



A RARE CAUSE FOR PALPITATIONS - BILATERAL PHEOCHROMOCYTOMA

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Abstract : Pheochromocytoma is a very rare neuroendocrine tumor during childhood, which originates from the chromaffin cells, mostly of the adrenals and sympathetic chain. According to literature its frequency is approximately 1 in 1,00,000 population. The classic clinical presentation includes paroxysmal attacks of headache, pallor, palpitations, and diaphoresis. However it can present with any sign and symptom due to catecholamine excess like hypertension, palpitation, headache, sweating, nausea, vomiting, tremors, irritation, epigastric pain, chest pain, dyspnoea, red warm face, numbness or paresthesia, blurred vision, dizziness, convulsion, tinnitus, dysarthria. These symptoms can be observed every day in severe disease. The clinical manifestation can be variable and resembling many other diseases, so the pheochromocytoma is called the Great imitator.

Diagnosis can be made based on elevated levels of urinary catecholamines, but localization may require various modalities of investigations. Early diagnosis and treatment is important because the tumor may be fatal, if undiagnosed. We are presenting this case - a 10 years old girl, admitted with complaints of headache, palpitation and giddiness for 1 year, who on clinical examination was found to have hypertension. After a series of biochemical investigations and imaging studies, the diagnosis of bilateral pheochromocytoma was made. Child underwent surgery, bilateral adrenalectomy was done. The child is on regular follow up, remaining asymptomatic and normotensive till now. We present this case for its rarity. There had been only 23 cases of bilateral pheochromocytoma reported worldwide in children less than 10 years.

Keyword : Headache, palpitation, hypertension, bilateral pheochromocytoma A 10 years old female child got admitted in our hospital with complaints of headache, palpitation and giddiness for the past 1 year. There was also history of numbness of fingers and poor weight gain. There was no history of breathlessness, syncopal attacks, chest pain, or abdominal pain. She didn't have excessive sweating or tremors. There was no history of seizures, vomiting, visual disturbances. There was no fever, ear discharge. Sleep, appetite, bowel

and bladder habits were normal. The child had been hospitalised for two weeks at the age of 5 years and was treated for meningitis. Antenatal, birth and perinatal period had been uneventful. Child was immunised upto the age and developmentally normal for age.

On clinical examination, head to foot and general examination were normal. No thyroid swelling seen or felt. Oral cavity and ENT examination were normal. The height and the weight of the child were appropriate for the age. During cardiovascular system examination there was tachycardia and increased blood pressure in all the four limbs (130-100 mm hg). There was no murmur, no rise in JVP. Respiratory system and abdomen examination were normal, with normal external genitalia. On central nervous system examination, higher functions, cranial nerves and spinomotor system showed no abnormality. Visual examination revealed no abnormality. Fundus examination was normal.

The initial blood investigations showed normal renal parameters, lipid profile and liver function tests. Complete blood count was normal. Urine examination showed albumin 1+, no deposits. Chest xray revealed no significant abnormality. USG abdomen and KUB was normal with normal renal echoes. Echo evaluation showed concentric left ventricular hypertrophy with normal valves and normal ejection fraction. CT abdomen and CT brain were normal. Arterial blood gas analysis was within normal limits. Second line investigations for hypertension was done. Serum cortisol, renin and aldosterone were found to be normal. 24 hours urine was negative for vanillyl mandelic acid. ANA and anti ds DNA were negative. Complement C3, C4 levels were within normal range. Next set of investigations measuring 24 hours urine metanephrines (4200 mcgs) and serum catecholamines (1800 mcgs) were found to be elevated. To confirm the diagnosis, MIBG Scintigraphy was done which showed hot spots in left adrenal with delayed uptake in right adrenal. Thus a diagnosis of bilateral pheochromocytoma was made.

During the course of evaluation child blood pressure was brought under control after trying wide range of multiple antihypertensive drugs like Prazosin, CCBs, Enalapril, Clonidine, Losartan, Methyl dopa, Beta blockers and Diuretics. The child was then taken up for surgery. Bilateral adrenalectomy was

Done. Post operative period was uneventful. Post operatively 24hrs urinary metanephrines was not undetectable. Child was started on oral Prednisolone and oral Fludrocortisone. Histopathology of the resected adrenal specimen revealed numerous cells with scanty cytoplasm, increased nuclear cytoplasmic ratio, arranged in Zellballen pattern, nucleoli are prominent, suggestive of chromaffin cells. The child is now under regular follow up with good compliance. Now the child is remaining asymptomatic, normotensive with normal renal functions at present. Follow up 24hrs urinary metanephrines remained undetected. Family Screening was done and found to be negative.

Discussion :

Introduction :

Pheochromocytoma is a rare, catecholamine secreting tumour derived from chromaffin cells. Around 30 percent pheochromocytomas are part of hereditary syndromes like Von hippel landau, MEN 2, and Neurofibromatosis 1. About 85 percent are located within the adrenal glands. Tumours located outside the adrenal gland are called as extra adrenal pheochromocytoma which develop in the paraganglion chromaffin cells. Common locations for extraadrenal pheochromocytomas are organ of Zuckerkandl, wall of the urinary bladder, mediastinum. Approximately 10 percent of Pheochromocytomas are malignant, however the number is little higher upto 20 percent in children.

Pathophysiology :

The catecholamine secretion from the tumour may be intermittent or continuous depending on which the symptoms vary. Norepinephrine and epinephrine are the main catecholamines secreted, the uncommon one being dopamine. Alpha adrenergic stimulation is the reason for the clinical manifestations.

Etiology :

Though majority of the cases are sporadic, few are due to inherited mutations. MEN 2A Syndrome is characterised by medullary thyroid carcinoma, parathyroid adenoma and pheochromocytoma due to mutation in the *ret* proto-oncogene of chromosome 10. Mutation in MYC associated factor X (MAX) gene, GDNF gene, TMEM127 gene are also found to have a role in pheochromocytoma. Also, succinate dehydrogenase complex gene SDHD mutations are involved.

Incidence :

The worldwide incidence is 1 in one lakh population with bilateral adrenal pheochromocytomas accounting for 15-20 percent in children.

Clinical Presentation :

Headache, diaphoresis, palpitations, tremors, weakness, pallor, weight loss. Signs – Hypertension, pallor, tachyarrhythmias, cardiomyopathy, retinopathy, weight loss, fever, anemia. Syndromes associated are Von hippel landau, neurofibromatosis, tuberous sclerosis, sturge weber syndrome. Features of these syndromes should be looked for.

Differential diagnosis :

Renovascular causes : Glomerulo nephritis, polycystic kidney disease, renal artery stenosis Cardiac causes : Tachyarrhythmias, valvular disease Endocrine causes : neuroblastoma, congenital adrenal hyperplasia, thyrotoxicosis, hyperaldosteronism. Generalised anxiety disorder.

Complications :

Hypertensive encephalopathy,
Myocardial dysfunction,
Dilated cardiomyopathy,
Pulmonary edema .

Work up :

Urine for vanillyl mandelic acid is a screening test. Diagnosis of pheochromocytoma is made by measurement of plasma free metanephrines, or urinary metanephrines. CT or MRI imaging can identify the site of the lesion depending on the size. Confirmation of the diagnosis is by MIBG Scintigraphy, PET scan or gene mutation analysis. Recent advancement is measuring plasma chromogranin A levels which is elevated in pheochromocytoma and it is found to

be 95percent specific. Postoperatively, histopathological diagnosis can be made by confirming the presence of chromaffin cells arranged in *zellballen* pattern.

Treatment :

Treatment of hypertension is with antihypertensive drugs. It is ideal to start alpha blocker first to avoid uninhibited alpha stimulation. Phenoxybenzamine is started 2 weeks prior to surgery usually to allow adequate volume expansion. Intraoperative hypertensive crisis is managed with phentolamine. Metyrosine is a newer drug, a tyrosine hydroxylase inhibitor which is under trial now. Surgery is the definite treatment of choice.

Prognosis :

Pheochromocytoma has good prognosis in general with recurrence rate of 10 percent for both benign and malignant type. Familial screening is mandatory in diagnosed cases. We have presented this case because of its rarity.

