

A pelvic paraganglioma presenting as a hypertensive emergency in pregnancy

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Introduction

Paraganglia are neuroendocrine organs that originate from the neural crest cells that are closely associated with the autonomic nervous system.¹ Paragangliomas and pheochromocytomas are tumours that arise from these organs. Paragangliomas are extra-adrenal tumours that can be divided into sympathetic and parasympathetic, and are further categorised by site.¹ The term "pheochromocytoma" is reserved for intra-adrenal tumours. The most common location of these extra-adrenal paragangliomas is the inferior para-aortic region (also known as the organ of Zuckerkandl).¹ Other extra-adrenal sites that have been described include the bladder, pelvis, prostate, ovaries and thorax.¹ According to McNicol, the estimated incidence of paragangliomas is 1:300 000. At least 30% of paragangliomas have a hereditary occurrence. Approximately 10% are syndromic.¹ We describe a case of extra-adrenal pelvic paraganglioma that caused hypertension in pregnancy.

Case report

A 31-year-old black woman, pregnant for the fifth time, presented at 31 weeks' gestation with pre-existent hypertension, superimposed pre-eclampsia and acute heart failure. She had a previous history of three stillbirths and one miscarriage due to uncontrolled hypertension. After her fourth pregnancy, she remained on antihypertensive medication. On admission, her blood pressure was 266/195 mmHg and she was treated with intravenous labetalol. A Caesarean section was performed and a 1.44 kg baby boy was delivered.

It was very difficult to control the blood pressure postpartum and the patient was treated with hydrochlorothiazide, atenolol, enalapril and amlodipine. At this stage, baseline investigation results included normal

urea and creatinine, a normal renal sonar and a creatinine clearance of 81 ml/minute, with no proteinuria. Echocardiography was normal, with a left ventricle ejection fraction of 52%.

Five months postpartum, the patient was referred to the division of endocrinology with a possible pheochromocytoma. The patient provided a history of experiencing feelings of impending doom when in the supine position just after micturition, as well as headaches, palpitations and sweating. These spells started during her fifth pregnancy at three months' gestation and disappeared approximately two months postpartum. A clinical examination did not reveal any target organ damage and her blood pressure was 122/70 mmHg on medication.

Twenty-four-hour urine results were as follows: metadrenaline 1 539 nmol/24 hour (n: 264-1 729), metnoradrenaline 227 641 nmol/24 hour (n: 480-2 424), metadrenaline/creatinine ratio of 170 nmol/mmol (n: 15-89) and metnoradrenaline/creatinine ratio 25 085 nmol/mmol (n: 28-158).

A computerised tomography scan showed a presacral mass measuring 6.6 x 6.6 cm (units were standardised throughout the case), with significant post-contrast enhancement. The mass extended inferior between the rectum and uterus. Possible sacral infiltration was noted superiorly. The mass was in keeping with a pelvic paraganglioma or possible ovarian mass. The adrenals appeared to be normal.

One month later, magnetic resonance imaging revealed a large tumour in the pelvis, just anterior to the sacrum. It measured 6.9 x 9.1 x 7.2 cm and was situated slightly left of the midline. It seemed to infiltrate the sacrum, with no extension into the spinal canal. The lesion was nonhomogenous on T2-weighted imaging and isointense to muscle on T1-weighted imaging, with a prominent vascular supply (see Figure 1).

An I-123 metaiodobenzylguanidine (MIBG) scan showed a solitary presacral mass lesion with high MIBG uptake. This picture was compatible with a functional paraganglioma. No metastases were identified (see Figure 2).

Surgical excision of the tumour was planned. The patient was adequately α -blocked with doxazosin preoperatively. In addition, she was given paracetamol and hydroxyzine as premedication.

Intraoperatively, the paraganglioma was located in the pelvis, inferior to the bifurcation of the aorta. It was not attached to any other organs. The patient had massive hypertensive responses during tumour manipulation and systolic blood pressures of up to 250 mmHg. This response was difficult to control with a nitroglycerine infusion, remifentanyl infusion, magnesium sulphate and sevoflurane in oxygen and air.

After the arterial and venous blood supply of the tumour was tied off, the patient had a severe hypotensive episode. The mean arterial pressure fell below 60 mmHg for a period of nine minutes. This was accompanied by substantial blood loss during removal of the tumour. The hypotension was managed with aggressive fluid resuscitation with packed cells. Intraoperatively, the patient received eight units of packed cells, eight units of cryoprecipitate, four units of fresh frozen plasma and one unit of platelets. She was also placed in the Trendelenburg position. The patient showed poor response to adrenaline and phenylephrine infusions. Subsequently, she was given hydrocortisone and calcium gluconate. Aortic compression was also applied during this period.

It was possible to remove the tumour in its entirety. The tumour was well circumscribed and tan-brown in colour. It measured 11 x 8.5 x 5 cm and weighed 140 g. Histology showed pleomorphic tumour cells arranged in well-defined nests (Zell ballen) set in a fibrovascular stroma. Immunohistochemical stains for synaptophysin and chromogranin were positive and the features were consistent with those of a paraganglioma (see Figure 3).

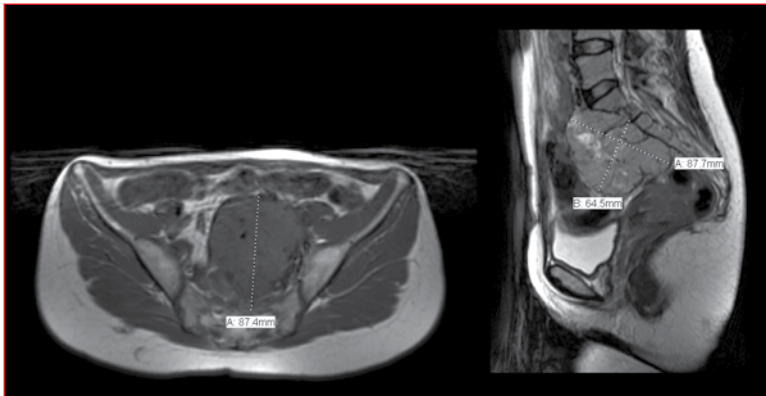


Figure 1: Magnetic resonance imaging demonstrating a large pelvic tumour

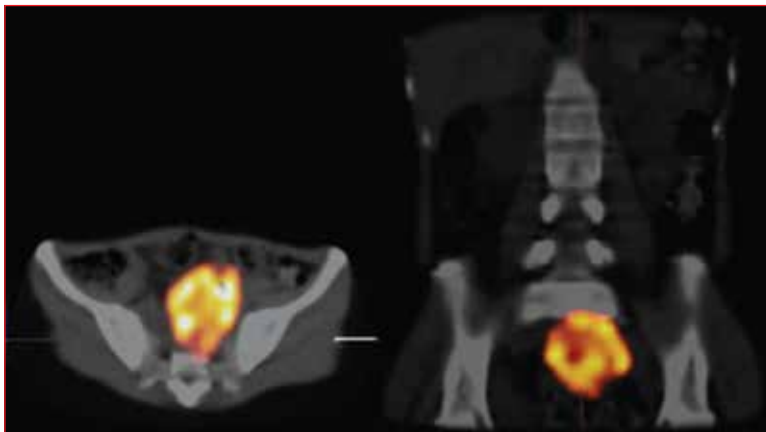


Figure 2: I-123 metaiodobenzylguanidine (MIBG) scan showing a presacral mass with high metaiodobenzylguanidine uptake

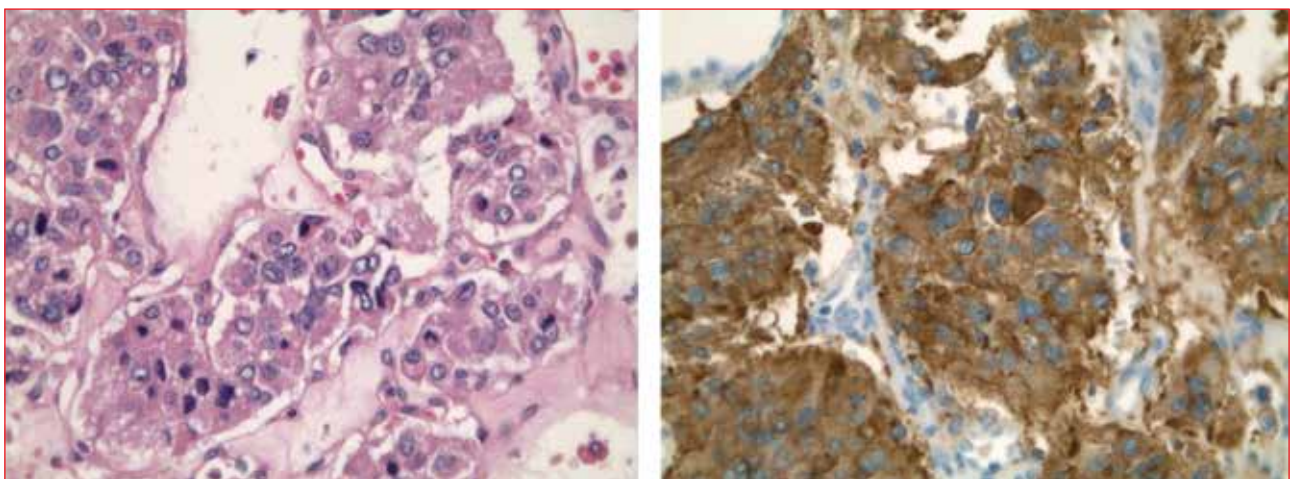


Figure 3: Haematoxylin- and eosin-stained section demonstrating Zell ballen set in a vascular stroma, and a chromogranin stain indicating strong cytoplasmic positivity

The patient recovered postoperatively and was discharged a few days later with normal blood pressure. She required no antihypertensive treatment. The postoperative neurological examination was normal.

At the six-month follow-up visit, she was normotensive and was not on any antihypertensive medication. The 24-hour metadrenaline and metnoradrenaline levels were normal, and I-123 MIBG and computed tomography scans of the abdomen and pelvis showed no evidence of recurrence or distant metastases.

Discussion

Paragangliomas and pheochromocytomas are rare causes of hypertension and only 0.1–1% of all cases of hypertension are due to these tumours.² The prevalence of paragangliomas and pheochromocytomas during pregnancy is five per million.³ The diagnosis is often missed during pregnancy, as the clinical picture mimics that of pre-eclampsia, leading to potentially lethal complications for both the mother and the foetus.² Prior to 1970, maternal mortality was as high as 50%, but it subsequently declined to 2%, mostly because of increased antepartum diagnosis.^{2,4} Foetal mortality has declined from 56% to approximately 10%.^{2,4}

During pregnancy, an undiagnosed paraganglioma can lead to a potentially fatal hypertensive crisis which can be precipitated by anaesthesia, the process of delivery, mechanical effects of the gravid uterus, abdominal palpation, uterine contraction and foetal movements.^{2,5} The foetus is protected from the direct effects of the high catecholamine levels by an enzymatic barrier at the placental level.² However, uteroplacental insufficiency can occur, leading to intrauterine growth restriction, miscarriage and stillbirth.^{2,5}

The diagnosis of paraganglioma should be considered in all pregnant women who present with hypertension in early pregnancy, and severe or intermittent hypertension, particularly if associated with headaches, palpitations, tachycardia and sweating, or episodes of sudden collapse.²

It is more common for extra-adrenal sympathetic paragangliomas to be malignant than pheochromocytomas.

Up to 50% give rise to metastases. The incidence of malignancy also varies depending on the particular inherited mutation in the case of familial disease. Malignancy is only diagnosed when there is metastasis to sites where paraganglial tissue is not usually found.¹ No definite histological criteria predict malignant behaviour. Only four features, extra-adrenal location, coarse nodularity of the primary tumour, confluent tumour necrosis and absence of hyaline globules, have been found to correlate statistically with malignancy.¹

A number of syndromes are associated with pheochromocytomas and paragangliomas, including multiple endocrine neoplasia types 2A and 2B, von Hippel-Lindau syndrome and neurofibromatosis type 1.¹ Familial cases show autosomal-dominant inheritance caused by germline mutations in one of 10 susceptibility genes: RET, VHL, SDHA, SDHB, SDHC, SDHD, SDHAF2, NF1, TMEM127 and MAX.⁶

Conclusion

We describe a patient who presented with multiple foetal losses due to uncontrolled hypertension secondary to a noradrenaline-secreting pelvic paraganglioma. The paraganglioma, which did not originate from the organ of Zuckerkandl, was located in a site that has rarely been described in the literature before.¹

This case demonstrates the importance of a high index of suspicion and the rewards of diagnosing a resectable, curable cause of hypertension. Ideally, this condition should be diagnosed early and managed aggressively in order to prevent maternal and foetal mortality.

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