Nocturnal enuresis is a possible symptom of pediatric paraganglioma: A case report

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Introduction

Paraganglioma is a rare catecholamine-secreting tumor that arises from chromaffin cells of the sympathetic nervous system. For adequate management and outcomes, early diagnosis is essential. However, particularly in children, early diagnosis is challenging. This is because of the extremely low incidence of pediatric paraganglioma (up to 0.3 per million, annually). Another reason for the challenging early diagnosis of paraganglioma in children is its atypical clinical symptoms. The classical triad of adult paraganglioma, i.e., headache, tachycardia, and sweating, may not always be present in pediatric paraganglioma. In order to diagnose pediatric paraganglioma without delay, careful clinical examination and assessment are essential.

Recently, we encountered a case of pediatric paraganglioma involving a patient whose chief complaint was secondary nocturnal enuresis. Despite the absence of the triad and a family history of paraganglioma, our routine physical examination revealed that the patient was hypertensive, leading to the diagnosis of paraganglioma in children. The classical triad of adult paraganglioma, i.e., headache, tachycardia, and sweating, may not always be present in pediatric paraganglioma. In order to diagnose pediatric paraganglioma without delay, careful clinical examination and assessment are essential.

Case Report

A 9-yr-old girl visited our pediatric general outpatient clinic with “nocturnal enuresis” as the chief complaint. Her family did not have any history of endocrine disorder or malignant diseases. For the last 2 years, she experienced increased thirst accompanied by frequent urination throughout the day. She had never experienced these symptoms before. During the previous year, she developed repeated emesis induced by physical exercise. She did not show any signs of dehydration and body weight loss. Her body weight and height were 28.2 kg and 131.1 cm (height SD-score: –0.2SD), respectively, with a body mass index of 16.40 kg/m2. Although her body temperature and heart rate were within normal range for her age, 96.8°F and 90/min, respectively, she was hypertensive (blood pressure: 161/125 mmHg). Neither a goiter nor an abdominal tumor was detected. Although there was no particular finding in our routine laboratory examination, the plasma levels of norepinephrine were significantly elevated (Table 1). On the other hand, the plasma epinephrine and dopamine levels were normal. Consistently, the accumulated urinary norepinephrine and vanillylmandelic acid levels were elevated. Computed tomography (CT), abdominal ultrasonography (Fig. 1a) and magnetic resonance imaging (MRI) (Fig. 1b) revealed a solid mass 39 × 34 × 38 mm in size in the right abdominal cavity. Within the same area, isotope imaging revealed a hot spot of radiolabeled [123I] m-iodobenzylguanidine (Fig. 1c).

Given the findings, solitary, norepinephrine-producing paraganglioma was suspected. We therefore performed tumorectomy after careful blood pressure control using alpha blockers (Fig. 1d). The histological analysis confirmed our clinical diagnosis. There was no...
malignant finding. We did not perform genetic analysis of the succinate dehydrogenase (SDH) enzyme, whose haploinsufficiency has been suggested to cause familial paraganglioma. This is because she had no family history of paraganglioma and the tumor was not malignant.

After surgical treatment, antihypertensive agents were discontinued and enuresis subsided completely. During the 9-yr period following surgical treatment, no clinical symptoms or signs of hypertension or enuresis was detected.

Table 1. Laboratory findings of the patient

| Blood test       | Urine test                   |
|------------------|------------------------------|
| free T3 (pg/dL)  | 17α-OHP (ng/mL) 0.9          |
| free T4 (ng/dL)  | Testosterone (ng/mL) 0.07    |
| TSH (µIU/mL)     | Androstenedione (ng/mL) 0.3  |
| ADH (pg/mL)      | Aldosterone (pg/mL) 264      |
| ACTH (pg/mL)     | PRA (ng/mL/h) 9.1           |
| Cortisol (µg/mL) | Adrenaline (ng/mL) ≤ 0.01   |
| DHEAS (µg/dL)    | Noradrenaline (ng/mL) 4.6    |
| Na (mEq/L)       | Dopamine (ng/mL) ≤ 0.02      |
| K (mEq/L)        | Posm (mOsm/L) 286           |
| Cl (mEq/L)       | Vanillylmandelic acid (mg/d) 15.6 |
| Glu (mg/dL)      | Urine specific gravity 1.015 |

The pathological diagnosis is paraganglioma (extra adrenal paraganglioma). No malignant findings.

Fig. 1. (a) Abdominal ultrasonography. (b) Abdominal magnetic resonance imaging (MRI). (c) Scanning with radiolabeled [123I] m-iodobenzylguanidine. (d) Surgical finding; the size of the tumor is 50 × 40 × 35 mm. The pathological diagnosis is paraganglioma (extra adrenal paraganglioma). No malignant findings.

Discussion

To date, only a few cases of pediatric paraganglioma with secondary nocturnal enuresis have been reported in the literature (1, 2). However, in the aforementioned studies, nocturnal enuresis was not precisely discussed as a clinical symptom of paraganglioma. We suggest nocturnal enuresis to be a symptom of pediatric paraganglioma. Its exact pathophysiology is unknown. However, a possible cause of nocturnal enuresis is impaired antidiuretic hormone (ADH) secretion. In vivo experiments suggested that norepinephrine is
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capable of crossing the blood-brain barrier and can reduce ADH secretion through non-osmolar regulation (3–5). Accordingly, dysregulation of ADH through excess norepinephrine secretion would cause polyuria and polydipsia, including enuresis. However, our data suggests that ADH secretion in our patient is normal, and that ADH secretion is not likely to be the cause of the nocturnal enuresis.

Another possibility is that secondary enuresis occurred as a result of increased sodium excretion from the kidney (6). In previous studies, enuresis due to hypertension was observed only in elderly patients. Further, nocturnal polyuria due to hypertension is caused by the reversed circadian rhythm of urination of the patient. Additionally, polydipsia, which was observed in our patient, is not common in this condition. To elucidate the precise pathophysiology of enuresis due to paraganglioma in children, more reports of such cases are required.

Based on the case described in this report, we suggest that paraganglioma should be included as a differential diagnosis of secondary enuresis, and that blood pressure should be measured routinely during physical examination of children.

For this case report, informed consent was obtained from the parents of the patient.

Conflict of interest: The authors declare no conflict of interest.

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