CASE REPORT

Functional paraganglioma

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SUMMARY

Paraganglioma are tumours arising from neural crest cells of the sympathetic and parasympathetic paraganglia. Functional paraganglioma presents with symptoms of catecholamine excess that includes hypertension, flushing, diaphoresis, etc. Non-functional paraganglioma are usually found incidentally during imaging studies. Early diagnoses of functional paraganglioma are important because their removal is often curative. We present the case of a young man who presented with hypertensive crisis and severe headache, who was later found to have functional paraganglioma.

BACKGROUND

Functional paraganglioma, one of the rare curable causes of secondary hypertension, are catecholamine-secreting tumours arising from neural crest cells outside adrenal medulla. We present the case of a young man who presented with peri-renal paraganglioma.

CASE PRESENTATION

A 20-year-old man presented with sudden onset of severe headache associated with bilateral blurry vision for 2 days. He had headache on and off with intermittent palpitation. He denied watering from eyes, photophobia or nasal congestion. He denied heat or cold intolerance, recent change in weight, muscle weakness, etc. His medical history and family history were unremarkable.

On examination, he was afebrile with blood pressure (BP) 216/84 mm Hg, heart rate 92 bpm, respiratory rate 20/min, oxygen saturation 99% on room air and body mass index 23.2. Fundus examination showed bilateral papilloedema. Remainder of the examination was within normal limits.

INVESTIGATIONS

Laboratory studies revealed normal complete blood count and basic metabolic panel. CT of the head ruled out any intracranial pathology. Workup for secondary causes of hypertension was initiated. He had an elevated serum normetanephrine (2.9 nmol/L; normal range: <0.9 nmol/L) and norepinephrine (718 ng/L; normal range: 50–440 ng/L) while his serum thyroid stimulating hormone (1.36 μIU/L; normal range: 0.34–4.82), serum calcium (9.2 mg/dL; normal range: 8.5–10.1), serum parathyroid hormone (36 ng/L; normal range: 10–65 ng/L) and serum epinephrine (42 ng/L; normal range: 9–75 ng/L) were within normal limits. Twenty-four hour urine collection revealed elevated metanephrine level of 1063 μg/day (normal range: 60–700 μg/day) with creatinine level of 1103 mg/day. CT of the abdomen revealed a 5×4×2 cm heterodense right peri-renal mass (figure 1). A meta-iodobenzylguanidine (MIBG) scan showed increased uptake of the right peri-renal mass, suggestive of paraganglioma.

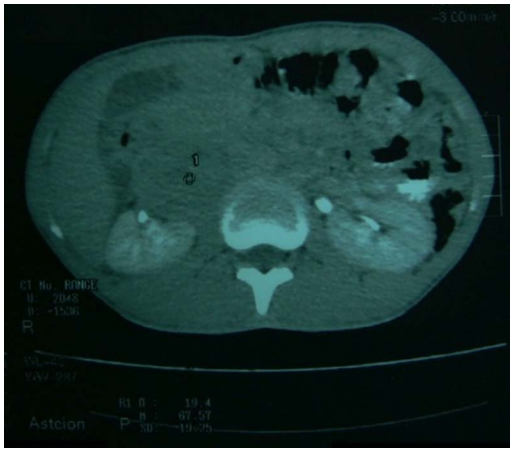

Figure 1 CT of the abdomen and pelvis showing 5×4×2 cm right peri-renal mass.[1]

TREATMENT

BP control was achieved with combined α-adrenergic and β-adrenergic blockers. He was started on prazosin and titrated to achieve target BP of 120/80 mm Hg. After a week of prazosin, propranolol 10 mg twice daily was initiated and titrated to achieve target heart rate of 60–80 bpm. He subsequently underwent open resection of the right peri-renal mass (figures 2 and 3). There was no intraoperative haemodynamic compromise. Histopathological examination revealed uniformly arranged cells with abundant granular cytoplasm and mild nuclear pleomorphism that was consistent with paraganglioma without any capsular or vascular invasion (figures 4 and 5).

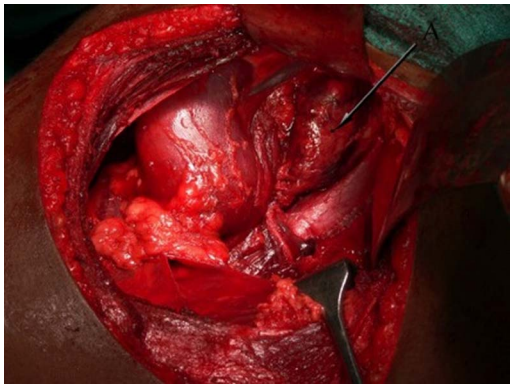

Figure 2 Intraoperative image of right peri-renal paraganglioma.

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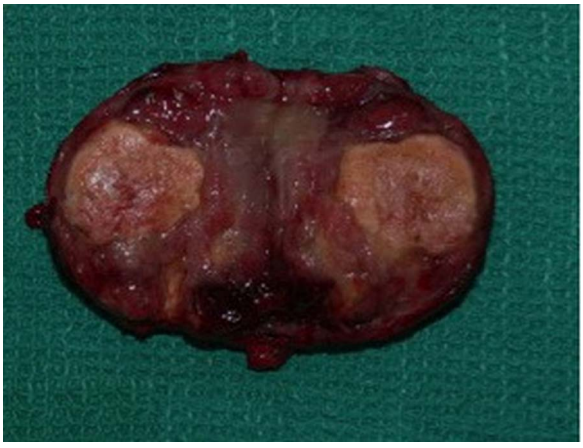

Figure 3 Cross-section of resected right peri-renal paraganglioma showing capsulated structure with a yellowish nodule measuring 2.5 cm with focal areas of haemorrhage.

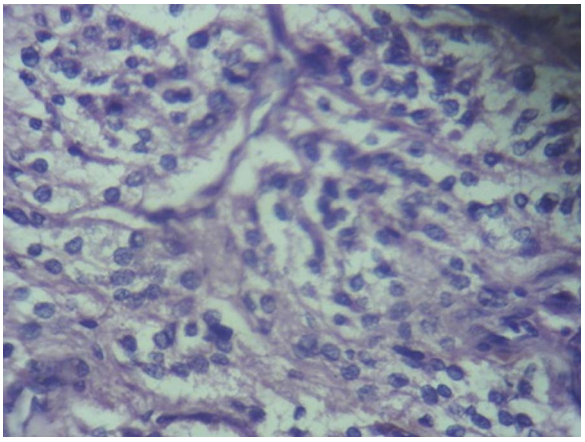

Figure 5 Histopathological examination under high power field (H&E ×100) revealing abundant granular cytoplasm and round to oval vesicular nuclei with mild nuclear pleomorphism.

OUTCOME AND FOLLOW-UP

His BP was normal in the immediate postoperative period and remained within range without the need of any antihypertensive medication until discharge from hospital. He is asymptomatic and normotensive during his follow-up visits.

DISCUSSION

Kohn[1] coined the term 'Paraganglioma' in 1900. According to the WHO classification of tumours of endocrine organs, paraganglioma are neuroendocrine tumours that can be intra-adrenal paraganglioma/pheochromocytoma and extra-adrenal paraganglioma.[2 3] Extra-adrenal paraganglioma can occur in four types of locations[4]—branchiomeric, intravagal, aorticosympathetic and visceral autonomic. The branchiomeric and intravagal tumours are found in head and neck region and are rarely functional. The aorticosympathetic tumours are found along the length of aorta, between the renal arteries, around the iliac bifurcation and include the organ of Zuckerkandl. The visceroautonomic paraganglioma occurs in association with blood vessels or visceral organs like the bladder. The aorticosympathetic and visceroautonomic tumours are mostly functional.[4] Extra-adrenal sympathetic paraganglioma most commonly arise from chromaffin tissue around the inferior mesenteric artery and aortic bifurcation and less commonly from chromaffin tissue at other sites, whereas the extra-adrenal parasympathetic paraganglioma are most commonly found in the head and neck region.

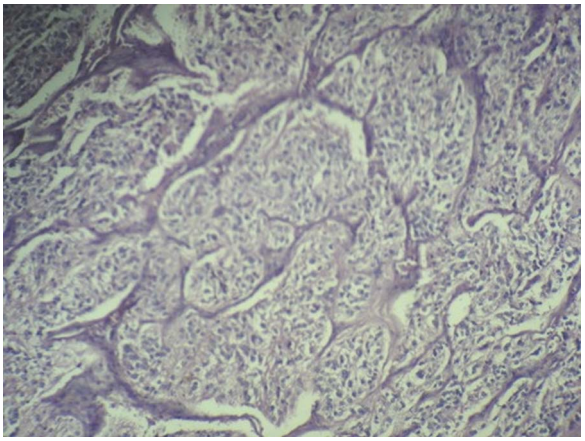

Figure 4 Histopathological examination showing cells arranged predominantly in alveolar pattern and occasionally in cords (H&E ×40).

Paraganglioma are a component of inherited syndromes in 10–50% of cases.[5] Four hereditary paraganglioma syndromes have been described—paraganglioma syndrome PGL1, PGL3 and PGL4 are associated with mutations in the succinate dehydrogenase complex subunit D, C and B, respectively, whereas PGL2 is not associated with any specific mutation.[6–8]

Paraganglioma are rare and are found in about 0.05–0.1% of patients with hypertension. The prevalence of pheochromocytoma and extra-adrenal paraganglioma in USA is 1:6500 and 1:2500, respectively, with the annual incidence of 500–1600 cases/year.[9] Malignant paraganglioma is rare and the reported incidence in USA was 93 cases/400 million persons.[10] About 20% of abdominal secreting paraganglioma are malignant.[11]

When compared with pheochromocytoma, paraganglioma occur at a younger age, are pathologically more malignant and have higher risk of recurrence after surgical removal. Pheochromocytoma secretes epinephrine and norepinephrine, whereas paraganglioma secretes norepinephrine only.[12] Clinical presentations are similar for pheochromocytoma and extra-adrenal sympathetic paraganglioma.

Most common presentation is hypertension. Common symptoms include headache, diaphoresis, palpitations, pallor and fever. Other rare symptoms include visual blurring, dyspnoea, vomiting, flushing, dizziness, paraesthesia and seizures. A thorough workup is important in patients presenting with these symptoms as pheochromocytoma and paraganglioma are curable in most patients and are fatal if not diagnosed early.

Initial evaluation involves 24 h urine catecholamines and serum metanephrines. CT scan has a sensitivity of 95–100% and specificity of 67%. CT scan will show a homogenous mass with intense enhancement following administration of contrast. MRI gives better information about the adjacent vascular structures. Diagnostic sensitivity of MRI is 98–100% and specificity is 70%. MIBG scintigraphy with ^{123}I has sensitivity of 78% and very high specificity of 100% for diagnosis and ^{131}I can also be used as a therapeutic modality in inoperable cases of malignant paraganglioma.[13–15]

Surgery is the treatment of choice for paraganglioma. Before surgery, appropriate medical preparation with α-blocking and β-blocking agents is very crucial to avoid intraoperative hypertensive crisis. Use of β-blockers prior to α-blocker can lead to

unopposed α-adrenergic vasoconstriction that predisposes to hypertensive crises. Traditionally, patients are started on phenoxybenzamine for α-blockade preoperatively. Recent data suggest use of newer agents like prazosin or doxazosin for the purpose of α-blockade.[16] Calcium channel blocker is suited for patients with cardiovascular disease because of its inhibition of catecholamine-induced coronary vasospasm and myocarditis.[17 18] Propranolol is commonly used for β-blockade. Preoperative volume expansion with saline infusion is often used to prevent postoperative hypotension secondary to chronic volume contraction.[19] Preoperative localised arterial embolisation may help reduce blood loss during surgery.[20] Adjuvant radiation therapy following surgery may improve median survival in malignant paraganglioma.[21] Long-term follow-up is very important following resection as patients can have persistent or recurrent disease or develop metachronous primary paraganglioma.[22] Recurrence rate for paraganglioma is about 30%. In patients with metastatic disease, palliative chemotherapy with cyclophosphamide, dacarbazine and vincristine is recommended.[23]

Learning points

- Paraganglioma is a rare and curable cause of hypertension.
- Prompt recognition and early surgical resection is the key in management.
- Preoperative preparation with α-blocking and β-blocking agents and volume expansion are crucial before surgical resection.

Contributors VN was involved in the manuscript writing and GB was involved in the management of the patient and reviewing the manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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