A rare cause of hypertension in pregnancy: Pheochromocytoma

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Abstract

A 26-year-old primigravida at 35 weeks' gestation was transferred to our institution from a regional hospital for management of presumed preeclampsia. Due to the labile nature of her hypertension, further investigation was undertaken which revealed a right-sided pheochromocytoma. Alpha blockade was commenced, and an uncomplicated elective caesarean delivery was performed at 38 weeks' gestation under spinal anaesthetic. The patient underwent an elective right laparoscopic adrenalectomy six weeks post-partum. This case highlights the importance of investigating young women for secondary causes of hypertension to avoid mislabelling as essential or gestational hypertension.

Keywords

Hypertension, pheochromocytoma, high-risk pregnancy, maternal mortality

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Case report

A 26-year-old primigravida at 35 weeks' gestation was transferred to our institution from a regional hospital for management of presumed preeclampsia. Medical history included untreated hypertension and polycystic ovarian syndrome. Family history was significant for hypertension in her father diagnosed at the age of 48. At her 20-week antenatal visit, her blood pressure was 150/90 mmHg. She was commenced on methyldopa 250 mg twice a day at 25 weeks of gestation, and this was titrated to 500 mg three times a day. At 33 weeks of gestation, labetalol 100 mg daily was added.

Despite dual antihypertensive therapy, she remained hypertensive with a blood pressure of 158/110 mmHg at 35 weeks of gestation. She reported occasional palpitations but denied headaches, sweating, abdominal pain or leg swelling. She was admitted to the local hospital for blood pressure stabilisation, and labetalol was up titrated to 200 mg thrice daily. Further investigation revealed mild proteinuria of 0.04 g/mmol (normal <0.03 g/mmol). Fetal assessment with ultrasound and cardiotocography was reassuring. Due to the labile nature of her blood pressure (110/75 to 200/124 mmHg), a renal artery Doppler ultrasound was performed to exclude underlying renal artery stenosis. This revealed normal velocities in the renal arteries and an incidental 6.1 × 5.8 × 4.9 cm mildly heterogeneous right-sided suprarenal mass with a calcific centre.

She was transferred to a tertiary hospital for further management and investigation. Examination was unremarkable with normal body mass index and no evidence of abdominal mass, café-au-lait spots or lipoma. Blood pressure at presentation was 148/100 mmHg without tachycardia. Two separate plasma metanephrine samples revealed isolated elevated normetanephrine of greater than 9999 pmol/L (normal <900 pmol/L) and normal metanephrine (<500 pmol/L). Urinary fractionated metanephrines revealed elevated noradrenaline of 11,610 nmol/day (<780 nmol/day) with normal adrenaline excretion (<30 nmol/day).

The diagnosis of pheochromocytoma was made, and alpha blockade medication was started in conjunction with labetalol 200 mg twice daily. Due to the lack of availability of phenoxybenzamine, prazosin 0.5 mg twice daily was commenced and titrated up to 3.5 mg thrice daily, achieving good blood pressure control (122/80 to 155/95 mmHg). On day 9 of admission, phenoxybenzamine 30 mg twice daily was substituted for prazosin. Despite a high salt and fluid intake, she experienced side effects including postural dizziness and nasal congestion. After discussion with a multidisciplinary team including obstetric, medical, anaesthetic and endocrine surgical,

delivery was planned at term once adequate alpha blockade had been achieved.

On day 14 of her admission, an elective caesarean delivery was performed at 38 weeks' gestation under spinal anaesthetic. Perioperative management included blood pressure monitoring with an arterial line and intravenous 0.9% normal saline fluid for volume expansion to minimise potential hypotension secondary to spinal anaesthesia. Despite concerns regarding precipitating a hypertensive crisis, intraoperative blood pressure was well controlled with a total of 10 mg of phentolamine in divided doses.

However, in recovery the patient became hypertensive up to 192/160 mmHg. Further boluses of intravenous phentolamine had little effect on the elevated blood pressure, suggesting that full alpha blockade had already been achieved. Therefore, intravenous 60 mg labetalol was given in 20 mg boluses with some response. Additional treatment over the following 30 min included intravenous hydralazine 5 mg, oral nifedipine 20 mg and intravenous magnesium sulphate (4 g loading dose) followed by a 24-h infusion. Her blood pressure settled following administration of the magnesium sulphate infusion.

On the first postoperative day, blood pressure was well controlled at 130/70 mmHg on phenoxybenzamine 30 mg and labetalol 200 mg twice daily. In the absence of information on the safety of phenoxybenzamine and lactation, breast milk was expressed and discarded until definitive surgical management of the pheochromocytoma occurred.

A healthy baby girl weighing 4200 g was delivered with Apgar scores of 7 and 8 at 1 and 5 min, respectively. Initial management included a temporary admission to the neonatal intensive care unit for 1 h of continuous positive airway pressure for respiratory distress and blood pressure monitoring.

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The immediate post-partum period was unremarkable. Subsequent staging chest, abdomen and pelvis computed tomography scan did not reveal evidence of metastases. The patient underwent an uncomplicated elective right laparoscopic adrenalectomy six weeks post-partum. Histology was consistent with pheochromocytoma with no definite lymph vascular invasion. There was a normal pattern of staining for succinate dehydrogenase subunit B and succinate dehydrogenase subunit A, making succinate dehydrogenase complex gene mutation unlikely. Massive parallel sequencing did not identify a mutation associated with an inherited predisposition to pheochromocytomas. Repeat plasma metanephrines and urinary fractionated metanephrines three weeks post-adrenalectomy were normal.

Although pheochromocytoma is uncommon in pregnancy with a reported incidence of 2 per 100,000 pregnancies, this case highlights the importance of doing a secondary screening in young patients with hypertension prior to 20 weeks of gestation to avoid mislabelling as essential or gestational hypertension.^{1,2} In contrast to the plasma renin, aldosterone and cortisol levels, plasma metanephrines are easier to interpret in pregnancy, especially with assays with high sensitivity and negative predictive value.³ A timely diagnosis is particularly important due to the high fetal and maternal mortality of up to 30% associated with undiagnosed pheochromocytoma, and the risk of precipitating a hypertensive crisis by manual pressure on the adrenals and the stress of surgery.⁴ This case also highlights that symptoms of pheochromocytoma can be more subtle than the classic triad of 'headache, palpitations and sweating' and therefore a high index of suspicion is required by clinicians caring for pregnant women with hypertension. Other management issues that arose in this case and may similarly be faced by other clinicians include: availability and efficacy of phenoxybenzamine versus prazosin,⁵ timing of surgical resection; concomitantly with caesarean delivery or post-partum, careful preparation and planning for management of a hypertensive crisis perioperatively, safety of breastfeeding on phenoxybenzamine and role of genetic mutation testing. Management of these cases with a multidisciplinary team including the obstetrician, endocrinologist, anaesthetist, geneticist and endocrine surgeon is important to ensure the best outcome.⁶

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