

Extra-adrenal Paraganglioma: An Uncommon Cause of Secondary Hypertension in a Young Subject

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Abstract

A 8 year boy was admitted with features of tuberculous meningitis. He was detected to have hypertension. Further investigations revealed an extra-adrenal paraganglioma. Tuberculous meningitis and paraganglioma could be chance associations. Paraganglioma is a rare and potentially lethal cause of secondary hypertension, very uncommon at this age. If left untreated it leads to complications arising from unrelenting hypertension. We report a case report on this very rare disease of paraganglioma presenting in an unexpected way.

Key words: Paraganglioma, Tuberculous meningitis, Secondary hypertension

Introduction

The paraganglion system is formed by numerous collections of neuroepithelial cells¹. Paraganglioma are tumors of paraganglia. The most common site is adrenal medulla, where it is known as pheochromocytomas. Those located outside the adrenal gland as extra-adrenal paragangliomas (EAPs). They have a more aggressive course than their adrenal counterparts. The diagnosis of pheochromocytomas and paragangliomas provide a potentially correctable cause of hypertension, and their removal can prevent lethal hypertensive crises.

The Case

!Unexpected End of Formula

A 8-year-old boy was admitted with fever, headache, and vomiting of 1 month duration. In the past, he had occasional headache relieved by medicines. There was no significant illness in the family. On examination patient appeared sick, pulse rate was 110/minute being felt at all limbs, BP was 210/130 mmHg in the supine position without any asymmetry in limbs and postural drop. He had signs of meningeal irritation without focal neurologic deficits. Investigations revealed

hemoglobin 13.8 g%, total leukocyte count 13,400 /mm³ with polymorphs 75% and lymphocytes 23%. His blood sugar, renal function tests, liver function tests, and serum electrolytes were within normal limits. Cerebrospinal fluid analysis revealed lymphocytic pleocytosis in the cerebrospinal fluid with protein content of 134 mg% and sugar of 90 mg% (corresponding blood sugar 85 mg%). Computed tomography (CT) brain showed sulcal effacement. Ultrasonography abdomen showed a well-defined hypodense area in the epigastric region. Electrocardiogram and X-ray chest were normal. Twenty-four hour urinary Vanilmandelic acid (VMA) (35 mg/ 24 hrs, normal: 2-7 mg/24 hrs) and urinary metanephrines levels (2560 µg/ 24 hrs, normal: 140-760 µg/ 24 hrs) were elevated. Contrast enhanced CT abdomen showed soft tissue mass of 4.5 × 2.9. × 3.5 in the left paraaortic region with heterogenous enhancement (Figure 1). Minimal compression was noted in the inferior vena cava with preserved fat plane. There was no lymph node enlargement with normal adrenals and renal arteries. The possibility of aortosympathetic paraganglioma was entertained. Establishing a diagnosis of tuberculous meningitis with EAP, he was prescribed antituberculous drugs, α blockers followed by β-blockers and calcium



Fig 1: CT scan abdomen showing soft tissue mass of 4.5 × 2.9. × 3.5 in the left paraaortic region with heterogenous enhancement

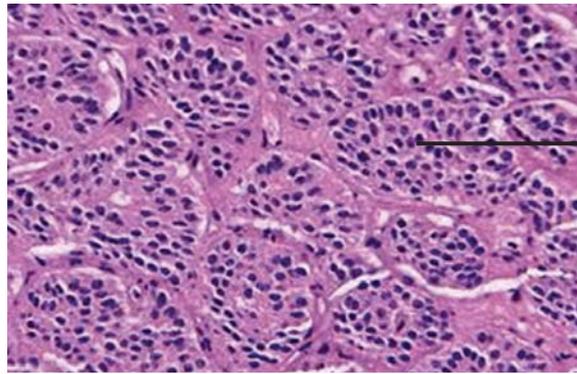


Fig 2: Histology of the biopsied specimen revealing characteristic organoid or zellballen nest of cells (hematoxylin-eosin stain, original magnification X 300)

channel blockers. Three weeks later, with proper BP control, the mass was surgically resected. Biopsy of the specimen revealed characteristic organoid or zellballen nest of cells confirming the diagnosis of paraganglioma (Fig 2). Patient was discharged after four days. One month later, patient was better without any recurrence of hypertension.

Discussion

Alezais and Peyron described extra-adrenal chromaffin tumors and called them paragangliomas in 1906. EAPs are divided into 2 categories: related to either parasympathetic or sympathetic system. The former, usually nonchromaffin, lie in the head and neck, including the carotid body, jugulotympanic, and mediastinal and aorticopulmonary paraganglia. The latter are chromaffin positive, associated with the peripheral sympathetic nervous system and secrete catecholamines. They lie in the para-axial region of the trunk close to the paravertebral and prevertebral ganglia². Rarely, paragangliomas have been described in other unusual sites, such as the gallbladder, mesentery, kidney, and prostate³.

Incidence of all EAPs is 2–8 per million. EAPs affect men in their 2nd or 3rd decade⁴. Our case was unique in its presentation in the first decade itself. EAPs can be inherited as an isolated autosomal dominant trait or as part of the multiple endocrine neoplasia type II syndromes, neurofibromatosis and von Hippel–Lindau disease. Germ line mutations in the succinate dehydrogenase (SDH) subunit genes SDHB, SDHC and SDHD⁵ predispose carriers to tumors of the paraganglia.

EAPs can be nonfunctional, but infradiaphragmatic ones are functional. The lower levels of phenylethanolamine *N*-methyltransferase (the enzyme responsible for the conversion of norepinephrine to

epinephrine by methylation) leads to higher levels of norepinephrine. Symptoms include hypertension (paroxysmal and/or sustained), headaches, sweating, palpitations, anxiety and tremors. It can present with heart failure, pulmonary edema, arrhythmias, and intracranial hemorrhage. There are clinical differences between adrenal pheochromocytomas and EAPs. Adrenal pheochromocytomas often affect females in 5th–7th decades. EAPs affect males in 2nd–3rd decade⁶. EAPs are more likely to be multifocal than are adrenal lesions.

In our patient the clinical scenario with raised urinary VMA and metanephrines and imaging evidence gives unequivocal confirmation of the diagnosis. Urinary tests for VMA, metanephrines (total or fractionated), and catecholamines are commonly used initially⁷. The fractionated metanephrines and catecholamines are the most sensitive. Plasma tests include measurements of catecholamines, metanephrines, and chromagranin A. False-positive elevations occur with stress, including venipuncture, medications (levodopa, labetalol, sympathomimetics). T2-weighted magnetic resonance imaging with gadolinium contrast is somewhat better than CT for imaging extra-adrenal pheochromocytomas and paragangliomas⁸. A heterogeneous, hypervascular, retroperitoneal mass with areas of necrosis with typical clinical setting is highly predictive of EAPs. The organs of Zuckerkandl are the most common site of involvement for paraaortic EAP. These are located along the aorta, beginning cranial to the superior mesenteric artery or renal arteries and extending to the level of the aortic bifurcation or just beyond. The highest concentration is typically seen at the origin of the inferior mesenteric artery. The organs of Zuckerkandl are not often visualized radiologically. The close relationship of paragangliomas to the aorta may be helpful in differentiating these tumors from other primary retroperitoneal tumors. Tumors can also be localized using radioactive tracers,

including I^{131} or I^{123} metaiodobenzylguanidine (MIBG), In^{111} - somatostatin analogs. However, there is a 10% false-negative rate with MIBG scanning. Most malignant tumors show an enhanced glycolytic metabolism with increased uptake of deoxyglucose that can be visualized by PET using $18F$ 2- fluoro- -2-deoxyglucose (FDG)⁹.

Complete tumor removal is the ultimate therapeutic goal. Preoperatively α blockers (phenoxybenzamine) should be initiated at low doses with gradual increment. Oral prazosin or intravenous phentolamine can be used to manage paroxysms, while awaiting adequate α -blockade. β -Blockers are added after adequate α blockade (10-14 days) and increased if tachycardia persists. Calcium channel blockers or angiotensin-converting enzyme inhibitors are used in cases of inadequate BP control¹⁰. Blood pressure can be labile during surgery, particularly at the onset of intubation or when manipulating the tumor. Nitroprusside infusion is useful for intraoperative hypertensive crises, and hypotension usually responds to volume infusion. No such complication was noted in our patient.

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