The many faces of adrenal glands pathology: imaging findings

Poster No.: C-2191
Congress: ECR 2012
Type: Educational Exhibit
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Keywords: Kidney, Abdomen, Oncology, CT, MR, Ultrasound, Diagnostic procedure, Endocrine disorders, Neoplasia
DOI: 10.1594/ecr2012/C-2191

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Learning objectives

1. To review multimodality imaging of adrenal glands pathologies.

2. To discuss the differential diagnosis with particular regard to the distinction between benign and malignant disease.

3. To highlight the imaging features that can lead to the best therapeutic approach.
Background

The adrenal gland is involved by a range of neoplasms, including primary and metastatic malignant tumors. However, the most common tumor detected is the incidental benign adenoma and the majority of lesions detected at CT are benign, be they myelolipomas cysts, or the sequelae of prior trauma.

Adrenal masses are occasionally found in 5% of CT examinations and in 3% of autopsy.

The prevalence of adrenal adenoma is age related and the majority of lesions are not functioning.

Adrenocortical carcinoma origins from adrenal cortex and it has an incidence of about 2/1,000,000 with female predominance. It has a bimodal peak (1st and 4th decades) and it is often identified earlier in children because it tends to be hormonally active. It presents a very heterogeneous clinical presentation manifesting as endocrine disorders (virilization, gynecomastia and testicular atrophy, Cushing's syndrome or mixed Cushing syndrome-virilization) or with mass effect symptoms (nausea, vomiting, abdominal or lumbar pain, palpable mass or gastrointestinal complains).

Pheochromocytoma is present in 0.1%-0.2% of adults with hypertension and its most frequent symptom is described as a new onset, refractory, paroxysmal or recently exacerbated hypertension. Other clinical manifestations of pheochromocytoma are palpitations, headache, diaphoresis, and flushing, however 10% of patients are asymptomatic.

Pheochromocytoma is associated in about 10% of patients with a number of syndromes including multiple endocrine neoplasia type 2, von Hippel-Lindau syndrome, neurofibromatosis, tuberous sclerosis, and Sturge-Weber syndrome. Approximately 10%-15% of pheochromocytomas are malignant.

Diagnosis of pheochromocytoma is made clinically by using a 24-hour urine assessment for vanillylmandelic acid, catecholamines, and metanephrines or by measuring of plasma-free metanephrine level.

Myelolipoma is a relatively uncommon benign tumor composed of hematopoietic tissue and mature adipose that is usually identified incidentally. Myelolipoma can arise in the adrenal gland or, much less frequently, from an extraadrenal location. When it is symptomatic it is generally due to due to mass effect, tumor necrosis, or hemorrhage, as myelolipomas are nonfunctioning tumors. Clinical symptoms may also occur when the tumors arise in conjunction with other adrenal masses or syndrome.
Lymphoma can involve the adrenal gland secondarily or uncommonly arise as a primary adrenal tumor; when it is primary the most frequent form is the Non Hocking type.

Neuroblastoma originates from the adrenal medulla (60%) and from sympathetic ganglia; it has an incidence of about 5/1,000,000/years with a peak incidence of 2-4 years and rarely over 10 years.

Adrenal glands are common site of metastases in many cancers such as thyroid, kidney, stomach, colon, pancreatic and melanoma. Lung and breast cancer are more common and their involvement is bilateral in about 50% of cases. Patients with lymphoma or with breast, colorectal, stomach, or prostate cancer may develop adrenal involvement more than 5 years after occurrence of their primary tumor.
Imaging findings OR Procedure details

Radiology has a critical role in not only the detection of adrenal abnormalities but in characterizing them as benign or malignant so it is important to practice the appropriate radiologic work-up for diseases affecting the adrenal gland.

US study represents the first level exam and it consents a good visualization of right adrenal gland but a poor visualization of left adrenal gland and it generally does not allow characterization of adrenal masses.

CT is the primary modality for both detection and characterization of adrenal masses. At CT, certain imaging findings are helpful in differentiating benign from malignant lesions. Larger lesions have a greater likelihood of being malignant; in particular, lesions greater than 4 cm in diameter tend to be either metastasis or a primary adrenal carcinoma. Also the change in lesion size is a useful indicator of malignancy because adenomas are slow growing and tend not to change size. Adenomas tend to have smooth margins and a homogeneous density, whereas metastases can be heterogeneous and have an irregular shape. Then, here are two independent properties of adrenal adenomas that can be exploited in characterizing them at CT.

Most adenomas contain large amounts of intracellular lipid so they present lower attenuation values at unenhanced CT than nonadenomas. In contrast, metastases have little intracytoplasmic lipid and thus do not have low attenuation at unenhanced CT. Second, all adenomas, including those without substantial lipid content, tend to have a more rapid loss of attenuation value soon after enhancement with intravenous contrast material. Unenhanced CT is commonly used to help diagnose lipid-rich adenoma measuring 10 HU or less. However lipid-poor adenomas, with attenuation values greater than 10 HU, remain indeterminate on unenhanced CT images. In these cases delayed enhanced CT performed 10-15 minutes following the intravenous administration of contrast material is highly accurate in characterizing lipid-poor adenoma when combined with portal venous phase CT.

A Hounsfield unit of less than approximately 30 at 10 minutes after injection has been shown to be diagnostic of a lipid-rich adenoma; however, most adenomas have an attenuation value higher than 30, so it is a specific but not a sensitive test. A more useful parameter is the percentage of washout of contrast material in which the attenuation of the adrenal gland at delayed CT is compared with its attenuation at dynamic CT. Loss of 60% of the attenuation value of the adrenal mass at delayed CT is specific for an adenoma while less than 60% washout is indicative of either a metastasis or an atypical adenoma. Percentage of washout is typically calculated by the following formula: \((1 - \text{delayed enhanced HU value}/\text{initial enhanced HU value}) \times 100\). Quantitative
region-of interest measurements (in Hounsfield units) are important because degree of enhancement is difficult to quantify with the human eye.

It is important to stress that if a lesion in an oncology patient cannot be definitively called an adenoma after CT examination, the patient should undergo further evaluation with MR imaging or an adrenal biopsy to confirm a benign or malignant adrenal lesion. Although an attenuation value of less than 10 HU at nonenhanced CT is diagnostic of an adenoma, an attenuation value of greater than 10 HU is not diagnostic of a metastasis. A lesion greater than 10 HU at nonenhanced CT may be either an adenoma or metastasis.

Various MR imaging parameters can be used to characterize adrenal masses such as T1 and T2 characteristics, calculated T2 values, enhancement patterns, and chemical shift characteristics. In general, metastases and carcinomas contain larger amounts of fluid than adenomas and thus appear bright on T2-weighted images. However, there is significant overlap in T1 and T2 signal intensity between adenomas and metastases, and thus signal intensity is not useful to reliably differentiate between them. Enhancement patterns have also been investigated as a means of differentiating benign adrenal adenomas from metastases, and, similar to their appearance at CT, adenomas vigorously enhance and exhibit early washout of contrast material compared with metastases on MR images.

Chemical shift imaging relies on the different resonance frequency rates of protons in fat and water molecules. Fat protons are more shielded than water protons, experience less external magnetic field, and thus resonate at a slower frequency. The net effect of this physical phenomenon is that there is cancellation of signal between lipid and water protons within a voxel. Thus, tissues containing lipid and water have signal loss on out-of phase images and the chemical shift is the most sensitive method for differentiating adenomas from metastases.

On out-of phase images, there is signal drop-off in adenomas due to the intra-voxel signal cancellation of the lipid and water protons. Thus, on out-of phase images, the adenoma appears darker than on in-phase images. In adrenal masses that do not contain lipid (metastases), there is no significant signal loss on out-of-phase images, and thus the signal intensity of the adrenal gland is the same on in-phase and out-of-phase images. When in-phase and out-of-phase images are compared, an internal standard is useful to visually quantify signal drop-off.
The technique of double-echo chemical shift gradient-echo MR imaging with the fast low-angle shot (FLASH) sequence provides in-phase and opposed-phase images in a single breath hold and it is not compromised by section. Chemical shift MR imaging is more important in the differentiation of adenoma from malignancy, particularly when attenuation is higher than 10 HU. So it has a high sensitivity for hyperattenuating adrenal adenoma with attenuation values of 10-30 HU at unenhanced CT.
Adrenal masses

- Pheochromocytoma and adrenal carcinoma (0.1%) are more rare; adenoma and myelolipoma are the most common

- Adrenal masses occasionally found in 5% of CT examinations and in 3% of autopsy

- Incidence <1% (<30 years), V-VII decade

**Fig. 1:** Adrenal Masses: epidemiology.

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Adrenal Carcinoma

- Origin from adrenal cortex
- Incidence: 2/1,000,000; ♀ : ♂ = 5 : 1
- Bimodal peak of incidence: childhood/fourth and fifth decade
- Heterogeneous clinical presentation: endocrine disorders 50% (virilization, gynecomastia and testicular atrophy, Cushing's syndrome s.me), mass effect symptoms (nausea, vomiting, abdominal pain and lumbar)

Fig. 2: Adrenal carcinoma: epidemiology and clinic presentation.

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• Bilateral 10%
• Rapid growth (6 months)
• 5-year survival: 20% -25%
• Gold standard treatment: complete resection
• 75-85% relapse
• Medical therapy: Mitotane (recurrence, metastasis, control of hormonal hyper secretion, adjuvant therapy)

**Fig. 3:** Adrenal carcinoma: epidemiology and clinic presentation.

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**Fig. 4:** CT scans in adrenal carcinoma.

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Fig. 5: MPR in Adrenal Carcinoma.

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**Fig. 6:** CT scans in Adrenal Carcinoma.

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Fig. 7: Pheocromocytoma: epidemiology and clinic presentation.

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Fig. 8: CT scans of Pheochromocytoma.

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**Fig. 9:** MR images of Pheochromocytoma.

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US

• First level exam
• Good visualization of right adrenal gland
• Poor visualization of left adrenal gland
• Generally does not allow characterization adrenal mass

Fig. 10: US imaging in adrenal masses study.

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Fig. 11: CT findings for Adrenal Masses study.

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CT study protocol:

- Basal scans
- Arterial phase (18”-23”)
- Venous phase (60”-70”)
- Delayed phase (10’ in order to characterize lesions > 10 UH in basal scans)

Adrenal Imaging, M. Blake, C. Cronin, G. Boland, AGR 2010; 194:1450-1460

Fig. 12: CT study protocol.

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**Fig. 13:** CT findings for Adrenal Masses Characterization.

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**CT findings in Carcinoma**

- large lesion ( > 6 cm)
- inhomogeneous
- central hypodense area (necrosis)
- calcifications (40%)
- heterogeneous enhancement, (> periphery)
- wash-out < 60%

**Fig. 14:** CT findings in Adrenal Carcinoma.

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CT findings in pheochromocytoma

- usually > 3 cm at diagnosis
- greater than adenoma, less than metastases
- Hypervascular lesions (hemorrhagic necrosis)
- Homogeneous / heterogeneous (hemorrhage / necrosis)
- Intracellular fat or cystic degeneration
- Intense heterogeneous enhancement
- Variable wash-out
- Calcification is not common

Fig. 15: CT findings in Pheochromocytoma.

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Lymphoma

Primary adrenal lymphoma is rare, most common is LNH
Location : 1-4% of secondary cases

Fig. 16: Lymphoma.

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Neuroblastoma

- Originates from the adrenal medulla (60%) and from sympathetic ganglia
- Incidence: 5/1,000,000/years
- Peak incidence: 2-4 years, rarely > 10 years

- Heterogeneous mass
- Hypodense (necrotic) or hemorrhagic areas
- Calcifications
- Encasement / vascular compression

**Fig. 17:** Neuroblastoma.

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CT findings in metastases

Adrenal glands are common site of metastases in many cancers (thyroid, kidney, stomach, colon, pancreatic, melanoma)
Lung and breast cancer are more common (50% bilateral)

**Fig. 18:** CT findings in Metastases.

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Fig. 19: CT scans in Adenoma.

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Fig. 20: CT scans in Lipid-poor Adenoma.

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Fig. 21: Cystic Lesion and Myelolipoma.

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MR

• Multiplanar exam

• Study protocol:
  - FSE T1/T2
  - FSPGR double echo
  - Fat Sat
  - SSFSE, FIESTA

• Chemical shift

• Dynamic study GE e FSPGR  T1 after medium contrast administration

Fig. 22: MR protocol study.

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MR findings in carcinoma

- Iso-hypointense on T1wi, Iso-hyperintense on T2wi
- Hemorrhagic areas with different signal intensity
- Heterogeneous enhancement
- No signal loss
- Venous dissemination and hepatic involvement

**Fig. 23:** MR findings in Adrenal Carcinoma.

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Fig. 24: MR images of Adrenal Carcinoma.

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MR findings in pheochromocytoma

- Iso-hypointense on T1wi; hyperintense on T2wi
- Hyperintense areas of necrosis on T1wi/T2wi
- No signal loss in out of phase sequence
- Intense and persistent enhancement

Fig. 25: MR findings in Pheochromocytoma.

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Fig. 26: MR findings in Metastases.

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MR findings in adenoma

- Lipidic content, signal loss
- Iso/hypointense on T1wi and on T2wi, rarely hyperintense on T2wi
- More homogeneous enhancement
- Rapid wash-out

Fig. 27: MR findings in Adenoma.

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Fig. 28: MR findings in Myelolipoma.

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Fig. 29: MR findings in Cystic lesion.

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Therapy and follow up

• Lesions > 4 cm, without a history of malignant disease: surgery

• Lesions from 1 cm to 4 cm characterized as adenomas: follow-up CT after 12 months

• Myelolipoma and adrenal cyst may require surgical evaluation if symptomatic

Fig. 30: Therapy and follow-up.

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Conclusion

We give special emphasis to the correlation with clinical features and to the distinction between benign and malignant disease in order to select the best therapeutic approach. Characterizing adrenal masses is important to identify both malignant lesions and benign adenomas because it would obviate both percutaneous biopsy and repeated interval follow-up imaging.

We have provided a comprehensive look at the signatures of the various adrenal masses. Although CT characteristics as age, lesion size, washout values, the presence of calcification, fat, or hemorrhage, unilateral or bilateral distribution will not always allow one to arrive at a definitive diagnosis, attention to these findings is important to guide image interpretation.
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Adrenal Mass Imaging with Multidetector CT: Pathologic Conditions, Pearls, and Pitfalls

Comparison of Delayed Enhanced CT and Chemical Shift MR for Evaluating Hyperattenuating Incidental Adrenal Masses