Anita Philyaw. *Vashti…banished*, 1999. Acrylic on canvas, 30″ × 56″. Courtesy of Stella Jones Gallery, New Orleans, La.

Evaluation and Management of Adrenal Masses

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Background: The widespread use of abdominal imaging has led to increased detection of adrenal tumors. The significance of these masses, as well as the optimal management approach to treatment, has generated some controversy regarding further evaluation and therapy.

Methods: The authors reviewed the literature regarding the evaluation and management of these masses, particularly adrenal incidentalomas. Based on their institutional experience, they propose a diagnostic, evaluation, and management algorithm for treating adrenal masses.

Results: Appearance and clinical history should indicate how to perform the biochemical evaluation, keeping in mind that the presence of pheochromocytomas must be ruled out. Radiological evaluation by CT or MRI provides useful parameters to identify malignant lesions. Surgery is indicated for masses that are larger than 5 cm in diameter or suspected of malignancy. Fine-needle aspiration biopsy should be used when other extra-adrenal malignancies are suspected and after pheochromocytoma has been ruled out.

Conclusions: Careful analysis of each adrenal mass is essential to effectively avoid potential problems. Guidelines to manage patients with adrenal masses are needed.

Introduction

The presence and importance of the adrenal glands as well as their physiology were initially described more than 500 years ago. In the 1850s,

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Addison[1] and Brown-Séquard[2] proved the essential role of the adrenal glands in mineral and corticoid function.

The etiology of adrenal masses includes benign or malignant adrenal cortical tumors, adrenal medullary tumors, and other benign lesions. A review of reported series of incidentally found adrenal masses shows that adrenal cortical adenomas are 60 times more common than primary adrenal cortical carcinomas, that primary adrenal cortical carcinomas are rare, and that many of the malignant lesions are metastatic from extra-adrenal neoplasms.[3] The approaches to the different types of adrenal masses are discussed in this report. Special attention is given to adrenal incidentalomas since the

increasing frequency in the diagnosis of this entity has become a common clinical problem.

Etiology

Incidentally Discovered Adrenal Masses (Incidentalomas)

Incidentalomas are adrenal tumors discovered on an imaging study performed for indications exclusive of adrenal-related conditions.[4] The frequent use of imaging studies, particularly computed tomography (CT) scans, which consistently detect adrenal lesions greater than 1 cm, has resulted in the detection of incidentalomas in 0.35% to 5% of studies.[5] The majority of incidentalomas are biochemically nonfunctional and benign. However, in approximately 10% of cases, an incidental adrenal mass may be functional.[6]

Several reports have addressed the topic of incidentalomas, and many controversies exist regarding evaluation and management methods of these entities. The approach to incidentalomas is directed towards distinguishing benign from malignant neoplasms and determining the functional status of these lesions.

When functional, these masses may manifest as Cushing's syndrome, a rare entity that describes the symptom complex caused by an excess of circulating glucocorticoids. It is also important to rule out an exogenous source of hormone excess since therapeutic corticosteroids are the most common cause. The term *preclinical Cushing's syndrome* was introduced in 1981 to describe adrenal incidentalomas with autonomous cortisol-secreting cortical adenomas in patients who lacked the typical signs and symptoms of hypercortisolism.[7] The incidence of preclinical Cushing's syndrome is approximately 5% to 10%.[8]

Primary aldosteronism is another disorder of excess adrenal hormone production to consider in a patient with an adrenal incidentaloma. In 1955, Conn[9] described the clinical syndrome consisting in hypertension, hypokalemia, hypernatremia, alkalosis, and periodic paralysis caused by an aldosterone-secreting adenoma. Primary aldosteronism is a rare but important cause of secondary hypertension. Recent data suggest that this pathology may be more common than previously reported (as much as 5% to 15% of the hypertensive population) and may become the most common form of curable hypertension.[10] The hallmark of primary aldosteronism is hypertension with hypokalemia, suppressed plasma renin activity, and elevated plasma aldosterone. All patients with adrenal incidentalomas who have hypertension should be evaluated for primary aldosteronism.

Clinically silent pheochromocytomas are a third disorder of excess adrenal hormone to consider in a patient with an adrenal incidentaloma. Approximately 5% of patients with adrenal incidentalomas have pheochromocytomas, and 10% of adrenal pheochromocytomas have presented as adrenal incidentalomas.[11] The clinical features of pheochromocytomas are discussed later.

Benign Adenomas

Distinguishing adenoma from carcinoma by pathologic examination can be challenging for pathologists. All large adrenal lesions do not behave biologically as carcinomas. Some lesions that appear benign on histologic evaluation eventually metastasize. Hence, surgical removal is recommended for all lesions larger than 5 cm.

Adrenal adenomas often manifest on CT scans as smooth, well defined, homogeneous, smaller than 4 cm in diameter, and low in attenuation. Several reports in the literature indicate that an adrenal mass with a value of 10 Hounsfield units (HU) or fewer on unenhanced CT scan is likely to be an adenoma.[12] The low attenuation of these lesions is attributed to their rich lipid content. Radiological findings are discussed later.

Myelolipomas

Benign neoplasms are composed of mature adipose cells and hemopoietic tissue in varying proportions, and most are hormonally inactive. They are generally small (<5 cm) and unilateral. The most common symptom is pain. The fatty component is evident and characterized on CT scans by low-density and inhomogeneous images (Fig 1). On magnetic resonance imaging (MRI), the fat appears hyperintense on T1-weighted images and intermediate on T2-weighted
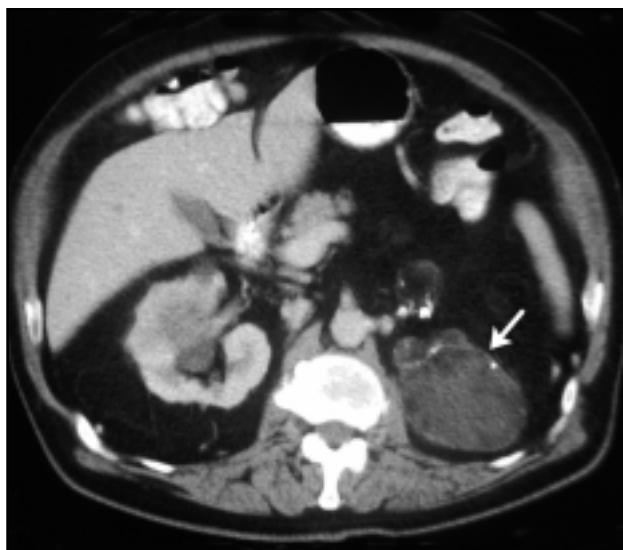

Fig 1. — Myelolipoma of the left adrenal (arrow).

images. The treatment for these lesions, if asymptomatic, is conservative unless there is a possibility that they may be confused with necrotic adrenal carcinoma. Tumor progression or hemorrhage is uncommon.

Adrenal Carcinoma

Adrenal carcinoma is a rare disease that carries a poor prognosis and accounts for 0.2% of all cancer deaths.[13] Adrenal tumors are classified as either functional or nonfunctional. Approximately 80% are functional, and they are usually larger than 6 cm. In a recent series published by Kendrick et al,[14] cortisol-secreting tumors were the most common functional tumors (67%), followed by mixed hormonal-secreting tumors (15%), sex hormonal excess (11%), and aldosterone-secreting tumors (7%). It is important to note that nonfunctional tumors may eventually become functional.

Due to the infrequency of adrenal carcinoma and the lack of randomized prospective trials, determining the optimal treatment can be difficult. Surgical resection is the principal treatment for stage I to II disease. For patients with stage III or IV disease, adjuvant therapy may improve survival, with mitotane being the agent of choice. Patients diagnosed at an earlier stage have an improved 5-year survival. However, the clinical benefits are questionable.

Adrenal Cysts

Adrenal cysts are rare, often unilateral lesions, and more prevalent in women. Endothelial cysts account for almost 50% of adrenal cysts. Pseudocysts, which are less common (40%), result from previous adrenal hemorrhages and may compress adjacent structures. Epithelial and parasitic cysts are uncommon.[15]

Adrenal Hemorrhage

Adrenal hemorrhage presents as a unilateral or bilateral mass on CT scan. It may occur spontaneously or may be the result of anticoagulation or trauma. On MRI in the acute phase, a signal loss is observed on T1 and T2 images due to the presence of deoxyhemoglobin. In the subacute and chronic phases, the intensity on both T1 and T2 images is increased due to calcification and hemosiderin deposition.[4]

Pheochromocytomas

Pheochromocytomas are tumors of neuroendocrine origin that arise in the adrenal medulla in approximately 80% to 90% of cases. They are the cause of hypertension in less than 1% of the hypertensive population. Detection of these tumors is critical, not only to cure the

hypertension, but also to avoid the potential lethal effects of the tumor. Pheochromocytomas can be large, ranging in size from 2 g to 3,600 g. Symptoms associated with these tumors usually are referable to their production of catecholamines.[16] The catecholamine-induced symptoms are mediated by the normal sympathetic neural pathway and not primarily by serum catecholamines. Any direct stimulus to the sympathetic nervous system can induce a crisis without a large rise in serum catecholamine levels. Hypertension is the most consistent sign, involving three basic patterns: sustained, paroxysmal, and sustained with superimposed paroxysms.[15] The signs and symptoms of pheochromocytoma are variable,[17] and 10% are found in normotensive patients. In addition to hypertension, the sequelae of chronic exposure to catecholaminic excess include plasma volume contraction and catecholamine-induced cardiomyopathy. Approximately 10% to 20% of pheochromocytomas are malignant. Although some patients may live decades, the mean 5-year survival rate is 40%.[18] Malignancy may be reflected in local invasion or by metastatic spread in decreasing frequency to the bone, lymph nodes, liver, lungs, or brain.

Several syndromes of familial pheochromocytoma have been described. The most common are multiple endocrine neoplasia type 2 and von Hippel-Lindau disease. A lower incidence of pheochromocytoma is seen in patients with neurofibromatosis type 1. Some families seem to have familial disorders characterized by pheochromocytomas without other abnormalities.

Manifestations of pheochromocytomas in children vary from those in adults and are not addressed here. The radiological and laboratory diagnosis is discussed later. Preoperative medical preparation is essential and includes expansion of plasma volume and alpha-adrenergic receptor blockade, with either selective alpha-blockers (prazosin)[19] or nonselective alpha-blockers (phenoxybenzamine). Beta-blockers are used to protect this patient against arrhythmias and should be started only after alpha-blockade has been established to avoid a significant rise in the total peripheral vascular resistance. Another option is alpha-methylparatyrosine, which decreases the rate of catecholamine synthesis.

Adrenal Metastasis

Metastatic tumors to the adrenal gland are more common than primary adrenocortical carcinoma. The most common tumors to metastasize to the adrenal gland are melanomas, carcinomas of the breast and lung, and renal cell carcinoma. Other tumors include carcinomas of the contralateral adrenal, bladder, colon, esophagus, gallbladder, liver, pancreas, prostate, stomach, and uterus.[20] In general, the adrenal lesion is part

of the clinical picture of diffuse metastatic disease. Therefore, the finding of an unsuspected adrenal mass should heighten the clinical suspicion of a neoplasm elsewhere. Adrenal insufficiency may occur.[21]

Other Causes of Adrenal Masses

Rare causes of benign nonfunctioning masses include adrenolipoma, amyloidosis, angiomyolipoma, ganglioneuroma, fibroma, neurofibroma, teratoma, and granuloma. Rare causes of malignant nonfunctioning masses include ganglioneuroblastoma, neuroblastoma, lymphoma, lymphangioma, liposarcoma, malignant schwannoma.

Evaluation of Adrenal Masses

An adrenal mass is characterized according to *functional status*, with a medical history, physical examination, and hormonal assessment, and *malignant potential*, with an assessment of the imaging phenotype and mass size. Most patients diagnosed with adrenal lesions had previous complaints of extra-adrenal origin, such as hepatic and biliary problems, lumbar pain, nephropathy, and abdominal pain that was nonspecific in nature. However, many lesions are associated with subtle symptoms of hormone excess, such as generalized obesity, hypertension, abnormal glucose tolerance, and depression. Also, several inherited syndromes are associated with adrenal gland pathology, such as multiple endocrine neoplasia (MEN) types 1 and 2, von Hippel-Lindau syndrome, neurofibromatosis, Beckwith-Wiedemann syndrome, and congenital adrenal hyperplasia.[4]

The optimal diagnostic approach to a patient with an adrenal mass is not well established. While several different algorithms and methods of determining the optimal treatment of these lesions have been published, most physicians would agree that the evaluation of the patient should start with a careful history and physical examination focusing on signs and symptoms of adrenal hyperfunction and malignancy.

Hormonal Evaluation

Adrenal Incidentalomas: Abnormalities of endocrine function have been observed in a substantial number of patients with adrenal incidentalomas. Adrenal incidentalomas may retain some hormonal activity, although most are clinically silent. This finding has clinical relevance because endocrine hyperfunction (ie, hypercortisolism, aldosteronism, pheochromocytoma) may be associated with significant morbidity. Measurement of adrenal cortical autonomy is mandatory in all patients with adrenal incidentalomas. Hormonal evaluation includes basal determinations and dynamic tests of cortical and medullary adrenal function.

Hypothalamus-Pituitary-Adrenal Axis: It is important to determine when glucocorticoid secretory autonomy in an adrenal cortical adenoma leads to clinical morbidity. Low adenocorticotropic hormone (ACTH) levels have been reported in approximately 5% to 34% of patients with adrenal incidentalomas, altered circadian cortisol rhythm in 8% to 20%, and elevated urinary-free cortisol in 0% to 21% and serum cortisol in 0% to 12%. Plasma dehydroepiandrosterone sulfate (DHEA-S) concentration may predict the hormonal activity of adrenal incidentalomas and serve as an indicator of hypothalamic-pituitary-adrenal axis suppression.[22] However, in a recent study, the plasma DHEA-S concentration was a poor predictor of hormonal activity.[23] Most centers utilize the overnight 1-mg dexamethasone suppression test. If the cortisol level at 8 AM following dexamethasone given the night before is greater than 5 mg/dL, a formal 2-day, low- or high-dose dexamethasone suppression test is indicated to confirm the autonomy. Some studies suggest a high rate of false-positive results. Until more is learned from the results of long-term follow-up studies, it is reasonable to consider that patients with nonsuppression to both a 1-mg dexamethasone suppression test (8 AM serum cortisol >5 mg/dL) and a formal 2-day, low- or high-dose dexamethasone suppression test (24-hour urinary-free cortisol >20 mg/dL) are candidates for adrenalectomy. Slightly elevated urinary-free cortisol and/or serum cortisol with abnormal rhythm incompletely suppressed by low-dose dexamethasone and decreased ACTH responsiveness to corticotropin-releasing hormone may be observed in clinically silent cortisol hypersecretion.

Baseline serum 17-hydroxyprogesterone is elevated in patients with rare adrenal masses associated with congenital adrenal hyperplasia, whereas adrenal masses have been reported in 82% of those with homozygous 21-hydroxylase defect.[24] Despite extensive experience, there is little consensus regarding selection of the most appropriate and cost-effective tests for endocrine evaluation of adrenal incidentalomas.

Renin Angiotensin Aldosterone Axis: Aldosteronomas have been reported in less than 3% of adrenal incidentalomas. Hypertensive patients with hypokalemic alkalosis should be evaluated by determining plasma renin activity and plasma aldosterone concentration, although essential hypertension may cause hypokalemia. An elevated plasma aldosterone-renin ratio is diagnostic of primary aldosteronism. Other methods, such as posture test and sodium load-

ing have been suggested but are not commonly used in clinical practice. Adrenal vein sampling of aldosterone is the gold standard for localization of aldosterone production; however, it is invasive, labor-intensive, and more challenging.

Adrenal Medulla: Even when clinically silent, pheochromocytomas can be lethal. Autopsy studies have shown that up to 76% of pheochromocytomas are clinically silent and unsuspected before death.[4] However, this lesion should always be suspected to avoid the risk of lethal hypertensive crises, especially during biopsy or surgery. Ninety-nine percent of patients with adrenal pheochromocytomas have increased levels of 24-hour urinary total metanephrines, catecholamines, or both.[25] Most clinicians advocate screening tests with measurements of urinary catecholamines and/or metanephrines in all patients with adrenal incidentalomas. Plasma catecholamine and/or metanephrine determinations are also sensitive and specific tests to detect pheochromocytomas. Less common dynamic tests (eg, glucagon stimulation, clonidine inhibition) may be useful to confirm the diagnosis.

Screening for Other Hormonally Active Processes: Sex hormone-secreting adrenal cortical tumors occur rarely. Patients with these tumors usually have symptoms and do not present with adrenal incidentalomas (except for testosterone-secreting adrenal tumors in men). Routine screening for sex hormone excess in a patient with an adrenal incidentaloma is not warranted.

Nonclassic congenital adrenal hyperplasia can cause unilateral or bilateral adrenal masses, and some investi-gators have suggested routine corticotropin stimulation testing in all patients with adrenal incidentalomas. This recommendation cannot be supported in view of the relative infrequency of congenital adrenal hyperplasia. Genetic screening and corticotropin stimulation testing should be reserved for patients in whom congenital adrenal hyperplasia is suspected on clinical grounds or for patients who have bilateral adrenal masses.[26]

Diagnostic Algorithm: Several hormonal screening protocols have been suggested, most based on evidence and the experience of the authors. Ross in 1990[27] suggested that a minimal evaluation consisting of screening tests for pheochromocytoma, serum potassium in hypertensive patients, and glucocorticoids or androgens only in the presence of suggestive clinical features may fail to identify those with mild hypercortisolism or congenital adrenal hyperplasia. Favia et al[28] recently suggested that patients with incidentalomas should be tested for (1) baseline plasma cortisol levels, (2) upright plasma aldosterone and plasma renin activity, (3) serum DHEA-S concentration, and (4) 24-hour urinary epinephrine and norepinephrine. For patients with clinical suspicion of hypercortisolism, Barzon and Boscaro[4] recently suggested a protocol for endocrine evaluation of adrenal masses, mainly incidentalomas, in which urinary-free cortisol and ACTH are measured and the 1-mg dexamethasone suppression test is utilized. When hyperaldosteronism is suspected, serum potassium levels and the aldosterone-to-plasma renin ratio should be obtained. Urinary catecholamines and metanephrines are performed to rule out pheochromocytomas.[4] Lenders et al[29] suggested that plasma-free metanephrines provide the best test for excluding or confirming pheochromocytoma. Definitive endocrine evaluation and appropriate management should follow positive results of any screening test. A practical algorithm for metabolic evaluation is suggested in Fig 2.

Abdominal sonography can detect adrenal masses greater than 2 cm in diameter with low costs and risk, although it cannot accurately define lesion size and morphological characteristics. In select cases, abdominal sonography can be used for follow-up, especially for masses in the right adrenal gland. Endoscopic ultrasonography has recently been demonstrated to be more accurate than a transabdominal approach in detection of the left adrenal gland, although it often cannot visualize
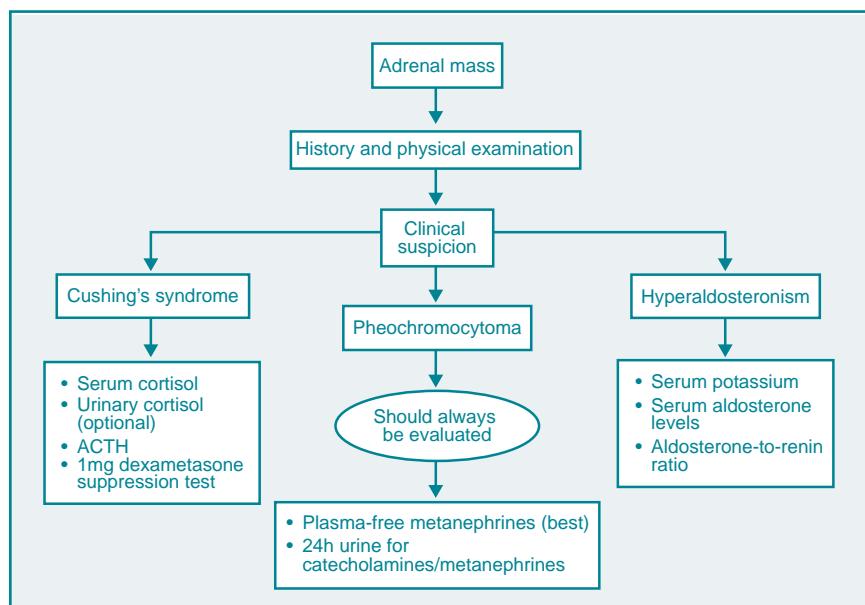

Fig 2. — Suggested algorithm for metabolic evaluation of an adrenal mass.

the right gland.[30] Therefore, routine use of this procedure is limited due to technical difficulty.

Imaging of the Adrenal

Computed Tomography

CT is the most effective technique for examining the adrenal glands. Perinephric fat allows the gland to be displayed clearly, and tumors as small as 10 mm in diameter are routinely identified with a sensitivity of up to 100%. The adrenal gland is be examined using contiguous 5-mm collimated slices; even narrower collimation may be used to clarify equivocal findings. CT has become the imaging procedure of choice for most patients with known or suspected adrenal lesions. CT can demonstrate the adrenal glands in virtually all patients and can usually identify the size, location, appearance, and presence of local or vascular invasion, lymph node involvement, and presence of distant metastases. In patients with adrenal lesions, the contralateral adrenal gland must be carefully evaluated to determine whether the disease is unilateral or bilateral. Intravenous contrast is generally not required for evaluation of the presence of an adrenal mass, although it is mandatory in defining vascular involvement, including the vena cava.

An adrenal adenoma usually appears as a small, well-defined, homogeneous, round mass, with low enhancement with contrast medium. Calcification, hemorrhage, and necrosis are uncommon. Due to the high cytoplasmic lipid content, the density is low and varies from 0 to 30 HU. Unenhanced images of less than 18 HU have been reported to diagnose an adenoma with 100% specificity and 85% sensitivity, whereas a more conservative cutoff of 10 resulted in a specificity of 96% to 100% and sensitivity of 68% to 79%. Delayed scans taken 15 minutes after injection of contrast show that lesions less than 37 HU are adenomas. However, it is necessary to ensure that the lesions are homogeneous and devoid of thickened walls.[31] CT of adrenocortical carcinoma reveals a large mass with central areas of low attenuation due to tumor necrosis with calcifications in 30% of cases. Evidence of metastatic spread to regional lymph nodes and the liver or direct invasion of adjacent structures, such as the kidney and inferior vena cava, suggests a malignant process. Adrenal metastases are solid masses of variable size with central necrosis or areas of hemorrhage and may be bilateral. Pheochromocytomas of the adrenal gland are usually 2 to 5 cm in diameter, vascular, and rich in intracellular water. On CT they are rounded or oval masses of soft-tissue density, frequently with central necrosis and marked enhancement after intravenous contrast material. Glucagon should not be used as an antiperistaltic agent because it may induce a hypertensive crisis and, similarly, injection of ionic contrast medium can precipitate such a crisis in some patients who have not received α-adrenergic blockade.

Magnetic Resonance Imaging

MRI of adrenal masses by several pulse sequences provides not only anatomical details, but also tissue characterization and extension into adjacent structures, and it defines the relationship between adrenal tumors and major vessels. Chemical shift MRI has become a popular technique for diagnosing adrenal adenomas with 96% to 100% accuracy.[31] Benign adrenal adenomas, which typically are composed of approximately 16% lipid based on in vitro studies, can demonstrate measurable differences in signal intensity when their appearance on in-phase gradient-echo images is compared with that on out-of-phase counterparts (Fig 3). Compared with benign lesions, metas-
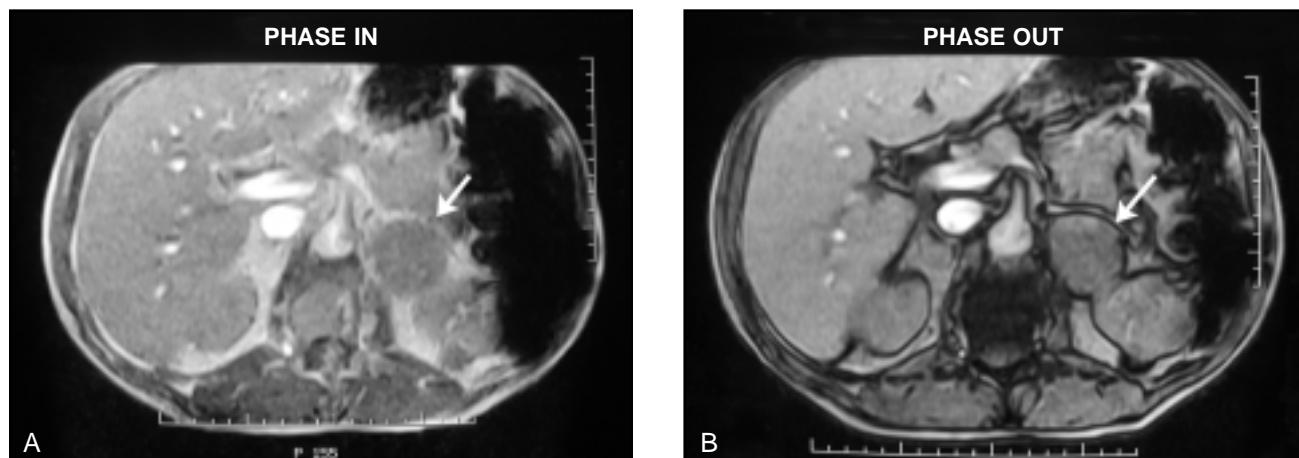

Fig 3. — Benign adrenal adenomas on in-phase gradient-echo MRI images compared with out-of-phase counterparts (arrows). (A) In-phase gradient of left adrenal mass. (B) Out-of-phase gradient in the same patient demonstrating a decrease in signal intensity.
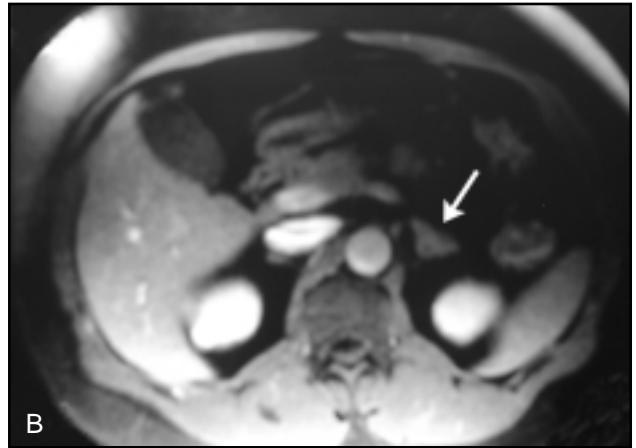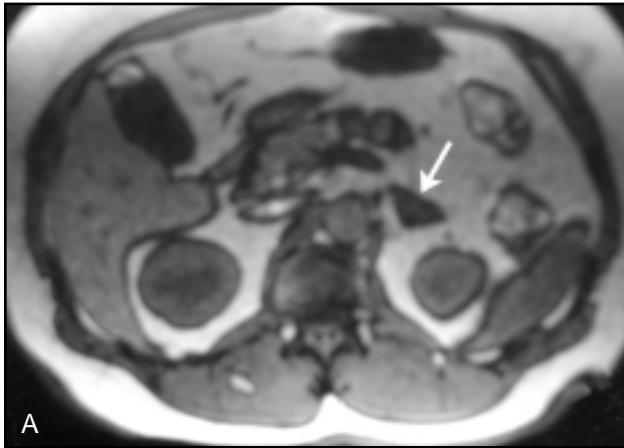
Fig 4. — (A) MRI of small left adrenal mass on T1. (B) The same lesion on T2. The pathologic diagnosis was an aldosteronoma.

tases usually show higher signal intensity on T2-weighted images, although there is a substantial overlap in signal intensities between them. However, metastases from hepatocellular carcinomas, renal cell carcinomas, liposarcomas and, rarely, adrenocortical carcinomas can contain fat, thus resulting in false-negative images. In contrast, some functioning adenomas (aldosteronomas) may contain insufficient lipid to result in signal loss (Fig 4). Although experience with MRI in the evaluation of adrenocortical carcinomas is limited, tumors are usually heterogeneously hyperintense on T1- and T2-weighted sequences due to frequent hemorrhage and necrosis. Postcontrast studies often demonstrate peripheral nodular enhancement and central hypoperfusion. MRI is particularly useful in patients with suspected pheochromocytomas and is the imaging procedure of choice when a patient presents biochemical data suggesting catecholamine excess. Pheochromocytomas tend to be hypointense on T1-weighted images and characteristically hyperintense on T2-weighted images. Tumors often have a heterogeneous appearance on the latter image due to the presence of cystic regions, necrosis, and fibrosis. MR angiography using gadolinium may be useful to delineate the anatomic relationships between adrenal tumors and vascular structures. This technique has been refined to the point where it is unusual to require invasive angiographic procedures, even in the setting of large invasive tumors.

Radioisotope Scanning/Positron Emission Tomography

Adrenal Scintigraphy: The widespread application of adrenal scintigraphy is limited by the lack of experienced nuclear medicine centers. In addition to anatomical localization, adrenocortical scintigraphy provides a functional characterization of the adrenals based on the uptake and accumulation in functioning adrenocortical tissues of radiotracers, such as iodocho-lesterol-labeled analogs (^{131}I-6-β-iodomethyl-19-norcholesterol [NP-59] and ^{75}Se-6-β-selenomethyl cholesterol). Hypersecreting tumors (eg, cortisol, aldosterone, and androgen secreting adenomas) and nonhypersecreting adenomas show radiocholesterol uptake, whereas primary and secondary adrenal malignancies appear as "cold" nodules. Incidentalomas may show different radiocholesterol uptake patterns related to their nature and functional status.

Adrenal medullary scintigraphy requires radioiodinated guanethidine analogs, ^{131}I-MIBG and ^{123}I-MIGB, which are specifically concentrated in the sympathomedullary system by the active high-affinity type 1 transport mechanism. ^{123}I-MIGB scintigraphy localizes pheochromocytoma as focal increased adrenal uptake with 86% sensitivity and 99% specificity. Masses less than 1.5 to 2 cm in diameter and large tumors with extensive tumoral necrosis and/or hemorrhage may not show sufficient MIBG uptake for visualization. False-negative results also may be due to drugs that interfere with uptake.

Positron Emission Tomography (PET): PET is a promising imaging modality in oncology to measure noninvasively biochemical and/or physiological processes in vivo. In a study performed to differentiate adrenal masses of unknown nature in patients with cancer, 2-[^{18}F]-fluoro-2-deoxy-D-glucose PET correctly distinguished benign adrenal lesions that showed no uptake and adrenal metastases characterized by high uptake with 100% sensitivity and specificity.[32] A feature unique to PET is the use of intravenous radiopharmaceuticals that closely mimic endogenous compounds. Specific inhibitors of adrenal steroidogenesis, etomidate and metomidate, have recently been used to develop suitable PET tracer. These molecules seem to be suitable as in vivo tracers for specific visualization of the normal adrenal cortex and positive identification of adrenocortical tumors.

Angiography: Arteriography and venography were once commonly used in the preoperative evaluation of large adrenal lesions. However, due to the unique sensitivity of spiral CT and MRI scans, these invasive techniques have become obsolete. The exception is in the patient with a small aldosteronoma in whom venous samples may be required for localization. An experienced interventional radiologist is required because the right adrenal vein can be difficult to catheterize.

Fine-Needle Aspiration Biopsy (FNAB): Percutaneous biopsy using either CT or ultrasound guidance can be performed to evaluate adrenal lesions. Adrenal FNAB cannot differentiate between an adrenal cortical carcinoma and an adrenal adenoma. FNAB of adrenal masses is invasive and produces significant morbidity. Complications such as pneumothorax, septicemia, and hemorrhage have been reported in 8% to 13% of cases. Although Favia et al[28] recently showed a 100% sensitivity and a 100% accuracy with FNAB for any incidental adrenal mass, most would agree that FNAB should be reserved only for suspected metastases (sensitivity 80% to 100%). Also, FNAB should not be performed in patients with occult adrenal lesions who have not undergone a biochemical evaluation to rule out pheochromocytoma.

Treatment Options

All adrenal lesions that do not meet the criteria for nonfunctional benign disease require a carefully performed history and physical examination and biochemical workup to evaluate adrenal function. The majority of reports recommend that all functional adrenal tumors require treatment. Others, however, would agree that while aldosteronomas and pheochromocytomas, although clinically silent, should be surgically removed, the appropriate management of nonclinical hypercortisolism is still unclear. In these patients, surgical treatment would depend on several factors, including the degree of cortisol hypersecretion and concomitant hypertension, obesity, diabetes mellitus or impaired glucose tolerance and osteoporosis.

If the biochemical data are negative and the imaging characteristics are consistent with benign disease, the issue becomes whether the size of the adrenal lesion mandates removal or whether it can be followed safely with a non-operative intervention. As already noted, FNAB of an adrenal tumor cannot reliably distinguish between adrenal cortical carcinoma and a benign adrenal adenoma and should be reserved for patients with neoplasms elsewhere and when there is suspicion of metastatic disease. Because adrenocortical carcinomas are larger than benign masses (90% being more than 6 cm in diameter), mass size has been considered the most important predictor of the risk of malignancy, and there is general consensus that adrenal incidentalomas greater than 6 cm should be removed. Accordingly, most experts agree that any lesion larger than 5 cm should be removed unless classic characteristics are present that demonstrate unequivocal benign disease, such as a simple adrenal cyst or a myelolipoma. Most experts agree that lesions smaller than 4 cm can be followed with a serial imaging study. The ideal management of lesions between 4 and 5 cm remains unclear, and individual institutional variation exists. Some studies demonstrated that prevalence of adrenal nodules increases with age and suggested vascular rearrangements as a pathogenetic mechanism. Based on this concept, it is conceivable that the risk of malignancy of an adrenal mass may be lower in older than in younger patients and thus age, in addition to size, can be considered as a criterion for removing adrenal masses.[33] Therefore, adrenalectomy for a 3-cm adrenal mass would be advisable in a patient younger than 50 years of age, considering the low morbidity and mortality of surgery in young subjects, the risk of malignancy, the possibility of subclinical hyperfunction, and the elimination of the need for long-term follow-up.

The surgical approach consists of open or laparoscopic adrenalectomy. Several authors have compared both approaches retrospectively and concluded that laparoscopy is not inferior in terms of safety, efficacy, reliability, patient outcome, and side effects or complications. For patients with primary adrenal cancer, open surgery remains the technique of choice.[34] If an adrenal lesion is managed without surgery, a serial imaging study should be obtained, initially at 2 to 3 months from the diagnosis and then at 6 months. If the lesion has grown, surgical intervention is indicated. If the lesion remains stable, a second serial imaging study can be obtained at 6 months to 1 year. If the study is unchanged, it is unlikely that the lesion represents a malignant tumor, and additional imaging studies may not be required. Others would advise follow-up for the following 3 to 4 years, especially when factors such as an exclusive radiocholesterol uptake or subtle endocrine abnormalities at diagnosis indicate higher risk of progression of adrenal disease.

Conclusions

With the increased use of cross-sectional imaging techniques, the diagnosis of adrenal masses will undoubtedly increase. The challenge for practitioners is to minimize the need for potentially complex and expensive imaging for what is usually a benign process.

Appearance and clinical history should indicate how to perform the biochemical evaluation, keeping in mind that the presence of pheochromocytomas must be ruled out. Radiological evaluation by CT or MRI provides useful parameters to identify malignant lesions. Surgery is indicated for masses that are larger than 5 cm in diameter or suspected of malignancy. FNAB should be reserved for cases suspected of other extra-adrenal malignancy. Meticulous analysis of each adrenal mass is essential to effectively avoid potential problems.

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