Non Functional Adrenal Disease: Comprehensive Review of Imaging and Clinical Implications

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Content

• Introduction and principles of adrenal imaging.
• Cased-based review of findings, clinical implications and management
• Simplified image-based algorithm to aid diagnosis and management
• References
Introduction and principles of adrenal imaging

The goal of adrenal imaging is to confidently differentiate between benign and malignant adrenal masses and accordingly direct medical management.

This can be done by examining 4 key factors:
- Temporal stability or progression
- Pathognomonic benign features
- Enhancement pattern
- Chemical shift
Temporal stability or progression

- Any lesion that grows within 6 months is concerning for a malignant process.
- Any lesion that is stable for 12 months is very likely benign.*

Pathognomonic benign features

- Predominant component is macroscopic fat – myelolipoma
- Simple cyst – adrenal cyst
- Large amount of calcium content

*Beware of the pitfall of an adrenal mass remaining stable or regressing while a patient is on chemotherapy
Intracellular lipid content by CT or MRI

• Using a CT threshold of < 10HU has 98% specificity for a lipid rich adenoma
• Loss of signal on chemical shift MRI either by subjective assessment comparing the adrenal lesion to the spleen or calculated signal intensity index (> 16.5% signal loss on out of phase sequence) is diagnostic of lipid rich adenoma.

Enhancement pattern

• Lipid poor adenomas can be categorized by washout criteria.
  • Absolute washout > 60% \((E-D)/(E-N)\)
  • Relative washout > 40% \((E-D)/E\)

\(E\) = Enhancement – venous phase (80 sec)
\(D\) = 15 minute delay
\(N\) = Non enhanced
Did the nodule lose signal?

\[
\frac{S_{\text{ip}} - S_{\text{op}}}{S_{\text{ip}}} = S_{\text{index}}
\]

\[
\frac{766 - 554}{766} = 29\%
\]

>16.5% is consistent with a lipid rich adenoma on MRI
Case 1
Lipid Rich Adrenal adenoma

Usually incidentally detected on CT. Nearly 3% incidence at autopsy series; 1% incidence on abdominal CT. 7% for patients 70 years old. 37% of incidentally detected adrenal nodules are functional.

Radiology:
Well-defined, round and homogeneous. Calcification is uncommon and central necrosis or hemorrhage is rare. Usually 3 cm or less in size.

80% are lipid-rich (< 10HU on non-contrast CT) or lose signal on chemical shift MRI (> 16.5% signal loss on out-of-phase sequence). Identification of this lipid allows confident diagnosis of an adenoma.
Case 2

NCCT = 25HU
Venous CT = 68HU
Delayed CT = 37HU

Washout = \( \frac{68 - 37}{68 - 25} = \frac{31}{43} = 72\% \)
Case 2

Lipid Poor Adrenal adenoma

NCCT = 25HU
Venous CT = 68HU
Delayed CT = 37HU

Washout
\((68-37)/(68-25)\)
\(31/43 = 72\%\)

Lipid Poor Adrenal adenoma

Similar clinical implications to a lipid rich adrenal adenoma.

Radiology:

Lipid poor adenomas can be categorized by washout criteria

Absolute washout > 60% \((E-D)/(E-N)\)
Relative washout > 40% \((E-D)/E\)
Case 3

Case courtesy of Christine Peterson, M.D.
Adrenocortical Carcinoma

Two age peaks; 1st decade and 5th to 7th decades. Children have a higher incidence of clinically evident hormone hypersecretion. Associated with Beckwith-Weideman syndrome and hemihypertrophy.

Radiology:
Usually large at presentation with nodular contour, typically >4 cm; bilateral in 10% of cases. Central tumor necrosis and hemorrhage are common. Calcium is seen in 30% of tumors.
Typically heterogeneous with hyperintensity on both T1 and T2 sequences. Heterogeneous enhancement.
Metastases present in 2/3 of patients at time of diagnosis.

Case courtesy of Christine Peterson, M.D.
Case 4
Adrenal metastases

Even in patients with a known primary neoplasm, an adrenal mass is a benign adenoma in more than 50% of the cases.

The most common primary cancers that metastasize to the adrenal are lung, breast, melanoma, and renal. Small metastases (<3 cm) are usually homogeneous and solid. Larger metastases may undergo necrosis and hemorrhage and occasionally may have calcification.

Keys to distinguish a benign adenoma from malignancy or metastasis:

- Lipid rich adenomas (80% of adenomas) have HU < 10. Sensitivity of 71% and specificity of 98%.
- Lipid rich and lipid poor adenomas have characteristic washout features:
  - Absolute washout > 60% \( \frac{(E-D)}{(E-N)} \)
  - Relative washout > 40% \( \frac{(E-D)}{E} \)
- MRI shows loss of signal compared to muscle or spleen on chemical shift out-of-phase sequence for a lipid rich adenoma. One may also use a signal intensity drop of 16.5% as an objective measure.
- Metastases also typically will show increased signal on T2 images whereas adenomas show less signal increase.

Case 4

Adrenal metastases

Left adrenal mass showed no signal loss on opposed phase MRI and progressively enlarged in this patient with renal cell carcinoma; presumptive adrenal metastasis.
Case 5
Case 5
Myelolipoma

Myelolipoma:
Tumor composed of mature adipose cells and hematopoetic tissue (slightly higher attenuation than the adipose components).

Radiology:
Typically unilateral. Can be extra-adrenal (pre-sacral or other areas of the retroperitoneum). The presence of macroscopic fat on CT is diagnostic. One-third of myelolipomas have areas of calcification and ossification. Fat can be seen in some cases of adrenocortical carcinoma and metastatic adenocarcinoma. In these malignant tumors the proportion of fat is usually minor compared to the remainder of the tumor. May be difficult to differentiate from lipoma or liposarcoma.

Clinical implications:
Usually managed conservatively but large tumors may be removed if they are symptomatic or to prevent hemorrhage.
Case 6

HU = 56

HU = 53
Case 6
Adrenal hematoma

Adrenal hemorrhage
Causes include trauma, anticoagulation (1/3 of cases), and spontaneous. Associated with numerous conditions such as septicemia or systemic illness. Can be seen in primary antiphospholipid syndrome, presumably because of adrenal vein thrombosis. 25% of patients with severe trauma have adrenal hemorrhage, most commonly on the right; 20% are bilateral. Rarely, symptoms from adrenal hemorrhage and adrenal insufficiency will occur if bilateral.

Radiology:
US: hyperechoic → mixed echogenicity → hypoechoic
CT: high density of 50-90HU with follow-up studies showing progressive resorption and low density near that of a cyst
MRI:
Acute: deoxyhemoglobin (high T1, low T2)
Subacute (1 week): extracellular methemoglobin (high T1, high T2)
Chronic: Resembles a cyst. The low- and high-signal rims on MR images strongly support the diagnosis of hematoma.
Case 7
Case 7
Adrenal pseudocyst

Adrenal cysts and pseudocysts

Usually asymptomatic

Causes include endothelial (45%), pseudocyst (39%), epithelial (9%) origin. Most common type is lymphangioma. Pseudocysts are caused by adrenal hemorrhage, up to 54% have calcifications.

Radiology:
US, CT and MR show imaging characteristics of a simple cyst.

One feature that can help distinguish pseudocyst from other causes of adrenal cysts is the shape of the inferior border of the cyst, which it is often flattened. The dependent calcification tends to be thick.

Neoplasms can be cystic, however typically show a thick wall, internal septations and a soft tissue component.
Case 8

\[
\frac{S_{ip} - S_{op}}{S_{ip}} = S_{index} \quad \frac{(167 - 150)}{167} = 10\%
\]
Case 8
Adrenal Lymphoma

Adrenal Lymphoma

Primary adrenal lymphoma is rare. Up to 4% of cases of lymphoma have adrenal involvement. 50% of cases involve both adrenal glands.

Radiology

MRI typically shows an iso-/hypointense T1, hyperintense T2 signal adrenal mass with a mild uniform enhancement pattern; mildly heterogeneous enhancement is also possible.

In this case, a mass with similar signal characteristics was seen in the liver, and was biopsy-proven hepatic lymphoma.

CT findings and washout characteristics are similar to other malignancies. Rounded mass or generalized enlargement of the gland with homogeneous density and contrast enhancement, although less than the adjacent kidney.

\[
\frac{\text{SI}_{\text{ip}} - \text{SI}_{\text{op}}}{\text{SI}_{\text{ip}}} = \text{SI}_{\text{index}} \quad \frac{167-150}{167} = 10\%
\]
Case 9
Case 9
Pheochromocytoma

Enhancing right adrenal mass. Absolute washout (non-contrast, venous, and 15 minute delayed) calculated at 72%.

Pheochromocytoma

Up to 10% of patients with pheochromocytomas can have lesions that do not produce sufficient catecholamines to cause symptoms. The Rule of 10’s is often described in the context of pheochromocytomas: 10% of pheochromocytomas are extra-adrenal, 10% malignant, 10% bilateral, 10% familial and 10% not associated with hypertension. Associated with multiple syndromes including Multiple Endocrine Neoplasia syndromes and Neurofibromatosis type I.

Radiology:

CT has 95% sensitivity for intra-adrenal pheochromocytoma. Non functional pheochromocytomas tend to be large and may occasionally have cystic changes and calcium. NECT shows >10 HU, rapid washout kinetics are possible. Prominent early enhancement is a key to suggest pheochromocytoma.

MRI shows pheochromocytomas often have high T2 signal (this is no longer considered a diagnostic feature) and hypervascular solid components.

Teaching Point: Highly vascular adrenal tumors such as pheochromocytoma or metastases from hypervascular primary tumors like hepatoma or renal cell carcinoma can have washout characteristics similar to adrenal adenoma.
IAL Detected at Imaging (NO signs/symptoms of hyperfunctioning)

Prior Exams

- Stable
  - Benign
  - Larger
    - Malignant

No Extra-adrenal Malignancy

- < 4cm + Homogeneous
  - Follow up 6 months

≥ 4cm or Non-homogenous

Refer to Surgery

Extra-adrenal Malignancy

Next Algorithm

Modified from Radiology: Volume 249: Number 3—December 2008
IAL Detected at Imaging
(NO signs/symptoms of hyperfunctioning + Known Extra-adrenal Malignancy)

- Imaging features diagnostic for a benign lesion; myelolipoma or simple cyst

- Unenhanced CT
  - ≤ 10 HU
    - Benign
  - ≥ 30 HU
    - Indeterminate

- Perfusion CT
  - APW ≥ 60%
    - RPW ≥ 40%
      - Benign
  - APW < 60%
    - RPW < 40%
      - Very Likely Metastasis

- Consider Chemical Shift MRI
  - No Signal Loss or $S_{index}$ ≤ 16.5%
    - Indeterminate
  - Signal Loss or $S_{index}$ > 16.5%
    - Benign

Inhomogeneity of lesion (necrosis, etc.) and lesion size > 4cm are concerning features for malignancy

Modified from Journal of the American College of Radiology 2010; 7:754-773DOI: (10.1016/j.jacr.2010.06.013)
Imaging findings concerning for a malignant process:

- Size greater than 4 cm at presentation has a 70% chance of malignancy. If larger than 6 cm, this increases to 85%.
- Enlargement within 6-12 months.
- Heterogeneity or areas of solid enhancement in a cystic mass.
- Known extra-adrenal malignancy and the adrenal lesion doesn’t meet criteria for an adenoma on CT density, chemical shift MRI or CT washout.
- Atypical adenoma, surgically removed.

Adrenocortical Carcinoma

Renal Cell Carcinoma Metastasis
Summary and Clinical Implications

• Accurate diagnosis of non-functional adrenal lesions by the radiologist is critically important, as they can be malignant in up to 30% of the oncology population.

• The key clinical dilemma of differentiating between benign and malignant adrenal disease can be effectively done with a diversity of imaging options.

• An adrenal CT protocol with an initial non-enhanced phase followed by washout, if necessary, is usually recommended as the initial study for evaluation of adrenal disease. Additional options include adrenal protocol MRI and PET-CT for specific scenarios.
References