Phaeochromocytoma: Experience with 12 cases in Tikur Anbessa, Addis Ababa, Ethiopia.

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Background: The incidence of phaeochromocytomas in Europe and the USA is well documented. From Africa, including Ethiopia, there are few reports on the disease. This paper describes 12 cases of phaeochrocytomas managed in Tikur Anbessa Hospital Addis Ababa between 1981 and 2001 inclusive.

Methods: A retrospective study of 40 patients undergoing adrenalectomy during the years under review was undertaken. The indications for surgery were Cushing's Syndromes in 24 cases, Phaeochromocytoma in 12 and adrenocortical tumours in 4 patients.This paper describes our experience with the management of the twelve patients with the phaeochromocytomas.

Results: The patients' ages ranged between 21 and 60 years. There were 5 males and 7 females. The majority of patients presented with clinical features related to episodic elevation of cathecolamines. Vanilylmandelic acid (VMA) in 24 hour urine was elevated in 10 patients. Localization of the tumours was made by ultrasonography or on exploration. The phaeochromocytomas were unilateral in 10 cases, seven of them on the left side. One patient had bilateral tumours and one other patient had an ectopic tumour. The tumours were operated through transabdominal or lower transthoracic approach.

Introduction

Phaeochromocytomas, a tumour of the adrenal glands or the sympathetic ganglia and causing hypertension, was first mentioned in medical literature in 1886 by Frankel in a purely pathological description. The name phaeochrocytoma was coined by Pick in 1912, who demonstrated black coloration of the tumour by application of chromsalts. The first surgical removal of adrenal phaeochrocytomas was done by Roux and Mayo in 1926 and 1927 respectively. The first accurate preoperative diagnosis and excision was made in 1929 by Pincoff and Shipley[1].

It was in 1947 that Physiologists first discovered catecholamines in urine (urosympatin)[2] and in 1949 that it was isolated in large amounts from phaeochromocytomas[3]. In 1950, Engels and Euler[4] in Sweden noted the diagnostic importance of finding large amounts of urinary catecholamines in two patients with phaeochromocytomas. In 1957 Armstrong[5] demonstrated that the end product of catecholamines metabolism in urine was vanilymanderic acid (VMA). Phaeochromocytomas, though very rare, are now well decribed in series from Europe and USA[1]. The aim of this study was to describe the findings in 12 patients presenting with the disease in Tikur Anbessa Hospital (THA) in Addis Ababa.

Patients and methods

The Operation registers of THA Surgery department were reviewed for cases undergoing adrenalectomy cases between 1981 and 200i inclusive. A total of 40 patients were found to have undergone the operation, 24 of which were cases of Cushing's syndrome, twelve of phaeochrocytoma and four of adrenocortical tumours. This paper analyses the findings among the twelve cases of phaechromocytomas.

Results

The indications for adrenalectomy and their yearly distribution are shown in Tables 1 and 2. Six of the phaeochromocytomas were operated on during the last five years. The patients' ages ranged between 21 and 60 years. There were five males and 7 females.

Nearly all the patients presented clinical features related to episodic elevation of catecholamines. The clinical

features included headaches, perspiration, palpitations and hypertension which were episodic in most of the cases. Two cases were monosymptomatic.

Table 1. Yearly distribution of adrenalectomy cases done in Tikur Anbessa Hospital, Addis Ababa: 1981-2001.

Yrs	Cushing's	Phaeos	Adrenocort.
81-84	4	-	-
85-87	3	3	-
88-90	2	2	-
91-93	4	1	-
94-96	2	-	-
97-99	2	3	3
2000-01	7	3	1
Total	24	12	4

Vanilyimandelic acid (VMA) in 24 hours was elevated in 10 patients and marginal in the remaining two cases. The tumours were located in the left adrenal in 3 patients, in the right adrenal area in 7 cases and were bilateral in only one case. One patient had the phaeochromocytoma in the organ of Zuckerkandel at the bifurcation of the aorta and another in the lower part of the paravertebral Sympathetic chain of the chest. These are now called paragangliomas. The largest tumour weighed 750 Grams but the majority of these tumours were of moderate size of between 50 and 100 Grams. In the case of the bilateral tumours, the total weight of the two tumours was 500 Grams.

The anaesthetic management in cases 1 to 7 was based on intraoperative blockade using pentholamine and propranolol and a smooth intra-anaesthetic handling of the cases. Hypotensive episodes occurring intraoperatively or postoperatively were managed by volume replacement with crystalloids and blood. Cases Two received pre-operative blockade with phenoxybenzamine. There were no postoperative deaths.

Three cases who had atypical presentations are described in details here below.

Case 1.

A 60-years old male patient known hypertensive for 7-years was admitted in 1991 with a one-year history of polydipsia and polyuria, episodic profuse sweating and palpitations which were followed by a headache and sometimes vomiting, Two years prior to admission, he had had thyroidectomy.

On examination, he was found to be in good general condition with a blood pressure (BP) of 140/70 and a pulse of 112 per minute. He had a post-thyroidectomy scar.

A 24-hour urine VMA estimated twice was elevated to 837 and 117 micromols respectively (NR = 12-30 micromols / 24 hours). Abdominal ultrasonography showed a 7 x 7.4 cm right adrenal mass and a 4.4 x 5.3 cm left adrenal. Thyroid function tests were within normal range. While on the surgical ward, his BP was within normal range most of the time but had several episodes of raised BP ranging between 160/110 and 170/130. Pre-operative treatment included phenoxyebenzamine 10mg b.i.d and increased to 10mg t.i.d at the time of surgery. His BP stabilized to within normal range.

In Mach 1991, the patient had surgery at which a tumour of the size of a fist was found and removed piece meal since it was attached to the inferior vena cava. A tumour twice the size of a lemon was removed from the left side. The intraoperative course was smooth. Phenoxybenzamine was discontinued postoperatively and patient started on replacement therapy with corticosteroids.

The histology confirmed a diagnosis of phaeochromocytoma with partial necrosis of the right adrenal mass.

Case 2.

A 33-year woman was admitted with over 10-year history of right upper abdominal pain. The pain was relieved by analgesics. She had previously been treated for dyspepsia with different drugs. She had a history of hypertension but no episodes of headaches or excessive sweating. On examination, there were no significant physical findings. Her BP was 110/70.

Ultrasonography showed a 5 by 6 cm cystic mass in the right lobe of the liver that was posteriorly located.

On exploration, no liver mass was seen. The right kidney was normal but the adrenal appeared suspicious. The ovaries and uterus were atrophic. Generally the operation was uneventful with no rise in BP.

During the postoperative repeat abdominal ultrasonograpy was done which revealed a 5 by 6 cm solid mass of the right adrenal gland. VMA estimation was 4 micromol in 24 hours (NR= 21-38). Daily recordings of the BP were within normal except on two occasions when the blood pressure rose to 190/110 and 160/100 respectively.

Table 3 Phaeochromocytmas in Africa, including Ethiopia 1996 - 2001

Author & Year	Country	NO.	Localization	Diagnostic
AC Templeton 1996 (7)	Uganda	10	Adrenal 7; Paraganglioma 2 bladder 1	Clinical 5 Postmortem 5
ENDEMARIAM Tsega Aklog H. Michiael 1997 (8)	Ethiopia	2	Adrenal 2	Clinical 2
Yemaneberhan Bahta et al 1991 (10)	Ethiopia	1	Paraganglioma 1	Clinical 1
KR Huddle et al 1991 (10)	South Africa	10	Adrenal 7 Paraganglioma 3	Clinical 10
HA N' Guessan 1990 (11)	Cote D'Ivoir	9	_	Clinical 9 Postmortem 1
EH Sibede at al 1997 (12)	Senegal	2	_	Postmortem 2
Chaiaeb et al 1990 (13)	Tunisia	7	_	Clinical 7
O. Johnson 2001	Ethiopia	12*	Adrenal 10 Bilateral 1 paraganglioma 1	Clinical 12

* Includes cases by Yemaneberhan Bahta, et al 1987.

The patient was put on phenoxybenzamine 10 mg b.i.d later was increased to t.i.d. when the blood pressure stabilized; exploration of the right adrenal was done through a right thoraco-abdominal approach in February 1999. A 5 by 5 by 4 cm adrenal tumour was found and removed. Her blood pressure remained stable throughout the operation and her postoperative period uneventful. When reviewed in July 1999, her BP and VMA were normal.

Histology showed a phaeochromocytoma with central necrotic degeneration.

Case 3.

A 37-years old male patient presented on referral from the Medical Department with a 3-years history of episodic attacks of palpitations, perspiration and headaches. He reported that although he had been found to be hypertensive two years earlier, he had never been treated for it. He also suffered from excessive thirst and polydipsia.

While in the medical Department, a diagnosis of phaeochrocytoma had been made based on the VMA results of 75 micromol in 24 hours (NR 12 - 38) and CT finding of a 13 by 10 cm mass in the left adrenal area.

While on the surgical ward for a month, the patient remained asymptomatic and had a normal BP and pulse. A repeat VMA estimation done on 26/9/2001 was 37 micromol in 24 hours.

On exploration through a low left transthoracic approach, a well-encapsulated tumour measuring 15 by 12 cm weighing 750 grams was removed from the left adrenal area. However, the left adrenal gland was found intact posteromedial to the tumour. The intraoperative and postoperative period was uneventful.

The histopathology was consistent with a phaeochromocytoma.

Discussion

Phaeochrocytomas are very rare tumours. Its incidence in a large autopsy series was 0.1% and 0.4% in patients with hypertension[6]. The tumour is well described in representative series from Europe and the US[1].

Few reports have come from Africa. Table 3 shows the cases from different countries in Africa reported during the past three decades7-13. The association between phaeochromocytoma and the multiple endocrine neoplasia and the anaesthetic management of the tumor have been described in reports from South Africa[14,15].

Although many of the patients present with the typical clinical features of episodic hypertension, headaches and perspiration, others present with vague signs and symptoms that are atypically of phaeochromocytomas which cause delay in diagnosis and management as exemplified by the three cases presented in our series. Long-standing effects of catecholamines make such patients liable to vascular complications and sometimes death.

Complications related to pregnancy in cases of phaeochromocytomas are well documented. Abortion in such cases is common and cases delivering at term face the risk of vascular crises and arrhythmias which often lead to death[7,9].

Diagnosis in clinical and suspected cases is nowadays made by bioassay of catecholamines and degradation products of catecholamines in urine[16]. Refined laboratory techniques have now made these bioassays highly sensitive and specific for phaeochromocytomas. Catecholaminsecreting neoplasmas are heterogeneous and have a varying temporal secreting pattern. Accordingly, combined assays of free catecholamines, metanephrines and vanilymandelic has become highly relevant and is used where assay methods are available 16. In our setting we have found the assay of vanilymandelic acid valuable. Localization of phaeochromocytomas is nowadays made using modern imaging techniques [16]. In the present series, cases 8, 9 and 11 were well visualized and described with ultransongraphy, in case 12 CT scan was successful. In the earlier part of the series, use of IVP showed depression of the kidney on the side of the tumor in few cases; and chest x-ray for a case of paraganglioma in the sympathetic chain was useful. In the majority of cases, however, localization was made after abdominal exploration of both adrenal and paraaortic areas.

The anesthetic management was, before the introduction of preoperative alphablockade, the most critical part of management. Anesthesia and surgery are highly conducive to hypertensive crises and arrythmias of the heart and the removal of the catechol-secreting tumor often followed by severe hypotension and shock. Meticulous attention to detail by the anesthetist and use of pentolamine and propanolol was earlier used intraoperatively [6]. Shock treatment included infusion of large volumes of crystalloids, plasma and blood. The current preoperative alphablockade, done most often using

Dibenyline (phenoxybenzamine), has almost eliminated the these problems [17]. The volume expansion is as well achieved preoperatively by blood and fluid infusions. The preoperative preparation may take up to two weeks and increasing doses of phenoxybenzamine are given until BP is normalized and stabilized. This type is well illustrated in the last five cases in our series.

Our case 1 is an extra-adrenal phaeochromocytoma. Localized in the organ of Zuckerkandel and in the right chest. Such localizations are reported to occur in 9-10% of cases 6. Malignant transformation is more common in familial cases (Men II) and in bilateral cases. Malignancy based on the presence of metastases is 3% whereas malignancy based on observation of features of of malignancy in the primary tumor is 9% [6]. In case 1, the thoracic phaeochromcytoma showed bizarre nuclei and also had an infiltrative pattern of growth. This patient was seen eleven months after excision and at that time was asymptomatic and had normal BP.

Otherwise, there were no recurrences in our series from TAH. After surgery, BP usually returns to normal and VMA in urine will be in the normal range. A few cases show residual hypertension after surgery. Multiple phaeochromocytomas should be ruled out in such cases. Otherwise such patients can be treated as essential hypertension [6].

There was no mortality in the presented series of cases. Mortality nowadays is very rare provided cases are completely diagnosed and an appropriate preparative management undertaken. In undiagnosed cases that are exposed to surgery, delivery or trauma, the mortality is still considerable. A high index of suspicion in cases of hypertension and screening for catecholamine-metabolites in urine should help to sort out such cases.

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