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Case Report

Pheochromocytoma in a 44-Year-Old Female

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ABSTRACT

Pheochromocytomas are rare neuroendocrine tumors that arise from the adrenal medulla and rarely from extra-adrenal locations. Although rare, they are potentially lethal tumors [1]. The pathognomonic biochemical features of these tumors are markedly elevated plasma catecholamines and their metabolites. The high plasma catecholamines are the reasons for the hypertension seen in patients with these tumors.

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Introduction

Pheochromocytomas are rare chromaffin-cell tumors of adrenal medulla and some extra-adrenal sites. The first reported case of pheochromocytoma is attributed to Frankel in 1886 [2]. Alezias and Peyron described extra-adrenal chromaffin tumors and called them paragangliomas in 1906 [2]. In 1912, Pick recommended that intra-adrenal chromaffin tumors be called pheochromocytomas and that all extra-adrenal chromaffin tumors be termed paragangliomas [2].

The most common feature of these tumors is their elaboration of high levels of catecholamines which in turn cause marked elevations in blood pressure in patients with these tumors. About 1 in 1,000 people with hypertension have pheochromocytoma [2]. A life-threatening hypertensive crisis is a risk incurred by patients with these tumors. Thus, prompt diagnosis, localization and surgical excision of these tumors can be life-saving. The classic triad of symptoms is headache, palpitations, and sweating [3]. This symptom-complex in someone with hypertension,

has a high specificity (93.8%) and sensitivity (90.9%) for the diagnosis of pheochromocytoma [3, 4]. However, in some patients with pheochromocytoma, the tumor may not produce symptoms or signs [5, 6]. The age-long and popular teaching describing pheochromocytoma as ‘the 10% tumor’ is being disproved in the face of recent evidence and findings [6-8]. Diagnosis of pheochromocytoma is confirmed by elevated levels of plasma and/or urine catecholamines and their metabolites. Localization of the tumor is done by radiologic studies.

Case Presentation

A 44-year-old lady was referred from the general outpatient department to the Endocrine Medical Unit of our center on account of hypertension and diabetes mellitus, both of one year duration prior to referral. About two (2) months before this referral, patient had amenorrhea for which she had gone to a peripheral hospital where she was found to be hypertensive. The random plasma glucose on initial review at the Endocrine Unit was 600mg/dl and the blood pressure was 200/120mmHg. The patient had facial puffiness and pitting edema of

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both feet and legs, up to knee-level. Following extensive evaluation by the medical team, she was diagnosed to have secondary hypertension, resulting from adrenal tumor, with strong suspicion of pheochromocytoma. Her diabetes mellitus was in fairly good control. There was no family history of similar illness of diabetes mellitus, of hypertension, or of any chronic illness. The medical team sent her for a number of investigations including complete blood count (CBC), erythrocyte sedimentation rate (ESR), fasting lipid profile, serum urea and electrolytes/creatinine levels, fasting blood glucose and HbA1c. She was placed on oral anti-hypertensives (Aldomet and Atenolol), subcutaneous insulin and oral hypoglycaemics.

Serum electrolytes, urea and creatinine results showed potassium value of 2.4mmol/L, with the rest of the parameters being within normal limits. Lipid profile results were all within normal values. Haemoglobin was 14.5g/dl and ESR was 10mm/hr. Fasting blood glucose was 6.9mmol/L and her glycated haemoglobin (HbA1c) level was 9.8%. She was assessed by the medical team as having stable hypertension and unstable diabetes mellitus.

As she had suffered frequent episodes of collapses, diaphoresis, and palpitations, she was subjected to further investigations. Abdominal CT scan showed a left suprarenal mass, strengthening the suspicion of pheochromocytoma. On account of this finding and suspicion, she was referred to the surgeons for further evaluation and management. The surgical team reviewed her and upheld the diagnosis of left adrenal pheochromocytoma. She was further evaluated by means of biochemical tests of urine levels of metanephrine, normetanephrine and vanillylmandelic acid. These parameters were all found to be markedly elevated.

She was worked-up for surgery. This work-up included correction of the hypokalaemia, commencement on Glucose-Potassium-Insulin (G-K-I) infusion, and discontinuation of subcutaneous insulin the day prior to surgery. The night before surgery, oral diazepam was administered. In theatre, she was connected to the routine non-invasive monitoring: five (5) ECG leads, pulse oximeter, blood pressure monitors and temperature probe. Two (2) wide-bore intravenous canulae (16G) were used to secure venous accesses for administration of fluids and medications. Baseline vital signs immediately before surgery were as follows: BP 194/102mmHg; pulse rate 101b/min and SPO2 of 93% at room temperature. Injection tramadol and lidocaine with propofol were used for induction and tracheal intubation was facilitated by intravenous suxamethonium. A size 7.0mm cuffed endotracheal tube was used to secure the airway. The capnograph was connected and equality of air entry in both lungs confirmed. Isoflurane was commenced. Vital signs after induction of anaesthesia and endotracheal intubation were BP 191/101mmHg, pulse rate 88b/min and SpO2 of 99%.

She had open total left adrenalectomy. The tumor weighed 27 grams and measured 15 cm x 6.5 cm {Length x Width} (See Figures 1 & 2). During the procedure, which lasted for about eighty (80) minutes, the blood pressure fluctuated between 201/111mmHg and 85/58mmHg, in spite of conscious efforts at gentle and meticulous handling of the tumor. At the end of surgery, anesthetic reversal was achieved using neostigmine and atropine, after which patient was extubated. Patient was transferred to the intensive care unit (ICU) fully awake, with stable vital signs. Her immediate post-operative condition and recovery were essentially

uneventful. On post-op day one, her random plasma glucose was 89mg/dl, and the blood pressure was 200/120mmHg. She was placed on intravenous verapamil and subcutaneous insulin until post-op day two when she was commenced on graded oral sips. On that same post-op day 2, she was transferred to the female surgical ward. She graduated to low residue diet, followed by regular diet. At this time, she was placed on oral hypoglycaemic medication (Glibenclamide) and oral anti-hypertensive (Lisinopril). On post-op day 3, her blood pressure was 135/90 and her pulse was 77/min, regular, with good volume.



Figure 1: The black spot identifies the adrenal tumor *in-situ*.



Figure 2: Resected left adrenal tumor.

Histopathology study of the specimen found overall features to be those of neuroendocrine tumor in favour of pheochromocytoma. In the six (6) fortnightly follow-up visits at the surgical outpatient department, patient continued to show normal control of both the blood pressure and the blood glucose. The patient was lost to follow-up four months after surgery.

Discussion

Pheochromocytoma is a rare cause of surgically-correctable hypertension and diabetes mellitus. Pheochromocytomas are commonest from the fourth through the sixth decades of life [9]. Our index patient was 44 years. Pheochromocytoma is a diagnosis of exclusion and

requires a high index of suspicion before the diagnosis is made. Hypertension is the commonest sign in patients with this tumor and headache is the commonest symptom. The diabetes seen in these patients is essentially functional; it is explained by the marked glycogenolysis and relative insulin resistance due to the very high levels of catecholamines in the circulation.

Normal adrenal gland secretion is 85% adrenaline but most pheochromocytomas secrete predominantly noradrenaline. An exception to this is familial pheochromocytoma which secretes mainly adrenaline. Adrenaline is produced from noradrenaline by methylation through the action of the enzyme phenylethanolamine-N-methyl transferase (PNMT). Confirmatory tests for pheochromocytoma include:

- i. Free catecholamine level in 24-hour urine sample.
- ii. Plasma free metanephrine level.
- iii. Urine vanillylmandelic acid (VMA) level.
- iv. Clonidine suppression test: clonidine lowers plasma catecholamine levels in patients without pheochromocytoma but not in patients with the tumor.

Localization tests include:

- i. Computerized tomography (CT) scan.
- ii. Magnetic Resonance Imaging (MRI); these two can identify most pheochromocytomas.
- iii. Meta-Iodo-Benzyl-Guanidine (MIBG) is a radiopharmaceutical agent and an analogue of guanethidine, with structural similarity to adrenaline. It is taken up and concentrated in catecholamine-secreting tumors. Scintigraphy detects MIBG in tissues where MIBG is taken up.

In the work-up of patients with pheochromocytoma for tumor excision, it is important to ensure that Roizen preoperative conditions are observed [10]. The conditions are:

- i. Blood pressure <160/90mmHg for 24hrs prior to surgery.
- ii. Postural hypotension >80-45mmHg.
- iii. ECG should be free of any ST-T changes for a week.
- iv. No PVCs more than 1 in 5 minutes.

Conclusion

Pheochromocytoma is a rare pheochromocyte tumor of the adrenal medulla. Its relevance lies in its propensity to cause hypertension that is

mostly paroxysmal and refractory to the usual anti-hypertensives, diabetes mellitus that is very unstable, high surgical mortality in patients who were inadequately prepared before surgery and least suspicion of this tumor by health care providers. In the management of a patient with refractory hypertension and unstable diabetes mellitus, efforts should be made to rule out pheochromocytoma.

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