Case Report

Uneventful Cesarean Section in A Woman with Normotensive Asymptomatic Bifocal Pheochromocytoma Without Preoperative Alpha Blockade Preparation

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ABSTRACT

Context: There are no guidelines on the management of pheochromocytoma (PCC) diagnosed during pregnancy due to the rarity of the condition.

Case Description: A 30-year-old woman with MEN 2A due to a germline mutation in exon 11 of the RET oncogene. She underwent a prophylactic total thyroidectomy at the age of 12 with pathology showing multifocal microscopic medullary thyroid carcinoma. At the age of 20, she was found to have elevated catecholamines and CT of the abdomen revealed a 2.1 cm left adrenal pheochromocytoma. She was asymptomatic and normotensive. She underwent an eventful laparoscopic left adrenalectomy preceded with taking doxazosin 1 mg daily for 3 weeks. At the age of 29, she was found again to have elevated catecholamines while being pregnant. MRI of the abdomen revealed a 3.3 cm right adrenal pheochromocytoma. She remained asymptomatic and normotensive throughout the pregnancy. Elective uneventful C-Section was performed at week 38 without preoperative medical preparation. Postpartum, she remained asymptomatic while breastfeeding. She underwent uneventful laparoscopic right adrenalectomy eight months after delivery proceeded by taking phenoxymenzamine 10 mg twice/day for 10 days during which time she suffered stuffy nose, fatigue, and orthostasis. Pathology interestingly revealed bifocal pheochromocytomas in both adrenal glands.

Conclusion: We present a normotensive asymptomatic pregnant with PCC who underwent an elective uneventful C-Section without alpha-blockade preparation with excellent maternal/fetal outcomes. To the best of our knowledge, no similar case has been reported thus far. Preoperative medical preparation may not be needed in asymptomatic normotensive pregnant patients with PCC undergoing C-Section.

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Introduction

Pheochromocytoma (PCC) is a catecholamine-secreting tumor derived from chromaffin cells located in the adrenal gland. PCC presenting during pregnancy is a rare entity with a reported incidence of 0.007% of pregnancies [1, 2]. PCC during pregnancy can be asymptomatic or cause a variety of nonspecific symptoms [1]. Management can be challenging as there is no consensus or guidelines for optimal management.

Case Description

30-year-old Caucasian woman with multiple endocrine neoplasia (MEN) 2A due to a germline mutation in exon 11 of the RET oncogene at codon 634 with a strong family history of MEN 2A (Figure 1). She underwent a total prophylactic thyroidectomy at the age of 12 with pathology showing multifocal microscopic medullary thyroid carcinoma (MTC) without any biochemical or structural evidence of recurrence. At the age of 20, she was found to have elevated 24-hour urine metanephrines during routine surveillance. Computed tomography (CT) of the abdomen revealed a 2.1 cm left adrenal hyperdense mass (Figure 2A). She was asymptomatic and normotensive (118/66 mmHg) with heart rate (HR) of 65 beats per minute (BPM). She underwent left laparoscopic adrenalectomy preceded with taking doxazosin 1 mg daily for 3 weeks. Intraoperatively, she required a low rate of phenylephrine drip (rate could not be obtained). Final pathology revealed bifocal pheochromocytoma measuring 1.8x1.5x1.5 cm and 2.1x1.8x1.5 cm. At the age of 29, she was found to have elevated 24-hour urine metanephrines during routine surveillance again [metanephrine 2099 mcg/24 hrs (normal 19-140 mcg/24 hrs) and normetanephrine 617 mcg/24 hrs (normal 52-310 mcg/24 hrs)]. She was also found to be pregnant at 7-week gestational age. Magnetic resonance imaging (MRI) of the abdomen revealed a right adrenal mass measuring 3.3 cm (Figure 2B). The patient remained asymptomatic and normotensive throughout the pregnancy with blood pressure (BP) ranging between 110-120/60-74 mmHg and HR between 73-86 BPM. Elective C-Section was scheduled for week 38. Preoperative preparation with alpha-blockade was offered but she declined it. She agreed, however to keep monitoring BP and HR at home 2/day. C-Section was uneventful with fetal APGAR score was 10 at 10 minutes. She required a minimal rate of phenylephrine drip (80 mcg/min) for less than 30 minutes after the epidural anesthesia. Postpartum, she remained asymptomatic and normotensive (BP and HR within the same above ranges) while breastfeeding. She underwent elective right laparoscopic adrenalectomy eight months later after she finished breastfeeding. Preoperatively, she took phenoxybenzamine 10 mg twice a day for 10 days according to the surgeon recommendation who did not feel comfortable operating without preoperative medical preparation. She suffered stuffy nose, fatigue and dizziness during those ten days. Intraoperatively, she developed hypotension and required phenylephrine 80 mcg/min drip for 60 min and 2500 ml of intravenous Lactated Ringer’s to maintain blood pressure stability. Final pathology interestingly revealed bifocal PCC again measuring 4.2 cm and nodule 1.5 cm. Plasma metanephrines normalized.

Discussion

We present a case of a normotensive asymptomatic PCC in a pregnant patient who underwent an elective uneventful C-Section without alpha-blockade preparation. To the best of our knowledge, no similar case has been reported thus far. Catecholamines may induce clinical symptoms that can mimic other common disorders of pregnancy like essential hypertension, gestational hypertension, gestational diabetes, hyperemesis and/or preeclampsia [2]. Five to 15% of patient with PCC during pregnancy have normal blood pressure, 50% have orthostatic hypotension, 50% have sustained hypertension and 35 to 45% have paroxysmal hypertension [2]. A subgroup of patients don’t develop symptoms/hypertension even with high circulating catecholamines. This could be explained by desensitization due to internalizations of receptors and reduction of their number on the cell surface and/or decrease binding affinity of the catecholamine to the receptor [3].

Despite the apparent general agreement regarding the need for preoperative α-blockade to prevent perioperative cardiovascular complications, not all feel this is necessary [4]. Work from the Cleveland Clinic has demonstrated that non-pregnant patients undergoing PCC resection may be safely managed intra-operatively with vasodilator therapy without undergoing preoperative α-blockade [5]. Shao et al showed that preoperative α1-adrenoceptor antagonist had no benefit in maintaining intraoperative hemodynamic stability in patients with normotensive PCC in a controlled prospective study. In fact, those patients had a higher rate of use of vasoactive medications and coloids [6]. Recent series of laparoscopic adrenalectomy for PCC showed that this procedure is now associated with experienced hands with no mortality and a morbidity rate of about 10%, regardless of the preoperative medical preparation [7].

Undiagnosed and/or untreated pheochromocytoma carries an increase the risk of maternal and fetal mortality, up to 12-18 and 40-50% receptively [1, 2]. A recent review showed improvement of survival rate with reported maternal and fetal mortality of 8 and 17% respectively [1, 2]. This improvement may be simply due to earlier diagnosis and better antepartum and intra-operative care, rather than preoperative α-blockade per se [8]. There are no guidelines on the management of PCC diagnosed during pregnancy and most recommendations come from case reports, case series and expert opinion due to the rarity of the condition. Surgical resection of the tumor is the definitive treatment of pheochromocytoma; with the optimal time for surgical resection being during the second trimester. Otherwise, adrenalectomy could then be scheduled in the same session or later several days to weeks after delivery [2]. Pretreatment with α-adrenergic receptor blockade for at least 10–14 days before surgery (C-Section or adrenalectomy) has been considered necessary in all pregnant patients even if they are normotensive to prevent paroxysmal peaks in blood pressure [2, 3]. There are no clear criteria to identify an adequate alpha-adrenoceptor blockade. However, orthostatic hypotension has been used as an indicator of the sustained blockade; but blood pressure should go below 80/45 mmHg [2, 3]. One of the main objectives of treatment with α-adrenergic receptor blockers is to counteract the effects of catecholamines that induce profound vasoconstriction of the maternal uterine arterial circulation, resulting in a compromised uteroplacental circulation [2, 3]. It is unclear though if above is still relevant in asymptomatic normotensive patients due to the desensitized receptors. In addition, the use of α-receptor blockers can result in hypotension compromising uteroplacental circulation as well. Antihypertensive drugs during pregnancy may indeed cause fetal complications including hypoxia, intrauterine growth retardation and placental ischemia [2, 3].
Searching Pub Med and Google scholar, we found only 3 cases of PCC diagnosed in normotensive (BP< 140/90 mmHg) asymptomatic pregnant patients who underwent C-Section followed by adrenalectomy [9-11]. The characteristics of those 3 cases, as well as our index case, are summarized in (Table 1). One of the patients was kept in the maternal intensive care unit from the time of diagnosis at 25 weeks of gestational age till delivery at 38 weeks of gestational age because she rapidly experienced symptomatic orthostatic hypotension, bradycardia and dyspnea even with small doses of prazosin and propranolol. Similarly, Almeida-Rodrigues et al reported that their patient was admitted to the antenatal care unit and kept there for a full week before the elective C-Section to monitor maternal blood pressure and fetal well-being tighter [11]. On the other hand, our patient underwent an uneventful C-Section without alpha nor beta-blockade preparation with excellent maternal/fetal outcomes comparable to the outcomes of the other 3 cases which were preceded by medical preparation. In fact, our approach was more cost-effective and convenient to the patient and did not put her at the risk of experiencing side effects nor developing potential fetal complications. She required a minimal rate of phenylephrine drip for less than 30 minutes after the epidural anesthesia which is commonly encountered in obstetrics cases following epidural analgesia. In addition, she had the opportunity to follow the World Health organization (WHO) recommendation by exclusively breastfeeding her newborn which is known to have many benefits for both the infant and the mother. Indeed, our patient suffered from many unpleasant side effects on a small dose of phenoxybenzamine in preparation for the adrenalectomy during which she required phenylephrine infusion for longer time.

In conclusion, we report the first case (to our knowledge) of a normotensive asymptomatic pregnant with PCC who underwent an elective uneventful C-Section without alpha-blockade preparation with excellent maternal/fetal outcomes. Asymptomatic normotensive pregnant patients with PCC may undergo C-Section safely without preoperative medical preparation. In addition, they may consider breastfeeding their infants after delivery without rushing into PCC resection.

Figure 1: Family pedigree Grandfather had total thyroidectomy for MTC, subtotal parathyroidectomy and bilateral pheochromocytomas resected. Father had a total thyroidectomy for MTC and had bilateral pheochromocytomas resected. Sister had prophylactic total thyroidectomy and primary hyperparathyroidism which is being watched currently.

Figure 2A: Computed tomography (CT) of the abdomen revealing a 2.1 cm left adrenal hyperdense mass (arrow).

Figure 2B: Magnetic resonance imaging (MRI) of the abdomen revealing a 3.3 cm right adrenal mass (arrow).

Disclosure statement

Authors has nothing to disclose.
Table 1: Summary of the characteristics of normotensive asymptomatic patients with PCC diagnosed during pregnancy and underwent C-Section before adrenalectomy including our index case

<table>
<thead>
<tr>
<th>First Author</th>
<th>Age (years)</th>
<th>Time of diagnosis (WGA)</th>
<th>24 hrs urine catecholamines (× UNL)</th>
<th>Preoperative blockade</th>
<th>End of pregnancy (wks)</th>
<th>Time of adrenal surgery/PCC size</th>
<th>Maternal-Fetal outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benmoussa</td>
<td>1.0</td>
<td>18</td>
<td>↑ MN (×4.7 UNL) and NMN (×2.5 UNL)</td>
<td>NO</td>
<td>38</td>
<td>8 months PP/bifocal 4.2 and 1.5 cm</td>
<td>Good/good</td>
<td>MEN 2A, second PCC</td>
</tr>
<tr>
<td>Orioli</td>
<td>27</td>
<td>24</td>
<td>↑ MN (×7.8 UNL) &amp; NMN (×8 UNL)</td>
<td>Prazosin/propranolol I/ High salt diet</td>
<td>38</td>
<td>Right after CS/ 4 x 3.5 cm</td>
<td>Good/good</td>
<td>MEN 2A, first PCC</td>
</tr>
<tr>
<td>Tingi</td>
<td>22</td>
<td>16</td>
<td>↑ MN (×3.2 UNL) &amp; NMN (×1 UNL)</td>
<td>Phenoxybenzamine</td>
<td>36</td>
<td>6 weeks PP/7.3 x 6.5 cm</td>
<td>Good/premature</td>
<td>MEN 2A, second PCC</td>
</tr>
<tr>
<td>Almeida-Rodrigues</td>
<td>36</td>
<td>20</td>
<td>MN and NMN intermittently elevated,</td>
<td>Doxazosin</td>
<td>37</td>
<td>NA</td>
<td>Good/good</td>
<td>MEN 2A, History of bilateral PCC resection. 2. Recurrence in the left side</td>
</tr>
</tbody>
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REFERENCES