Phaeochromocytoma in pregnancy: timing of surgery, mode of delivery and magnesium

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Summary: Phaeochromocytoma in pregnancy is rare. It is associated with high rates of fetal and maternal mortality especially in undiagnosed cases. There are no reliable data comparing outcomes regarding the timing of removal of tumour, or comparing outcomes between vaginal and caesarean delivery. Management should be individualized based upon consultation between the mother, obstetrician, anaesthetist, surgeon and physician. Magnesium infusion should be considered peripartum and/or at the timing of tumour resection.

Keywords: endocrinology, phaeochromocytoma, pregnancy, magnesium, genetic testing

CASE REPORT

A 28-year-old woman of Tongan ethnicity gravida 4 para 3 at nine weeks gestation was found to have a right suprarenal mass on ultrasound performed because of hypertension and dipstick proteinuria (subsequent urine protein:creatinine estimations were normal). Plasma normetadrenaline was 4350 pmol/L (normal <900) and 24 hour urine normetadrenaline was 18.5 µmol/day (normal <2.3) consistent with a diagnosis of phaeochromocytoma. There were no symptoms of obstructive sleep apnoea as an alternative cause of hypertension and elevated metanephrines. There was no clinical or biochemical evidence of Cushing's or Conn's syndromes. The patient had no history of paroxysmal symptoms, no relevant family history, and no clinical or biochemical features to suggest multiple endocrine neoplasia, neurofibromatosis or von Hippel-Lindau syndrome. Her three previous pregnancies had been uneventful. She was morbidly obese (body mass index 39.8 kg/m²), and her previous anaesthetic history was significant for previous inability to insert a bougie or endotracheal tube, a grade 3 laryngoscopy, and requiring intubation with a fast-track laryngeal mask airway.

Magnetic resonance imaging revealed a 35 mm diameter solid mass in the right adrenal gland with inhomogenous high signal on T2-weighted imaging, with no synchronous or metastatic disease (Figure 1). Echocardiography was performed to exclude left ventricular dysfunction due to catecholamine cardiomyopathy. The mother was commenced on phenoxybenzamine with the dose gradually increased to 40 mg twice a day.

Multidisciplinary meetings were held involving the mother, obstetrician, anaesthetist, surgeon and physician regarding the timing of surgery. Concerns regarding laparoscopic adrenalectomy in second trimester or removal of the tumour at the time of caesarean section included the mother's and the anaesthetist's reservation regarding awake intubation (felt to be indicated in view of her previous anaesthetic history), the possibility the tumour may not be able to be removed laparoscopically requiring conversion to an open procedure, and her morbid obesity. It was decided to attempt vaginal delivery with an assisted second stage to avoid pushing, with subsequent laparoscopic adrenalectomy approximately six weeks postpartum.

The mother was commenced on beta-blockers two days prior to delivery at 38 weeks gestation. Analgesia was achieved with epidural blockade, a magnesium sulphate infusion commenced, membranes were ruptured and a syntocinon infusion commenced. The cervix was fully dilated 13 hours after artificial rupture of membranes; a live male infant weighing 3742 g was delivered by Neville Barnes forceps with Apgar scores of 9 at 1 and 5 min. Other than transient hypotension after the epidural was commenced the mother's blood pressure was stable with systolic readings 115–140 mmHg and diastolic readings 60–90 mmHg during labour. No maternal arrhythmias occurred during monitoring with electrocardiographic telemetry.

Iodine-131-meta-iodobenzylguanidine (MIBG) scintiscan one month postpartum showed intense uptake in the right adrenal gland with no evidence of avid disease elsewhere. The mother proceeded to laparoscopic right adrenalectomy without complications when six weeks postpartum. Histology confirmed a 33 mm phaeochromocytoma, positive staining for succinate dehydrogenase complex subunit B (SDHB) excluding mutations of SDHB, SDHC and SDHD. Genetic tests for von Hippel-Lindau syndrome and RET-proto-oncogene are pending. Postoperatively maternal blood pressure has been normal off phenoxybenzamine, and urine and plasma metanephrines are normal.

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The mother gave written informed consent for publication of this case report.

Figure 1 T2-weighted MRIs

DISCUSSION

No reliable data for phaeochromocytoma in pregnancy exist comparing outcomes regarding timing of surgery (prior to 24 weeks where diagnosed, at term, postpartum) or mode of delivery (vaginal or caesarean).^{1,2} Management should be individualized based upon discussion within a multidisciplinary team. Surgical removal before 24 weeks gestation is generally associated with a good outcome provided alpha-blockade is adequate.³ Delay in surgery until the postpartum period however enables the use of MIBG, positron emission tomography and octreotide-labelled scintigraphy to exclude multiple or metastatic disease. Where vaginal delivery is attempted active pushing should be avoided to minimize the risk of tumour stimulation due to raised intra-abdominal pressure. Magnesium reduces catecholamine release from both the adrenal medulla and peripheral adrenergic nerve terminals. It is thought the mechanism of magnesium action is via interference with movement of calcium into chromaffin cells, calcium ions being responsible for increases in cell membrane permeability.⁴ Magnesium is also a highly effective direct alpha-adrenergic antagonist and antiarrhythmic in the setting of high dose epinephrine infusions. Magnesium infusions are efficacious in the management of hypertension and arrhythmias during surgical removal of phaeochromocytoma, and case reports describe its successful use in individuals with phaeochromocytoma crisis including catecholamine cardiomyopathy.^{5,6} Germline mutations account for a quarter of phaeochromocytomas – patients are more likely to be younger, tumours are more likely to be bilateral or extra-adrenal (parangliomas). Genetic screening should be considered in all pregnant women with phaeochromocytoma, especially those with paranglioma, bilateral adrenal phaeochromocytoma, a positive family history, onset at age less than 20 years, and those with clinical findings suggestive of associated syndromic disorders.

In conclusion we present a case of phaeochromocytoma diagnosed early in pregnancy where surgical removal of the tumour was delayed until after vaginal delivery with excellent outcome for mother and baby.

Points for consideration from this case report are:

- (1) Decisions about the mode of delivery and timing of surgery with phaeochromocytoma should be made by a multidisciplinary team in each case;
- (2) If vaginal delivery is attempted, early epidural analgesia should be considered to minimize pain, and active pushing in second stage should be avoided;
- (3) Magnesium sulphate infusion should be considered for delivery and/or removal of the tumour;
- (4) Echocardiography should be performed to exclude left ventricular dysfunction due to catecholamine cardiomyopathy;
- (5) In the setting of hypertension and mildly elevated urine or plasma catecholamines or metanephrines where a tumour cannot be localized, obstructive sleep apnoea should be excluded as a cause of the biochemical abnormalities;
- (6) Beta-blockers are often not required in the treatment of phaeochromocytoma, and should not be started until adequate alpha-blockade with phenoxybenzamine has been achieved;
- (7) Gene testing should be considered in all women of reproductive age with phaeochromocytoma.

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(Accepted 14 October 2010)