas do not contain sufficient fat to be less than 10 HU and be considered benign. They may therefore mimic malignancy on non-contrast CT.
- CS MRI principle: adrenals look bright on IP (in-phase) and darker in OOP (out-of-phase). Signal drop-off from IP to OOP of >16.5% is considered lipid-rich adenoma. Lipid poor lesions demonstrate no signal drop-off.
- This method cannot distinguish between benign and malignant lipid poor lesions.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Physiologic CT washout test

Absolute percentage washout:

$$APW = \frac{dynamic\ enhanced\ HU - 15\ minute\ delayed\ HU}{dynamic\ enhanced\ HU - unenhanced\ HU}\ X\ 100$$

Relative percentage washout:

$$RPW = \frac{dynamic\ enhanced\ HU - 15\ minute\ delayed\ HU}{dynamic\ enhanced\ HU}\ X\ 100$$

Principle: IV contrast is washed out rapidly in benign lesions, whereas it is retained longer in malignant ones due to porous vasculature.
If APW > 60% and/or RPW > 40%, then the lesion is safely considered a benign adenoma.
This method is more specific than lipid sensitive methods and almost 100% sensitive for all adenomas, whether lipid-rich or lipid-poor.

Metabolic Imaging

PET and PET-CT using FDG: differentiation of benign versus malignant masses with sensitivity 93-100% and specificity 90-100%.

Because a small percentage of benign adenomas can present with increased glucose uptake, the specificity is not 100%.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Objectives

- Index Patient Presentation
- Primary aldosteronism
- Initial radiologic evaluation
- Differential diagnosis of adrenal masses
- Radiologic workup of adrenal masses
- Index Patient diagnosis
- Adrenocortical carcinoma
- Conclusions

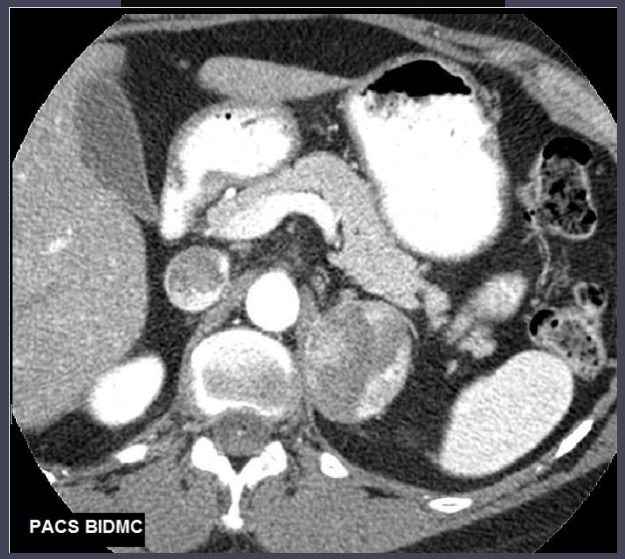
Beth Israel Deaconess Medical Center
Odise Cenaj, MSIII
Gillian Lieberman, MD

Index Patient: Physiologic CT Washout Test

Unenhanced CT

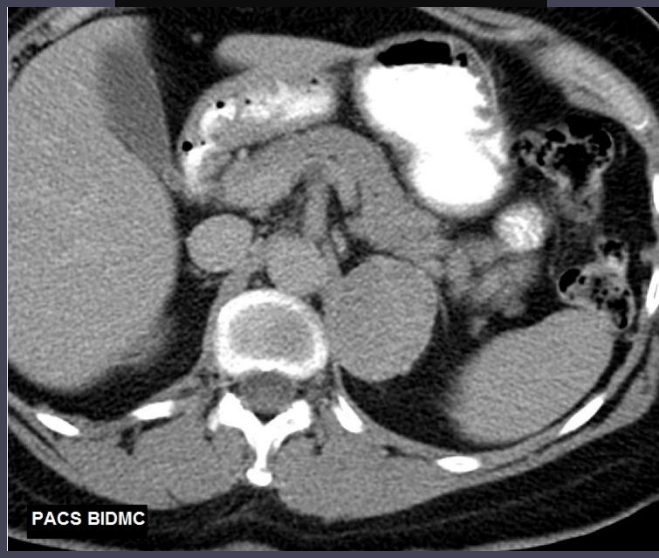
45 HU

Dynamic enhanced CT



138 HU

15 min delayed phase CT



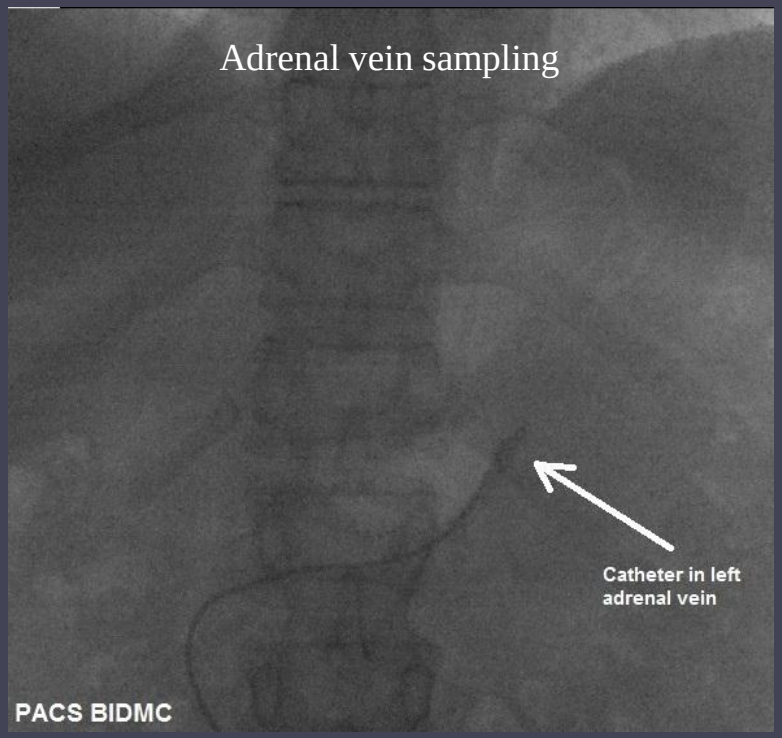
78 HU

APW = 65%, consistent with benign left adrenal adenoma

Odise Cenaj, MSIII
Gillian Lieberman, MD

Index Patient: Diagnosis, Management and Course #1

- The patient remained symptomatic. She initially refused treatment with surgical resection and months later agreed to undergo laparoscopic left adrenalectomy.
- Left and right adrenal vein sampling was performed preoperatively to make certain that the hormone gradient is in agreement with the imaging test, indicating that the aldosteronoma is on the left side and that there is no right adrenal hyper-production.



Index Patient: Diagnosis, Management and Course #2

- Pathology revealed **adrenocortical carcinoma** with positive tumor margin and periadrenal adipose tissue invasion and capillary lymphatic infiltration.

- The patient was referred to oncology for adjuvant chemotherapy, endocrinology for postoperative adrenal insufficiency treatment, and chest and abdomen CT scan for staging of disease. Long-term follow-up with surveillance imaging and plasma aldosterone levels were recommended.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Objectives

- Index Patient Presentation
- Primary aldosteronism
- Initial radiologic evaluation
- Differential diagnosis of adrenal masses
- Radiologic workup of adrenal masses
- Index Patient diagnosis
- Adrenocortical carcinoma
- Conclusions

Odise Cenaj, MSIII
Gillian Lieberman, MD

Adrenocortical Carcinoma: Facts

- Highly malignant with poor prognosis
- Incidence = two cases per million annually in the US
- Bimodal age distribution: <5yo and 4^{th}-5^{th} decade of life
- Functional ACC: women > men
- Nonfunctioning tumors: men > women
- 60% are secretory :Cushing syndrome, virilization, feminization, and aldosteronism in <10% of cases
- Survival in unresectable cases = 6 months
- 5-year survival after resection = 32-48%
- 18-39% initial presentation with distant metastasis to lung, bone, liver, brain, pleura or contralateral adrenal
- CT abdomen is important for detection, staging, evaluation of resectability, and surgical treatment planning

Odise Cenaj, MSIII
Gillian Lieberman, MD

Adrenocortical Carcinoma: Typical Radiologic Manifestations

- Size > 6cm 93% sensitive and 62% specific for ACC
- Punctate, patchy, or irregular nodular calcifications
- Hypoatenuated or unenhanced central area
- Well-defined margins in 70% of ACC
- Direct invasion to adjacent organs
- Direct spread to IVC and renal vein with thrombus formation
- CT washout characteristics of ACC are similar to non-adenomas:
  - -Average APW = 50% +/-17%
  - -Average RPW = 27% +/-12%

Odise Cenaj, MSIII
Gillian Lieberman, MD

Companion Patient #5: Typical Presentation of Adrenocortical Carcinoma on CT

Contrast-enhanced CT showing 8.2cm heterogeneous left adrenal mass with peripheral vascular enhancement (long arrow) and inferior vena cava invasion (short arrow), typical of adrenocortical carcinoma.
From Boland GW. Adrenal imaging: from Addison to algorithms. *Radiologic clinics of North America*. 2011 May;49(3):511-28, vii.

Odise Cenaj, MSIII
Gillian Lieberman, MD

Objectives

- Index Patient Presentation
- Primary aldosteronism
- Initial radiologic evaluation
- Differential diagnosis of adrenal masses
- Radiologic workup of adrenal masses
- Index Patient diagnosis
- Adrenocortical carcinoma
- Conclusions

Odise Cenaj, MSIII
Gillian Lieberman, MD

Conclusions

- Our patient had an atypical presentation of adrenocortical carcinoma both in physiologic CT washout values and lesion morphology.
- Rare cases of adrenocortical carcinoma have been reported with CT washout values in the range of benign adenomas.
- CT washout studies may not be as accurate in discriminating adenomas from non-adenomas as was initially thought.
- Morphological evaluation of adrenal lesions should be used a in complementary manner along with CT washout studies.
- FTG PET-CT is indicated for indeterminate lesions.
- No single study is perfect.

References

- Zhang HM, Perrier ND, Grubbs EG, Sircar K, Ye ZX, Lee JE, Ng CS. CT features and quantification of the characteristics of adrenocortical carcinomas on unenhanced and contrast-enhanced studies. *Clinical Radiology*. 2012 Jan;67(1):38-46.
- Boland GW. Adrenal imaging: from Addison to algorithms. *Radiologic clinics of North America*. 2011 May;49(3):511-28, vii.
- Song JH, Mayo-Smith WW. Incidentally discovered adrenal mass. *Radiologic clinics of North America*. 2011 Mar;49(2):361-8.
- Vlahos I. CT of the adrenal: not just distinguishing non-adenoma versus adenoma. *Clinical Radiology*. 2012 Jan;67(1):47-8.
- Szolar DH, Korobkin M, Reittner P, Berghold A, Bauernhofer T, Trummer H, Schoellnast H, Preidler KW, Samonigg H. Adrenocortical carcinomas and adrenal pheochromocytomas: mass and enhancement loss evaluation at delayed contrast-enhanced CT. *Radiology*. 2005 Feb;234(2):479-85.
- Korobkin M, Brodeur FJ, Yutzy GG, Francis IR, Quint LE, Dunnick NR, Kazerooni EA. Differentiation of adrenal adenomas from nonadenomas using CT attenuation values. *American Journal of Roentgenology*. 1996 Mar;166(3):531-6.
- Funder JW, Carey RM, Fardella C, Gomez-Sanchez CE, Mantero F, Stowasser M, Young WF Jr, Montori VM; Endocrine Society. Case detection, diagnosis, and treatment of patients with primary aldosteronism: an endocrine society clinical practice guideline. *The Journal of clinical endocrinology and metabolism*. 2008 Sep;93(9):3266-81.

Acknowledgements

Lisa M. Fortin, MD

Iva Petkovska, MD

Andrew Bennett, MD, PhD

Claire Odom

Gillian Lieberman, MD