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Research Article

Diagnostic and Therapeutic Elements of an Adrenal Incidentaloma, a literature review. About a Case

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Abstract

The use of imaging has increased dramatically over the past 3 decades due to technological advances, these diagnostic modalities lead to the increasing discovery of unexpected pathological findings. Consequently, the occurrence and diagnosis of adrenal tumors have increased up to 10-fold, such as adrenal incidentaloma (IS), defined as an asymptomatic adrenal mass detected during an imaging study performed for reasons other than suspected adrenal disease.

Clinical case: A 77-year-old female patient describes chronic abdominal pain; therefore, an abdominal CT scan was requested where a left adrenal space-occupying lesion measuring 5 x 3 cm was observed, due to its malignant potential a laparoscopic left transperitoneal adrenalectomy was performed.

Methods: A retrospective, multicenter study was conducted through a systematic online search from 1990 to 2024, using search terms such as "Risk of malignancy in hypofunctioning adrenal incidentalomas, practice guidelines on the diagnosis and treatment of adrenal incidentalomas, case reports."

Results: 294 studies were identified, of which, after review, 266 did not meet the inclusion criteria or met the exclusion criteria. Of the 28 included studies, 26 conducted a literature review and 2 clinical practice guidelines.

Conclusions: Having an algorithm is essential for surgeons to understand the critical diagnostic and therapeutic steps of an IS, identify characteristics of suspected malignancy, and be able to adequately select those patients who merit surgical intervention.

Keywords: adrenal incidentaloma; adrenal mass; adrenalectomy

Kew Words & Abbreviations: kidneys; ureters; urolithiasis; ureteric calculus; vdr fok1 factor; ureteroscopy; urinary stone relocation /push back, until= urinary tract infections

Introduction

The use of diagnostic imaging has increased dramatically over the past 3 decades due to technological advances, a growing awareness of preventive care, an increasing number of imaging centers, and the prevalence of chronic diseases. Improvements in these imaging modalities, combined with their considerable use, are leading to the increasing discovery of unexpected pathologic findings. [1] Consequently, the occurrence and diagnosis of

adrenal tumors (ATs) have increased up to 10-fold over the past two decades, with smaller ATs being diagnosed at a rate of 1.4%. [2,3]

Among the most common unexpected ATs revealed by CT, MRI, or ultrasound is an incidental adrenal mass, or incidentaloma. An adrenal incidentaloma (IS) is defined as a clinically inapparent adrenal mass greater than 1 cm in diameter detected during an imaging study performed for reasons other than suspected adrenal disease. [4]. The term "incidentaloma" was coined in 1982 by Geelhoed and Druy [5], [who] recognized that, with the advent of improved resolution of radiological techniques, physicians were faced with the unfamiliar dilemma of early diagnosis of an asymptomatic adrenal mass. This strict definition, recognized by the European Society of Endocrinology and the European Network for the Study of Adrenal Tumours (ESE/ENSAT), excludes adrenal lesions discovered during screening of patients with hereditary syndromes or extraadrenal tumors. [2] The overall prevalence of IS increases with age and reaches 3.2% among individuals aged 65 years and older. Approximately two-thirds of patients with IS undergo laboratory studies; 69% have nonfunctioning adenomas, 20% have autonomous cortisol secretion (usually mild), and 12% have primary aldosteronism. [3] The risk of malignancy in SI <4 cm is 0.2% and 4.8% in those measuring 4-6 cm, while those measuring more than 6 cm increase to 37.7%. [6]

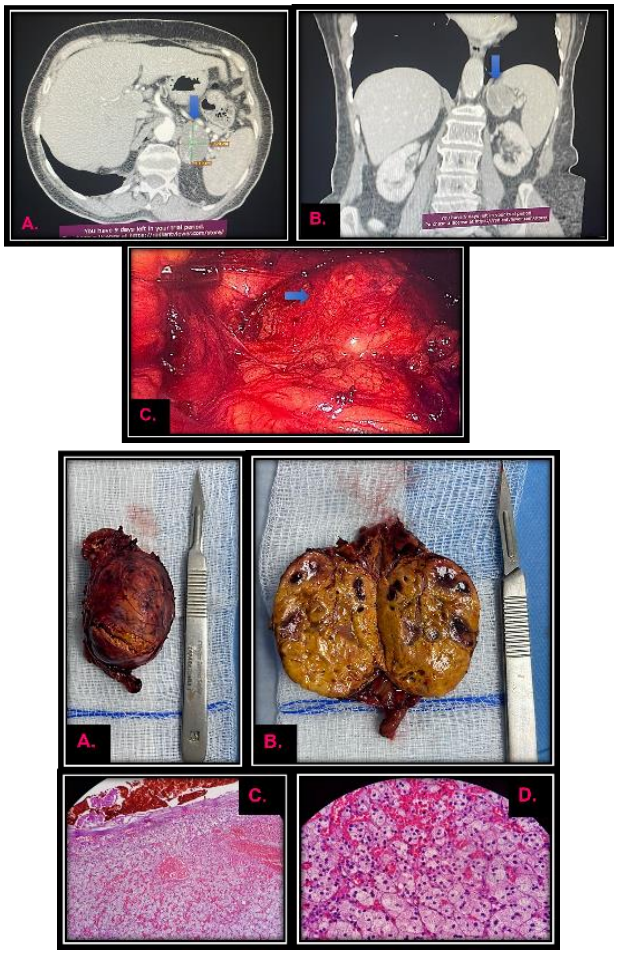
We present the clinical case of a female patient with a TS, whose diagnosis was made fortuitously during a medical radiological examination performed for reasons other than adrenal disease, with a high index of suspicion of malignancy preoperatively.

Case Presentation

A 77-year-old female patient with a history of controlled hypertension describes chronic, poorly localized, mild to moderate abdominal pain with a dull ache. For this reason, an imaging study was requested, a contrast-enhanced abdominal and pelvic tomography (Fig. 1. A - B), where a heterogeneous space-occupying lesion was observed on the left adrenal gland with the presence of neovascularization and indeterminate post-contrast enhancement, where the possibility of neoproliferative origin was not ruled out, size: 51 x 33.8 mm, Hounsfield units 30. Thus, serum laboratory analysis was performed that reported: The nocturnal dexamethasone cortisol suppression test (cortisol less than 1 mcg / dL), Aldosterone 8.3 ng / Dl, Renin 0.8 ng / mL / h, Epinephrine 63 pg / ml, Norepinephrine 203. 3 pg / ml, Dopamine 21.2 pg / ml, Total catecholamines 287.5 pg / ml, post-menopausal LH 14 mU / mL, Basal insulin (fasting) 9.5 uU/mL, Androstenedione 0.85 ng/mL, Cortisol 18.09 µg/dL, Dehydropiandrosterone 260ng/mL, Progesterone <0.1ng/mL, Total testosterone 0.1ng/mL, Estradiol <5ng/mL, and in urine: Aldosterone 2.4mcg/24h, Norepinephrine 31mcg/24h, Epinephrine 3.0 mcg/24h, Dopamine 117 mcg/24h. On physical examination, the patient was in stable general condition, with a BP of 130/80 mmHg, HR 67 BPM, RR 16 RPM, a flat abdomen, present bowel sounds, soft, depressible, nontender to superficial palpation, mild generalized tenderness to deep palpation, no palpable masses, and the remainder of the evaluation was within normal limits.

Treatment Performed

The patient was prepared for surgery and taken to the operating table, where a laparoscopic left transperitoneal adrenalectomy was performed. The findings were: a left adrenal gland measuring 8 x 5 cm with a superficial cortex adenoma measuring 5 x 4 cm (Figure. 1. C). The sample was sent for pathology (Figure. 2. A – B), which concluded that a non-neoplastic adrenal gland with a normal configuration and benign neoplastic nodular structure was determined as a cortical adenoma (Figure. 2. C – D). With satisfactory clinical progress, the patient was discharged 24 hours postoperatively.



Methods

A retrospective, multicenter study was conducted using a systematic search of MEDLINE, Embase, Cochrane, PubMed, and Google Scholar, both in Spanish and English, from 1990 to 2024. The search terms used were "Risk of malignancy in hypofunctioning adrenal incidentalomas, practice guidelines on the diagnosis and treatment of adrenal incidentalomas, case reports," and 294 results were obtained.

- **Inclusion criteria**: Studies in English and Spanish that described the risks of malignancy in hypofunctioning adrenal incidentalomas, practice guidelines on the diagnosis and treatment of adrenal incidentalomas, and clinical case reports with diagnoses of hypofunctioning adrenal incidentalomas with indication and cure by surgical removal were included.
- **Exclusion criteria**: Studies that did not describe the risks of malignancy in hypofunctioning adrenal incidentalomas were excluded. Studies and case reports that did not include surgical removal or surgery as a treatment indication were also excluded.

Results

A total of 294 studies were identified, of which, after reviewing the title, abstract, and keywords, 266 did not meet the inclusion criteria or met the exclusion criteria. Of the 28 included studies, 26 conducted a literature review, and 2 included clinical practice guidelines.

Discussion

Adrenal masses discovered incidentally on imaging studies, initially unrelated to adrenal symptoms, are known as incidentalomas. Patients with this diagnosis, by definition, must not have a history, signs, or symptoms of adrenal disease prior to the imaging procedure that led to their discovery. This strict definition excludes cases in which symptomatic adrenal-dependent syndromes are "overlooked" during the history or physical examination, but it is also subject to some controversy regarding a priori suspicion. An adrenal tumor detected in a patient undergoing abdominal imaging for staging and evaluation of an extra-adrenal malignancy should not be considered an incidentaloma. [7] In this case, the female patient had no history, symptoms, or signs suspicious for adrenal pathology, and her discovery on imaging studies was incidental. The overall prevalence increases with age and reaches 3.2% among people aged 65 years or older. The age of the patient presented in the clinical case is 77 years, relating to the prevalence range of IS. The reason for consultation is usually chronic abdominal pain [8], which is why the patient consulted the medical center where the imaging study was requested. When detected, the diagnostic evaluation aims to determine whether the lesion is hormonally active or not, or if it is a malignant or benign lesion. The result of the study will determine whether the lesion is treated surgically or managed medically. The recommended hormonal evaluation consists of measurements of plasma cortisol and metanephrines, which allows the diagnosis of the most frequent functioning lesions: subclinical hypercortisolism (or subclinical Cushing's syndrome) and subclinical pheochromocytoma. In hypertensive patients, serum potassium, plasma aldosterone concentration, and plasma renin activity should be measured, which will allow for the diagnosis of primary hyperaldosteronism, the leading cause of endocrine hypertension [10]. In the case presented, given a history of arterial hypertension, serum potassium levels were measured and reported to be within normal limits. Regarding the hormonal profile, the nocturnal dexamethasone cortisol suppression test reported less than 1 mcg/dL. Aldosterone and renin values, along with their ratio, were also within normal limits, thus classifying this patient as having nonfunctioning or hormonally inactive IS. [8,9]

Imaging evaluation of IS aims to determine which lesions are at higher risk for malignancy, with the size and appearance of the lesion on CT being the parameters to be evaluated. Although an arbitrary cutoff of 1 cm or more has been used to define an adrenal lesion as an IS, this cutoff may be challenged by the higher resolution offered by modern imaging modalities, primarily MRI and CT [(2)]. Available imaging assessment data for IS suggest dividing lines based on tumor size (<4 cm and >4 cm) and laterality (unilateral vs. bilateral), indicating the proportion of each tumor entity that falls within each cutoff point. Most lesions smaller than 4 cm are benign, and those larger than 6 cm have a significantly increased likelihood of malignancy [8]. This was determined by *Ebbehoj A. et al.* [10], who indicate that "the risk of malignancy is proportional to the size of the tumor", demonstrated this in their population study with 1287 patients, in their results 6% of adrenal tumors <2 cm and 9% of adrenal tumors between 2 and 4 cm were malignant, unlike 34% of adrenal tumors >4 cm that were malignant. In a study of 705 patients with large adrenal tumors >4 cm evaluated in a tertiary center, the prevalence of malignancy was similar to the population setting (31%). [11]. The size of the IS brought for review presented the following measurements: 5.1 cm x 3.38 cm, to be correlated with the aforementioned studies, it is described as a potentially malignant lesion due to this characteristic.

In addition to the size of the IS, Hounsfield units (HU) are also used to assess the risk of malignancy. Since most adrenal adenomas contain a significant amount of intracellular fat and therefore have low attenuation on unenhanced computed tomography (CT), the cutoff value is also used to assess the risk of malignancy. In contrast, almost all malignant lesions have a low intracellular lipid component, and therefore, their attenuation on CT is higher. The threshold value used to diagnose adrenal adenoma by unenhanced CT is 10 HU. If the lesion has fewer than 10 HU on unenhanced CT, it is benign, whereas if it has more than 10 HU, further evaluation is warranted. This cutoff value can be accurately applied to large adrenal tumors >4 cm and to patients at high risk of malignancy, such as those with extraadrenal malignancy. For example, in a study of 705 patients with adrenal tumors >4 cm, the minimum HU values on unenhanced CT in pheochromocytomas, adrenal carcinoma, and metastases were 18 and 14 HU, respectively [8,9]

CTs are now performed with contrast enhancement, so unenhanced attenuation measurements cannot be obtained unless dual imaging is initially performed; and up to 30% of adenomas are lipid-poor and therefore have attenuation values greater than 10 HU. Imaging features that can help distinguish benign or malignant IS on contrast-enhanced CT include enhancement of less than 30 HU in benign adenomas and post-contrast enhancement greater than 30 HU in malignant lesions such as carcinomas and metastases. Another characteristic of contrast-enhanced CT scans is the phenomenon known as contrast washout, in which adenomas rapidly absorb intravenous contrast but also rapidly lose contrast medium on delayed images. Malignant lesions generally enhance rapidly but have slower washout of contrast medium. Therefore, contrast washout kinetics allows a distinction between lipid-poor adenomas and malignant lesions, with an accuracy of 50% or greater on images with a 10-minute delay from a contrast-enhanced CT scan. [12]

Homogeneous, well-circumscribed lesions with attenuation less than 20 HU on contrast-enhanced CT strongly suggest a diagnosis of benign adrenal adenoma. Suspicious or atypical features include heterogeneous lesions with poorly defined borders, the presence of necrosis, hemorrhage, calcification, and an attenuation coefficient greater than 20 HU. [8,9,13] Contrast-enhanced CT of the presented SI revealed a heterogeneous nodule with poorly defined irregular borders and neovascularization. The mean attenuation coefficient was 30 HU and was classified as indeterminate or suspicious. The suitability of surgical intervention should be guided by the likelihood of malignancy, the presence and degree of hormonal excess, age, general health, and patient preference. [6] The female patient is 77 years old, in adequate physical and psychosocial condition. As a comorbidity, she has a diagnosis of controlled arterial hypertension not associated with hypertension of endocrine origin and a nonfunctioning SSc, but with malignant potential based on the imaging findings described above.

Regarding imaging characteristics, tumor size alone should not determine the need for adrenalectomy. For example, a purely nonfunctioning tumor with benign imaging characteristics larger than 4–6 cm does not necessarily require resection based on size alone. Myelolipomas and other benign adrenal tumors can grow to quite large sizes without causing significant

symptoms. Local symptoms of compression in the form of pain or early satiety are not well studied, but tumors can grow to quite large sizes and result in minimal symptoms. If a benign-appearing tumor reveals evidence of rapid growth at 6–12-month follow-up examinations, resection is indicated. The decision to perform resection may also be made for benign-appearing nonfunctioning tumors that reach 6 to 10 cm because tumors of this size are still potentially amenable to a minimally invasive approach. With growth, an open approach is more likely to be needed simply to remove the tumor through one incision because morcellation of an adrenal tumor must be avoided to allow for adequate pathologic examination. Furthermore, patient age and comorbidities should be considered to aid in the decision-making process regarding resection of benign nonfunctioning tumors. In younger patients, continued follow-up for many years increases medical costs, and the patient may prefer resection sooner rather than later, especially when the patient is still healthy and has few comorbidities. [8,9,13]

Patients with evident hormonal excess due to a unilateral adrenal tumor are more often offered surgery rather than medical treatment. Each patient's anatomy must be carefully considered when selecting a surgical approach. The approach is not based solely on size, but also includes prior surgical history, concern for malignancy, and cardiac and pulmonary status in terms of tolerance to laparoscopy. The position of the adrenal gland relative to the renal vasculature and the upper pole of the kidney is important in the selection of an anterior or posterior approach. [8,9,13] These anatomical features are important when choosing between a laparoscopic or retroperitoneal approach. The laparoscopic transperitoneal approach is the most common for small benign tumors; an alternative approach, for those experienced in adrenal surgery, is the posterior retroperitoneal approach. Mobilization of the spleen and liver is not necessary, and blood loss is often reduced due to increased insufflation pressures and the need for less mobilization of adrenal structures. [8,9,13]

To summarize, there are four fundamental critical steps that must be followed in the management of an IS: the first is to evaluate adrenal hormone excess; the second is to assess the risk of malignancy; the third step is to identify which patients should undergo surgery and what type of approach; and finally, the fourth step is to determine the appropriate follow-up for those patients who do not undergo surgery. [8,9,13] The IS in this case was classified as hormonally nonfunctioning, with malignant potential and with surgical criteria. Therefore, the patient underwent surgery and a laparoscopic transperitoneal adrenalectomy was performed. The pathological findings reported a benign cortical adenoma.

Conclusion

It is important for surgeons evaluating patients with IS to understand the critical diagnostic and therapeutic steps through appropriate biochemical and radiological interpretation. They must be familiar with the imaging characteristics of various benign and malignant adrenal lesions to appropriately select patients for surgery. There are multiple pathologies that can affect the adrenal glands, both local and metastatic; therefore, having a diagnostic algorithm is essential, allowing for appropriate management of IS.

Conflict Of Interest: The authors declare that they have no conflict of interest.

Informed Consent: Informed consent was obtained from all participants included in the study.

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