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Adrenal Incidentalomas: Diagnostic, Etiological and Therapeutic Aspects

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Abstract

Introduction: Adrenal incidentalomas have been increasingly diagnosed, thanks to advances in medical imaging and its growing use in the general population. They represent a diagnostic challenge due to their heterogeneous nature and malignant potential. This work illustrates the importance of optimal and appropriate management and, above all, of limiting exploration and morphological follow-up when the mass is initially benign in appearance. **Patients and Methods:** In a retrospective study spanning 12 years and including a total of 25 patients, all had an adrenal mass discovered incidentally. **Results:** In our study, adrenal incidentalomas had a prevalence of 11.27%, with a mean age of 54.9 years, and were mainly discovered incidentally during abdominal imaging. Clinical, hormonal and radiological evaluation, dominated by the use of a CT scan in 80% of cases, identified mostly non-functional adenomas in 64% of cases, pheochromocytoma, Conn's adenoma, MACS in equal proportions, with appropriate management based on risk of malignancy or hormonal activity. **Ethical Considerations**: in accordance with the regulation in force, informed consent, written and verbal, was provided by the patients concerned by the study.

Keywords

Adrenal Incidentalomas (AI), Non-Functioning Adenoma, Medical Imaging

1. Introduction

Diagnostic imaging has undergone a revolution over the last three decades, with major advances aimed at improving the prevention and early diagnosis of numerous pathologies. These advances are particularly important as the prevalence of certain diseases continues to rise, especially among vulnerable populations [1].

This scientific progress has led to an ever-increasing detection of unexpected pathologies, among which incidental adrenal masses, commonly known as "inci-

dentalomas", are among the most frequently observed [1].

The term "adrenal incidentaloma" refers to an adrenal mass identified incidentally on abdominal imaging, without any pre-existing clinical suspicion of adrenal pathology [1] [2].

The main challenge is therefore to know when to opt for surgery, without unnecessarily increasing the cost of the procedure, or to opt instead for monitoring, after having carried out a thorough evaluation of the load-bearing mass in terms of both secretion and morphology [3] [4].

Several recommendations have been attributed to this pathology, the most recent of which dates from 2023, produced by the European Society of Endocrinology (ESE) in collaboration with the European Network for the Study of Adrenal Tumors (ENSAT) [1] [3].

In this context, this study is based on data from the literature and on a retrospective analysis of cases recorded in the Endocrinology and Diabetology departments of the Mohamed V Military Training Hospital in Rabat, in order to gain a better understanding of the clinical and radiological features of adrenal incidentalomas and to identify risk factors to guide their clinical management [4].

2. Patients and Methods

This study is a retrospective descriptive analysis of 25 cases of adrenal incidentalomas (AI), collected in two hospitals: the Mohamed V military training hospital (2012-2024) and the Avicenne hospital (2020-2024).

Patients included were those presenting with an adrenal incidentaloma with a complete clinical record.

Patients with a previous diagnosis of adrenal pathology, signs suggestive of adrenal pathology or pregnant women were excluded.

The study involved a total of 295 adrenal pathology cases at the Mohamed V military training hospital (2012-2024) and 176 cases at the Avicenne hospital (2020-2024). Of these, 33 cases of adrenal incidentalomas (AIs) were identified at Mohamed V Hospital, of which 15 were actionable, and 20 cases at Avicenne Hospital, of which 10 were actionable.

The data analysed included: Epidemiology; Circumstances of discovery; Clinical, biological and radiological analysis; Anatomopathological analysis, Selected etiology, Management and finally Follow-up according to the nature of the mass.

This protocol enables a complete evaluation of SI, from diagnosis to management and evolution.

3. Result

Epidemiology

The average prevalence of IS in this population is estimated at 11.27%, with a mean patient age of 54.9 years, ranging from 16 to 80 years.

Circumstances of discovery

Adrenal incidentalomas (AIs) were mainly discovered during investigations for

abdominal or lumbar pain (9 cases) and renal colic (6 cases).

Other situations have led to their discovery, notably during investigations for hepatic colic with cholecystitis, chronic cough, haemoptysis, bilateral sciatica, flu-like symptoms with dizziness, or following the chance discovery of an abdominal mass.

In terms of the radiological examination used to detect IS, CT was the main imaging modality. Abdominal CT scans were used in 50% of cases.

Clinical analysis

Questioning revealed several antecedents cited below (Figure 1).

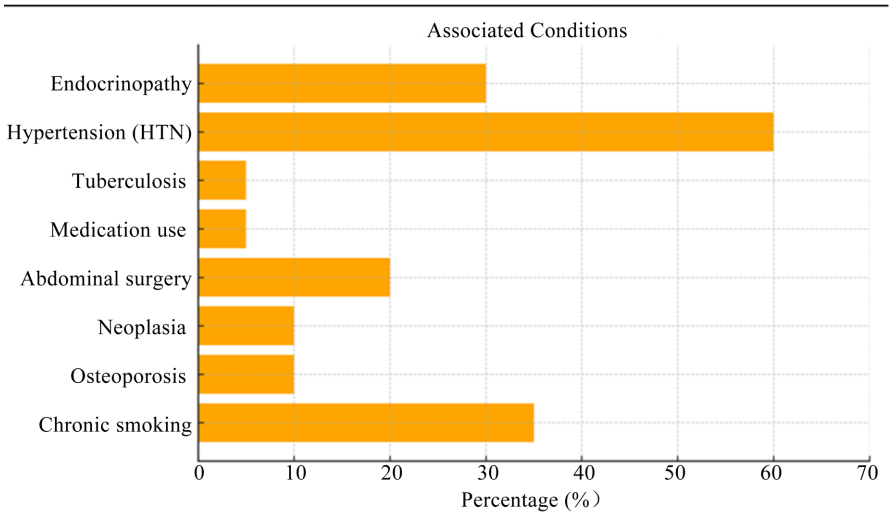

Figure 1. Bar chart representing the antecedents sought in our series.

With regard to functional signs related to hormonal impregnation, our patients were mostly asymptomatic, while a menard's triad and a state of hypercorticism were found, as well as an altered general condition.

Hormone analysis

All patients underwent a secretory profile guided by clinical symptoms and the suggestive picture, *i.e.* urinary methoxylates, urinary free cortisol, dexamethasone brake test and exploration of the renin angiotensin aldosterone system, the latter being requested in the presence of arterial hypertension and/or hypokalemia.

Tumor marker assays were performed in a category of patients presenting with bilateral incidentalomas with altered general condition, and returned negative.

Of the 25 cases of adrenal incidentaloma, 16 were non-secretory, *i.e.* a prevalence of 64%.

X-ray analysis

Radiological analysis of adrenal incidentalomas relies mainly on computed tomography (CT), which is used in 80% of cases. In some cases, additional examinations have been carried out, in particular adrenal MRI, PET-SCAN in cases of suspected neoplasia, and thoraco-abdomino-pelvic and cervico-thoraco-abdomino-pelvic CT.

Overall, the choice of examination depends on the nature of the mass, the initial imaging and the patient's history.

Radiological imaging can be used to analyze the characteristics of the mass, including its size, density and absolute and relative wash out.

In our study, lesion size was less than 4 cm in over 76% of patients. Suspicious density (> 20 HU) was observed in 28% of cases, while non-suspicious density (< 10 HU) was also found in 28% of cases. When the density was suspect, the calculated wash-out was mostly reassuring, with values above 60% absolute and 40% relative in more than 60% of cases.

Moreover, in the face of diagnostic impasse using the means described above, an adrenal biopsy was indicated in one patient after ruling out a pheochromocytoma, which was not performed due to the inaccessible location to the radiologist.

In the end, after all these clinical, biological and radiological investigations, the diagnosis retained was dominated by non-functioning adrenal adenomas in 64% *cases* (**Figure 2**).

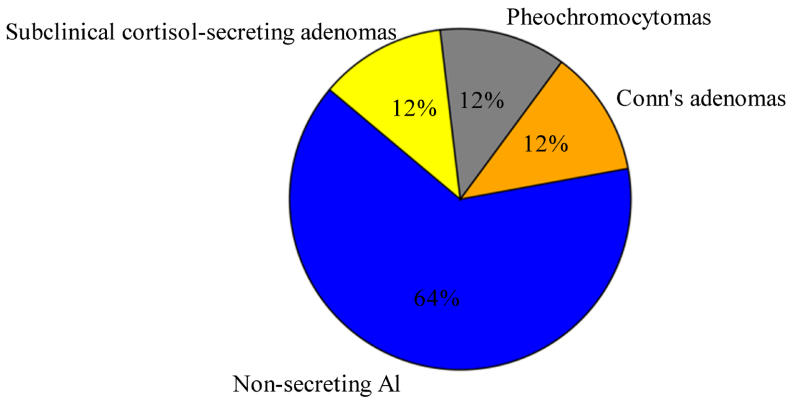

Figure 2. Pie chart showing the percentage distribution of IS etiologies in our series.

Therapeutic management

After establishing the diagnosis by evaluating the secretory character or suspicion of malignancy on morphology, the indication for surgical resection was established in 4 patients with the presence of a pheochromocytoma, congenital adenoma, MACS with a suspicious appearance on imaging, a mass exceeding 4 cm and displaying signs suggestive of malignancy on imaging.

A medical preparation was started before any surgery to neutralize hormonal impregnation.

In cases where surgical treatment was not chosen, medical treatment was initiated to curb hypersecretion, using a corticoid mineral antagonist in the case of bilateral primary hyperaldosteronism, or ketoconazole in the case of MRI-negative cushing's disease.

As part of the follow-up of non-functioning adenomas, an endocrinology consultation was scheduled at 6 months, with a biological workup (fasting blood glucose, urinary methoxylates, dexamethasone minute braking test, kalemia) and an

adrenal CT scan. Biological and scannographic re-evaluation was then scheduled at 2 and 5 years.

Operated adrenal masses were followed up biologically and morphologically to assess the efficacy of surgery and detect any recurrences.

4. Discussion

The prevalence of adrenal incidentalomas varies according to the size considered pathological and the type of radiological examination used. Generally speaking, only tumors larger than 1 cm are taken into account; below this size, they are rarely clinically significant [5].

According to the European Society of Endocrinology, autopsy and radiological studies estimate this prevalence at 2 to 3%, with a range from 1% to 10% [6].

In the study conducted, the observed prevalence is higher, reaching 11.27%, and this can be explained by:

- IS discovered by any type of imaging test
- Adrenal lesions of all sizes, including those < 1 cm

This high rate found in our series may also be explained by the performance of the imaging techniques used, and also by the existence of obesity, diabetes or hypertension) found predominantly in our patients [5].

The rate of SI is also influenced by age, and is higher the older the subject is [7] [8].

In our study, the mean age was 54.9 years, with extremes of 16 and 80 years, and a peak age of discovery between 50 and 70 years, which is in line with the literature and with the results of Dr. Jaafor's study (mean age 56.6 +/− 16.8).

There is a slight female predominance in our series, with a sex ratio of 0.92, *which is in line with data in the literature and Dr Bensbaa's series, and can be explained by iterative consultations by women* [9].

In our series, adrenal incidentalomas were most frequently discovered during abdominal-lumbar pain, closely followed by renal colic. These circumstances are broadly in line with the literature, which, although heterogeneous, also reports a predominance of abdominal pain as the main reason for discovery [7] [10] [11].

Radiological examination by *CT scan accounts for* 96% *of adrenal incidentalomas, while abdominal ultrasonography accounts for only* 4%. *This is in line with data in the literature and with the Tabuchi et al. series and that of Dr. Jaafor* [12] [13].

In the literature, MRI is the second most revealing examination for SI, whereas in *our series it was not revealing in any case. This is an expensive examination, which is still not very accessible for our population* [5].

The patient's history is a key step in guiding the clinician to the underlying cause, and also in detecting possible comorbidity secondary to excessive hormone impregnation.

Over 80% *of patients showed signs of catecholamine or cortisol impregnation, and only* 4 *patients in our series were asymptomatic, in contrast to the literature.*

This richness is explained by the systematic search and analysis, in line with international consensus recommendations, of all data that could be linked to the various possible diagnoses of SI.

One of the two main questions to ask when faced with an adrenal incidentaloma is: Is it secretory? To answer this question, it is necessary to carry out a hormonal evaluation to look for subclinical secretion of cortisol, aldosterone, catecholamines and steroid sex hormones.

The methoxylate assay was requested in all patients, although in accordance with the latest ESE 2023 guidelines, this assay should only be performed in patients with adrenal lesions whose characteristics are not typical of a benign adenoma (DS > 10 HU) [6].

In our series, two assays came back conclusive and concordant with the CT scan

Research into autonomous cortisol secretion, recently referred to as MACS, using dexamethasone minute braking at a dose of 1 mg with a cut-off of 1.8 ug/dl, should be carried out systemically, particularly in the presence of a metabolic syndrome, except in the frail elderly population over 65, in whom this test is of little relevance [14] [15].

All guidelines recommend measuring the plasma aldosterone-to-renin ratio in patients with concomitant hypertension and or unexplained hypokalemia in order to assess primary hyperaldosteronism [6].

Exploration of this system should have been carried out in 18 patients, but in our context only in 10, given the meticulous conditions of preparation prior to carrying out the workup, which remains restrictive in a category of patients [6].

Finally, sex steroids were found to be negative in all patients who benefited from this assay, and it is therefore recommended that they be measured by multi-steroid mass spectrometry profiling in the event of clinical or radiological suspicion of adrenocortical disease [6].

In the literature, non-functioning tumors predominate, accounting for 40% - 70% of adrenal incidentalomas, which *is in line with the results of our study, which showed that* 64% *of IS found were non-secreting* [16].

In the presence of a bilateral lesion, it is essential to first rule out adrenal insufficiency by measuring cortisol levels at 8 hours, or even performing a Synacthen test. In addition, the aforementioned investigations should be completed by measuring 17-hydroxyprogesterone [16].

Once the secretory or non-secretory nature of the mass has been determined, it is essential to distinguish benign from malignant adrenal tumors. Three main imaging techniques are used: computed tomography (CT), magnetic resonance imaging (MRI) and 18F-FDG tomsitometry (FDG-PET/CT).

The ESE 2023 guidelines call for a rigorous assessment of the risk of malignancy from the very first imaging. Non-contrast-injected computed tomography (CT) is preferred to analyze the size, homogeneity and lipid content of the lesion, notably by calculating its spontaneous density [16].

All our patients underwent a CT scan.

Finally, in the absence of any conclusion after the investigations previously de-

scribed, adrenal biopsy remains a diagnostic option. In our context, it was recommended for a single patient, but was not performed.

This invasive procedure is discouraged by all learned societies, and is only considered in specific cases, notably in the presence of a history of extra-adrenal malignancy associated with a high risk of metastasis to the adrenal gland [6].

The indication for surgical resection was based on the tumor's secretory nature, size and suspicious morphological appearance.

The surgical indications for our patients were consistent with international recommendations in terms of size, probable malignancy and secretory profile of IS.

Hormonal follow-up at 6 *months*, 1 *year and* 2 *years. None of these adenomas became functional, supporting the value of changing the recommendations in* 2023*. In our study*, 90.9% *of non-functioning adrenal adenomas were discovered before the recommendations were modified in* 2023*.*

However, ESE guidelines, including the 2023 guidelines, do not recommend additional functional testing for adrenal tumors deemed non-functional at initial hormonal evaluation, except in the event of new clinical symptoms [14].

Furthermore, they point out that MACS rarely progresses to overt Cushing's syndrome (<1%) and that the dexamethasone suppression test can sometimes lead to false-positive results [14].

However, patients with MACS should be monitored for possible metabolic complications.

From a morphological point of view, adenomas initially classified as benign on imaging and reassessed at 6 months either remained stable in size or regressed. Morphological follow-up is therefore not necessary for nodules with a spontaneous density of less than 10 HU, regardless of size.

5. Conclusions

At the end of this work, we note that the discovery of SI has become increasingly frequent, thanks to the population's improved accessibility to medical services and radiological imaging techniques.

At the end of 2023, the *European Journal of Endocrinology* published new ESE recommendations on the management of IS in adults. Compared to those of 2016, they favor a more individualized approach, with adjustments in malignant risk assessment, hormone testing and surgical indication.

These modifications aim to improve the prognosis of IS by optimizing etiological diagnosis, therapeutic orientation (surveillance, medical treatment or surgery) and follow-up modalities. They also make it possible to limit unnecessary investigations, thereby reducing the financial and mental burden on patients.

Declarations

Ethics Approval and Consent to Participate

The study did not require approval from an ethics committee. Verbal consent was

obtained from all patients involved.

Consent for Publication

Verbal consent for publication was obtained from all patients.

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Authors' Contributions

Dr Malak Riznat contributed to data collection, analysis, and drafting of the manuscript. Prof Jade Issouani and Dr Hajar Srifi supervised the clinical aspects and contributed to manuscript revision. Prof Ahmed Anas Guerboub provided senior oversight and critical revision of the manuscript. All authors read and approved the final manuscript.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that they have no competing interests.

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