



## Biochemical analysis and management of pheochromocytoma: A case report

Familoni O.M, Uwanuruochi V.N, Uwanuruochi K, Elendu K.C.

Department of Medicine, Federal Medical Centre, Umuahia, Nigeria

### Abstract

Pheochromocytoma is a tumour from chromaffin cells in adrenal medulla or extra-adrenal autonomic ganglia, usually releasing catecholamines and metanephrines. It is an unusual cause of severe hypertension in the young. This is the first report from our hospital, the Federal Medical Centre, Umuahia. There are important steps in management which if unattended to results in high peri-operative mortality. This article highlight these issues in its management.

Keywords: Biochemical, management, analysis, Pheochromocytoma

### Introduction

There have been few reports of pheochromocytoma from various centres in Nigeria.<sup>1-4</sup> It is a rare cause of hypertension and diagnosis is often delayed. Our case report highlights the need for higher index of suspicion, understanding of current guidelines for diagnosis and modalities of management that enhance early diagnosis and reduce morbidities and mortality in patients.

### Case report

A 27 year old male complained of recurrent abdominal pain, headache and palpitations for 4 years. The headache was severe, frontal and associated with light headedness and diaphoresis. He also had nausea, vomiting, recurrent constipation and generalised body weakness and occasional shortness of breath. He was not hypertensive, and did not abuse drugs. For the past one year, he had increased urination, thirst, appetite and progressive unintentional weight loss and undue fatigue. He was not known to be diabetic. He sought care at a private hospital where abdomino-pelvic ultrasound scan showed left

hypoechoic mass suspected to be splenic. He was given some medications for splenic enlargement. At the Babcock University teaching hospital a computer tomography of the abdomen was done, localised a tumour in the adrenal gland (Figure 1). There was a rim enhancing isodense mass in the left suprarenal region. The mass has a Hounsfield unit value ranging from 10 to 65 and measures 76 x 71 x 57mm in its widest longitudinal, anterior-posterior and transverse dimensions. No area of macroscopic fat is seen. The mass is seen to compress the left kidney but no definite invasion of adjacent structures is seen, revealing features of left large adrenal mass likely adrenal carcinoma with no evidence of metastasis to any intra-abdominal organs.

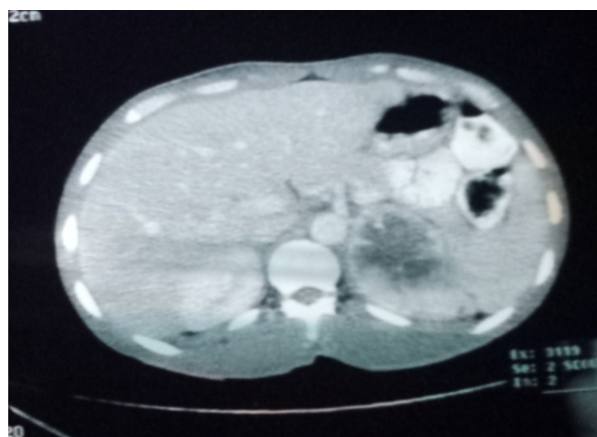


Figure 1: A left 7 cm pheochromocytoma seen on a CT scan

Corresponding Author: Dr. Kelechukwu Uwanurochi

Department of Medicine,  
Federal Medical Centre,  
Umuahia, PMB 7001, Nigeria

E-mail: kcgrace2002@yahoo.com, Phone number: +2348037407703

He could not follow up his treatment in the hospital due to financial constraints and came to our hospital, which is near his home and family. He was first seen at general out-patient, and sent to the Endocrine clinic. He was acute on chronically ill-looking, wasted and lethargic.

His random blood sugar record was above 33.3 mmol/L on the Accu-chek glucometer. His pulse was 87beats per minute, blood pressure was 130/90mmHg, respiration 23per minute, and oxygen saturation 97% at room air. He had left flank pain, radiating to the epigastrium. He was lethargic, but well oriented with no muscle weakness.

We entertained pheochromocytoma with secondary diabetes in hyperosmolar, hyperglycaemic state. The following investigations were requested: serum cortisol (9am), plasma free metanephrine, 24 hour urine creatinine, total catecholamine, vanillylmandelic acid and

metanephrine, serum testosterone, dihydrotestosterone, dehydroepiandrosterone, Hemoglobin A1C, Brain magnetic resonance imaging.

He was rehydrated with normal saline and hyperglycaemia was controlled with regular insulin. He was placed on phenoxybenzamine 10mg daily and doxazosin 2 mg daily. Laboratory results obtained are shown in Table 1. It showed biochemical evidence of pheochromocytoma.

Brain magnetic resonance imaging and C-peptides were not done due to financial constraints. By the following day, he was better, with good glycaemic control (random blood sugar 198 mg/dl (11 mmol/L). His pulse was 128 beats/minute, so propranolol 40mg daily was added. He was discharged to the clinic on the fourth day. He is being prepared for adrenalectomy, with continued alpha and beta adrenergic blockade.

**Table 1: Biochemistry results of patient**

Test name	Result	Reference range
Urine Volume	4530 mL	
Urine Creatinine	1.54	3 – 23 mmol/l
24 hour urine Creatinine	6.98	7-14mmol/24h
HVA/creatinine ratio	0.307	
VMA /creatinine ratio	0.116	0.7---4.3
24 hour urine serotonin	355.95	50---250ug/24hrs
24 hr urine dopamine	3595.97 high	65---400ug/24hrs
24hr urine homovalinic acid (HVA)	53.42	1.4—8.8mg/24 hrs
24 hr urine norepinephrine	1451.58	15----80 ug/24 hrs
24 hr urine normetanephrine	8349.88	100---500ug/24 hrs
Plasma metanephrine	31.97	0—90pg/ml
24 hour urine epinephrine	285.95	0—20ug/24hrs
24 hour Urine metanephrine	173.88	50---250ug/24hrs
24hr urine vanillylmandelic acid (VMA)	20.14	1.4---6.5mg/24hrs
Cortical fasting	410.9mmol/l	240----618mmol/l
Cortisol random	412.8	Less than 270nmol/l
Dehydroepiandrosterone sulphate	1.2	2.31—6.5mg/dl
Testosterone	5.98	9—35nmol/l
Serum Creatinine	68	39—91umol/l
Serum Urea	3.2	2.5—6.4mmol/l
Serum Sodium	136	135---145mmol/l
Serum Chloride	100	98---110mmol/l
Serum Potassium	4	3.5—5.1mmol/l
Estimated glomerular filtration rate	>90ml/min /1.73m <sup>2</sup>	

## Discussion

Pheochromocytoma is a rare cause of secondary hypertension, with a prevalence of about 0.2–0.6%.<sup>5</sup> This is the first documented case in our centre. Management is demanding as it may precipitate life-threatening hypertension or cardiac arrhythmias because of excessive catecholamine secretion.<sup>6</sup>

Headaches, palpitations, and sweating which were all present in our patient are the classic triad of symptoms seen in pheochromocytoma.<sup>6</sup> The triad has a specificity of 93.8%, a sensitivity of 90.9% and an exclusion value of 99.9% for the diagnosis of phaeochromocytoma.<sup>7</sup> Their presence in hypertensive patients justifies assays of blood or urinary catecholamines. Their absence virtually excludes phaeochromocytoma.

Proper interpretation of biochemical analysis is important. Initial biochemical tests of paragangliomas (PPGLs) should include measurements of plasma free metanephrines.<sup>8</sup> Metanephrines are normetanephrine and metanephrine, the degradation products of noradrenaline and adrenaline respectively.

Elevated plasma free metanephrines is considered the gold standard for diagnosis, with a sensitivity of 99% and specificity of 89%.<sup>9</sup> Positive results is greater than > 2-3 folds elevation, 24h Urine catecholamines above 2-fold elevation, 24h Urine total metanephrines above 1.2 ug/d (6.5 umol/d), 24h Urine VMA > 3-fold elevation. Sensitivity approaches 90% and specificity 98% when urinary catecholamine is combined with urinary total metanephrines. Urinary fractionated metanephrines have equivalent sensitivity, but much lower specificity (about 45%). They are useful for initial screening.<sup>9</sup>

24hr urine normetanephrine, dopamine, epinephrine and norepinephrine were markedly elevated in our patient, but 24 hour urine metanephrine and plasma metanephrine were normal. Separate measurement of metanephrine and normetanephrine is required (fractionating) and an elevation in either is considered positive.<sup>10</sup> Normal plasma metanephrine in the presence of markedly elevated urine catecholamines suggest a dopamine secreting paraganglioma, a very rare occurrence.<sup>10</sup> VMA is a metabolites of the norepinephrine and HVA is a metabolites of the dopamine. They were

elevated in our patient. Elevated HVA supports a diagnosis of neuroblastoma and malignant pheochromocytoma. Measurements of urinary dopamine and plasma 3-methoxytyramine are useful for the biochemical diagnosis of PPGLs with predominantly dopamine secretion and/or high risk for metastases.<sup>11</sup> Low levels of HVA in presence of high levels of dopamine suggest poor conversion of dopamine.

After biochemical confirmation, the tumour is localized using either computed tomography or magnetic resonance imaging.<sup>12</sup> The location in the suprarenal region, variable display and enhancement with contrast are features helpful for its identification.

Preparation for surgery is multidisciplinary, involving endocrinologists, anaesthesiologists, surgeons and cardiologists. Most commonly, phenoxybenzamine is used for pre-operative blockade of catecholamines. It should be started at least 10-14d preoperatively, at starting dose of 10 mg twice a day, with stepwise increases of 10 to 20 mg every 2-3 days until until blood pressure and paroxysms are controlled. The final dose of 1mg/kg of body weight is reached. The Maintenance is usually 40-80 mg/day.<sup>9</sup> To reduce tachycardic reflex responses while patients are on alpha-blockers, a low dose beta-blockade is started only after effective a-blockade. It also prevents arrhythmia during surgery. Propranolol is usually started at 10 mg twice a day, and increased to control the heart rate.

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