Case Report

Secondary hypertension: A rare cause

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ABSTRACT

A 13-year-old, previously asymptomatic girl was admitted with features of tuberculous meningitis. She was found to be hypertensive and further investigations revealed an extra-adrenal paraganglioma. Tuberculous meningitis and paraganglioma could be chance associations. Paraganglioma is a very rare and potentially lethal cause of secondary hypertension. We are reporting a very rare disease, which has come to light in a most unexpected manner.

Key words: α-Blockers, extra-adrenal paraganglioma, tuberculous meningitis

Introduction

Paraganglioma is the generic term applied to tumors of paraganglia, regardless of location. Paragangliomas of the adrenal medulla, the most common site of paragangliomas, are known as pheochromocytomas, whereas those located outside the adrenal gland as extra-adrenal paragangliomas (EAPs). Extra-adrenal retroperitoneal paragangliomas 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 hypertensive crises that can be lethal.

Case Report

A 13-year-old girl was admitted with a history of fever, head ache, and vomiting of 1 month duration. She did not give any history of significant illness in the past, other than occasional headache, which was relieved by medicines. Her blood pressure (BP) had not been checked before at any time. She had 2 siblings. There was no significant illness in the family. On examination she was sick looking. Her pulse rate was 120 beats per minute, BP was 180/130 mmHg in the supine position and 140/110 mmHg in the upright position. She had signs of meningeal irritation but no focal neurologic deficit.

Her blood investigations revealed a hemoglobin of 14.2 g%, total leukocyte count of 12,900 /mm^3 with polymorphs 85%, lymphocytes13%, packed cell volume 45%. Her blood sugar, renal function tests, liver function tests, and serum electrolytes were within normal limits. She was not immunosuppressed. She had lymphocytic pleocytosis in the cerebrospinal fluid with protein content of 139 mg% and sugar of 92 mg% (corresponding blood sugar 85 mg%). Computed tomography (CT) brain showed evidence of sulcal effacement. Ultrasonography abdomen showed a well-defined hypodense area in the epigastric region. She had normal electrocardiogram and X-ray chest. Twenty-four hour urinary Vanilmandelic acid (VMA) and urinary metanephrines levels were elevated. CT abdomen with nonionic contrast showed a well-defined lobulated heterogeneously enhancing soft tissue mass lesion of size 4.3 × 3.4 × 3.7 cm in the right para-aortic location at the level of L3 vertebra with no necrosis or calcification. Fat plane with aorta and adjacent bowel and vertebrae was well preserved. Minimal compression was noted in the inferior vena cava with preserved fat plane. There was no lymph node enlargement. Both the adrenals and renal arteries were normal. The possibility of aortosympathetic paraganglioma

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was entertained. With the clinical and investigation results a diagnosis of tuberculous meningitis with EAP was made. She was started on antituberculous drugs, α- and β-blockers, and calcium channel blockers. Surgery is being planned.

Discussion

The diagnosis of pheochromocytomas and paragangliomas provide a potentially correctable cause of hypertension.

The first reported case of pheochromocytoma is attributed to Frankel in 1886. Alezais and Peyron described extra-adrenal chromaffin tumors and called them paragangliomas in 1906. The paraganglion system is formed by numerous collections of neuroepithelial cells.[1] EAPs are divided into 2 categories: those related to the parasympathetic system and those connected with the 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 ganglia.[2] Rarely, paragangliomas have been described in other unusual sites, such as the gallbladder, mesentery, kidney, and prostate.[3]

Incidence of all EAPs is only 2–8 per million. EAPs affect patients in the 2nd or 3rd decade of life. Men are affected more frequently than women.[4]

EAPs can be inherited as an isolated autosomal dominant trait or as part of the multiple endocrine neoplasia type II syndromes, as well as with neurofibromatosis and von Hippel–Lindau disease. Germ line mutations in the succinate dehydrogenase (SDH) subunit genes sdh b, sdh c, sdh d, and sdh af2[5] predispose carriers to tumors of the paraganglia.

Clinical features

Although EAPs can be nonfunctional, the majority of EAPs occurring below the diaphragm are functional with the symptoms related to the excessive secretion of catecholamines, namely, norepinephrine. In EAPs, the lower levels of phenylethanolamine *N*-methyltransferase (the enzyme responsible for the conversion of norepinephrine to epinephrine by methylation) may lead to higher production of norepinephrine. Commonly reported symptoms include hypertension (paroxysmal and/or sustained), headaches, sweating, palpitations, anxiety, and tremors. Catecholamine crises can lead to heart failure, pulmonary edema, arrhythmias, and intracranial hemorrhage. There are several important clinical differences between adrenal pheochromocytomas and EAPs. First, sporadic adrenal pheochromocytomas often affect patients in the 5th to 7th decades of life, with a slight female predilection. EAPs affect patients in the 2nd or 3rd decade of life, with genetic tumors having a male predilection.[6] Extra-adrenal tumors are more likely to be multifocal than are adrenal lesions.

Diagnosis

The diagnosis is based on documentation of catecholamine excess by biochemical testing and localization of the tumor by imaging. In this patient the clinical scenario as well as biochemical evidence of raised urinary VMA and metanephrines and also imaging evidence give unequivocal confirmation of the diagnosis.

Pheochromocytomas and paragangliomas synthesize and store catecholamines, which include norepinephrine (noradrenaline), epinephrine (adrenaline), and dopamine. Elevated plasma and urinary levels of catecholamines and the methylated metabolites, metanephrines, are the cornerstone for the diagnosis. Urinary tests for VMA, metanephrines (total or fractionated), and catecholamines are commonly used for initial testing. Among these tests, the fractionated metanephrines and catecholamines are the most sensitive. Plasma tests include measurements of catecholamines, metanephrines, and chromagranin A, a secretory product of endocrine cells. False-positive elevations occur due to stress, including venipuncture, medications (eg, levodopa, labetalol, sympathomimetics).

Diagnostic imaging

CT should be performed with contrast. T2-weighted magnetic resonance imaging with gadolinium contrast is somewhat better than CT for imaging extra-adrenal pheochromocytomas and paragangliomas. A heterogeneous, hypervascular, retroperitoneal mass with areas of necrosis with typical clinical setting, is highly predictive of the presence of EAPs. Of the paraganglionic tissues adjacent to the aorta, the organs of Zuckerkandl are the most common site of involvement. The organs of Zuckerkandl 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 unless they are involved by a pathologic process.

CT features of EAP overlap those of other types of tumors found in the retroperitoneum. Specifically, tumors of neural or mesodermal origin and those of metastatic disease must be considered. The close relationship of paragangliomas to the aorta in all instances may be of

some value in differentiating these tumors from other primary retroperitoneal tumors. Tumors can also be localized using radioactive tracers, including ^{131}I or ^{123}I metaiodobenzylguanidine (MIBG), ^{111}In-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-D-2-deoxyglucose (FDG).

Treatment

Complete tumor removal is the ultimate therapeutic goal. Preoperative patient preparation is essential for safe surgery. α-Adrenergic blockers (phenoxybenzamine) should be initiated at relatively low doses. Adequate α-blockade generally requires 10–14 days. Oral prazosin or intravenous phentolamine can be used to manage paroxysms, while awaiting adequate α-blockade.

β-Blockers can be added after starting α-blockers, and increased as needed, if tachycardia persists. Because β-blockers can induce a paradoxical increase in BP in the absence of α-blockade, they should be administered only after effective α-blockade. Other antihypertensives, such as calcium channel blockers or angiotensin-converting enzyme inhibitors, have also been used when BP is difficult to control with phenoxybenzamine alone. 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.

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