Uncontrolled Hypertension in a Child with Phaeochromocytoma: Management Challenges In A Resource-Limited Setting

Type of Article: Case Report

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ABSTRACT

BACKGROUND
Hypertension in childhood which is usually uncommon and secondary to renal or other diseases, poses significant challenges to the health system in resource-limited settings due to lack of access to diagnostic and management facilities.

METHODS
The case records of an affected 11 year old male and the review of literature were utilised to highlight the diagnostic and management challenges in this case.

RESULTS
An 11 year old male was diagnosed with hypertension secondary to a pheochromocytoma following presentation with severe hypertension (220/180mmHg) associated with frontal headache, easy fatigueability and deterioration in vision. Urinalysis, microscopy and culture, Renal and thyroid function tests, lipid profile, full blood count and abdominal ultrasound and Computerised Tomographic scanning were normal. Electrocardiogram and echocardiography showed features of hypertensive heart disease. Urinary vanylylmandelic acid and homovanillic acid assays suggested phaeochromocytoma. No anti-hypertensive combination controlled the blood pressure. He was referred to India where abdominal magnetic resonance imaging revealed a left sided retroperitoneal, adrenal, para- aortic tumour which, on resection, was confirmed as phaeochromocytoma. Post-operatively all clinical features resolved and he became well.

CONCLUSION
The challenges posed by delayed presentation, lack of access to adequate facilities and skilled health manpower required for the management of challenging health situations in resource-limited settings have been highlighted.

Running title
Pheochromocytoma; Uncontrolled hypertension in Children; management challenges; resource- limited settings.

KEYWORDS
Hypertension, Phaeochromocytoma, Childhood, Resource-limited settings.

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INTRODUCTION

Hypertension, defined as blood pressure (BP) greater than or equal to the 95th percentile for age and sex or BP greater than 120/80mmHg for children aged less than 10 years or greater than or equal to 140/90mmHg for those aged 10 years or older is uncommon in children[1]. In Nigeria, the prevalence of hypertension in children is low, ranging from 0.3 to 3.7% among adolescents, depending on the age group[2,3]. Hypertension in children is usually

secondary and in more than 80%, an underlying kidney disease will be found[4,5]. Phaeochromocytoma, a catecholamine-secreting solid tumour is rarely reported among children, especially in resource-limited settings such as Nigeria due to several management challenges[6,7]. It is also a very rare cause of secondary hypertension in children. Hypertension results from the cardiac and peripheral vascular effects of the excessive epinephrine and norepinephrine produced by the tumour[8]. Children with phaeochromocytoma usually have sustained, rather than the intermittent hypertension with wide swings in blood pressure pattern found in adults, and their blood pressure is difficult to control[8].

We report a case of an eleven year old male who presented with severe, sustained and uncontrolled hypertension secondary to phaeochromocytoma and the challenges we faced in the diagnosis and management of his condition.

CASE REPORT

Master AS, 11 year- old male, was first seen in October, 2008 with a two-year history of persistent headache and chest pain, and 6-month history of easy fatigueability and poor vision. The headache was generalized, continuous and associated with pain in the neck but no fever, nausea or vomiting. The headache waxed and waned in severity but was continuous. The chest pain, localised to the praecordium was dull, severe, recurrent and non-radiating. Six months before presentation, he was noticed to be breathless on minimal exertion. Additionally, he became less active and no longer played with other children. He also complained of poor vision but had no diplopia. He had been well with no significant past medical or surgical histories.

The pregnancy, birth and developmental histories were normal. He was a primary 6 pupil with good academic performance. He was the last of five children in a monogamous family and all children were alive. The father was a known hypertensive but the mother was well and not hypertensive. The review of systems was essentially normal.

Physical examination revealed a young appropriately sized male, with no obvious physical deformities, not in any obvious distress, mildly pale and not cyanosed. His weight and height were 35kg and 1.44m respectively and are within the normal limits for his age. The pulse was 134beats/min, regular, synchronous, non-collapsing with no radio-femoral delay. The blood pressure was 220/180mmHg in both arms and 230/180mmHg in the lower limbs, the apex beat was located at the 5th left intercostal space, along the mid clavicular line and heaving. The 1st heart sound was normal but the 2nd had a loud aortic component (A2). The examinations of the respiratory, digestive and genitourinary systems were normal. The central nervous system examination was normal except for the findings in the eyes where fundoscopy revealed papilloedema, retinal haemorrhages, exudates, and arterial constriction consistent with grade 3 hypertensive retinopathy. A diagnosis of severe hypertension with hypertensive heart disease and grade III retinopathy of unknown cause was made.

Investigations conducted included urine for analysis, microscopy and culture, assays of serum electrolytes, urea and creatinine, abdominal ultrasound scanning, Full Blood Count (FBC), Thyroid function tests (T3, T4 and TSH) and lipid profile assay. The results were within normal limits. The electrocardiogram and echocardiography showed features of hypertensive heart disease. The assays of urinary vanylylmandelic acid and homovanillic acid could not be carried out at the University of Port Harcourt Teaching Hospital. A 24 hour timed urine collection was done and the sample sent to a private laboratory which transferred it to Lagos for analysis. The report, obtained after 4 weeks, showed markedly elevated levels suggestive of phaeochromocytoma and advised on the assays of plasma urinary metanephrine and normetanephrine and plasma chromogranin

to confirm the diagnosis. These could not be done because of the cost and lack of facilities in Port Harcourt. Consequently a tentative diagnosis of hypertension secondary to phaeochromocytoma was made and computerized tomographic scanning of the thorax and abdomen was done at the University of Port Harcourt Teaching Hospital but the tumour was not detected. Further investigation with Magnetic Resonance Imaging could not be done due to lack of facilities and the cost of doing the test outside Rivers State.

Treatment: Definitive treatment for the tumour could not be done because of the inability to localise the tumour. The child was therefore given supportive management for the hypertension till definitive treatment could be offered. He received a combination of antihypertensives such as twice daily doses of atenolol 50mg, captopril 12.5mg, prazosin 1mg, and daily doses of Adalat® 20mg and moduretic. The blood pressure however remained poorly controlled ranging from 140/90 to 160/100mmHg with intermittent spikes of acute blood pressure rise up to 200/120mmHg.

Frustrated by our failure to detect the tumour site and offer definitive treatment, the parents requested for the child's referral to India. There, a Magnetic Resonance Imaging (MRI) of the abdomen done in February 2009 revealed a solitary left sided, adrenal, retroperitoneal para-aortic tumour. The tumour mass, measuring 22mmx24mm in size, was successfully removed operatively. The histology confirmed the diagnosis of phaeochromocytoma. The child had an uneventful post operative recovery and subsequently returned to Nigeria. Subsequently, his symptoms and signs resolved and his blood pressure remained normal six months after surgery and untill when he was last seen about 4 years after surgery.

Results of Laboratory Investigations

Urinary Vanyl Mandelic Acid Assay using 24 hour urinary sample (16/11/2008)
Height =1.44m
Weight=35kg
Urine VMA 3.1mmol/l, Urinary Creatinine 147.7ml/24hr, Urinary VMA: Creatinine Clearance ratio-19.10, 24 hour urinary volume 2,500ml

Comment: The levels were markedly elevated and suggestive of phaeochromocytoma but the following tests should be done to confirm the diagnosis-urinary metanephrine and normetanephrine and plasma chromogranin assays which could not be done at the centre

Echocardiogram Report (10/10/2008)
Weight =35kg, Height=1.44m
M Mode Measurements
Left ventricular systolic function:
Left ventricular (LV) Internal diameter diastole= 24mm, LV Internal Diameter Systole 17mm,
Interventricular septal thickness in diastole =14mm, Interventricular septal thickness in systole=16mm, LV posterior wall thickness in diastole=19mm, LV posterior wall thickness in systole=21mm, Ejection fraction=54.3%, Stroke volume=11ml, Cardiac output=1.15L/min, Left ventricular mass (indexed for weight)=140
Two dimensional echocardiogram:
LV End diastolic volume=20ml, LV End systolic volume=9ml

Doppler echocardiogram:
Aortic Outflow: Mean velocity=145.7cm/s; VTI=34.2cm, LVOT=15mm; CSA=1.79cm2
SV=61ml; HR=118b/min; CO=7.23l/min
Pulmonary Outflow: Mean velocity=98.3cm/s; VTI=30.4cm; RVOT=14mm; CSA=1.45 cm2, SV=44ml; HR=102b/min; CO=4.52l/min
Mitral E-velocity=73.7cm/s;
Mitral A Velocity=69.0cm/s; E/A ratio=1.07
Mitral E wave deceleration time=262ms
Tricuspid E-velocity=39.4cm/s;
Tricuspid A Velocity=48.8cm/s; E/A ratio=0.81
Tricuspid E wave deceleration time=214ms

Comment: The ratio of left atrium to the aorta was[1.15], implying a mild left atrial enlargement. There was dense LVH and also a mild RVH with grade II LV diastolic dysfunction and grade I RV diastolic dysfunction. The pressure in the left ventricular outflow tract was very elevated. Valves were normal. There was no obvious systolic anterior wall motion.

Echocardiographic Diagnosis: Hypertensive heart disease with left ventricular dysfunction

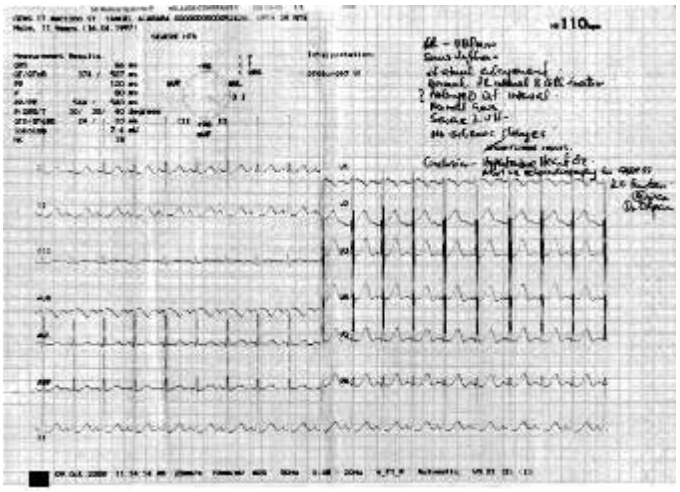

Fig 1: ECG tracing of patient showing evidence of left atrial enlargement and left ventricular hypertrophy.

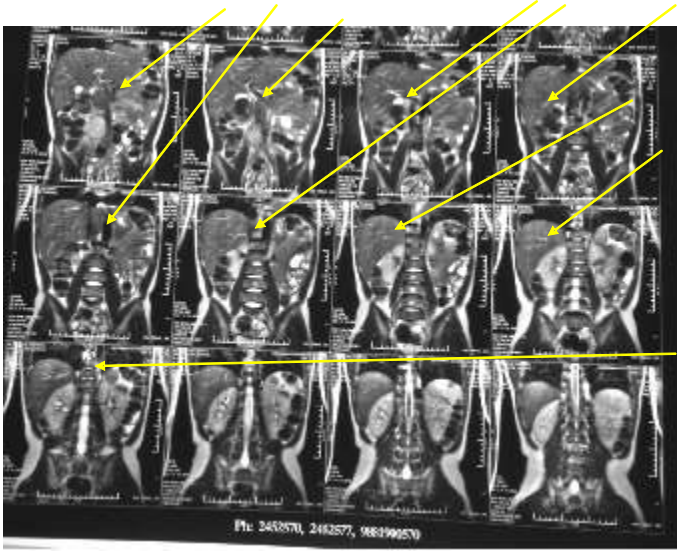

Fig. 2. Magnetic Resonance Imaging of the Child's abdomen showing the tumour mass(arrows) in serial films(photographs taken in an Indian Hospital)

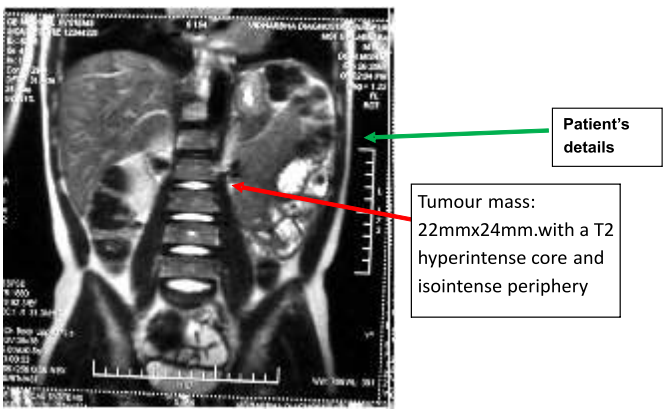

Fig. 3: Tumour mass and Patient's details in the MRI scan done on Feb 26th, 2009

DISCUSSION

Phaeochromocytoma is a catecholamine-secreting tumour that arises from chromaffin cells. The most common site of origin (approximately 90%) is the adrenal medulla; however, tumours may develop anywhere along the abdominal sympathetic chain and are likely to be located near the aorta at the level of the inferior mesenteric artery or at its bifurcation.1Phaeochromocytomas are uncommon tumours in children even in Nigeria[4,5]. Ten percent (10%) of them occur in children, in whom they present most frequently between the ages of 6 and 14 years[8]. The age at presentation of this patient of 11years, about 2 years after the onset of symptoms is thus in keeping with the usual age of presentation. However, as is common in resource-limited settings, the late presentation accounted for the complications such as the hypertensive retinopathy and cardiomegaly reported in this child. The tumours vary in diameter (size) from 1 to 10 cm and they are found more often on the right than the left side. However in more than 20% of affected children, the adrenal tumours are bilateral and in 30-40%, the tumours may be found in both the adrenal and extra-adrenal areas or only in an extra-adrenal site[9]. The tumour in our patient was adrenal in location and within the normal size limits but was located on the left.

The clinical features of phaeochromocytoma result from excessive secretion of epinephrine and norepinephrine and all patients have hypertension at some time during the course of their illness. Paroxysmal hypertension should particularly suggest phaeochromocytoma as a diagnostic possibility. The hypertension in children is however more often sustained rather than paroxysmal, in contrast to the situation in adults[9]. When there are paroxysms of hypertension, the attacks are usually infrequent at first but become more frequent and eventually give way to a continuous hypertensive state[8,10]. It is however probable that our patient had continuous hypertension from the beginning of his illness because of the presence of persistent headache

from the onset of his symptoms. The hypertension is also associated with palpitations and dizziness as was shown in the review of 54 black African patients with phaeochromocytoma (children and adults) in which 77% presented with palpitations and headaches[7]. Furthermore, in another review of ten patients with phaeochromocytoma 90% had palpitations and headaches[10]. Thus a high index of suspicion for phaeochro-mocytoma should be entertained in hypertensive children with histories of palpitations and continuous or paroxysmal headaches. Furthermore, in patients with long standing severe uncontrolled hypertension, there may be praecordial pains which radiate to the arms, acute pulmonary oedema, congestive cardiac failure and retinal changes consistent with hypertensive retinopathy. The praecordial pain in these patients may be due to myocardial ischaemia from prolonged and severe blood pressure elevation and although rare, may portend a serious clinical deterioration[11]. Thus, the pattern of presentation of this patient was consistent with the findings in other series[9].

The diagnosis of phaeochromocytoma is established by demonstration of elevated blood or urinary levels of catecholamines and their metabolites[8]. However, in adults with phaeochromocytoma both norepinephrine and epinephrine levels are elevated while in children norepinephrine is commonly elevated[8]. The total urinary catecholamine excretion usually exceeds 300 μg/24hour and the urinary excretion of vanillylmandelic acid (VMA, 3-methoxy-4-hydroxymandelic acid), the major metabolite of epinephrine and norepinephrine, is increased, as is the excretion of metanephrine-homovanillic acid. There are no facilities for the estimation/assay of urinary catecholamine and their metabolites at the University of Port Harcourt Teaching Hospital or any other centre in Port Harcourt further contributing to delayed diagnosis as the test had to be done in a private laboratory in Lagos. This situation is not peculiar to this case as several other specialised investigations for the diagnoses and management of other medical conditions are often unavailable both in public and private health facilities including many tertiary health facilities in Nigeria and have to be accessed outside the country thereby contributing to the high rate of medical tourism in Nigeria[12]. An additional challenge presented by this case was the failure to localise the tumour by ultrasound and CT (2 Slice helical GE CT) scan . This may be due to their types/ages some of which may have been replaced by machines of higher performance ratings. An additional reason could be that of the technical expertise of the operators of the machine and or the expertise of those who reported the scans.

The frustrations faced by health workers and patients in situations where confirmatory diagnosis and definitive treatment are not feasible in a centre have been highlighted by the frequent demands for referral abroad and the promptness with which these services are accessed outside. Medical tourism, which has become a new trend in the country has far reaching consequences on the health system, the economy and the morale of the public. It highlights the need for governments of resource-limited countries to increase their investments in health care and man-power development. This will make the services accessible to those who cannot afford the cost of care outside the zones where they live and worse still, outside the country. Thus, if the national goal of ensuring health for all by the year 2000 and beyond is to be achieved, the country must invest in health care.

CONCLUSION

Childhood hypertension is usually secondary and therefore often treatable if definitive diagnosis and appropriate treatment are promptly accessed. Delayed presentation, lack of diagnostic facilities and appropriate skills may delay the confirmation of diagnosis and therefore definitive treatment. Thus, the need for the governments of resource-limited countries to invest in health if the goal of health for all is to be attained cannot be over emphasised. Evolving and increasing cases of

medical tourism outside Nigeria and the associated cost of care should not be allowed to continue.

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