Review Article

Radiological imaging in endocrine hypertension

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ABSTRACT

While different generations of assays have played important role in elucidating causes of different endocrine disorders, radiological techniques are instrumental in localizing the pathology. This statement cannot be truer in any disease entity other than endocrine hypertension. This review makes an effort to highlight the role of different radiological modalities, especially ultrasonography, computed tomography and magnetic resonance imaging, in the evaluation of different causes of endocrine hypertension.

Key words: Adrenal imaging, endocrine hypertension, pituitary imaging

Introduction

Idiopathic (primary or essential) hypertension accounts for approximately 85% of the cases of hypertension, whereas in rest of 15% of cases, the cause of hypertension is secondary with known conditions that result in blood pressure elevation (secondary hypertension). Endocrine hypertension accounts for approximately 3% of the secondary hypertension due to excess production of hormones from various endocrine glands. The importance of endocrine or hormone-mediated hypertension resides in the fact that the cause is clear and can be treated surgically in most of the cases. The surgical intervention may result in complete cure, obviating the need for lifelong antihypertensive treatment. Imaging plays a very small role in evaluation of primary or essential hypertension. The need of imaging is obvious in patients with secondary hypertension and may be an integral part of clinical decision making. Moreover, in younger age group, the secondary form of hypertension is more prevalent. Therefore, it is prudent to pursue diagnostic imaging in young patients with hypertension.

With the advent of more sophisticated diagnostic imaging techniques, there is paradigm shift in imaging of hypertension. Computed tomography (CT), magnetic resonance imaging (MRI), ultrasonography (USG), and various nuclear medicine imaging techniques can be used to evaluate the adrenal, thyroid and pituitary gland. Imaging is necessary in the problematic case in which the clinical and laboratory data support the possibility of endocrine hypertension. This article focuses on those abnormalities where radiological imaging plays a paramount role in establishing a firm diagnosis. Below is an outline of abnormalities that are frequently encountered in clinical practice, presenting with endocrine hypertension.

- Hyperfunctioning adrenal medullary neoplasm
  - Pheochromocytoma
- Hyperfuntioning adrenal cortical neoplasm
  - Aldosteronoma
  - Cushing's disease
- Congenital adrenal hyperplasia (CAH)
- Hyperthyroidism
- Hyperparathyroidism
- Acromegaly

This discussion will focus mainly on the role of imaging in evaluating the causes of hypertension listed above.

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Pheochromocytoma

Pheochromocytoma arises from the adrenal medulla which secretes excess catecholamine leading to hypertension and palpitations. It is commonly known as 10% tumor as it is bilateral, extra-adrenal and malignant in 10% of patients.[1] The clinical diagnosis is suspected in a younger patient with hypertension, which can be established by measuring free plasma or fractionated urinary metanephrines and normetanephrines, with sensitivities ranging from 89 to 100%.[2]

Whenever the clinical suspicion is very high in corroboration with laboratory data, multi-detector computed tomography (MDCT) [Figure 1] is usually performed to exclude an adrenal mass. Once the adrenal mass is demonstrated, surgery is usually the next treatment after adequate control of the blood pressure. Paraspinal and organ of Zuckerkandl close to aortic bifurcation also need to be evaluated properly to exclude extra-adrenal mass which is preferably known as paraganglioma. Approximately 35% of extra-adrenal pheochromocytomas are malignant as opposed to approximately 10% of those arising in the adrenal gland. The risk for malignancy increases when the tumor exceeds 5 cm in size.[3]

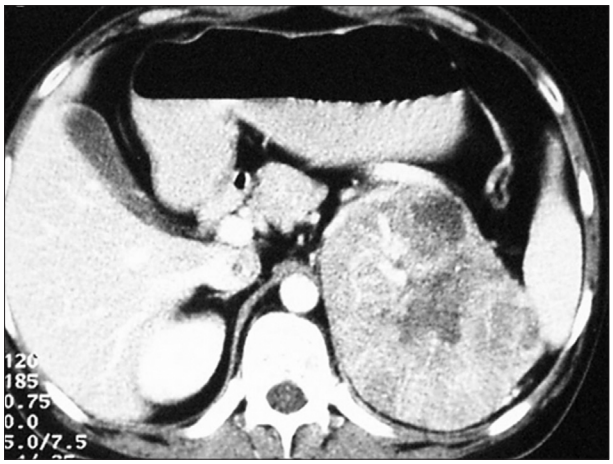

Figure 1: Multi-detector computed tomography showing large heterogeneously enhancing necrotic left supra renal mass which was confirmed to be malignant pheochromocytoma at histopathology

USG has proved its accuracy in detecting pheochromocytoma confined to the adrenal, as these are usually large and well-marginated masses. In a small series,[4] histopathologically confirmed pheochromocytomas appeared both homogenous [Figure 2] and heterogeneous, the later appearance being characterized by areas of hemorrhage and necrosis. Cystic appearance with or without fluid level has also been described. However, USG has limited role in detecting small adrenal tumors and extra-adrenal pheochromocytomas such as those found in the retroperitoneum.

MRI [Figure 3] is more specific and may show "light bulb sign" on T2/STIR images due to presence of more interstitial space.[5] MRI is also very useful for detecting extra-adrenal lesion to assess the recurrences after surgery.

Nuclear medicine imaging can be used when CT or MRI could not demonstrate a mass in patients with high index of suspicion. I-131 iodine-131-meta-iodobenzylguanidine (MIBG) and In-111 octreotide are the two radiopharmaceuticals used to evaluate suspected cases of pheochromocytoma. Abdominal imaging is performed 24–72 hours after IV administration of I-131 MIBG, whereas imaging is performed at 4 and 24 hours after

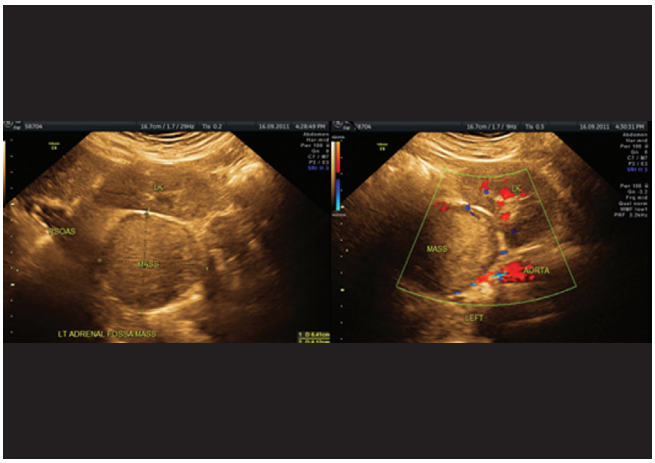

Figure 2: Large, well-circumscribed, homogenous mass in the left adrenal; biochemical tests confirmpheochromocytoma

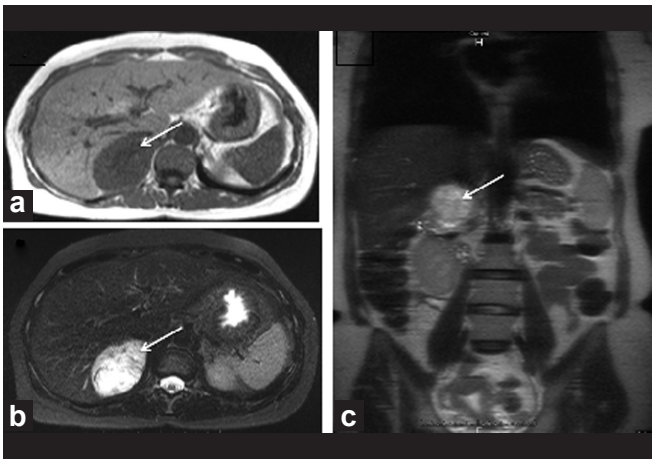

Figure 3: Pheochromocytoma: The mass is hypointense (arrow) on (a) axial T1-weighted image. The mass shows bright signal – "light bulb sign" (arrow) on (b) T2 axial and (c) coronal mages

injection of In-111 octreotide. When pheochromocytoma is suspected, any focal uptake of I-131 MIBG in the adrenal gland is abnormal. The reported sensitivity of I-131 MIBG for detection of a pheochromocytoma is 80–90%, with a specificity of 90–100%,[6,7] whereas In-111 octreotide has a sensitivity of 75–90%.[8] 50% of pheochromocytomas are visualized with both agents, 25% of pheochromocytomas are seen only with I-131 MIBG and another 25% are seen only with In-111 octreotide.[9] For malignant pheochromocytomas, 18F-fluorodopamine positron emission tomography (PET) appears to be very helpful.

Hyperfunctioning Adrenal Cortical Neoplasms

The adrenal cortex is composed of three separate zones: the zona glomerulosa (produces aldosterone), fasciculate (produces cortisol) and reticularis (produces androgens). For hormone secretion, positive feedback is provided by adrenocorticotropic hormone (ACTH) from the pituitary gland, whereas negative feedback is given by cortisol.[10] Cortisol overproduction causes Cushing syndrome, whereas aldosterone overproduction causes Conn's syndrome.

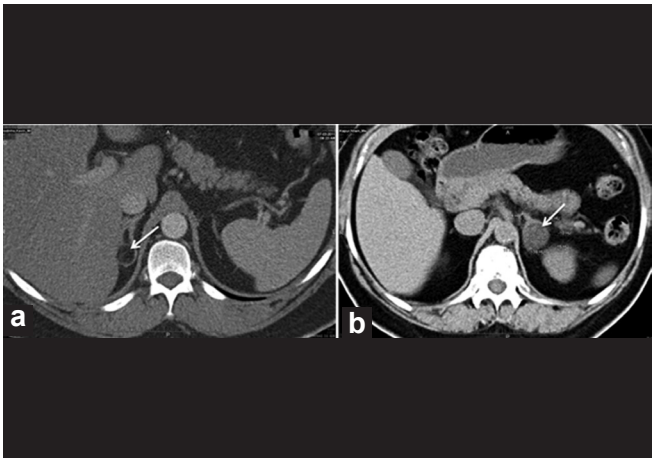

Figure 4: Adrenal adenoma: Axial CT image in (a) shows hypodense fat containing mass (arrow) in the right adrenal. Axial CT image in (b) shows a lipid-poor adenoma in left adrenal (arrow) in a patient with Conn's syndrome

Cushing syndrome is either ACTH dependent or ACTH independent. In Cushing disease, which accounts for approximately 80% of Cushing syndrome, a pituitary adenoma secretes excess ACTH that stimulates the adrenal gland to release cortisol. MRI shows a pituitary mass with symmetrically enlarged adrenal. Up to 30% of patients may have normal-sized adrenal glands.[11] In 15–25% of cases of Cushing syndrome, the cause is a primary adrenal neoplasm, most likely an adenoma.[12] Adrenal adenomas causing Cushing syndrome are usually greater than 2.0 cm in diameter. The role of scintigraphy for the evaluation of patients with Cushing syndrome is limited, particularly with the advances in CT and MRI. Adrenal cortical scintigraphy may be performed in patients who have persistent elevated cortisol levels after adrenalectomy.[13]

Primary aldosteronism is caused by adrenal adenoma in about 80% of cases and is characterized clinically by hypertension and hypokalemia. The cause is adrenal gland hyperplasia in 20%.[14] Adrenal carcinoma is a rare cause. MDCT with thin (3 mm) collimation is usually the first-line imaging examination [Figure 4]. Adrenal adenomas are often small and difficult to detect.[15] Chemical shift MRI is emerging as one of the most sensitive and specific investigations for differentiating adenoma from non-adenoma of the adrenal gland. Adenomas contain abundant amount of intracytoplasmic lipids (cholesterol, fatty acids and neutral fat) in clear and compact cells. The chemical shift imaging is used to identify this intracytoplasmic lipid and is the most sensitive and specific MRI technique in characterization of adrenal adenoma.[16] Out-of-phase imaging reveals loss of signals from these intra-cytoplasmic lipids, which helps in characterizing the adenoma [Figure 5]. Adrenal carcinomas are usually large tumors of more than 5 cm in size. donot contain fat and show heterogeneous

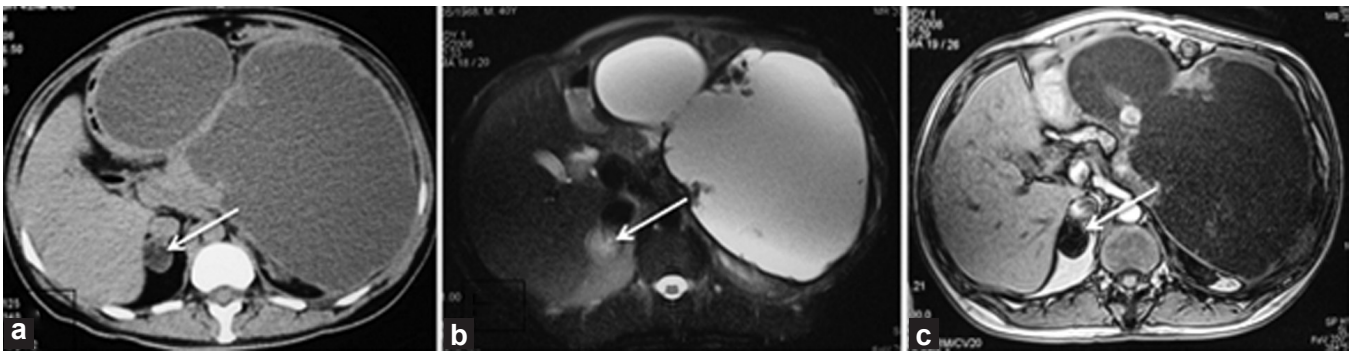

Figure 5: Adrenal adenoma: Axial CT image in (a) shows hypodense fat containing mass (arrow) in the right adrenal. (b) The mass is hyperintense (arrow) on fat-saturated axial T2-weighted images although the rest of the fat gets suppressed. (c) The mass shows signal drop (arrow) on out-of-phase T1 axial image

signal intensity in MRI [Figure 6].

Congenital Adrenal Hyperplasia

The most common cause of CAH is 21-hydroxylase deficiency. Hypertension *per se* has not been regarded as a component of this syndrome. Abnormal steroidogenesis due to defective 11 beta-hydroxylation is the second most common form of CAH. Due to excess accumulation of 11-deoxy corticosterone (11-DOC), patient presents with hypertension (unlike in classic CAH) and hyperandrogenism (like in classic CAH).[17] The 17 alpha-hydroxylase deficiency is rarer and leads to diminished production of cortisol and sex steroids. Chronic elevation of ACTH causes subsequent hypertension and hypokalemia.[18] CT or MRI findings are nonspecific and show diffuse bilateral enlarged adrenal with preserved shape of the limbs. Genitography may be needed in case where of ambiguous genitalia is a presenting feature.

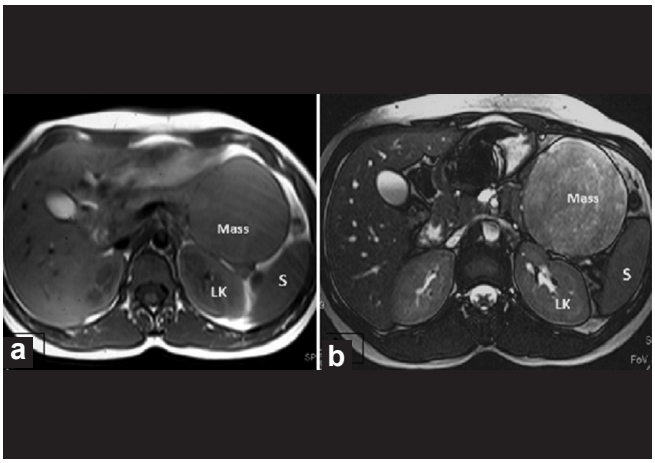

Figure 6: Adrenal carcinoma: Axial T1W image in (a) shows well-defined, large suprarenal mass and axial T2 image in (b) shows the mass being hyperintense. The mass is separate from left kidney (LK) and spleen (S)

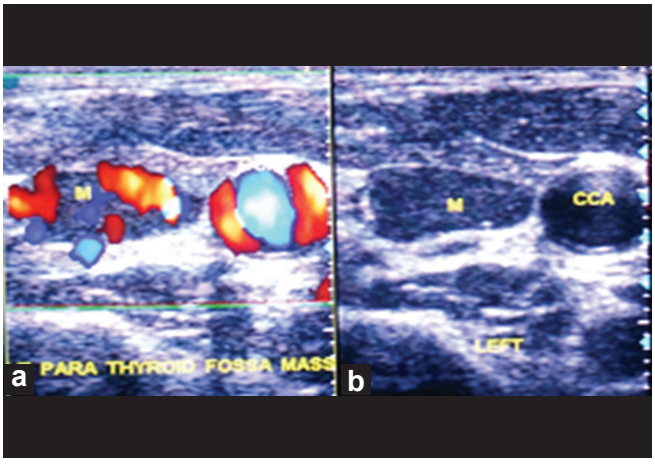

Figure 8: Parathyroid adenoma (M) detected by neck ultrasound. Note the oval shape, high vascularity (a) and hypoechoic appearance (b)

Hyperthyroidism

Hyperthyroidism increases systolic blood pressure by increasing heart rate and raising cardiac output. In thyrotoxicosis, patients usually have tachycardia and high cardiac output with an increased stroke volume and elevated systolic blood pressure. The pulse pressure is significantly increased due to vasodilatation. Approximately one-third of patients with hyperthyroidism have hypertension which often resolves after achieving euthyroidism. The sonographic appearance of Graves' disease is characteristic. Usually, the gland is diffusely hyperechoic or may show heterogeneous echotexture [Figure 7].[19] Color Doppler shows extensive hypervascularity within the gland, also described as thyroid inferno [Figure 7]. Peak systolic

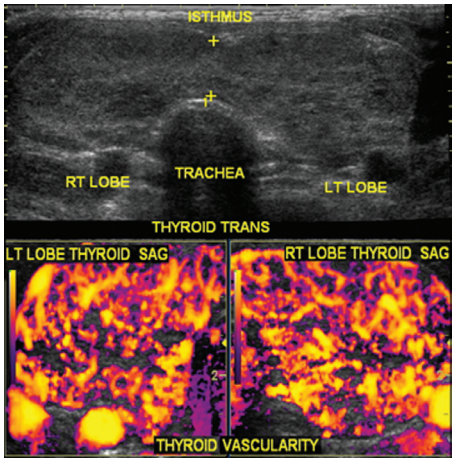

Figure 7: Thyroid sonography in a Graves' disease patient. The gland appears enlarged and diffusely heteroechoic (upper panel). On Doppler, there is significant increase in vascularity, also described classically as *thyroid inferno* (lower panel)

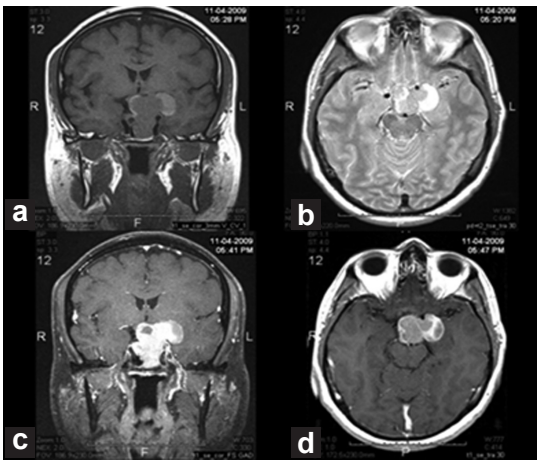

Figure 9: Pituitary macroadenoma in a patient with acromegaly: Coronal T1 (a) and axial T2 (b) showing a mass in sella with suprasellar extension having "figure of 8" appearance. The mass shows avid enhancement in post-contrast coronal T1 (c) and axial T1 (d) images with central nonenhancing area suggesting necrosis

velocity exceeds 70 cm/s on spectral Doppler.[19] It can be used to monitor therapeutic response in patients with Graves' disease[20] as there is decrease in flow velocities in superior and inferior thyroid arteries after successful medical treatment. CT and MRI are nonspecific, showing only diffusely enlarged gland.

Hyperparathyroidism

There seems to be a close association of prevalence of systemic hypertension with primary hyperparathyroidism. Up to 50% of patients with primary hyperparathyroidism seem to have high blood pressure. Interestingly, elevated parathyroid hormone has been reported to be more common among patients with essential hypertension.[21]

However, it is arguable that such an association is merely statistical, as more than 50% of such patients will continue to be hypertensive even after a successful parathyroidectomy. It is also worth mentioning that both essential hypertension and primary hypertension are conditions which are more common after 5th decade of life.[22,23]

Parathyroid adenomas of sporadic origin are the most common cause of primary hyperparathyroidism. They appear characteristically oval, but may appear oblong or elongated or even bilobar when enlarged. Due to uniform hypercellularity, they are typically hypoechoic, with the echogenicity being substantially lower than the overlying thyroid [Figure 8]. Most parathyroid adenomas measure 0.8–1.5 cm in their largest diameter.[24]

Acromegaly

The prevalence of hypertension in patients with growth hormone (GH) excess is approximately 50% and more frequent than in the general population.[25] Because GH-secreting pituitary adenoma is the most common cause, MRI of the sella is the investigation of choice which provides detailed information about the mass as well as the surrounding structures such as the optic chiasm and cavernous sinuses [Figure 9].

In conclusion, endocrine hypertension is a special clinical entity in which imaging has definite role in its evaluation to guide the endocrinologist as well as the endocrine surgeon. A detailed clinical work with laboratory evaluation will be necessary before shortlisting the radiological imaging procedure which the patient would be subjected to.

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