CASE REPORT

Pelvic paraganglioma: a rare and unusual clinical presentation of paraganglioma

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SUMMARY

Paraganglioma of the urinary bladder is a rare tumour of the urinary bladder causing palpitation, headache, paroxysmal hypertension, tachycardia, blurring of vision and haematuria. Patients may present with these exaggerated symptoms during or just after micturition. We present a case of a 15-year-old girl who presented to us with accelerated hypertension, headache, palpitation and blurring of vision. On the basis of a positive family history, laboratory investigations and imaging studies, she was diagnosed to have an extra-adrenal paraganglioma. Complete enucleation of the tumour with preservation of the bladder was done. This case is reported because of the rarity of the disease in urology.

BACKGROUND

Paraganglioma are defined as neuroendocrine tumours that arise from the extra-adrenal autonomic paraganglia, small organs consisting of neuroendocrine cells derived from the embryonic neural crest, that have the ability to secrete catecholamines. As per the 2004 WHO classification, pheochromocytoma are classified as intra-adrenal paraganglioma, whereas those arising from extra-adrenal sympathetic or parasympathetic paraganglia are classified as extra-adrenal paraganglioma. In the abdomen, extra-adrenal paraganglioma are located in association with the coeliac, superior and inferior mesenteric ganglia and organ of Zuckerkandl. In the urinary bladder, embryonic cell rests of chromaffin tissue arising from the sympathetic plexus of the bladder wall are the source of these tumours.¹ Extra-adrenal paraganglioma constitutes <0.06% of all bladder tumours.² So, the urinary bladder and pelvic organ involvement is a rare entity. Urinary bladder paraganglioma presents with haematuria and paroxysmal hypertension induced by micturition along with symptoms due to raised catecholamines (headache, palpitation, blurred vision).

CASE PRESENTATION

A 15-year-old girl presented to our hospital with a 6-month history of pulsatile headache, palpitation and gradual loss of vision. No history of haematuria or dysuria was present. The patient's family history was significant, as her two elder cousins had a history of episodic hypertension and died at an age <20 years due to a mediastinal mass most likely due to paraganglioma. On physical examination, her pulse was 92 bpm and blood pressure (BP) 190/90 mm Hg in the left arm in a supine

position. Routine haematological and biochemical workup was within normal limits.

INVESTIGATIONS

In view of the positive family history and uncontrolled hypertension, further workup revealed urinary metanephrine (7950 µg/24 h) and normetanephrine (4577 µg/24 h) to be elevated. The plasma free metanephrine was 489 pg/mL. Ultrasonography (USG) of the abdomen revealed a large solid, heterogeneous mass measuring 61×45 mm in the pelvis on the left side of the urinary bladder, which was indenting the left lateral wall of the urinary bladder without any intraluminal urinary bladder lesion; the bilateral adnexa were normal in size and echo texture (figure 1A). A CECT (contrast-enhanced CT) abdomen scan revealed a large, heterogeneously enhancing soft tissue mass, measuring 68×36×64 mm in size, along the left lateral wall of the urinary bladder. In the CECT, the mass was abutting the uterus, left ovary and left ureter; however, no obvious hydronephrosis was noted and bilateral kidneys were normal in size and shape (figure 1B). MRI of the pelvis revealed a heterogeneous signal intensity mass lesion in left lateral wall of the urinary bladder measuring 56×42×39 mm, appearing hyperintense on the T2 and short τ inversion recovery images and hypointense on the T1 W images (figure 1C); the mass was extending into the left pelvic side wall with loss of fat planes with uterus.

TREATMENT

After proper optimisation of BP, cystoscopy was done which did not reveal any abnormal findings. With a working diagnosis of urinary bladder paraganglioma in mind, the patient was preoperatively optimised with α and β-blockers and planned for partial cystectomy. The patient underwent exploratory laparotomy via a low midline incision. After a thorough dissection, the mass was seen to arise from the left pelvic wall, abutting the left lateral wall of the urinary bladder. It was dissected meticulously and completely enucleated from the pelvic side wall and bladder. The bladder and ureters were safeguarded completely. Pelvic lymph node dissection and biopsy were performed to rule out secondaries in lymph nodes. The postoperative course was uneventful. BP was normal on the first postoperative day and the patient was discharged on the fourth postoperative day without any antihypertensive drugs. Surgical specimen morphology showed a 6×4×3 cm yellowish brown mass (figure 2). A histopathological report revealed a neoplasm

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Figure 1 (A) Preoperative ultrasonography kidney, ureter, bladder showing a solid heterogeneous mass measuring 61×45 mm in the pelvis on the left side of the urinary bladder indenting the left lateral wall, (B) contrast-enhanced CT of the pelvis showing a focal enhancing mass of size 68×36×64 mm along the left lateral wall of the urinary bladder, abutting the left ureter without any hydronephrosis and (C) MRI of the pelvis showing a heterogeneous, hypointense mass along the left lateral wall of the urinary bladder in T1 sequences.

composed of monotonous looking cells arranged in the Zellballen pattern and separated by sinusoids (figure 3A, B). Tumour cells were large, arranged in nests separated by fibrovascular stroma, and nuclei were small and round with bland appearance and fine chromatin. Lymph nodes were negative for malignant cells. Immunohistochemistry was strongly positive for chromogranin A, consistent with paraganglioma.

OUTCOME AND FOLLOW-UP

In the 3-month follow-up, the patient's previous symptoms disappeared completely; BP was within normal range and urinary metanephrine levels were also within normal limits. After 6 months of surgery, the CECT abdomen scan showed no tumour recurrence in the pelvis or metastasis in the abdomen.

Figure 2 Surgical specimen showing a 6×4×3 cm yellowish brown mass.

DISCUSSION

Paraganglioma can arise in any position of the paraganglionic system or the organ of Zuckerkandl. Paraganglioma of the urinary bladder is a rare neoplasm, accounting for <0.06% of all bladder tumours. In the urinary bladder, paraganglioma arises from the chromaffin tissues of the sympathetic nerves in the bladder wall. The patient may present with palpitation, headache, paroxysmal hypertension, tachycardia, excessive sweating and blurring of vision due to excessive catecholamine secretion especially associated with micturition, and there may be haematuria and dysuria.^{3 4}

Our index patient presented with pulsatile headache, palpitation and gradual loss of vision, but with no haematuria or no other urinary symptoms. The dizziness and palpitations were exaggerated immediately following micturition. The most useful laboratory tests to diagnose paraganglioma are blood or urinary levels of epinephrine and norepinephrine and their metabolic by-products. As per the Endocrine Society Guidelines, the current recommendation for biochemical analysis for paraganglioma states that initial testing for paraganglioma must include measurement of fractionated metanephrine in plasma. In our case, 24 h urinary metanephrine, 24 h urinary normetanephrine and plasma free metanephrine were markedly raised.

A majority of paraganglioma appears to be sporadic. However, one-third to one-half of the cases are associated with an inherited syndrome. Certain hereditary syndromes such as the Von Hippel-Lindau (VHL) syndrome, multiple endocrine neoplasia type 2 (MEN2), neurofibromatosis type 1 (NF1) and the hereditary paraganglioma-pheochromocytoma (PGL-PCC) syndromes can be associated with development of paraganglioma. About 15 genes have been identified as being associated with the development of paragangliomas.⁵ In our case, genetic

Figure 3 (A and B) Histopathology revealing monotonous cells arranged in the Zellballen pattern separated by sinusoids.

testing was required as the patient's age was <30 years and she had a family history of mediastinal paraganglioma, but it could not be done due to financial constraints. Her two cousins died due to some mediastinal mass, most likely paraganglioma. Both were managed non-operatively at some other centre and no genetic testing was done. Genetic testing is expensive and should be done in a stepwise fashion. The patient should be tested to identify the specific genetic mutation, and then other family members should be tested for that genetic mutation so as to decrease the number of tests performed. To choose a proper genetic test, the biochemical profile of catecholamine secretion, age of the patient, localisation of the primary tumour and family history should be carefully evaluated and included in the genetic algorithm.⁶

USG and CT abdomen are required to locate the extra-adrenal paraganglioma and to exclude multifocal and metastatic lesions. A CT scan is more sensitive than USG in detecting adrenal and extra-adrenal paraganglioma. CT scan can define the tumour relationship with the bladder muscles, mucosa, perivesical extension and pelvic lymph node status. The MIBG scan (¹³¹I metaiodobenzylguanidine) and PET-CT (positron emission tomography) helps to evaluate the functional status of paraganglioma. Radiotracers used in PET-CT are 18F-fluoro-2-deoxy-d-glucose and 18F-dihydroxyphenylalanine.⁷

Cystoscopy has a limited role in localising the pelvic or urinary bladder paraganglioma. Cystoscopic biopsy is not recommended as it may provoke a hypertensive episode during tumour biopsy and artefactual changes in a small biopsy may cause diagnostic confusion.⁸

The treatment of pelvic or urinary bladder paraganglioma is primarily surgical. In case of pelvic paraganglioma, complete excision of the tumour is recommended, while for bladder paraganglioma partial or total cystectomy is the treatment of choice.⁹ To exclude metastatic disease, pelvic lymph node dissection has been recommended for all urinary bladder paragangliomas.^{10–11} Preoperative optimisation of BP with α and β -blockers and intraoperative BP monitoring and minimum tumour tissue handling are required to achieve a successful outcome. In our patient, we found a tumour on the left pelvic wall just abutting the left lateral wall of the bladder. Complete enucleation of the mass was done, preserving the bladder and ureter. Postoperatively, the patient had normal BP and recovered well.

Histological features of paraganglioma are similar to those of intra-adrenal paraganglioma. The tumour cells grow in a Zellballen pattern or nested pattern separated by sinusoids and fibrovascular stroma. Immunohistochemistry gives the definitive diagnosis and shows positive staining for chromogranin and synaptophysin.

Lifelong follow-up with annual determination of serum or urinary catecholamines or their metabolic by-products is required in extra-adrenal paraganglioma.

Learning points

- ▶ Pelvic paraganglioma often mimics urinary bladder paraganglioma.
- ▶ A combination of specific signs and symptoms, family history, laboratory test, imaging and histology is critical to diagnosis this rare disease.
- ▶ Genetic testing and screening play a very important role in identification of hereditary paraganglioma.
- ▶ Treatment is surgical exploration.

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Competing interests None declared.

Patient consent Obtained.

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