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Overview of Adrenals Tumors in Dakar Hospitals

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Abstract

Introduction: Adrenal tumours (AT) are commonly encountered in clinical practice. For any patient presenting an adrenal mass, there are two crucial points to consider: is the adrenal mass malignant and is it hormonally active? The objective of our study was to evaluate the epidemiological, diagnostic, therapeutic, and evolutionary aspects of AT in a developing country. **Methodology:** We conducted a retrospective study spanning 17 years (from January 2005 to October 2022) in four Dakar hospital services. We included all patient medical records with explored AT. **Results:** AT was diagnosed in 35 patients who had a mean age of 36.62 years (range: 12-79), and a female predominance (26 women to 9 men). Among these patients, 17.2 % had incidental AT. Hypertension was the commonest presenting symptom in 27 patients (77%), which was associated with Ménard's triad in 14 patients (40%). Abdominal pain was reported by 20 patients (57%), and 14 presented with an abdominal mass. Among the patients, 29 had functional AT: 22 with pheochromocytoma, 5 with primary hyperaldosteronism, and 2 with hypercortisolism. Imaging evaluations revealed that 33 patients had unilateral AT and one had bilateral AT. Tumour sizes varied, 5 patients had tumours <4 cm, 20 patients had tumours between 4 and 10 cm, and 10 patients had tumours >10 cm. Two patients presented with metastases. The therapeutic approach involved adrenalectomy in 32 patients. Perioperative complications were observed in five patients, including haemorrhage (two patients), hypotension (two cases), and hypertensive crisis (one case). One patient with bilateral pheochromocytoma developed acute adrenal insufficiency postoperatively, followed by abdominal herniation. Histopathological examination confirmed

pheochromocytoma in 21 patients, Conn's adenoma in 5, adrenocortical carcinoma in 3, cortisol adenoma in 2, and adrenal cyst in 1 patient. Non-functional AT included adrenocortical carcinoma (three patients), adrenal cyst (one patient), and pheochromocytoma (two patients). After a one-year follow-up, 29 patients with benign tumours had favourable outcomes, while death occurred within six months of diagnosis in five cases. A patient who had bilateral pheochromocytomas, with complications, died before surgery. **Conclusion**: In our practice, AT are predominantly pheochromocytomas, being typically diagnosed when they become symptomatic large tumours and, due to this large size, laparotomy is the preferred surgical approach. Unfortunately, the prognosis for malignant tumours is poor.

Keywords

Tumour, Adrenal, Pheochromocytoma, Conn, Adrenocortical Carcinoma, Dakar

1. Introduction

Before the advent and widespread availability of cross-sectional imaging, adrenal tumours (AT) were considered a rare entity that largely went undetected unless they were of large size and compressed adjacent organs or manifested with clinically overt hormone excess [1]. With ongoing advances in cross-sectional imaging techniques, the rate of incidentally discovered adrenal masses has increased to approximately 5% of patients undergoing abdominal computed tomography (CT) [2]. The most prevalent types of benign AT are adenomas followed by pheochromocytomas [3]. The two most frequent primary malignant AT are adrenocortical carcinoma (ACC) and pheochromocytoma [4]. Based on the hormone type, functioning adrenal masses can be classified as cortisol-producing tumours, aldosterone-producing tumours, and androgen-producing tumours, which originate in the adrenal cortex, as well as catecholamine-producing pheochromocytomas, which originate in the medulla [5]. CT is often the first-line approach for adult adrenal imaging due to its wide availability, reproducibility, good temporal resolution, and better spatial resolution than MR (magnetic resonance) imaging [6]. The therapeutic approach depends on the clinical context, whether the AT are secreting hormones or not, and the presence of malignancy criteria [7]. Our study aimed to evaluate epidemiological aspects, diagnostic circumstances, therapeutic strategies, and evolutionary outcomes of AT in a developing country.

2. Patients and Methods

We conducted a retrospective study over 17 years (from January 2005 to October 2022) based on four Dakar-based hospital-university services: Internal Medicine-Endocrinology, Internal Medicine, and two General Surgeries. We col-

lected data from the medical records of all patients hospitalized in these four services to manage AT. Only patient records with hormonal measurements were considered, including corticotrope axis, renin and aldosterone secretion, and catecholamine levels.

The following information was gathered from the selected patient medical records:

- Epidemiological data: age, sex, personal or family history of neuroendocrine tumours, or conditions related to genetic syndromes associated with AT.
- Clinical data: circumstances of AT discovery, associated signs.
- Paraclinical data: results of hormonal exploration, tumour localization, size, and number of AT, presence or absence of metastases, and genetic study.
- Therapeutic and follow-up data: therapeutic indication (surgery or medical treatment), histological report, and treatment response with a one-year follow-up.

Descriptive statistics were performed using SPSS version 26.0. Quantitative variables were expressed as mean (±SD) and qualitative variables as numbers and percentages. All patients treated at our university hospital centres were informed that their medical records may be used for scientific publications while respecting their anonymity. Being an observational study, there were no ethical concerns.

3. Results

This study included 35 observations of patients with AT.

3.1. Epidemiological Data

The mean age of patients was 39.62 years (range: 12 - 79); twenty-four patients were under 40 years of age. There was a predominance of females, with 26 women (74%) and 9 men (26%). Any personal or family history of neuroendocrine tumours or a context suggestive of genetic syndromes was reported.

3.2. Diagnostic Data

AT were functional in 29 patients; two patients had Cushing's syndrome. In 27 patients (77%), the circumstance for discovery was hypertension, which was associated with a triad of headaches, palpitations, and sweating in 14 patients (40%). The hypertension was of Grade 3 in 31%, Grade 2 in 34%, and Grade 1 in 12% of patients; the permanent or paroxysmal pattern of hypertension was not specified. Hypertension complications included hypertensive heart disease in eight patients (22%), hypertensive retinopathy in two, and nephroangiosclerosis in one. Abdominal pain was reported in 20 patients (57%), and an abdominal mass was noted in 14 patients (40%). In five patients, AT were incidental. Poor general health was reported in three patients. No signs suggestive of hyperandrogenism were outlined in any of the records. Hormonal exploration revealed catecholamine hypersecretion in 22 patients (62%), primary hyperaldosteronism

in 5 (14%), and non-ACTH-dependent hypercortisolism in 2. Adrenal insufficiency was observed in six patients (18%). None of the patients had undergone androgen level measurements or genetic investigation. Abdominal ultrasound, performed on 15 patients (42%), consistently detected an adrenal mass. All patients were subjected to an abdominal CT, which allowed the objective assessment of the adrenal mass and its characteristics: dimensions, number, and possible presence of metastases. CT scans revealed unilateral AT in 33 patients and bilateral AT in 2 patients. Among these patients, five had a tumour size <4 cm, 20 had tumours of between 4 and 10 cm, and 10 patients had tumours >10 cm. Two patients with pheochromocytomas presented with metastases; one had hepatic metastases and invasion of the right renal vein, while the other had pulmonary metastases, retro-caval vascular invasion, and involvement of the right hepatic and homolateral renal areas. Intra-tumoural necrosis was noted in three patients. No female patient underwent MRI or nuclear imaging

3.3. Treatment Data

All symptomatic patients had received medical treatment based on antihypertensive and/or analgesic medications. Adrenalectomy was performed in 32 patients, including one case of bilateral adrenalectomy. The surgical approach was laparotomy in 29 patients and laparoscopy in 3. Histological findings revealed pheochromocytomas (21 patients), Conn's adenoma (5 patients), and ACC (3 patients). Additionally, there were two patients with cortisol-secreting adenomas and one with a renal cyst. Unfortunately, a female patient with bilateral pheochromocytoma died before surgery. In two patients, the diagnosis of malignant pheochromocytoma was promptly established due to secretory syndrome and the presence of metastases. Following a multidisciplinary consensus meeting, chemotherapy based on Cyclophosphamide, Vincristine, and Dacarbazine (CVD) was decided. The diagnosis of corticosurrenaloma was only confirmed postoperatively, in which postoperative polychemotherapy with CVD was also proposed.

3.4. Evolutionary Data

Immediate postoperative outcomes were simple in 27 patients. Three patients experienced haemodynamic instability during surgery, which was successfully managed, and two had haemorrhagic complications. Notably, a case of acute adrenal insufficiency occurred in the patient with bilateral pheochromocytoma, which required reanimation and subsequent endocrinological care. This same patient developed an abdominal eventration 12 days post-procedure, requiring surgical intervention with an unremarkable outcome. Unfortunately, the evolution of the two patients with malignant pheochromocytoma was poor; one patient died before commencing chemotherapy, while the other died after two cycles. The three patients with ACC also did not survive. Outcomes were uneventful in the other patients. A female patient with bilateral pheochromocytoma and hypertension-related complications, including hypertensive cardiopathy,

stage 4 nephroangiosclerosis, and hypertensive retinopathy, died before surgery. Table 1 summarises the epidemiological, diagnostic, therapeutic, and evolutionary patterns depending on the type of AT.

4. Discussion

The prevalence of AT varies depending on the study, with most results reported in the literature deriving from radiological or autopsy series [1]. The most prevalent types of benign AT are adenomas followed by pheochromocytomas. Additionally, adrenocortical adenoma is the primary cause of adrenal incidentaloma [3]. The two most frequent primary malignant AT are ACC and pheochromocytoma [4]. Overall, adrenal metastases are the most common malignant lesions affecting the adrenal glands [3]. Although exceedingly rare, lymphoma and

Table 1. The distribution of patients according to epidemiological, diagnostic, therapeutic, and evolutionary patterns depending on tumour type.

Type of tumour	Pheochromocytoma	Conn's adenoma	Cortisol-secreting adenoma	Adrenocortical carcinoma	Adrenal cyst
Number of cases	24	5	2	3	1
Mean age (years)	37.9	42.6	63.5	34	28
Sex	6 Men 18 Women	1 Man 4 Women	1 Man 1 Woman	1 Man 2 Women	1 Woman
Circumstances of discovery	Systematic = 22 Incidental = 2	Systematic = 3 Incidental = 2	Systematic = 2	Systematic = 3	Incidental
Secreting pattern	Functional: 22 Non-functional: 2	Functional: 5	Functional: 2	Non-Functional: 3	Non-functional
CT scan	Unilateral AT = 2 Bilateral AT = 2 Metastases = 2 Size (4 - 10 cm): 18 Size > 10 cm: 6	Unilateral AT = 5 Size < 4 cm: 4 Size (4 - 10 cm): 1	Unilateral AT = 2 Size < 4 cm: 1 Size (4 - 10 cm): 1	Unilateral AT = 3 Metastases = 2 Size > 10 cm: 3	Unilateral AT Size (4 - 10 cm)
Treatment	Surgery = 21 Chemotherapy = 2	Surgery = 5	Surgery = 2	Surgery then chemotherapy = 3	Surgery
Outcomes	Favourable outcomes in 21 benign operated pheochromocytomas Death: -2 malignant pheochromocytomas -1 bilateral benign pheochromocytoma before surgery	Favourable outcomes	Favourable outcomes	Death: 3 patients	Favourable outcome

sarcoma may also originate from the adrenal glands [3]. In our series, pheochromocytoma was the most frequent AT type, followed by adenomas and corticosurrenaloma. One patient presented with an adrenal cyst and malignant tumours accounted for 14.28% of AT. The higher prevalence of pheochromocytomas compared with adenomas could be partly explained by the circumstances under which AT were discovered in our patients. Specifically, 85% of patients had symptomatic adrenal pathologies, whereas, in larger series, the most common mode of AT discovery is incidentaloma [1] [3] [4].

The most frequent circumstance in which adrenal pathology was discovered was hypertension, accounting for 77% of our patients with functional tumours. Primary hyperaldosteronism (PA) is the leading cause of secondary hypertension, with a prevalence ranging from 2.6% to 12.7% among hypertensive individuals. The prevalence of PA is related to the severity of the hypertension, reaching 20% in patients with resistant hypertension [8]. Other adrenal causes of hypertension are rarer: cortisol-secreting adenomas (occurring in less than 0.5% of hypertensive patients) and pheochromocytomas (affecting 0.2% to 0.5% of hypertensive individuals) [9]. Secondary hypertension should be suspected in patients under 30 years old with no other risk factors, resistant hypertension, grade 3 or paroxysmal hypertension, non-dipper subjects, and the presence of complications at the time of diagnosis [9]. This hypertension was found in all patients who had a functional pheochromocytoma and a cortisol adenoma, however, it was only present in four of the five patients with Conn's adenoma. For our patients, hypertension was grade 3 in 31% of cases and was complicated by hypertensive heart disease in eight patients, hypertensive retinopathy in two, and nephroangiosclerosis in one. The association of hypertension with the triad of headaches, palpitations, and sweating is pathognomonic of pheochromocytoma [10]. This was present in 14 out of 22 patients, accounting for 63.63% of functional pheochromocytomas. Twenty patients (57%) reported abdominal pain and an abdominal mass were noted in 14 patients (40%). The abdominal tumour syndrome is more commonly reported as the mode of presentation of malignant tumours [4], which has also been described in other African series [11] [12]. This unusual clinical presentation could be attributed to the large size of AT in our patients, 20 had AT of between 4 and 10 cm, and 10 had tumours larger than 10 cm. The large size of the tumours could also explain the performance of abdominal ultrasound in our study [13], which was performed in 15 patients (42%) and consistently revealed an adrenal mass. CT is often the preferred initial imaging approach for adult adrenal evaluation due to its widespread availability, reproducibility, good temporal resolution, and superior spatial resolution compared with MR imaging. Other imaging techniques, such as MRI and PET (positron emission tomography) with fluorodeoxyglucose (FDG) or other specialized radioactive tracers like gallium-68 DOTATATE, are valuable complementary tools when CT results are negative or inconclusive [6].

The size of an adrenal mass can be predictive of malignancy. When larger than 6 cm, the proportion of malignant tumours is 25%. Regarding ACC, the

specificity is 98% for tumours >10 cm [14]; in our series, all three patients with an ACC diagnosis had tumours >10 cm. Intra-tumoural necrosis is also suggestive of ACC. In the case of pheochromocytoma, the only criterion for malignancy was the presence of secondary locations in organs lacking chromaffin tissue, which, in order of frequency, include lymph nodes, bones, liver, lungs, and kidneys [4] [6] [13]. In our two patients, the diagnosis of malignant pheochromocytoma was confirmed based on the presence of hepatic metastases associated with renal vein invasion in one case, and pulmonary metastases associated with vascular invasion in the other. The diagnosis of ACC could only be established postoperatively. In all three cases, the tumours were non-functional. Approximately 40% of patients with ACC present hormonal manifestations such as Cushing's syndrome; virilization or feminization secondary to excess androgen or oestrogen, respectively; or Conn's syndrome. ACC usually presents as a large (>6 cm) heterogeneous mass due to haemorrhaging and central necrosis, and calcification is present in 30% of ACC [6]. In the patients with corticosurrenaloma, only cortisol hypersecretion was evaluated, and none underwent sex steroid testing. However, no signs of virilization or feminization were reported in their observations. The other non-functional tumours included two pheochromocytomas and one adrenal cyst.

The role of percutaneous biopsy in the aetiological diagnosis of non-functional AT is very limited. First and foremost, infraclinical pheochromocytomas must always be ruled out. In cases of suspected ACC, a biopsy is contraindicated due to the risk of tumour dissemination associated with capsular rupture. Exceptionally, it may be necessary to confirm the diagnosis of an initially unresectable metastatic adrenal lesion or differentiate adrenal metastasis from a non-secreting ACC [15]. All our patients with non-functional AT underwent adrenalectomy. This option could be justified by the large size of the tumours and the presence of intra-tumoural necrosis in three patients, as well as the relatively young age of the affected patients, with an average age of less than 40 years [14] [15].

The management of functional AT is surgical [6] [14] [15]. All our patients with functional tumours underwent surgery. The standard treatment for pheochromocytoma is surgery, which should always be performed electively, following premedication to control blood pressure and decrease the heart rate, thus avoiding complications during surgery due to extreme blood pressure variability. This variability is linked to catecholamine discharges triggered by tumour manipulation during surgery [16]. The surgical approach should be guided by the potential for malignancy, the presence of other conditions, or multiple tumour locations. The presence of a large tumoural lesion, an extra-adrenal localisation, or an SDHB mutation is high-risk situations of malignancy. Considering pheochromocytomas, 40% have a genetic origin; germline and somatic mutations involving 15 genes have been reported in patients with pheochromocytoma. There is a genotype-phenotype association based on these mutations. Patients with germline mutations in RET, VHL, or NF1 have a low risk of developing metastatic disease, while germline mutations in SDHB, FH, or MAX carry a higher

risk, which can reach up to 90% in patients with an SDHB germline mutation [17]. Patients with germline mutations in RET, VHL, and NF1 are at high risk of developing bilateral synchronous or metachronouspheochromocytoma; therefore, given the low risk of malignancy, adrenal-sparing adrenalectomy is advocated in patients harbouring these mutations to avoid life-long steroid replacement as well as an Addisonian crisis [18]. One of the main limitations of our study is that none of the pheochromocytoma patients underwent a genetic study. The management of malignant pheochromocytomas depends on the resectability of the tumour [16]. Regarding our two malignant pheochromocytoma patients, the therapeutic option, following a multidisciplinary consultation, was chemotherapy due to vascular invasion and the presence of metastases. The surgical approach involved laparotomy in 29 patients and laparoscopy in 3, which seems judicious given the large size of the tumours in our patients.

The outcomes of all patients with benign tumours were good. Immediate post-operative outcomes were simple in 27 patients. Three patients experienced haemodynamic instability during surgery, which was managed successfully. Two patients experienced haemorrhagic complications and acute adrenal insufficiency occurred in the patient with bilateral pheochromocytoma. The five-year survival rate for malignant pheochromocytomas ranges from 40% to 77%. Several adverse factors have been proposed, including large tumour volume, the presence or number of visceral metastases, and carrying an SDHB gene mutation [19]. Our patients exhibited at least two poor prognostic factors: tumour size and the presence of metastases at the time of diagnosis. The prognosis was also poor in patients with corticosurrenaloma, with a 100% mortality rate during the first year. Overall, the prognosis of adrenocortical carcinoma is poor, with an overall five-year survival rate of approximately 30% across all stages [7].

5. Conclusion

In our study, AT occur in young patients, under the age of 40, and are diagnosed when they become symptomatic with large tumours. Pheochromocytomas are the leading cause of AT. The prognosis for malignant tumours is poor, with 100% mortality within the first year.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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