Clinical Reports

Anaesthesia for phaeochromocytoma in pregnancy

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Purpose: Pheochromocytoma in pregnancy is a rare occurrence. Details of the anaesthetic are even more rarely reported. Our purpose is to describe our management with reference to previous reports.

Clinical features: A 31-yr-old woman underwent resection of a pheochromocytoma at seven weeks gestation. Preoperative preparation included 2 mg prazosin *po* bid and 40 mg propranolol *po* bid. A balanced anaesthetic technique including 5 mg midazolam, 1500 µg alfentanil, 35 µg sufentanil, nitrous oxide and isoflurane was used. Blood pressure was controlled with 3.4 g magnesium and 2437 µg nitroglycerin. There were no episodes of hypertension intraoperatively. The patient made an uneventful recovery and delivered a normal baby at 37 wk gestation by caesarean section.

Conclusion: Anaesthesia for resection of a pheochromocytoma in early pregnancy can be successfully managed with preoperative alpha and beta sympathetic blockade and a balanced anaesthetic technique using magnesium as the main intraoperative hypotensive agent.

Objectif : La littérature médicale fait rarement mention du phéochromocytome durant la grossesse. La description de la gestion anesthésiste y est encore plus rare. Notre objectif est de présenter notre prise en charge d'un cas en faisant un rappel de comptes rendus antérieurs.

Éléments cliniques : À la septième semaine de sa gestation, une parturiente de 31 ans subissait une résection de phéochromocytome. Elle avait reçu en préopératoire prazosine 2 mg *po* BID et propranolol 40 mg *po* BID. Une technique d'anesthésie équilibrée a été réalisée avec midazolam 5 mg, alfentanil 1500 µg, sufentanil 35 µg, protoxyde d'azote et isoflurane. La pression artérielle a été contrôlée avec magnésium 3,4 mg et nitroglycérine 2437 µg. Il n'y a pas eu d'épisode d'hypertension peropératoire. Les suites opératoires ont été normales et la patiente a mis au monde un bébé normal par césarienne à la 37^e semaine de gestation.

Conclusion : Il est possible de bien gérer l'anesthésie du phéochromocytome en début de grossesse avec un blocage sympathique alpha et bêta et une technique d'anesthésie équilibrée associés au magnésium comme agent hypotenseur principal.

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Case report

A 31-yr-old woman presented with a two year history of headaches, often associated with vomiting, and a more recent history of sweating, palpitations, paroxysmal flushing and tremor. For one month, she had complained of right upper quadrant pain. An ultrasound revealed a right adrenal mass. Blood pressure measured during two different paroxysms was 180/120 mmHg.

Previous medical history and previous general anaesthetics were unremarkable. A pregnancy test at this stage was negative. Urinary metanephrines and vanillyl-mandelic acid (VMA) confirmed the diagnosis of pheochromocytoma. Urinary VMA was $99 \mu\text{mol}\cdot\text{day}^{-1}$ ($n = 0\text{--}50$) and metanephrines $20.8 \mu\text{mol}\cdot\text{day}^{-1}$ ($n = 0\text{--}7.1$). A CT scan before pregnancy was diagnosed showed a right adrenal mass 27×20 mm. Other laboratory work was unremarkable. Her ECG was reported to be normal but was suggestive of borderline left ventricular hypertrophy. An echocardiogram was not done.

At this stage, another pregnancy test was positive. She was estimated to be six weeks pregnant and expressed a strong desire to keep the baby. Initially, she was started on 3 mg terazosin *bid po* but this was changed to 2 mg prazosin *tid po* to which 40 mg propranolol *bid po* was later added because of the history of palpitations. She had no documented episodes of hypertension and no palpitations whilst taking these agents for about ten days before surgery.

On the day of surgery, she was given her usual medication plus 2 mg lorazepam *po* for pre operative sedation. On arrival in the OR, her blood pressure (BP) was 120/75 mmHg. She was sedated further with 3 mg midazolam *iv* and 5 μg sufentanil *iv*. An arterial line, an epidural catheter and a pulmonary arterial catheter were inserted prior to induction of anaesthesia. Central venous pressure (CVP) was 10 mmHg and the pulmonary capillary wedge pressure (PCWP) 17 mmHg. Prior to induction, she was given magnesium sulphate (MgSO_4) 2.25 g ($40 \text{ mg}\cdot\text{kg}^{-1}$) *iv* followed by an infusion at $1 \text{ g}\cdot\text{hr}^{-1}$.

Induction consisted of 15 μg sufentanil, 1500 μg alfentanil, 2 mg midazolam, 50 mg thiopentone with 6 mg vecuronium for muscle relaxation. Her BP decreased to 70/40 mmHg and responded to a rapid infusion of normal saline 0.9% together with two doses of 10 mg ephedrine.

Maintenance of anaesthesia consisted of isoflurane 0.5–1.0% together with an infusion of $0.25 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ sufentanil. Magnesium was continued and an infusion of nitroglycerin was given at a rate of 0.5–0.75 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. A test dose of 3 ml bupivacaine 0.5% was

used on insertion of the epidural, and at the start of the anaesthetic, 100 μg fentanyl were injected into the epidural catheter followed later during surgery by 4 mg morphine. No further local anaesthetics were used intra-operatively. Systolic BP stayed between 90 and 110 mmHg until after occlusion of the venous return from the tumour when it decreased to 70/40 mmHg. This responded to rapid infusion of normal saline 0.9%, ephedrine total dose 30 mg, and to stopping the infusions of MgSO_4 , nitroglycerin and sufentanil. At the end of surgery, the muscle relaxation was reversed with neostigmine and atropine, the trachea was extubated in the OR and she was taken to the PAR. A total of 3000 ml normal saline 0.9% were given intraoperatively. Blood loss was estimated at 300 ml and urine output was 900 ml.

There were no hypertensive episodes but treatment was required for hypotension. A total of 1.4 g MgSO_4 were given by infusion and the serum magnesium concentration half way through the procedure was $1.38 \text{ mmol}\cdot\text{l}^{-1}$ (0.7–1.05). This decreased to $1.05 \text{ mmol}\cdot\text{l}^{-1}$ 20 min after arrival in the PAR and to $0.75 \text{ mmol}\cdot\text{l}^{-1}$ eight hours later.

The patient made an uneventful post operative recovery. Pregnancy progressed until 37 wk when she showed signs of early intrauterine growth retardation which had occurred with her previous pregnancy. Labour was induced and she had a Caesarean section for a brow presentation with uneventful outcome for mother and baby. The baby's weight was 3035 g with Apgar scores of 8 and 9 at one and five minutes respectively. The baby is thriving and is now over a year old.

Discussion

Pheochromocytoma during pregnancy is rare. In 1987, Ellison¹ reported 128 cases in the world literature. In 1989, Harper² reported 139 patients with 162 pregnancies. Details of the anaesthetic are seldom reported in the literature. We have, therefore, reported details of the anaesthetic management of this case.

The initial question was whether to use alpha sympathetic blockade in this patient before surgery. Alpha blockade in non pregnant patients is controversial. It has been considered standard practice to provide at least 7–14 days of alpha blockade prior to surgery.⁴ As patients with pheochromocytoma are thought to be volume depleted, it is common in the preoperative period to utilize a high salt diet in combination with *iv* crystalloid to replete the patient's extracellular volume.⁴ Two questions arise. Do these patients really have a contracted intravascular volume and does preoperative alpha blockade together with *iv* fluid make any difference in outcome?

Bravo⁵ showed that, in non pregnant patients during steady state conditions, there was no difference between the haemodynamic features of patients with phaeochromocytoma and patients with untreated essential hypertension. In particular, this study showed no difference in plasma volume between the two groups. In both groups, hypertension was due to an increase in systemic vascular resistance (SVR). It did not examine haemodynamic variables during conditions of stress and did not compare plasma volume with that of normal patients. Bravo concluded that patients with phaeochromocytoma did not have a decreased intravascular volume but this can only be stated in relation to patients with untreated essential hypertension. In pregnancy, maternal ECFV is related to amniotic fluid volume and, therefore, maternal volume depletion may contribute to uteroplacental insufficiency and oligohydramnios.⁶ This may not have been a factor at this gestational age.

The routine use of preoperative alpha blockade in non pregnant patients has been questioned. Boutros⁷ reported a retrospective evaluation of 63 patients over 10 years and showed no difference in outcome. However, there were a number of questions raised by this study. The mean systolic pressure preoperatively was not different between those patients who were alpha blocked and those who were not, suggesting that alpha blockade may not have been optimal. They did not report differences in the amount of agent required to control blood pressure intraoperatively or the number of interventions required by the anaesthetist. Lastly, they did not specifically look for markers of complications such as electrocardiograms or cardiac enzymes. We feel that the intraoperative fluctuations in blood pressure may be less with preoperative blockade but have no evidence for this. For these reasons as well as ensuring adequate intravascular volume, we elected to alpha blockade our patient pre operatively and give intravenous fluids. After insertion of the pulmonary artery catheter but prior to induction of anaesthesia, the pulmonary artery wedge pressure was 17 mmHg. This implies that alpha blockade and fluid administration prior to surgery were effective.

Several different drugs have been used for preoperative preparation. Phenoxybenzamine, an irreversible alpha adrenoreceptor antagonist, has been widely used during pregnancy and is considered the drug of choice.² Other drugs with alpha blocking properties such as prazosin,³ labetalol² and alpha methyl tyrosine³ have also been used. Beta blockade has often been added to established alpha blockade to improve control of tachycardia, arrhythmias and blood pressure.⁴ There are no controlled trials of these drugs

during pregnancy. None have been associated with any problems except propranolol which, anecdotally, has been reported to be associated with intrauterine growth retardation, fetal bradycardia, fetal hypoglycaemia and premature labour when used long term during pregnancy.¹ Our patient had been started on 3 mg terazosin *po* bid before referral but this was changed to 2 mg prazosin *po* tid because the former is not on our hospital formulary.

Phaeochromocytoma and pregnancy have been associated with considerable morbidity and mortality for both mother and fetus. Ellison¹ reported that, if undiagnosed, the maternal mortality was 58% and the fetal mortality 56%. When the diagnosis was made before delivery, the maternal mortality was around 40% but the fetal mortality was as low as 10%. Harper² reported that, in the period between 1980 and 1987, the maternal mortality had fallen to 17%, and to 1% if the diagnosis was made antepartum. Over the same period, fetal mortality was 26% overall and 15% if the diagnosis was made antepartum. Until 1979, only one fetus of five survived surgical intervention up to 24 wk gestation but from 1980 to 1987, seven of eight survived. If pregnancy is allowed to proceed to term in a patient with undiagnosed phaeochromocytoma, there is considerable maternal and fetal mortality.

There has been controversy about the timing of surgical intervention. Many of the recommendations have been based on experience with single cases, some of which occurred many years ago before modern perioperative monitoring and intervention. Therefore, everything has been advocated in terms of timing. There is now a consensus that either the tumour should be excised during the first trimester or that the pregnancy should be allowed to proceed to fetal maturity when caesarean section should be performed followed immediately by removal of the tumour. Our interpretation was that maternal mortality was decreased with earlier surgical intervention. Fetal risk was still potentially high but there has been a trend to increased survival with more recent reviews.² Thus, we elected to proceed with early surgical intervention.

The anaesthetic management for surgical phaeochromocytoma removal is often not well documented. Epidural anaesthesia,^{9,10} trimetaphan,⁸ phentolamine,¹¹ nitroglycerine,⁹ nitroprusside, labetalol¹² and magnesium¹¹ have all been used to control blood pressure in pregnant patients with phaeochromocytoma. No adverse effects on the fetus have been demonstrated although there are theoretical reasons for avoiding nitroprusside as it has been shown to have adverse effects in fetal lambs¹³ and to reduce uterine blood flow in pregnant sheep.¹⁴ Magnesium has only recently been

described for controlling blood pressure in pregnant patients with phaeochromocytomas.¹¹ It is commonly used to prevent seizures in patients with pregnancy induced hypertension and its therapeutic levels are well known. Other advantages include a direct acting vasodilating effect, inhibition of catecholamine release from the adrenal medulla, reduction in sensitivity of alpha receptors to catecholamines and a potent anti arrhythmic effect.¹¹

James reported on 17 patients with phaeochromocytoma where magnesium was the primary agent used to control blood pressure intraoperatively, two of whom were pregnant.¹¹ These were also reported separately.¹⁵ Magnesium controlled blood pressure except when therapeutic levels were not achieved and during tumour handling when additional agents were required.

We used a balanced approach to anaesthesia and blood pressure control to avoid exposure to high concentrations of a single drug. Magnesium was used as the primary agent for blood pressure control but sufentanil, isoflurane, midazolam and nitrous oxide were all used to help prevent catecholamine release from inadequate anaesthesia. Alfentanil was used at induction to prevent the potential hypertensive response to laryngoscopy and intubation. Nitroglycerin was used to help with blood pressure control and theoretically to maintain uterine blood flow and prevent uterine muscle contraction. We have no evidence that this is true at this gestational age. Fentanyl, via the epidural catheter, contributed to intraoperative analgesia, but the main reason for the epidural was for post operative pain control with morphine.

There were no episodes of hypertension even when handling the tumour. Intervention for hypotension was required several times. This may have been due either to preoperative alpha blockade, to lack of catecholamine secretion during tumour manipulation, or to the multifaceted and balanced approach to anaesthesia and blood pressure control. Therapeutic levels of magnesium were not achieved. However, apart from the initial bolus of 40 mg.kg⁻¹ and the infusion at 1 g.hr⁻¹, blood pressure was controlled without further magnesium and a total of only 3.4 g magnesium were used.

In summary, we describe the preoperative management and details of anaesthesia for a patient with phaeochromocytoma in early pregnancy with successful outcome for mother and baby.

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