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Case Report

Pediatric Suprarenal Paraganglioma Presented as Blurred Vision — a Case Report

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Abstract

Ocular manifestations of hypertensive retinopathy such as vision impairment or even loss associated with pheochromocytoma or paraganglioma were rarely reported. In this paper, we report a case of a fifteen-year-old girl with unremarkable medical history but presenting with bilateral blurred vision for two months. Initial blood pressure (BP) was 218/159 mm Hg. Ophthalmoscopy showed bilateral hypertensive retinopathy with optic disc edema. Two-dimensional echocardiography revealed hypertrophy of the interventricular septum and left ventricular wall. Initial emergent hypertension was stabilized with phenoxybenzamine and calcium channel blocker. Renal ultrasound and abdominal computed tomography revealed a huge right suprarenal tumor with compressing renal hilar vessels. Urinary vanillymandelic acid (VMA) level was 56.5 mg/24 hr (normal, 2-7 mg/24 hr). Retroperitoneal suprarenal paraganglioma was highly suspected. Tumor resection was performed after blood pressure was stabilized for two weeks. Pathological study revealed a paraganglioma of 10 × 6.7 × 4 cm in size with potential of metastasis. Postoperative 18-fluorodeoxyglucose positron emission tomography scan revealed no metastasis. Her visual acuity, BP and VMA level returned to normal after tumor resection. While pediatric pheochromocytoma and paraganglioma are rare, blurred vision with hypertensive retinopathy may be induced by pheochromocytoma/paraganglioma in children. We deemed it worthwhile to report our experience with a patient who presented with initial blurred vision caused by paraganglioma.

KEY WORDS: paraganglioma, hypertensive retinopathy, vanillymandelic acid

Introduction

Pheochromocytomas in children, arising from chromaffin cells of adrenal medullary or extra-adrenal paraganglionic tissue, are rare. Tumors from extra-adrenal chromaffin tissues are referred to as paragangliomas or extra-adrenal pheochrocytomas. Incidence of pheochromocytoma and paraganglioma is 0.40-2.06 per million per year (1, 2). Most cases are found in adults with incidence in children lower than 5% (3). Most symptoms are due to elevated levels of catecholamines. Sustained hypertension in pediatric pheochromocytoma cases is more common than in adult cases.

Pheochromocytoma is estimated to be prevalent in approximately 1% of hypertensive pediatric patients and should be considered after exclusion of more common causes (4, 5). Paroxysmal hypertension or development of orthostatic hypotension against the background of sustained hypertension or amelioration or even inversion of circadian BP rhythm may be crucial to diagnosing pheochromocytoma (6). Palpitation, headache, excessive sweating and pallor are well-known symptoms of continuous or paroxysmal catecholamine excess and should arouse suspicion of pheochromocytoma (7). Sweating, nausea, vomiting, weight

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loss, polyuria and visual disturbances are reported more often in children than in adults (8, 9). While pediatric pheochromocytoma and paraganglioma are rare, they provide an important differential diagnosis for childhood hypertension. Ocular manifestations of hypertensive retinopathy such as vision impairment or loss associated with pheochromocytoma were reported.

Case Report

A fifteen-year-old girl visited an ophthalmologic clinic because of a two-month history of blurred vision. Excessive sweating had also been noted for three years. Her medical history was unremarkable with no family history of hypertension. Hypertensive retinopathy was suspected at ophthalmologic clinic and she was admitted for further observation. Her body weight was 51.8 kg (50^{th} percentile) and body height was 158 cm ($50\text{-}75^{th}$ percentile). She had best corrected visual acuity of 6/60 in both eyes, which was worse than visual acuity of 6/6 in both eyes before this hypertensive episode. Slit lamp examination and intraocular pressure were normal. Ophthalmoscopic examination showed papilledema over the optic disc with hemorrhage and cotton-wool spots at the retina in each eye. Heart rate was 122 beats/minute and respiration rate was 20/minute. Wide fluctuations in BP were noted: maximal of 218/159 mm Hg and minimal of 150/110 mm Hg. Auscultation revealed grade 2 short systolic murmurs over left middle sternal border and no palpable abdominal mass. Urine analysis was unremarkable. Complete cell count, blood urea nitrogen, creatinine, and electrolyte levels of blood were all within normal limits. Urinary VMA level was 56.5 mg/24 hr (normal, 2-7 mg/24 hr) and plasma renin activity was 9.62 ng/mL/hr during supine rest (normal, 0.15-2.33 ng/mL/hr). Chest roentgenography and electrocardiography also showed normal results. Two-dimensional echocardiography revealed hypertrophy of interventricular septum and left ventricular free wall. Ultrasound revealed a right, huge suprarenal mass with compression of right kidney. Computed tomography of the abdomen demonstrated a right retroperitoneal, suprarenal tumor of 7.2×5.5 cm in size with tortuous veins and displacement of right renal artery and inferior vena cava (Fig. 1). Captopril renoscintigraphy revealed no probability of renovascular hypertension. Before operation, right retroperitoneal, suprarenal paraganglioma was suspected. Her thyroid function, calcitonin and intact PTH level were within normal limits. The patient was treated with phenoxybenzamine, an alpha-adrenergic blocking agent, and calcium channel blocker. Initial phenoxybenzamine dosage was 30 mg/day but increased to 120 mg/day after 4 weeks of therapy to control systolic BP within the range of 130 to 100 mm Hg. Surgery was arranged after hypertension was controlled. Tumor resection was performed after BP was stabilized for two weeks. A $10 \times 6.7 \times 4$-cm tumor located between aorta and inferior vena cava with much collateral circulation and dense adhesion was noted intraoperatively. Microscopically, tumor mass is encapsulated and the tumor cells within the mass were characterized by round and focal pleomorphic nuclei, indistinct to small nucleoli, and pink cytoplasm (Fig. 2a). Tumor cells were arranged in nest or Zellballen pattern (Fig. 2b) and surrounded by thin fibrovascular channels. Both vascular and capsular invasion with patchy hemorrhage and confluent necrosis were noted. Nerve bundles both within and at the periphery of tumor mass were also noted. Several big vessels within tumor mass and vascular wall were focally invaded by tumor cells. There was no adrenal component in this specimen. Immunohistochemical study showed tumor cells with positive stain for synaptophysin (Fig. 2c) and chromogranin (Fig. 2d). Sustanticular frameworks were highlighted by S-100 (Fig. 2e). All section margins were free, but tumor nests were very close to section margins focally (less than 1 mm). Potential of malignancy and metastasis was highly suspected, with tumor necrosis, capsular invasion, vascular invasion and large vessels within tumor mass having invaded vascular wall observed. Ki-67 positive cells were about 4-5%. Paraganglioma with potential of metastasis was diagnosed. Postoperative 18-fluorodeoxyglucose positron emission tomog-

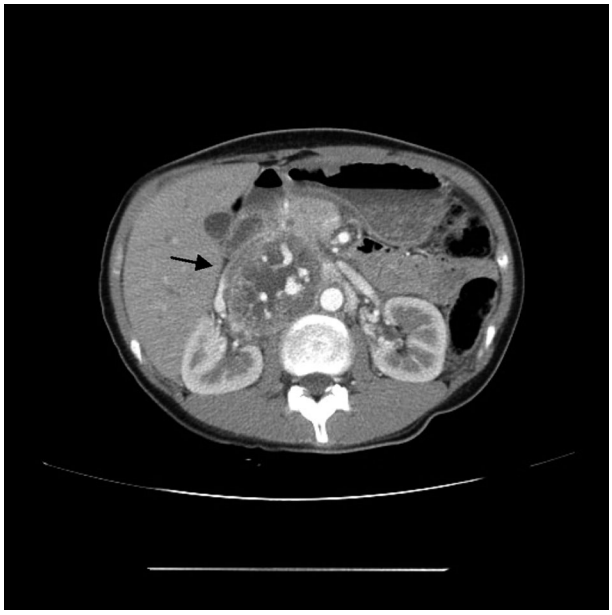

Fig. 1. Computed tomography of the abdomen demonstrating a 7.2×5.5-cm hypervascular mass lesion (arrow) over right retroperitoneum, suprarenal region with tortuous veins and displacement of right renal artery and inferior vena cava.

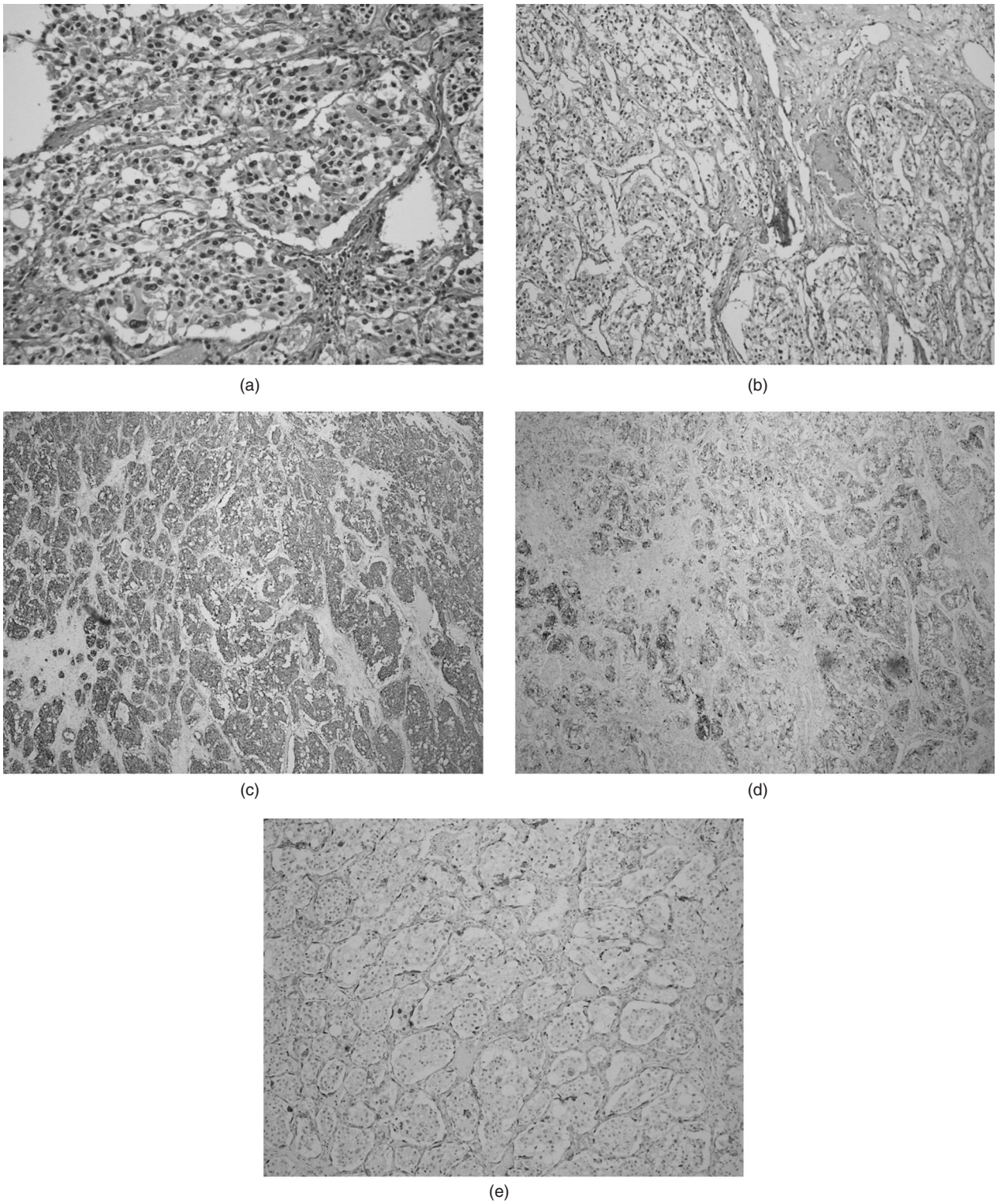

Fig. 2. Hematoxylin and eosin stain demonstrating tumor cells characterized by round and focal pleomorphic nuclei (1a) and arranged in nest or Zellballen pattern (1b). Immunohistochemical stain showed tumor cells with positive stain for synaptophysin (1c) and chromogranin (1d). Sustanticular frameworks highlighted by S-100 (1e).

raphy scan revealed no metastasis. She had complete resolution of presenting symptoms with normalized blood pressure 2 months postoperatively without antihypertensive medication. Visual acuity and VMA level normalized after tumor resection and were regularly monitored at our outpatient clinic for 6 months.

Discussion

Pheochromocytomas, originating from chromaffin cells of adrenal medullary or extra-adrenal paraganglionic tissue, are rare in children. Those that arise from the autonomic nervous system of abdomen, thorax, neck or head are more specifically termed as paragangliomas and often referred to as extra-adrenal pheochromocytomas. While the incidence of pheochromocytoma and paraganglioma in childhood is low, they represent the most common pediatric endocrine tumor and constitute a key cause of severe hypertension in children. Clinical presentations of childhood pheochromocytoma or paraganglioma are highly variable, with tumors found in some patients who are completely asymptomatic. Average age at onset is 11 years, with a male/female ratio of 2:1 (5, 10). Hypertension caused by secretion of one or more catecholamine hormones is the most prominent feature and may be paroxysmal or persistent. Compared with adults, children more often present with symptoms related to hypertension: headache, tachycardia, diaphoresis, postural hypotension, nausea, vomiting, abdominal or chest pain, weight loss, shortness of breath, polydipsia, polyuria, acrocyanosis, convulsions, and visual disturbances (11). Yet symptoms and signs of pheochromocytoma or paraganglioma are not so specific in children, thus making early diagnosis difficult. Clinical alertness and BP measurement are vital for detecting child hypertension. Sustained hypertension is found in 60-90% of pheochromocytoma in pediatric cases, versus 50% in adult cases. Pheochromocytoma or paraganglioma should be considered after excluding usual causes of pediatric hypertension such as cardiovascular or renovascular hypertension, renal parenchymal disease and renal congenital anomaly. Other endocrine causes of pediatric hypertension included thyroid disease, Cushing syndrome and congenital adrenal hyperplasia. Evaluation of suspected pheochromocytoma or paraganglioma should include 24-hour norepinephrine, epinephrine, total metanephrines, and VMA concentrations in urine. In more than 95% of patients of pheochromocytoma or paraganglioma, diagnosis can be established by increased urinary VMA concentration (12). Plasma catecholamine determination is generally less useful than urinary assessment, except in hypertension crisis. Upon diagnosis, surgical excision is the only curative treatment. Surgical complications may emanate from excessive and abrupt release of catecholamines (12). Adequate preoperative preparation and treatment with non-competitive alpha-adrenoreceptor blocker like phenoxybenzamine can treat adrenergic manifestations and hypertensive crisis during anesthetic induction or surgical manipulation of tumors as well as reduce morbidity and mortality effectively. Patients with adequate phenoxybenzamine are prone to orthostatic hypotension (13). This preoperative treatment should be given in the hospital; patients should be instructed on the need for and assisted in maintaining upright position to prevent complications. Hypertensive retinopathy is uncommon but a critical condition for children. Delay diagnosis may result in permanent visual damage owing to optic atrophy. In its early stages, fundus picture shows retinal arteriolar constriction. As the disease progresses, superficial hemorrhages and small white superficial foci of retinal ischemia in nerve fiber layer (cotton-wool spots) develop. In cases of severe hypertension, optic discs become congested and edematous. If elevated BP is controlled promptly with medication or surgery, retinal blood vessels may recover without permanent pathologic changes (14). In our case, fundus ophthalmoscopy revealed intraretinal hemorrhage, cotton-wool spots and optic disc edema; visual acuity returned dramatically to normal after tumor resection, indicating that early correction may reverse hypertensive retinopathy in a child.

Though pediatric pheochromocytoma and paraganglioma are rare, blurred vision with hypertensive retinopathy may arise from either of them. Permanent visual damage can be a severe complication without early treatment; 24-hour urine VMA, plasma catecholamine and localized image study can aid diagnosis. Preoperative stabilization of BP and surgical intervention can result in uneventful recovery.

In summary, pheochromocytomas or paraganglioma have varied clinical ocular manifestations of blurred vision and hypertensive retinopathy. While pediatric pheochromocytoma and paraganglioma are rare, they constitute a key diagnosis for child hypertension.

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