Retroperitoneal paraganglioma: a chameleon masquerading as an adrenal pheochromocytoma

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ABSTRACT

Retroperitoneal paragangliomas are rare tumours arising from neural crest cells located near or in the autonomic nervous system; right from the skull base to the pelvic floor. Often called the great masqueraders, their diagnosis and treatment is often difficult and fraught with danger, considering the close proximity of these tumours to important retroperitoneal organs.

A 29-year-old woman presented to the outpatient department with complaints of paroxysms of headache, sweating and palpitations for one year. She was found to have elevated urinary metadrenalines (metanephrines) and a suprarenal mass on contrast-enhanced computed tomography of the abdomen, which demonstrated increased tracer activity on I-131 iodine-123 meta-iodobenzylguanidine scintigraphy. Adrenal pheochromocytoma was diagnosed and she underwent laparoscopic adrenalectomy after stabilisation of her blood pressure. Laparoscopy revealed a large suprarenal mass with dense adhesions to the inferior vena cava that was carefully separated from the vein and surrounding structures. The cut section revealed a heterogeneous mass encasing a normal adrenal gland and histopathology confirmed the same, confirming the final diagnosis of retroperitoneal paraganglioma.

KEYWORDS

Paraganglioma – Pheochromocytoma – Great masquerader – Adrenal

Accepted 10 September 2018

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Introduction

Retroperitoneal paragangliomas are rare tumours arising from the neural crest cells along the autonomic nervous system, extending from the head and neck, to the pelvic organs. They may be found at any of the locations where paraganglia are found; superior para-aortic region being the most common (46%), followed by the inferior para-aortic area (29%), the bladder (10%) and the thoracic region (10%).¹ Primary paragangliomas are also reported in other abdominopelvic as well as in craniocervical sites.² These tumours are often difficult to diagnose as the wide spectrum of presentations and the close proximity to vital structures makes complete surgical resection of these functional tumours dangerous and demanding.

We present the case of a young woman suspected of having an adrenal pheochromocytoma on the basis of history and imaging. She underwent laparoscopic excision of the suprarenal mass. The cut section of the mass revealed a normal adrenal gland which was encased by the retroperitoneal tumour and the histopathology exhibited a retroperitoneal paraganglioma with a normal adrenal cortex and medulla.

Case history

A 29-year-old woman presented to the outpatient department with complaints of paroxysms of headache, sweating and palpitations for one year. She had also developed vertigo and postural dizziness for the preceding two months. She was found to have hypertension, with blood pressures of 170/100 mmHg supine and 140/100 mmHg standing. On examination, no abnormal findings were noted on general physical, cardiovascular and abdominal examination. There was no significant family history. She was started on amlodipine, metoprolol and prazosin to control her blood pressure. On evaluation, she was found to have elevated urinary metadrenalines (metanephrines; 6023 mg/day) with a predominance of normetadrenalines (normetanephrines; 5800 mg/day). Other blood investigations (serum cortisol, dehydroepiandrosterone, calcitonin, thyroid function tests) were within normal limits. She was further evaluated with contrast-enhanced computed tomography (CECT), which revealed a well-defined heterogeneously enhancing lobulated space-occupying lesion in the right suprarenal region with retrocaval extension measuring 6.7 × 6.3 × 5.1 cm (Fig 1A–C). On further evaluation with I-131 iodine-123

Figure 1 (A,B) CECT abdomen depicting a well-defined $6.7 \times 6.3 \times 5.1$ cm suprenal mass with retrocaval extension and no distinction of normal adrenal gland. (C) Well-defined planes with the kidney.

meta-iodobenzylguanidine (MIBG) scintigraphy, increased tracer activity was seen in the right suprenal region corresponding to the location of the mass, suggesting a diagnosis of a non-metastatic pheochromocytoma.

The patient was planned for laparoscopic adrenalectomy and underwent surgery after stabilisation of her blood pressure with blockade of the a and b sympathetic systems using metoprolol and prazosin. During surgery, ports were placed in the standard fashion and laparoscopy revealed a large suprenal mass with dense adhesions to the inferior

vena cava. The mass was carefully dissected from the vein and surrounding structures and the specimen was retrieved from a small subcostal incision. There were no intraoperative adverse events and patient was stable post-operatively. She did not require antihypertensive medication in the postoperative period elucidating a complete removal of the tumour. Three months after the surgery, the patient was doing well having regular follow-up with complete resolution of symptoms.

The mass measured $6 \times 5 \times 6$ cm in size with a lobulated smooth appearance (Fig 2A). The cut section of the mass revealed a heterogeneous mass with necrotic areas encasing a normal-looking adrenal gland (Fig 2B) and histopathology confirmed this finding. An encapsulated homogenous tumour was seen separate from the adrenal gland with markedly pleomorphic tumour cells with abundant eosinophilic cytoplasm and brisk mitosis (per 10–12 high-power fields; Fig 3A). There was no capsular or vascular invasion and normal adrenal medulla and cortex were separately identified (Fig 3B). The final histopathological diagnosis reported as a retroperitoneal paraganglioma. Retrospectively, the retroperitoneal paraganglioma encasing the normal adrenal gland was disguised as a pheochromocytoma on imaging.

Discussion

Retroperitoneal paragangliomas are rare tumours arising from chromaffin cells along the autonomic nervous system, with an estimated incidence of 2–8 per million,¹ accounting for 1–3% of retroperitoneal tumors.⁵ Those paragangliomas arising from the medulla are known as pheochromocytomas, which comprise nearly 70% of such cases.⁴ Paragangliomas are known to occur in various locations in the body such as the head and neck, thorax and abdomen. They may occur sporadically or as a part of hereditary syndromes like Von Hippel Lindau disease, multiple endocrine neoplasia type 2, hereditary paraganglioma/pheochromocytoma syndrome and neurofibromatosis type 12. No features

Figure 2 (A) The excised well-encapsulated mass measuring $6 \times 5 \times 6$ cm. (B) Cut section of the yellowish brown mass showing the normal adrenal gland (arrow) encased by the tumour and heterogeneous areas within the tumour.

of associated hereditary syndromes were present in our patient.

Paragangliomas can have varied manifestations, often described as kaleidoscopic, including sustained or paroxysmal hypertension, paroxysmal symptoms such as palpitations, headaches and sweating. Non-functional paragangliomas may remain asymptomatic or present as suprarenal or midline abdominal masses. Hypertension is the most common symptom, present in up to 90% of the patients.⁵ Excessive generalised sweating is seen in 60–70% of patients. Tumour-secreting adrenaline (epinephrine) may also present with hypotension.⁶

The diagnosis of paraganglioma is made on the basis of clinical findings, biochemical tests and imaging. Paragangliomas are known to secrete a wide gamut of hormones such as adrenaline, noradrenaline (norepinephrine), vasoactive intestinal peptides, which accounts for the wide spectrum of presentations. Catecholamine secretion is elevated in paragangliomas but their excretion may vary with various stresses, amounting to a sensitivity of 95% with an unacceptable specificity.^{1,2} Both plasma-free metadrenalines and urinary metadrenalines are accepted tests for diagnosis of paraganglioma and pheochromocytoma, with no consensus on the preferred test.⁷ Both tests are equally effective in excluding functional tumours and pheochromocytomas. It is worthwhile to note that paragangliomas invariably only produce noradrenaline and urinary normetadrenalines compared with phaeochromocytomas, which produce both adrenaline and noradrenaline, showing as urinary metadrenalines and normetadrenalines.⁸ Our patient had predominantly elevated urinary metadrenalines.

Radiological imaging is of paramount importance in the diagnosis of paraganglioma. CECT and magnetic resonance imaging (MRI) are preferred imaging modalities in identifying retroperitoneal paraganglioma. CECT provides

the initial method of localising these tumours, being widely available and relatively inexpensive. It can be used to localise extra-adrenal tumours greater than 2 cm with a sensitivity of around 95% and specificity of 70%.⁹ These tumours usually exhibit a density greater than 10 Hounsfield units with an inhomogeneous appearance.¹⁰ Although considered a risk factor leading to exaggerated response of catecholamines in functional tumours, it has been evident in recent studies that is essentially a theoretical risk.^{1,4}

MRI with or without contrast enhancement has proven to be reliable and superior to CECT in diagnosing extra adrenal paraganglioma. It offers excellent tissue characterisation and relationship to surrounding structures with no exposure to ionising radiation. It may help in identifying more than 95% of the tumours but its high cost and long duration is a drawback in using it routinely, especially in overloaded set-ups like ours. On T1 weighted images, tumours appear similar to liver and muscle with an enhancement observed in T2 and diffusion-weighted image, confirming the diagnosis.⁵

Nuclear imaging in the form of I123 MIBG and F18-fluorodopa positron emission tomography (PET) is also useful in the diagnosis of these enigmatic tumours. 123 MIBG has a sensitivity of 92–98% for non-metastatic tumours and 57–79% for detecting metastases.¹¹ The introduction of F18-fluorodopa PET has aided our armamentarium with a superiority over I123 MIBG, especially in patients with metastasis, with highest yield in detecting metastatic head and neck paragangliomas.⁹

Surgery remains the mainstay of management in these cases, with a shift from laparotomy to laparoscopy, especially for smaller tumours.^{1,2,12} Preoperative therapy with α -blocking drugs allows for re-expansion of blood volume and intraoperative management with halogenated compounds, volume replacement and cardiovascular

monitoring, and the advent of minimal access surgery has significantly reduced the morbidity and mortality associated with surgical excision of these tumours, lowering the operative mortality to 3% in most centres.^{1,4} The close proximity of these tumours to important retroperitoneal organs and major vessels calls for a thorough knowledge of retroperitoneal anatomy and meticulous dissection, allowing safe surgical excision. Preoperative three-dimensional reconstruction and the use of energy sources intraoperatively further aids the surgeon in safe excision of these difficult tumours without injury to surrounding structures and decreasing the chances of local recurrence.¹⁵

Extra-adrenal retroperitoneal paragangliomas have a more aggressive course compared with their adrenal counterparts and their prognosis can be difficult to predict. Approximately 20–42% of retroperitoneal paragangliomas metastasise compared with only 2–10% of pheochromocytomas. Dissemination occurs both lymphatically and haematogenously, with regional lymph nodes, liver, bone and lungs being common metastatic sites.⁴ This mandates intimate follow-up of these tumours. Diagnosis of malignant paragangliomas is based on evidence of extensive local invasion, which was absent in our case. A more reliable indicator may be documentation of metastasis to one or more sites where non-chromaffin tissue is not usually present. The present World Health Organization criteria, however, do not define malignancy only on the basis of local invasion as it is not always present in tumours that metastasize.¹⁴ MIBG scanning and CECT aid in follow-up of these cases. Moreover, therapeutic doses of I131 MIBG with or without combination chemotherapy may induce response in malignant paragangliomas.^{2,4}

Conclusion

Retroperitoneal paragangliomas are rare tumours which often have a wide variety of presentation and may mimic various retroperitoneal tumours. A multimodality approach

and keen clinical suspicion is required in diagnosis and treatment of these difficult tumours. Surgery remains the mainstay of treatment with emphasis on preoperative planning and meticulous dissection. Retroperitoneal paraganglioma must always be considered as a close differential while dealing with retroperitoneal pathologies, even when adrenal pheochromocytoma is suspected.

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