A Child with Paraspinal Paraganglioma: A Rare Case Presentation

Upander Kumar1, Nancy Raja2, Ganesh Bhat3, Rizhin Sooraj4, Poorvi Mathur5, Kul R Singh6, Chanchal Rana7, Pooja Ramakant8, Anand Mishra9

Abstract

Aim: To manage a rare case of paraspinal paraganglioma in an 8-year-old female.

Background: Functional paraspinal paragangliomas are exceptionally rare entities in both adult and pediatric age groups. These tumors are closely associated with major vascular structures like the aorta and are in close proximity to the spinal nerves and threatened with deadly vascular complications (e.g., hemorrhagic shock) and neurological complications (e.g., paralysis or paresis of the lower limb). So managing pediatric patients with safe outcomes is a challenge.

Case description: An 8-year-old female child presented with a two years history of headache, palpitations, sweating, and high blood pressure despite three antihypertensive medications. She was subsequently referred to a tertiary center for further evaluation. There was no significant family history.

Conclusion: Biochemical evaluation, perioperative care with adequate α-blockade, and timely follow-up is necessary for best outcomes in functional paraspinal paraganglioma.

Clinical significance: High suspicion of an index and multidisciplinary teamwork were key in diagnosing and managing this rare tumor.

Keywords: Blood pressure, Normetanephrine, Paragangliomas, Paraspinal, Pheochromocytoma.

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Background

Pheochromocytomas and paragangliomas are rare tumors of both sympathetic and parasympathetic origin. Pheochromocytomas are derived from the adrenal medulla (85–90%) whereas paragangliomas arise from extra-adrenal sympathetic and parasympathetic tissues (15–18%).1 Nonfunctional paraganglioma arises from the parasympathetic trunk, commonly located in the head and neck. Catecholamine secreting paragangliomas arise from the sympathetic trunk and are commonly located in the abdomen (85%) and thorax (10%).1,2 Paraspinal paragangliomas in the thorax are infrequent and patients present most commonly with back pain. Functional paraspinal paraganglioma with features of catecholamine excess are very rare and present diagnostic and therapeutic challenges. Herein, we present a case of pediatric functional paraspinal paraganglioma.

Case Description

An 8-year-old presented with complaints of paroxysmal headache, excessive sweating, palpitations, and left-sided chest pain for the past 2 years. She was diagnosed with hypertension by her primary pediatrician and her blood pressure was uncontrolled despite three antihypertensive medications. She was subsequently referred to a tertiary center for further evaluation. There was no significant family history.

On examination, the patient was found to be underweight for her age (BMI: 12.6 kg/m2). She had tachycardia with multiple readings of elevated blood pressure (average 220–180 mm Hg systolic/110–150 mm Hg diastolic). Apart from hyperdynamic precordium, the rest of her systemic examination revealed normal findings.

Biochemical investigations revealed grossly elevated 24-hour urinary normetanephrine (NMN) levels. However, urinary metanephrine was within the normal range (Table 1). A 2-D electrocardiography showed left ventricular hypertrophy. Fundoscopy was normal. Contrast-enhanced computed tomography (CECT) dorsal spine showed a relatively well-defined heterogeneously enhancing soft tissue lesion (47 × 33 × 56 mm) in the left paravertebral region extending from D6 to D8 vertebral level (Figs 1A and 8). She was diagnosed as having functional paraspinal thoracic paraganglioma. MRI, neck, thorax, and abdomen have similar findings and no evidence of any skeletal/spinal involvement. High-resolution ultrasonography (HRUSG) of the neck and CECT abdomen were also normal, although pediatric patients have a propensity for multiple tumors. Functional imaging as well as genetic testing, could not be performed due to financial constraints.
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Anatomical imaging studies of the neck, thorax, and abdomen were used as surrogates for functional imaging.

The patient was optimized preoperatively with an alpha-blocker (prazosin), calcium channel blocker (nifedipine), and beta-blocker (propranolol), along with volume and sodium replacement (Fig. 2). As the lesion was located near the abdominal aorta, a vascular surgeon was consulted. Left lateral thoracotomy was planned and an incision was made along with the 5th intercostal space. The left lobe of the lung and heart were mobilized to expose the thoracic aorta and caudal dissection was performed to expose the tumor. Intraoperatively, a well-circumscribed paraspinal lesion close to the descending thoracic aorta was visualized which was densely adherent to the left posterior-inferior rib cage, along the 6th and 7th ribs, reaching the body of D11 vertebrae. Manipulation of the tumor produced hemodynamic instability intraoperatively (maximum blood pressure (BP) was 220/160 mm Hg and minimum BP was 80/40 mm Hg), and inotropes were started immediately after removal of the tumor and tapered gradually over a day. The postoperative course was unremarkable with no neurological deficit or complications. In the postoperative period, the patient’s blood pressure normalized. The antihypertensive medications were tapered and stopped. The drain was removed on postoperative day 4 and the patient was discharged on day seven with instructions to return after 1 month for a repeat biochemical evaluation.

The examination of the gross surgical specimen revealed a well-circumscribed, encapsulated mass measuring 6.5 × 4.5 × 2 cm (Fig. 3). The cut surface of the tumor showed a tan-brown appearance. Microscopic examination revealed well-defined nests of cuboidal cells arranged in a “zellballen” pattern which were separated by highly vascular fibrous septae (Fig. 4). The individual cells had amphophilic granular cytoplasm and rounded nuclei with discernible nucleoli. Brown melanin pigment was also noted. On immunohistochemically, these tumor cells were positive for synaptophysin and chromogranin. The S-100 protein stained the sustentacular cells.

At 1 month follow-up, the patient was asymptomatic with normal BP and she was not on any medications. Repeat biochemical evaluation (24-hour urinary metanephrine and normetanephrine) was within the normal range. The patient was advised of regular follow-up, BP monitoring, and yearly biochemical evaluation.

Paragangliomas in pediatric patients are usually syndromic/hereditary, and those located in extra-abdominal

Table 1: Biochemical investigations

| Biochemical investigations   | Values       | Normal range               |
|-----------------------------|--------------|----------------------------|
| 24 hour urinary normetanephrine | 7171.60 mcg/24 h | <600 mcg/24 h             |
| 24 hour urinary metanephrine  | 207 mcg/24 h   | <350 mcg/24 h              |
| Serum calcitonin            | 52.82 pg/mL   | <10 pg/mL (male), <5 pg/mL (female) |

Figs 1A and B: (A) Cross-sectional; (B) Coronal sectional of CECT of thoracic paraspinal paraganglioma (depicted by red and black arrow respectively)

Fig. 2: Intraoperative pictures; showing thoracic exploration (purple arrow)

Figs 3A and B: Gross specimen (A) longitudinal dimension; (B) Horizontal dimension
locations are commonly associated with succinyl dehydrogenase (SDH) mutations. Paragangliomas associated with SDH-B mutation tend to recur and have high chances of malignant transformation (30–70%). Although no consensus exists on the duration of follow-up required in these patients, they may require lifelong monitoring. Yearly biochemical investigations and BP assessment are recommended, and imaging studies are to be done if there is biochemical evidence of recurrence.

**Discussion**

Pheochromocytoma and paraganglioma are rare disorders with an incidence of 0.3 cases per million. Approximately 20% of cases are diagnosed during childhood. Out of all the causes of hypertension in childhood, 0.8–1% are due to catecholamine secreting tumors (80% pheochromocytoma and 20% paraganglioma). Due to the rarity of these tumors in the pediatric age group, scant literature is available. The largest series included 95 pediatric cases.

Paragangliomas in the pediatric age group have a higher incidence of multicentricity and malignancy. These tumors are also associated with familial hereditary syndromes. Paraspinal paraganglioma tends to be even rarer, with only 90 cases reported in the literature. There are only two case reports of functional thoracic paraspinal paraganglioma in the literature (Table 2). Paragangliomas are more likely to be malignant (29–40%) as compared to pheochromocytomas. Among children, the most common presentation is hypertension (60–90%), typically sustained but may be paroxysmal or even malignant hypertension with its associated complications. Episodic sweating, tachycardia, or palpitations are present in 50–60% of cases, and headache is present in 50–80% of cases. An accurate 24-hour urine metanephrine and normetanephrine collection are difficult in infants, so measurement of plasma fractionated metanephrines can be a reasonable alternative initial test. Imaging studies, both anatomical (CT or MRI imaging) and functional (123I-metaiodobenzylguanidine (MIBG) scan or integrated positron emission tomography (PET)/CT using gallium Ga-68 DOTATATE or gallium Ga-68 DOTATOC) helps in accurate localization of the tumor and also rule out any multicentricity. Genetic testing should be done in pediatric paraganglioma as germline pathogenic variants are more common in children. Functional imaging and genetic testing could not be carried out in this case due to logistic and financial constraints. CT/MRI findings were used as surrogates’ markers to rule out multicentricity. Preoperative optimization in these patients is critical. Alpha-adrenergic receptor blockade is done to allow the chronically contracted extravascular space to expand and to prevent catastrophic chronic vagal tone suppression in the perioperative and immediate postoperative period. Beta-adrenergic receptor blockade is added perioperatively to control tachycardia as it was done in our case. Beta-adrenergic receptor blockade is not done before complete alpha blockade as it can cause a paradoxical increase in blood pressure due to inhibition of peripheral β2 receptors.

Gentle precise surgical techniques and a multidisciplinary team including the endocrine surgeon, expert anesthetist, and thoracic/vascular surgeon are required. Further studies are required in such cases, as they pose both diagnostic and therapeutic challenges.

**Clinical Significance**

- High suspicion of an index for the possibility of pheochromocytoma/paragangliomas is necessary for the pediatric age group presenting with resistant hypertension.

| Year | Author          | Age (yrs.) | Sex | Location | Symptom/sign                        | Surgical treatment           | Follow-up                        |
|------|-----------------|------------|-----|----------|------------------------------------|-----------------------------|----------------------------------|
| 2003 | Spector JA et al. | 8          | Male| T1–5     | Headache, erythema, and swelling of the hands | Complete resection           | Normotensive, no neurological deficits |
| 2018 | Yuan M et al.    | 9          | Male| T3–7     | Headache, vomiting, raised blood pressure | Complete resection           | Normotensive, no neurological deficits |
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- Preoperative α-blockade helps maintain perioperative and postoperative hemodynamic stability by allowing the chronically contracted extravascular space to expand and prevent catastrophic chronic vagal tone suppression.
- Paraspinal paragangiomas lie close to major vascular and neural structures. Hence, proper surgical planning with a multidisciplinary team is mandatory.
- Timely follow-up is necessary to rule out any recurrence or residual disease.

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