Paraganglioma (extra-adrenal pheochromocytoma) is a rare neuroendocrine tumor in children. Pheochromocytomas account for about 0.1% to 0.5% of cases of hypertension [1, 2]. Only 20% of pheochromocytomas are found in the pediatric population and less than half of these arise at extra-adrenal locations [1, 3]. The tumor can easily be recognized during workup from the classical presentation of hypertension. However, shock presents as the initial manifestation in only 2% of patients with such tumors [2, 4]. In this report, we describe the management of a girl with a retroperitoneal paraganglioma who presented with shock and pulmonary edema as the initial manifestation.

Case Report

A 12-year-old girl had headaches, palpitations, and sweating of the forehead occasionally during the past year. Hypertension had not been documented. Progressive dyspnea was noted for 2 days and she was referred to our pediatric intensive care unit because of shock. On admission, her height was 140 cm (between the 10th and 25th percentile for her age) and her weight was 26.5 kg (between the 3rd and 10th percentile for her age). Physical examination revealed a respiratory rate of 30 breaths per minute, a pulse rate of 160 beats per minute, and a body temperature 39°C. Her blood pressure was 50/20 mm Hg. Cardiac auscultation failed to detect any murmur but a gallop was noted. Signs of heart failure including engorgement of the bilateral jugular veins, basilar rales over both lung fields, and hepatomegaly (2 cm below the right costal margin) were noted at physical examination. Chest radiographs showed cardiomegaly and pulmonary edema. Electrocardiography revealed sinus tachycardia, left ventricular hypertrophy by voltage criteria, and T-wave inversion in leads V5 and V6. Echocardiography demonstrated left ventricular chamber enlargement and dyskinetic and hypokinetic movement of the left ventricle. At that time, her left ventricular ejection fraction (LVEF) was 29%. Myocarditis was the initial diagnosis. However, cardiac enzymes were not elevated (creatine kinase, 83 U/L; creatine kinase MB isoenzyme, 12 U/L; troponin I, < 0.5 ng/mL). Her blood pressure became stable after intravenous normal saline challenge and intravenous dopamine given for one night. However, after tapering the dose of dopamine, hypertension was noted. Physical examination showed a systolic blood pressure of 160 to 190 mm Hg. Funduscopic examination of the eyes revealed hypertensive retinopathy.

A series of studies was done to evaluate the cause of hypertension. Renal ultrasound disclosed a 4 x 4-cm perirenal tumor near the hilum of the left kidney and hydronephrosis of the left kidney. A peripheral blood sample showed elevated plasma renin activity (24.45 ng·mL⁻¹·hr⁻¹) and aldosterone concentration (55 ng/dL). Abdominal T1-weighted magnetic resonance (MR) imaging revealed a 5.8 x
4.7 x 3.2-cm mass with low central signal located near the left renal hilum, accompanied by displacement of the left renal artery and left hydronephrosis (Figs. 1 and 2). No evidence of focal stenosis of the left renal artery was detected by abdominal aortography. Renal vein sampling for renin activity also failed to demonstrate lateralization. The plasma renin activity was 28.45 ng/mL/hr in the right renal vein, 28.13 ng/mL/hr in the left renal vein, and 19.81 ng/mL/hr in the inferior vena cava. The 24-hour urine vanillylmandelic acid (VMA) and catecholamine excretions were elevated (VMA 18 mg/24 h, dopamine 917 µg/24 h, norepinephrine 1,162 µg/24 h, epinephrine 51 µg/24 h) 2 weeks after discontinuation of dopamine. Hence, I-131 metaiodobenzylguanidine (MIBG) scintigraphy was performed and a large mass was shown in the left abdomen (Fig. 3). Bone marrow biopsy was done to exclude bone marrow metastasis. During this period, the patient's cardiac function evaluated echocardiographically showed slight improvement, with an LVEF of 43% to 49% on four occasions.

After the diagnosis of paraganglioma was made, the patient was prepared for surgery with oral phenoxybenzamine 30 mg/day and normal saline infusion. The retroperitoneal tumor was excised and a left radical nephrectomy was performed due to severe adhesion of the tumor to the left kidney. Pathologic findings confirmed the diagnosis of paraganglioma with central fibrosis. The histologic features of the left adrenal gland and kidney were normal. The postoperative course was smooth and her blood pressure was 120/70 mm Hg after surgery. Twelve days after surgery, a follow-up 24-hour urine study showed excretion rates of VMA of 1.2 mg/24 hours, dopamine of 192 µg/24 hours, norepinephrine of less than 2.4 µg/24 hours, and epinephrine of less than 2.4 µg/24 hours, which were all within normal limits. At that time, follow-up echocardiography showed an LVEF of 43%. Captopril 25 mg/day and furosemide 20 mg/day were prescribed. Four months after surgery, the patient's blood pressure remained normal and her cardiac function had recovered (LVEF 64%).

**Discussion**

Pheochromocytoma is rare in childhood; only 10% to 20% of pheochromocytomas are found in the pediatric population [3]. Paragangliomas (extra-adrenal pheochromocytomas) arise from the chromaffin cells of the paraganglionic system and account for 30% to 50% of pheochromocytomas in children [1–3]. Urinary and plasma catecholamines are reliable tools for the diagnosis of pheochromocytomas and paragangliomas [3]. MR imaging and MIBG scintigraphy are also useful for radiologic localization of these tumors [3]. The diagnosis of paraganglioma in our patient was confirmed by these studies.

Paragangliomas are clinically different from pheochromocytomas. Pheochromocytomas secrete a combination of epinephrine and norepinephrine, whereas paragangliomas predominantly secrete norepinephrine. Hence, selective elevation of urine catecholamines was noted in this case.
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norepinephrine has been recommended as a diagnostic clue to predict the presence of an extra-adrenal pheochromocytoma [1]. The concentrations of catecholamines in this case confirm the diagnostic usefulness of this test.

Shock is a rare manifestation of pheochromocytoma. In a large study, only 2% of patients had shock as the initial manifestation [4]. The exact pathophysiology of shock accompanying pheochromocytoma has not been thoroughly elucidated [4, 5]. Hypertensive crisis induced by massive catecholamine release from tumor necrosis followed by depletion of the catecholamine store may result in shock, as has been confirmed in animal models [5, 6]. However, there was no evidence of tumor necrosis on pathologic investigation in the present case. Coronary vasospasm has also been reported as an important cause of shock in pheochromocytoma [7]. Norepinephrine is the major catecholamine secreted by paragangliomas [1]. Myocardial lesions from alpha-mediated coronary vasoconstriction due to norepinephrine and subsequent myocardial ischemia and necrosis have been shown experimentally [7–10]. However, there was no evidence of coronary ischemia in the electrocardiographic record of our patient. A greater increase in peripheral vascular resistance than in myocardial contractility, due to high catecholamine concentrations resulting in cardiac decompensation with shock, has also been proposed as the cause of shock in patients with pheochromocytoma. The patients may be so severely vasoconstricted that accurate blood pressure measurement cannot be obtained peripherally, yet these individuals may be severely hypertensive centrally [4, 5]. The term catecholamine cardiomyopathy has been used to describe myocardial impairment in pheochromocytoma [9–14]. In 1966, Van Vilet et al found focal myocarditis in 15 of 26 patients with pheochromocytoma at autopsy [15]. Direct toxicity of catecholamine to the cardiac muscle has been thought to cause catecholamine cardiomyopathy. Therefore, the cause of shock in patients with paraganglioma is complicated. It can also be caused by the combination of all these factors.

Patients with paraganglioma present with variable clinical manifestations. About 6% to 7% of patients with catecholamine cardiomyopathy present with acute left heart failure and myocardial infarction [10]. On the other hand, cardiomegaly, electrocardiographic evidence of left ventricular hypertrophy, and T-wave inversion are commonly seen in others [13]. Shock with pulmonary edema has occasionally been reported in these patients [5]. Although cardiogenic shock has been suggested as the cause, the possibility of direct toxic effects of increased catecholamine concentrations on the lung cannot be excluded [5].

Shock followed by death in patients with pheochromocytoma has been reported [12, 14]. Nonetheless, with appropriate management, shock can be corrected and the patient can survive [5, 7, 13]. However, it usually takes several months for cardiac function to completely recover [7, 11, 13]. In spite of the fact that our patient’s blood pressure became normal, her LVEF remained depressed 12 days after removal of the tumor. Her cardiac function recovered 4 months later.

The unusual presentation and findings in the present case emphasizes the importance of the consideration of pheochromocytoma in patients presenting with shock without any obvious cause.

References