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Multi-modality imaging of pheochromocytoma

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Pheochromocytoma, a rare neuroendocrine adrenal tumor, is often diagnosed by a combination of clinical, laboratory, and radiographic features. While the imaging features of this entity are variable, the use of complementary modalities often helps to target the diagnosis and assess the extent of the disease. We present a multi-modality evaluation of a pheochromocytoma, with CT, MR, MIBG, and pathologic findings, in an individual who initially presented to the Emergency Department with flank pain.

Case report

A 48-year-old male presented to the Emergency Department in the middle of the night with lower-back pain and dysuria. The patient had recently been treated with oral ciprofloxacin as an outpatient for a presumed urinary-tract infection. The patient's past medical history was significant only for hypertension, managed with clonidine. A urine analysis before imaging workup revealed positive urine nitrates, leukocytosis, and white blood cells, consistent with history of recent urinary-tract infection.

A contrast-enhanced CT of the abdomen and pelvis was then ordered to assess for causes of the patient's flank pain and to rule out an ascending genitourinary infection. The CT demonstrated a large 6.8cm left adrenal mass with predominantly peripheral enhancement and central areas of low attenuation, presumed to represent necrosis (Fig. 1). No imaging findings of cystitis or pyelonephritis were demonstrated.

The diagnostic considerations for the adrenal mass were broad and included primary adrenal carcinoma, metastasis, neuroendocrine etiologies, and (less likely) adrenal hemorrhage. The patient was subsequently admitted to the hospital; on the following day, he underwent an MRI of the adrenals performed without the use of intravenous contrast material. The lesion did not demonstrate any signal loss on out-of-phase imaging, as would be expected with lipid-rich lesions such as adenomas (Fig. 2). On the T2-weighted sequence, the lesion was heterogeneous but showed large regions of hyperintensity (Fig. 3).

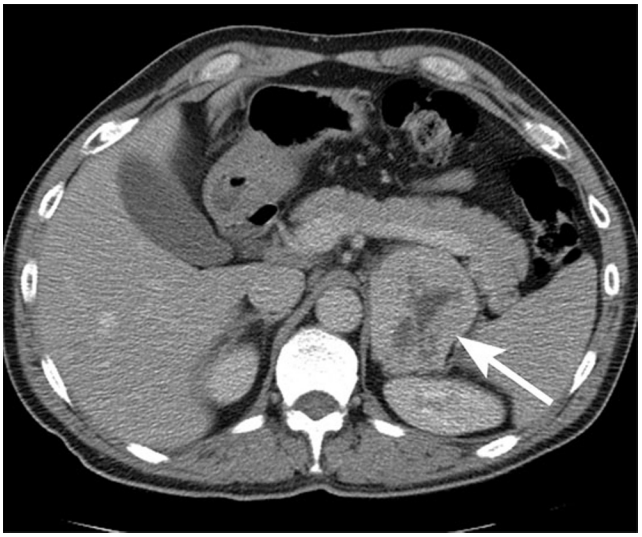

Figure 1. 48-year-old male with pheochromocytoma. Axial, contrast-enhanced CT demonstrated a 6.8cm left adrenal mass (arrow) with predominantly peripheral enhancement and central necrosis (arrow). The lesion implied mass effect and posterior displacement of the left kidney.

At this time, the patient was discharged and followed by the endocrinology service. On further review of systems, the patient indicated that he had been having intermittent palpitations, diaphoresis, and headaches. Laboratory

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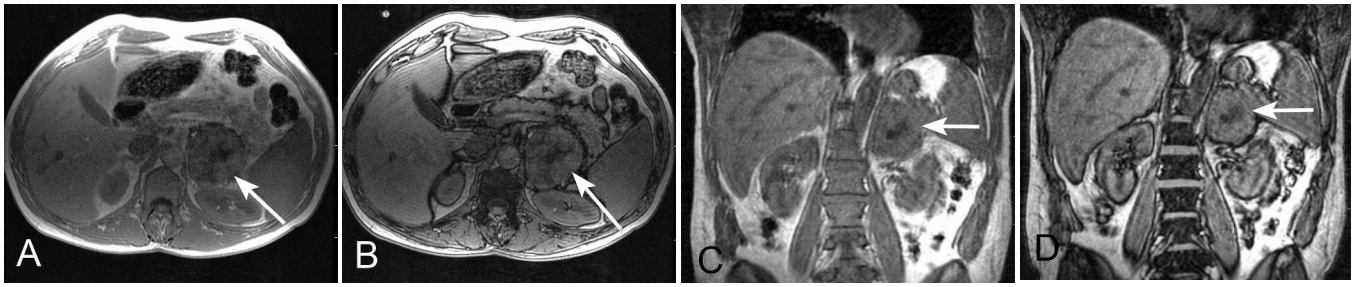

Figure 2.48-year-old male with pheochromocytoma. Axial (A) and coronal (C) in-phase MR images showed the heterogeneous left adrenal mass (arrows). During the axial (B) and coronal (D) out-of-phase images, there was no loss of signal in the mass (arrows).

evaluation revealed an elevated 24-hour level of urinary total metanephrines, measuring 14,168 mcg (normal range: less than 739 mcg/24 hours). At this point, a presumptive diagnosis of pheochromocytoma was made, and the patient

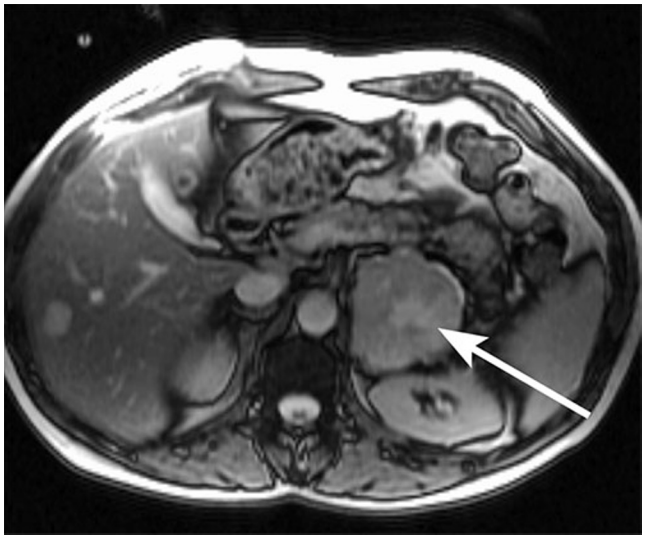

Figure 3. 48-year-old male with pheochromocytoma. Axial, T2-weighted MR showed a central area of hyperintensity (arrow) within the left adrenal mass.

underwent an I-123 MIBG nuclear-medicine scan to further evaluate the extent of disease and to confirm the diagnosis. The study demonstrated that the left adrenal mass was strongly MIBG-avid (Fig. 4), supporting the clinical diagnosis of pheochromocytoma. No focal MIBG uptake was identified elsewhere to suggest metastasis.

The patient was subsequently placed on the alpha-blocking antihypertensive phenoxybenzamine and underwent laparoscopic left adrenalectomy. Gross pathology (Fig. 5a) revealed an encapsulated rubbery, red-brown mass arising from the adrenal medulla with histologic findings (Fig. 5b) supporting the diagnosis of pheochromocytoma.

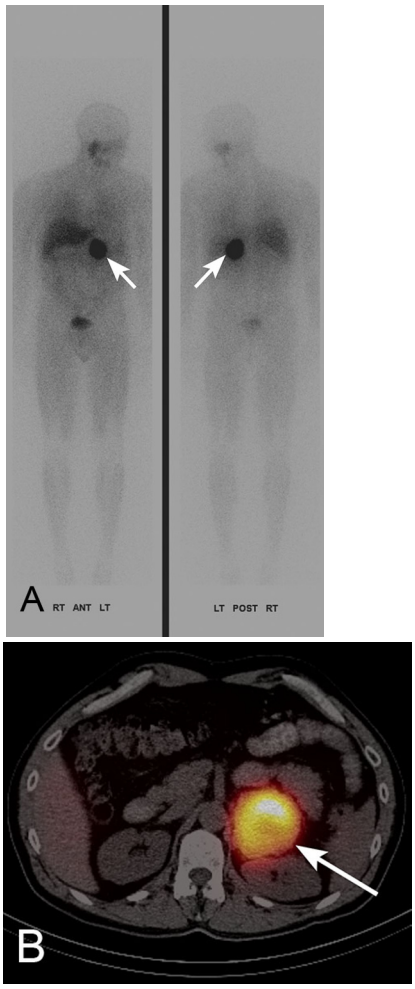

Figure 4. 48-year-old male with pheochromocytoma. Four hours following I-123 MIBG administration, anterior and posterior whole-body planar images (A) and fused SPECT-CT images (B) revealed focal concentrated uptake of MIBG (arrows) within the left adrenal gland consistent with a pheochromocytoma. No other areas of focal MIBG activity were seen to suggest metastasis. Physiologic uptake was identified within the salivary glands, liver, and urinary bladder on the planar images.

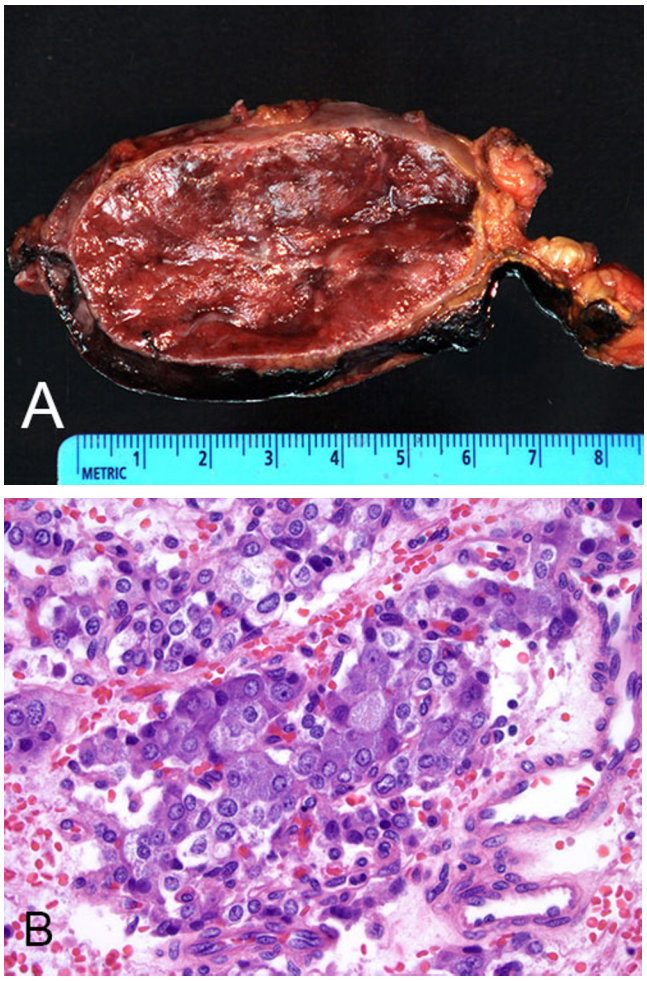

Figure 5. 48-year-old male with pheochromocytoma. Gross pathology (A) revealed an encapsulated red-brown pheochromocytoma, measuring 7cm and 139g. Hematoxylin and eosin stain (B) revealed pleomorphic nuclei with characteristic nests of cells ("zellballen") and abundant cytoplasm (1).

Discussion

Pheochromocytomas are uncommon neuroendocrine tumors arising from chromaffin cells of the adrenal medulla (2, 3, 4). In approximately 10% of cases, these tumors can arise from extra-adrenal paraganglionic chromaffin tissues and are referred to as paragangliomas (2, 5). The result of unregulated catecholamine secretion from these tumors can result in a classic clinical symptomatology of episodic hypertension, headaches, and palpitation; however, if left untreated, pheochromocytomas can lead to malignant hypertensive crises, cardiac arrhythmias, and death (2, 6, 7). Due to the risks of biopsy or manipulation of a pheochromocytoma, an accurate diagnosis and subsequent pre-operative alpha-blockade are essential in the workup of this condition (2, 3, 5, 7).

Classically, pheochromocytomas have been said to follow a "rule of 10s": 10% are bilateral, 10% are extra-adrenal, 10% are silent, and 10% of intra-adrenal pheochromocytomas are malignant (2, 6, 8, 9). Up to 25% of pheochromocytomas have an associated genetic predisposition, with a smaller percentage related to broader syndromic states such as multiple endocrine neoplasias (MEN) II and III, Sturge-Weber, neurofibromatosis, and von Hippel-Lindau (2, 5, 8).

The role of imaging in characterizing these lesions is important but complementary to the clinical presentation. In addition to the aforementioned clnical symptoms, first-line laboratory diagnostic evaluation entails measurement of plasma metanephrines and 24-hour urinary catecholamine and vanillymandelic acid levels (2, 7, 8, 9).

Pheochromocytomas larger than 3cm often have a variable appearance on CT and can mimic many other adrenal lesions (2, 8). While they are typically well-defined, with attenuation greater than 10 hounsfield-units, larger lesions can develop a more heterogeneous appearance due to internal necrosis and hemorrhage (Fig. 6a) (2, 5). Due to a rich capillary network, pheochromocytomas demonstrate

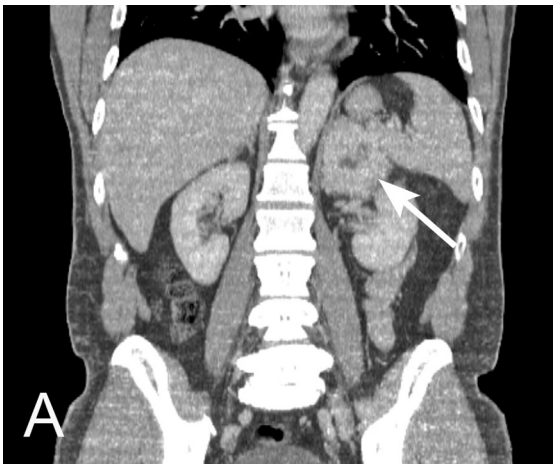

Figure 6A. 48-year-old male with pheochromocytoma. Coronal post-contrast CT demonstrated a heterogeneously enhancing left adrenal pheochromocytoma with central necrosis.

avid enhancement with variable washout dynamics on delayed images (2). While there are theoretical concerns regarding the use of iodinated intravenous contrast agents, several sources report the safety of using nonionic low-molecular-weight agents if necessary (3, 4, 6, 7, 8).

Although signal intensity is variable on MR imaging, pheochromocytomas have classically been described to have a "light-bulb" hyperintensity on T2-weighted sequences, due to a cystic component, and are hypointense on T1 sequences (2, 5, 9). However, the presence of T2 hyperintensity is neither sensitive or specific for pheochromocytoma, and considerable variability exists in the uniformity and distribution of T2-signal involving these lesions (Fig. 6b) (2, 10). A retrospective study of 44 cases of pheochromocytoma found only 11% demonstrating the

classic homogeneous, T2-hyperintense appearance; 34% were described as homogeneously hypointense to CSF T2 signal, 16% showed a heterogeneous "marbled" appearance, and 39% were heterogeneous with cystic pockets of T2 hyperintensity (10). Due to the rich vascular network within these tumors, punctate flow-voids are described as

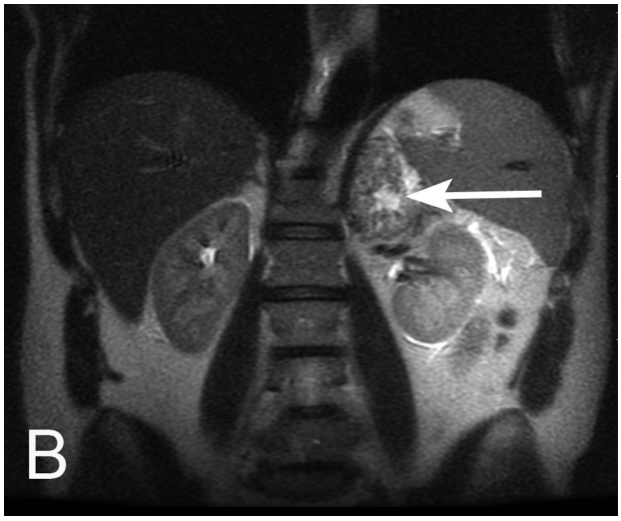

Figure 6B. 48-year-old male with pheochromocytoma. A companion coronal T2-weighted MR revealed characteristic T2 hyperintensity within the center of the pheochromocytoma.

having a "salt-and-pepper" appearance (2). While signal loss on out-of-phase imaging is more commonly associated with a lipid-rich adenoma, a pheochromocytoma can also occasionally show signal loss due to intracellular fat content (2).

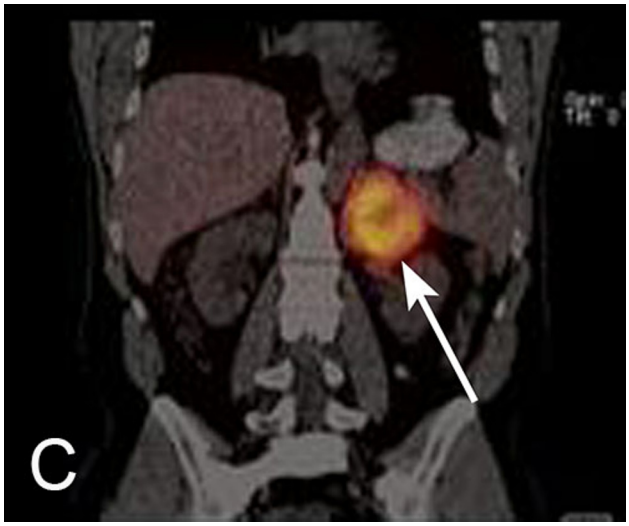

Figure 6C. 48-year-old male with pheochromocytoma. Fused coronal I-123 MIBG SPECT/CT showed avid uptake of radiotracer within the left adrenal pheochromocytoma.

Radionuclide scintigraphy, particularly when coupled with SPECT/CT, plays an important role in localizing extra-adrenal disease, assessing for distant metastases, and evaluating for tumor recurrence (2, 5, 11, 12). The most specific radiotracer used is metaiodobenzylguanidine (MIBG), labeled with radioiodine 123 or 131, whose specificity for detecting pheochromocytomas approaches 100% (Fig. 6c) (2, 9). MIBG acts as a norepinephrine analog and is stored in neurosecretory granules of chromaffin cells (9). Although less specific, In-111 octreotide, a somatostatin-analog, is a second agent that can be used to localize pheochromocytomas; it may serve a complementary role, particularly in evaluating nonfunctioning paragangliomas and dopamine-secreting metastases (2, 9, 12). The use of PET and PET/CT is also coming into practice, with new F-18-labeled tracers (DOPA, FDA) providing better sensitivity and specificity than the commonly used FDG (2, 9, 11, 12). However, due to continued investigation of these agents, cost, and limited availablity of these analogs, the use of PET is not yet widespread (2, 12).

As illustrated in this case, the use of multi-modality imaging provides an important role in guiding the diagnosis and directing pre-operative planning for pheochromocytomas.

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