CASE REPORT

Much more than anxiety...

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SUMMARY

Pheochromocytoma and paraganglioma are rare neuroendocrine tumours in paediatric ages. We report a case of a 14-year-old girl referred to our oncology centre due to an abdominal mass. She had an 11-month history of paroxysmal episodes of headache, nausea, dizziness, palpitations and visual disturbances. Imaging studies showed a left paravertebral mass measuring 5.8×4.6×3.5 cm. Metaiodobenzylguanidine scintigraphy revealed an abnormal hyperfixation on the left upper quadrant. Chromogranin A was elevated, as well as normetanephrine. The patient was submitted to surgery during which a connection between this mass and the adrenal gland was found. A diagnosis of pheochromocytoma was performed.

BACKGROUND

Pheochromocytoma is an entity rarely reported in paediatric ages and remains a diagnostic challenge.¹ This case was exceptionally difficult due to the unusual location outside the adrenal medulla, raising the possibility of other differential diagnosis. Pheochromocytoma is a potentially life-threatening disease, requiring a high index of suspicion for early diagnosis, particularly in the paediatric population.

CASE PRESENTATION

We report a case of a 14-year-old girl, with no relevant personal or family history, with an 11-month history of paroxysmal episodes of headache, nausea, dizziness, dyspnoea, palpitations and visual disturbances (foggy and floater), who was referred to our oncology centre by her primary care physician. These episodes had no relation with exercise and were described as very brief (a few seconds). No reference was noted to fever, night diaphoresis or weight loss. Physical examination was normal, with exception of an elevated blood pressure (systolic and diastolic pressure slightly above 95th centile for sex and age).

INVESTIGATIONS

ECG and echocardiogram evaluation were normal. Abdominal ultrasound described a hypoechoogenic nodule adjacent to the left renal hilar region, approximately 6.2×3.7×3.3 cm (longitudinal×transversal×anteroposterior axis). A subsequent non-contrast abdominopelvic CT confirmed the presence of a left retroperitoneal heterogeneous mass measuring 5.6×4 cm, located behind the pancreas body, pushing forward the renal vein, with intimate contact with the renal hilum, just below the adrenal gland, with intense contrast enhancement in arterial phase. Owing to imagiological

Figure 1 Metaiodobenzylguanidine scintigraphy showing an abnormal hyperfixation in left upper abdominal quadrant.

findings, the patient was referred to our oncology centre for further investigation.

Considering the possibility of a neuroendocrine tumour, iodine-131-metaiodobenzylguanidine (MIBG) scintigraphy was performed, which revealed an abnormal hyperfixation in the left upper quadrant. This finding was consistent with a malignant tumour associated with increased catecholamine activity (figure 1).

Abdominal angio-MRI showed a left paravertebral irregular mass measuring 5.8×4.6×3.5 cm (longitudinal×transversal×anteroposterior axis) with an intermediate signal on T1 and hyperintense signal on T2. Both renal artery and vein showed a reduced calibre, and invasion of these vessels could

Figure 2 Abdominal angio-MRI showing a left paravertebral irregular mass (coronal section).

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Figure 3 Abdominal angio-MRI showing a left paravertebral irregular mass (axial section).

not be excluded (figures 2 and 3). The relation between tumour and adrenal gland was not completely elucidated by imaging studies.

Laboratory studies showed a normal complete blood count. Chromogranin A level was 14.12 nmol/L (normal <6 nmol/L). A 24-h urinary collection revealed grossly elevated levels of normetanephrine (4681.93 µg/24 h, normal range: 88–444 µg/24 h) and vanillylmandelic acid (38.58 µg/mg, normal range <8.2 µg/mg).

DIFFERENTIAL DIAGNOSIS

Neuroendocrine tumours, such as paraganglioma and pheochromocytoma, although rare, must be included in the differential diagnosis when symptoms possibly associated with catecholamine secretion are present.

Neuroblastoma, Wilms' tumour or sarcomas can occur in similar locations and be associated with catecholamine secretion.^{1 2}

Paragangliomas and pheochromocytoma produce physiologically active catecholamines, and, thus, isolated assay of urinary vanillylmandelic acid and homovanillic acid is considered insufficient for differential diagnosis. The inability to differentiate them may lead to fatal consequences during surgery.

TREATMENT

Following a 10-day course of phenoxybenzamine, later associated with propranolol, the patient underwent surgery for abdominal mass excision. The operative and immediate post-operative periods were complicated by profound episodes of

Figure 4 Encapsulated and highly vascular tumour, connected to the left adrenal gland by membranous tissue.

Figure 5 'Zellballen' pattern (80×).

hypotension, requiring 24 h of inotropic support in paediatric intensive unit care.

Pathological examination of the specimen showed an encapsulated and highly vascular tumour, measuring 6.5×4.4×3.2 cm and connected to the left adrenal gland by membranous tissue (figure 4). Microscopically, the tumour was composed of cells arranged in a small nest surrounded by sustentacular cells ('Zellballen' pattern, a distinct characteristic of paragangliomas and pheochromocytomas). The tumour showed some aggressive features and a proliferation index (Ki-67) of 2–10% (figure 5). Capsular rupture was identified but no vascular invasion was found.

Given the fact that distance between tumour and normal adrenal gland was inferior to 0.5 cm, it was considered a pheochromocytoma.

OUTCOME AND FOLLOW-UP

MIBG scintigraphy performed 2 weeks later showed no evidence of residual or metastatic disease. Urinary catecholamines and chromogranin A levels were normal. Postoperatively, the patient's blood pressure remained stable within normal range for age and sex. The patient was discharged on day 6 and referred for genetic counselling.

DISCUSSION

Pheochromocytomas and paragangliomas are rare neuroendocrine tumours characterised by strong immunoexpression of chromogranin A.¹ The major differentiation between them relies on location—pheochromocytomas arise from the adrenal medulla whereas paragangliomas have an extra-adrenal location.³ Presenting symptoms in children are usually due to catecholamine hypersecretion or, more rarely, due to mass effect.^{1 2}

The majority are sporadic cases. Nevertheless, some tumours occur as part of hereditary syndromes, mainly von Hippel-Lindau disease and multiple endocrine neoplasia type 2A and 2B.⁴ Sporadic lesions are usually solitary, as opposed to the usually bilateral/multifocal types seen in familial disease.^{5 6}

In our case, given the proximity and connection to the adrenal medulla, the tumour was considered a pheochromocytoma, despite its location outside the gland. As such, no adrenalectomy was performed. This presents an exceedingly rare case of a pheochromocytoma.

Accordingly to the literature, patients with pheochromocytoma often present with symptoms secondary to catecholamine excess. Hypertension, headaches, palpitations and sweating are

common presenting symptoms, accompanied by elevated urinary catecholamine excretion.^{1 6 7} Surgical excision is the only effective treatment, and the prognosis is excellent if complete resection with free margins is achieved.^{1 8} Noteworthy is the fact that before any surgical procedure, it is imperative that these patients receive an adequate α -adrenergic and β -adrenergic blockade.^{1 9}

At present, no histological criteria can predict malignancy in this entity. Malignant disease is defined by the presence of metastases and represents less than 2% of paediatric pheochromocytomas.¹⁰ Although presenting some aggressive histological features, namely focal nuclear pleomorphism, moderate to high mitotic index and size >5 cm, the tumour was classified as benign pheochromocytoma, since no metastases were found.¹¹

Follow-up is crucial and includes urinary catecholamines, chromogranin A and imaging studies.^{1 8}

Learning points

- ▶ Pheochromocytoma is rare in paediatric age.
- ▶ It is a potentially life-threatening disease, requiring a high index of suspicion for early diagnosis, as its presentation can be mild with brief paroxysmal episodic symptoms.
- ▶ The neuroendocrine origin is given by strong immunoexpression of chromogranin A as well as elevation of urinary catecholamines.
- ▶ Distinguishing paraganglioma from pheochromocytoma is not simple and definite diagnosis can only be made after surgical excision.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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