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Pheochromocytoma Presenting as Diabetes Insipidus

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Background: Pheochromocytomas are catecholamine producing tumors that classically present with the triad of sweating, palpitations and headache. **Case characteristics:** 9-year-old boy whose only presenting complaints were polyuria and polydipsia for 2 years. **Observation:** Routine measurement of blood pressure detected mild hypertension, and subsequent investigations revealed bilateral pheochromocytoma. **Outcome:** Surgical removal of the tumors resulted in complete resolution of polyuria and polydipsia. **Message:** The case highlights the importance of measuring BP for children as part of physical examination.

Keywords: Diabetes insipidus, Pheochromocytoma, Polydipsia, Polyuria.

Pheochromocytomas and paragangliomas are rare, with an estimated annual incidence of 2-8 per million population [1]. Hypertension, paroxysmal or sustained, is the most consistent finding [2]. The classical triad of symptoms, headache, palpitations and excessive sweating, is present in up to 50-70% of patients [2]. Other relatively common symptoms are flushing, pallor, anxiety, diarrhea, fatigue and fever. Here, we report a 9-year-old boy with bilateral pheochromocytoma, whose only presenting complaints were polyuria and polydipsia for two years.

CASE REPORT

A 9-year-old boy was brought to the outpatient department with complaints of increased thirst and urination for last 2 years. The child drank 7-8 L of water and passed 6-7 L of urine per day (10-12 mL/kg/h), with multiple nocturnal awakenings. There was no history of weight loss, polyphagia, fatigue, headache, vomiting, visual complaints or any significant past illness/head injury. Parents had consulted many pediatricians in their city, but no cause had been found. He had been diagnosed as psychogenic polydipsia, and behavioral therapy advised. However, there was no improvement and the child was brought to us. On examination, the child had normal hydration, heart rate of 110/min, blood pressure

of 126/75 mm Hg (at 95th centile), and weight and height between 10th-25th centiles. Urine output was documented as 10 mL/kg/hr. The initial investigative work-up was as follows: blood sugar (fasting and post-prandial) 103 and 146 mg/dL, urine specific gravity-1.002, serum sodium 143 and potassium 4.1 mEq/L. Renal function, blood gas, serum calcium, thyroid function, serum cortisol, urine routine and urine calcium/creatinine ratio were normal. Water deprivation test was planned the next morning, but baseline urinary and plasma osmolarity were 170 and 301 mOsm/kg respectively, which established the diagnosis of diabetes insipidus (DI). It was decided to give vasopressin challenge to differentiate between central and nephrogenic DI. BP was measured before administration of vasopressin, and was found to be 130/90 mm Hg (>95th centile). Vasopressin was not administered in view of the hypertension. Ultrasonography of the abdomen revealed bilateral adrenal masses 4.1 × 3 cm (left) and 2.2 × 1.9 cm (right) with areas of cystic degeneration, suggestive of pheochromocytoma.

Plasma and urinary normetanephrines were markedly elevated (2187 pg/mL (normal <180), and 3810 µg/day (normal 0-600) respectively), while the metanephrines were within normal levels, suggesting that the

predominant catecholamine secreted by the tumor was norepinephrine. PET/CT showed tumor located in bilateral adrenals with no extra adrenal tissue involvement. MRI of the brain was normal.

The child was taken up for surgery after medical preparation. The left adrenal was completely removed, while a part of the right adrenal gland was left and secured in place. Antihypertensives were discontinued immediately after surgery and replacement doses of hydrocortisone and fludrocortisone were started. Inotropic support was needed for one day in postoperative period. Polyuria and polydipsia subsided completely within 3-4 days of surgery.

The child has been in regular follow up for the last 8 months. There is no polyuria, polydipsia or hypertension. Hydrocortisone and fludrocortisone were tapered successfully after six months of surgery, and serum cortisol documented to be within normal limits. Repeat MIBG and PET/CT done after 6 months of surgery to look for tumor recurrence were normal.

DISCUSSION

Presentation of pheochromocytoma with DI like symptoms is extremely uncommon. Only three earlier case reports have reported polyuria and polydipsia as major presenting complaints, and in two of these, there were other complaints that provided additional clues towards diagnosis [3-5]. Our case presented with polyuria and polydipsia as the predominant complaint, leading to delay in diagnosis despite consulting several physicians over a two year period. The hypertension in our case was not striking, and emphasized the fact that hypertension can be mild and paroxysmal in patients with pheochromocytoma.

Norepinephrine has been seen to have a role in the non-osmolar regulation of antidiuretic hormone (ADH) secretion. In experimental studies by Schrier, *et al*, it was seen that intravenous infusion of norepinephrine in rats led to diuresis by inhibition of endogenous ADH release. This diuresis could be blocked by baroreceptor denervation or by alpha-adrenergic antagonists, indicating that the inhibition of ADH was mediated by α -adrenergic stimulation of the baroreceptors [6-8]. Elevated BP also exerts a hemodynamic effect, mediated by peripheral baroreceptors, and contributes to suppression of ADH secretion [4, 6].

Moreover, in experimental and clinical studies, administration of norepinephrine has been seen to cause a reduction in insulin secretion [9], as well as sensitivity

[10]. The combined effect is therefore hyperglycemia, which can lead to solute mediated diuresis. In this child however, blood sugar was only mildly elevated, and therefore unlikely to be contributing to polyuria.

To conclude, we would like to state that polyuria and polydipsia can be the only presenting complaints in a child with pheochromocytoma, and BP measurement should be an integral part of initial evaluation of all children.

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