

Case Report

Diagnosis and Management of Pheochromocytoma in a Resource-Challenged Setting: A Case Report

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Abstract

Phaeochromocytoma (PCC) is a rare catecholamine-secreting tumor derived from the sympathetic nervous system's chromaffin cells. Pheochromocytomas are exceptionally rare in children and are responsible for about 1% of pediatric hypertensive patients [1]. They arise most commonly in the adrenal glands (approximately 85% of tumors)[1] but may also arise from chromaffin cells of the sympathetic nervous system, known as paragangliomas (PGLs). The tumors are more common in boys than girls, with a 2:1 ratio of boys to girls in pediatric PCC/PGL cohorts [2]. PCC/PGL often occur as sporadic tumors, but may sometimes occur as part of hereditary tumor syndromes, mainly Von Hippel Lindau (VHL) disease and multiple endocrine neoplasia (MEN) type 2A and 2B [1]. About 50% of cases are missed and discovered at autopsy because the diagnosis was not considered at presentation [3]. We report this case of phaeochromocytoma to draw the attention of clinicians in our environment to this unusual cause of pediatric hypertension and the need for a thorough investigation of the hypertension etiology of in children. We also underline the fact that this feared tumor can be successfully managed even in areas with limited resources, such as ours. Finally, we encourage physicians to measure blood pressure of children presenting to their clinics.

Keywords: Phaeochromocytoma, pediatric, hypertension.

Case Report

A 14-year old girl presented to the pediatric clinic with complaints of recurrent headaches, visual disturbances, and an incidental finding of elevated blood pressure (BP), during a home-measurement of blood pressure by her mother, who is a nurse. She first presented to a pharmacy shop where anti-hypertensives were given to her. However, her blood pressure remained high. She

subsequently developed palpitations and excessive sweating, necessitating admission to the pediatric cardiology clinic where examination findings included elevated blood pressure, ranging from 150/120 to 220/150mmHg at repeat measurements, an irregular heartbeat, and a displaced apex beat at the sixth left intercostal space, at the mid-clavicular line. Following an assessment of hypertensive heart disease (secondary hypertension), a series of investigations were requested.



Chest X-ray, electrocardiography (ECG), serum electrolytes and thyroid function tests were normal. Two-dimensional echocardiography showed a structurally normal heart with mid-left ventricular hypertrophy but good biventricular contractility. The ophthalmological assessment was normal, and cranial computed tomography (CT) showed no abnormality. The abdominopelvic ultrasound scan showed a left extrarenal pelvis and a right aortocaval mass, which was identified by an abdominal CT scan as a right adrenal pheochromocytoma. Urinary normetanephrine was markedly elevated: 46642 nmol/24h (450-1709 nmol/24h), with a normetanephrine-to-creatinine ratio of 5481 (21-308). However, urinary metanephrine was within normal limits: 366 (100-1262 nmol/24h), with a urine metanephrine-to-creatinine ratio of 43 (26-188).

She was managed with anti-hypertensives—a combination of an alpha-blocker (prazosin) and a beta-blocker (propranolol), which was started two days after the commencement of the alpha blockade. She subsequently had near-total adrenalectomy two months after the initial presentation. A variegated firm to hard, right suprarenal gland tumor was found intra-operatively, adherent to the adventitia of the posterior wall of the inferior vena cava (IVC), and displacing it anteromedially. The mass was free from other surrounding structures. The IVC, right renal, and supra-renal veins were distended. Intraoperatively, she had blood pressure surges and dysrhythmias; hypertension was controlled using magnesium sulfate infusions and labetalol. The diagnosis of pheochromocytoma was confirmed by histology of the sample. Following surgery, all symptoms resolved over ten weeks. Biochemical markers have all returned to normal reference ranges and the patient is stable on follow-up. Other family members are yet to be screened due to financial constraints.

Discussion

This case highlights the diagnosis of a rare adrenal tumor, pheochromocytoma in a pediatric patient. This was an incidental finding, following a thorough evaluation of an

adolescent female with an incidental finding of hypertension after monitoring blood pressure at home.

Pheochromocytomas are rare neuroendocrine tumors, with an incidence of 1 per 100,000 population reported in the United States, with pediatric cases accounting for 10 to 20% of all cases in the US [4]. Some reviews of pediatric cases have shown that pediatric pheochromocytomas account for 8.86% of all cases of PCC/PGL [2]. Besides, they account for 1.1 to 11% of adrenal masses found incidentally [5].

Cases are more common in males than females, with a male-to-female ratio of 2:1 [6]. Incidence peaks between 9 and 12 years of age [6], with a median diagnosis age of 13 years [2].

Our patient presented with all of the four characteristic features of the tumor: headaches, palpitations, excessive sweating, and severe hypertension [4]. Hypertension from pheochromocytomas accounts for 0.5 to 2.5% of all pediatric hypertension [7] and has been shown to be present in 80-90% of children at diagnosis. Some studies have demonstrated that sustained hypertension (rather than paroxysmal), is seen in up to 90% of pediatric patients with pheochromocytoma [8]. The diagnosis is, nevertheless, an important cause of correctable hypertension in children [5]. Headaches are the most frequent symptoms in children, and are present in about 75% of patients, while palpitations are present in about 64% of cases [4].

Diagnosis of this rare and extremely perilous tumor requires a high index of suspicion since up to half of the cases are discovered at post-mortem examinations. Therefore, the diagnosis should be considered in any patient presenting with symptoms of excessive catecholamine secretion such as hypertension, palpitations (with tachycardia or, less frequently, reflex bradycardia), and excessive and inappropriate diaphoresis. Other less common symptoms include orthostatic hypotension, excessive anxiety, paleness of the face and upper body, tremors, heat intolerance, and, rarely, seizures [3]. Unfortunately, in our environment with high medical costs and lack of health insurance, presentation to a pharmacy with the purchase of over-the-counter medications is usually the

first line of treatment of symptoms for many patients, resulting in late presentation to the hospital.

Measurement of 24-hour urinary metanephrines (catecholamine metabolites) is recommended for the diagnosis of pheochromocytoma, with higher sensitivity for normetanephrine (87.3%) compared to metanephrine (56.9%) [10], as shown in our patient. The specificity of both tests is 95%. Measurements of plasma and 24-hour urinary catecholamines (epinephrine, norepinephrine, dopamine) and urinary vanillylmandelic acid (VMA) are no longer used, owing to the lower sensitivity and specificity of these tests. The elevation of catecholamine metabolites four times the upper limit of normal is highly suggestive of a tumor, and our patient had a urinary normetanephrine level that was 27 times the upper limit of normal.

The gold standard for diagnosis is the measurement of plasma or 24-hour fractionated urinary metanephrines with imaging studies performed for the localization, identification of metastatic lesions, and surgical resection [7]. There are a few laboratories in our environment able to measure fractionated catecholamine metabolites, thus limiting the accuracy of diagnosis in many cases. However, efforts should be made to contact laboratories with this competency, if the patient can afford it.

Ninety-five percent of adrenal tumors measuring 1 cm or larger, and 90% of pelvic and abdominal tumors larger than 2 cm are identified by computed tomography (CT) [3]. CT and MRI of the abdomen and pelvis remain the imaging modality of choice in pediatrics, with a sensitivity of 90-100% for both tests, and specificity of 70-80% [5]. MRI, however, has the advantage of a better sensitivity for extra-adrenal tumors, and no radiation exposure [5]. Nonetheless, this imaging modality is less affordable and accessible in our environment, and therefore, computed tomography is more commonly used for diagnosis, as seen in our index case.

Owing to financial challenges in our environment, where health insurance is not widely available, diagnosis in the index patient was first made by abdominal ultrasonography (which has a sensitivity of 89%) before computed tomography

was done to confirm ultrasound findings. This was further confirmed by 24-hour fractionated urinary metanephrine values and post-operatively by histological findings. In all, the lack of adequate finances considerably prolongs intervention time for patients in our environment, as shown by the 2-month duration from presentation to intervention in the presented case. Therefore, it is necessary to reiterate the need for functional health-insurance systems to be made operational in third-world countries, particularly in Sub-Saharan Africa. This would improve management outcomes for the vast majority of children living in these environments. Additionally, there is an urgent need for the subsidized care of the ever-growing number of children with cancers in our environment.

Management of pheochromocytoma is multidisciplinary, involving the pediatric endocrinologists, pediatric surgeons, anesthetists, and geneticists. Except for the geneticist, these subspecialties are readily available in most tertiary institutions in our environment. Pheochromocytomas are managed by complete surgical resection, which carries the risk of hypertensive crisis intraoperatively. The occurrence of this feared complication has been greatly reduced in recent times by the preoperative use of the alpha- and beta-blockade [8]. As presented in the index report, alpha blockade usually precedes beta-blockade, never vice versa, to prevent unopposed alpha-receptor stimulation, which would lead to a severe hypertensive crisis [11]. Malignant cases are further treated with chemotherapy, with a 5-year survival rate ranging from 78% to 95% [8]. Recurrences are frequent, especially in patients with germline mutations, and may occur as early as one-year post-surgery, or as late as 35 years later [8]. In view of this, long-term follow-up of patients is necessary; yearly measurements of urinary/plasma metanephrines and imaging studies should be carried out at regular intervals.

Conclusion

Endocrine hypertension in general, and specifically pheochromocytoma, should be considered in the differential diagnosis of children

presenting with severe hypertension, especially if accompanied by the triad of headaches, palpitations, and excessive sweating. This is important, especially in an environment like ours, where pediatric endocrine disorders are mostly undiagnosed.

Proper management by a multidisciplinary team is associated with good outcomes, especially in children with benign tumors.

Additionally, a functional health-insurance system in developing countries would improve the treatment outcomes for children who may present with the same or similar tumors, leading to improved survival of these children.

Conflict of Interest

The authors declare no conflict of interest.

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