Adrenal Incidentalomas

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Epidemiology

Most cases of AI are due to cortical adenomas, whose prevalence in large series ranges from 70 to 90%. Although inactive adenoma is considered the most common adrenal lesion, other adrenal lesions may be functionally active, requiring hormonal investigation, along with subsequent medical and surgical treatment [1, 2] (Table 10.1).

Prevalence increases with age, especially in the fifth and seventh decades of life, but is regarded as uncommon in individuals with less than 40 years of age and is rare in children and adolescents. Hypertension, obesity, and diabetes have been frequently reported, particularly in bilateral lesions, and this may be due to the presence of subclinical hypercortisolism [3, 4].

Table 10.1 Etiology, prevalence, and laboratory evaluation of adrenal incidentalomas

Etiology	Prevalence (%)	Laboratory screening
Nonfunctional adenoma	85	Normal
Subclinical Cushing's syndrome	7	1 mg DST(serum cortisol >3 μ/dl) Plasma ACTH (<5 pg/ml)
Phaeochromocytoma	3.5	24-h urine metanephrines>2 mg/g Cr
Hyperaldosteronism	0.7	Plasma aldosterone ≥15 ng/dl with a APRR ≥20
Nonfunctional adrenocortical carcinoma	2	Normal

Imaging Procedures

CT scan is the primary and preferred method used for evaluation of adrenal glands because it is a procedure that is readily available while offering the highest spatial resolution. Contrast enhancement and deenhancement (washout) in late phases (15 min) are helpful to characterize the lesions; however, noncontrast CT is often sufficient for the diagnosis of AI (Fig. 10.1).

Among the characteristics for identification of potentially malignant lesions, the first to be observed is the size of the mass. Various cut points have been proposed ranging between 3 and 6 cm (more often 4 cm) of diameter based on the fact that primary carcinomas of the adrenal with measurements lower than these are quite rare. However, adrenal carcinomas of 2.5 cm have been documented, and the use of these cutoff limits can exclude patients harboring carcinomas that are still small and, therefore, offer the greatest likelihood of being able to be treated and cured if operated upon in early stages [5, 6].

The next, and probably the most important, aspect to be seen is related to the noncontrast attenuation of the lesion when evaluated by CT. The rationale is that adrenal adenomas, due to their high content of intracellular lipids, usually exhibit low attenuation. In this regard, using a cutoff level of 10 HU (Hounsfield units) or less, a sensitivity of 96–100%, and a specificity of 50–100% have been reported for diagnosing a benign lesion [4, 7–9]. However, 40% of the benign lesions have a pre-contrast attenuation above 10 HU [4, 9]. Several authors reported high sensitivity and specificity in CT after using contrast. Percentage deenhancement, the so-called washout, of at least 60% in 15 min has been shown to be 98% sensitive and 92% specific for benign lesion [8] (Fig. 10.1).

Other features of benign lesions that can be evaluated by CT, such as regular margins and homogeneous attenuation, have low accuracy and are less useful in diagnosis. Calcifications, necrosis, and hemorrhages are atypical events but occur more specifically in larger lesions.

In adrenal hemorrhage, a clinical condition associated with sepsis, coagulation disorders, adrenal tumors (such as pheochromocytomas), and abdominal trauma, CT scan initially shows high density that gradually decreases as the hematoma subsides which may in turn become a pseudocyst.

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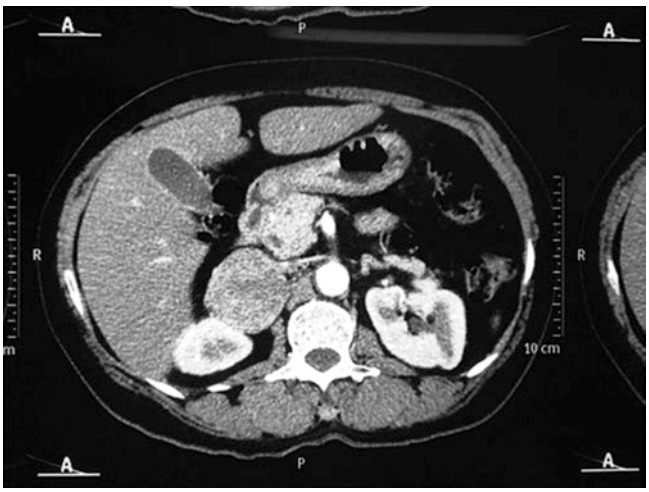


Fig. 10.1 A 52-year-old woman with primary hyperparathyroidism and hypertension had a CT scan to evaluate for renal calculi. A lesion (5.5 cm) in right adrenal gland was discovered. Noncontrast attenuation: 39 HU. Contrast washout: 42% in 15 min

Other lesions with characteristic features include cysts and myelolipomas. Endothelial cysts and pseudocysts are the most common, accounting for more than 80% of the cases. CT is useful in demonstrating the presence of liquid (hypodense) and generally thick capsules, whereas MRI shows hypointensity on T1 and hyperintensity on T2. Patients with adrenal cysts can, in some cases, benefit from fine needle aspiration (FNA) biopsy guided by ultrasound or CT for decompression and/or cytologic evaluation of the aspirated fluid. Since pseudocysts can originate from pheochromocytomas, measurements of serum or urinary catecholamines or metanephrines are always recommended [2, 5, 6].

Myelolipomas, in turn, are benign tumors composed of mature adipose tissue and normal hematopoietic tissue, corresponding to around 7–15% of AI cases. They are almost always asymptomatic lesions. Seen by CT, they appear as hypo-dense lesions (−40 HU), due to the presence of fat. Calcifications and hemorrhages may also be present [4]. Bilateral lesions occur in about 20% of AI cases and are usually due to metastases, granulomatous diseases, adrenal hemorrhage, or congenital adrenal hyperplasia. In this regard, positron emission tomography (PET) using 2-^{18}F-fluoro-2-deoxy-d-glucose has been used in cancer patients to evaluate the possibility of adrenal metastasis by demonstrating increased uptake, as well as being able to differentiate these cases from adenomas, which may not demonstrate the same uptake [8, 10].

Fine Needle Aspiration (FNA)

This procedure is useful in cases where there is known malignant disease (prior or concurrent) and suspicion that the adrenal nodule is metastatic [4, 6, 8, 10]. Diagnosis of metastasis in this situation has corresponded on average to about half the cases. The incidental finding of metastatic adrenal lesions in a patient with no clinical symptoms is considered to be rare. FNA should always be preceded by hormonal evaluation to rule out pheochromocytoma as catecholamines may be released with subsequent increase in blood pressure during the procedure. FNA should not be performed in the suspicion of adrenocortical carcinoma due to the risk of tumor seeding. FNA is now rarely necessary due to the improved accuracy of the emerging procedures [6, 8–10].

Hormonal Evaluation

The prevalence of autonomous adenomas that produce cortisol among cases of incidentalomas is from 5 to 20%. This condition has been classified as possible autonomous cortisol secretion (PACS), formerly named anteriormente denominada subclinical Cushing's syndrome (SCCS). Diagnosis can be made by a combination of 1 mg dexamethasone suppression test and plasma ACTH concentrations. Various cutoff values for cortisol have been proposed ranging from 2 to 5 μg/dl [4, 8, 11].

The natural history of SCCS is not completely understood. In many patients the condition does not progress, but in some it may evolve to clinical Cushing's syndrome. Patients must be evaluated for the presence of arterial hypertension, obesity, and glucose intolerance. Patients who demonstrate clinical consequences attributable to cortisol excess are likely to benefit from surgery. In asymptomatic patients, conservative management is appropriate, along with clinical and laboratory monitoring [4].

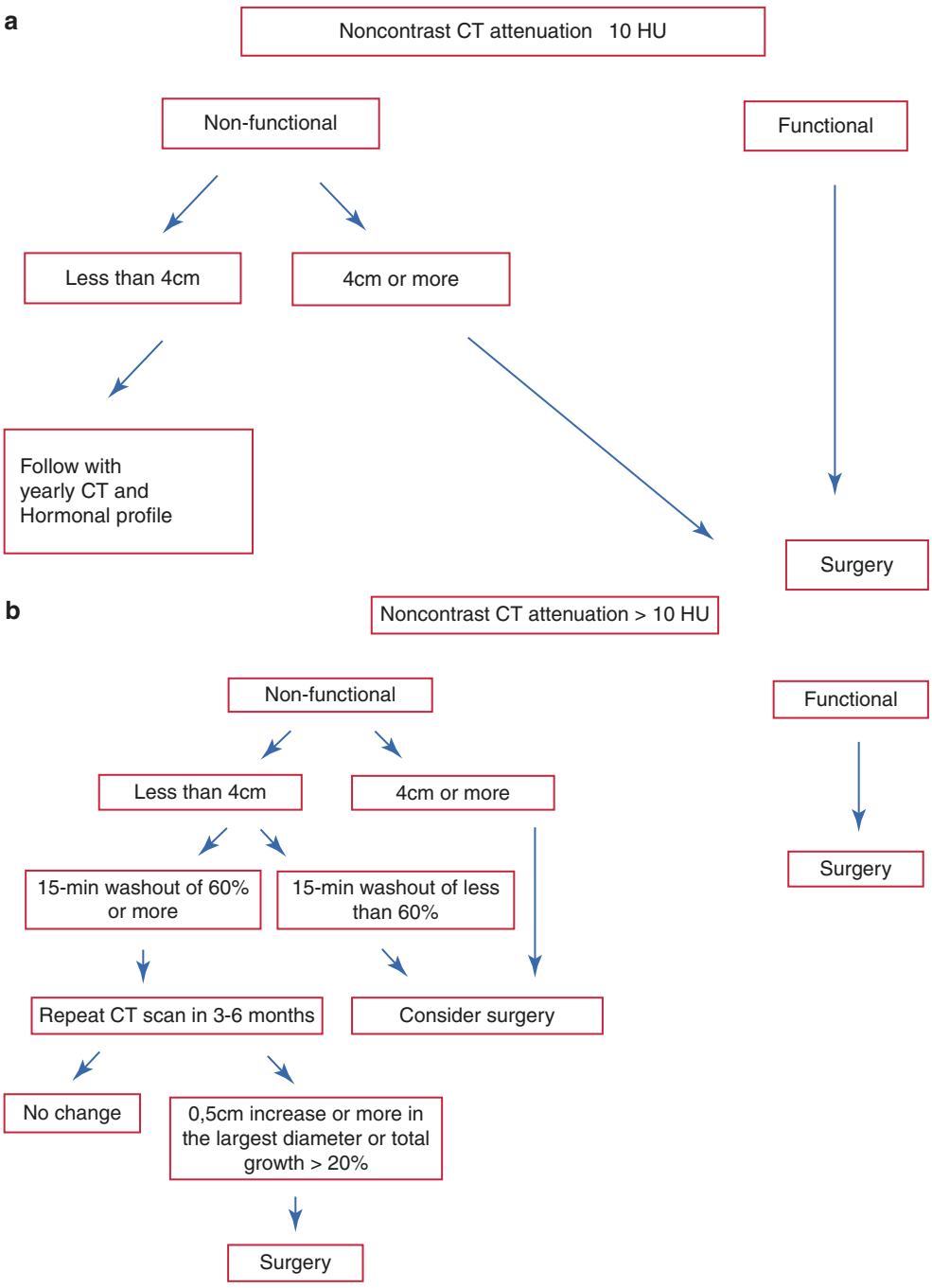
The prevalence of primary hyperaldosteronism, as a cause of arterial hypertension in the general population, has been growing due to its increasing recognition and diagnosis, especially in normokalaemic patients, through routine measurements of aldosterone and plasma renin activity (PARA). Hypertensive patients, hypokalemic or not, demonstrating AI should be evaluated, initially with the aldosterone-plasma renin activity ratio (APRR), providing a diet with normal amount of sodium and, if possible, stopping medications such as spironolactone, diuretics, and beta-blockers that may interfere with measurements [8, 10]. Plasma aldosterone values of more than 15 ng/dl in the presence of an APRR of 20 or more should be considered a positive screening, and dynamic tests are necessary. Additional test should include aldosterone suppression test with 2 L of normal saline infusion over 4 h followed by measurement of plasma aldosterone. Oral captopril 50 mg may be given after 2 h of infusion. At the end of 4-h infusion, plasma aldosterone level above 10 ng/dl confirms the diagnosis of hyperaldosteronism [4].

Pheochromocytomas comprise about 10% of AI cases. Many of these patients are asymptomatic, and half of them have arterial hypertension and adrenergic symptoms which may be paroxysmal. Metaiodobenzylguanidine scintigraphy (MIBG) has almost 100% specificity (albeit with much lower

sensitivity than MRI and CT) and can be used to confirm cases with positive hormonal screening. This should be done with measurements of plasma-free metanephrines or urinary fractioned metanephrines [4, 10]. Plasma catecholamines above 2000 pg/ml or urine norepinephrine above 100 μg/g urine creatinine/24 h or urine epinephrine above 10 μg/g urine creatinine/24 h or urine metanephrine above 2 mg/g urine creatinine is suggestive of the presence of phaeochromocytoma. Highest specificity may be obtained with a plasma free metanephrine value above 1.4 pmol/ml [1, 4, 7, 10]. If this initial endocrine evaluation is normal, a follow-up workup would be necessary only in the setting of clinical symptoms [4].

Patient Follow-Up

The clinical evolution of AI patients who exhibit radiological characteristics suggesting a benign and normal hormonal profile is usually favorable. Some patients (about 20%) progress to hormonal hyperfunction, notably clinically evident hypercortisolism, or PACS and more rarely pheochromocytomas. In those patients with nonfunction lesion with noncontrast attenuation less than 10 HU, a one-time follow-up CT scan in 12 months is recommended [7, 10]. Those with lesion less than 4 cm but more than 10HU should have a CT scan done in 3–6 months and then yearly for 2 years (Fig. 10.2a, b).



Figs. 10.2 (**a** and **b**) Approach to the patient with incidentally discovered adrenal mass, with low (**a**) and high (**b**) attenuation

Treatment

Most lesions can be removed by laparoscopic surgery, including pheochromocytomas, cortisol-producing adenomas (Cushing's syndrome), aldosteronomas, nonfunctional adenomas, lesions suspected of malignancy without signs of local invasion, and, more rarely, cysts or myelolipomas. Tumors larger than 10 cm in diameter should preferably be operated with conventional techniques due to the increased risk of malignancy and the greater difficulty involved in the laparoscopic procedure [4, 12]. Suspected malignancy lesions with evidence of local invasion at imaging should be addressed by open adrenalectomy [4].

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