Pheochromocytoma in Pregnancy
A Case Series and Review

Raymond Oliva, Peter Angelos, Edwin Kaplan, George Bakris

Hypertensive disorders in pregnancy remain among the most understudied areas despite the recent advancement in medical care and management. Although most of this is ascribed to a pregnancy-specific disorder, preeclampsia, there is a paucity of data and few recommendations about another potentially disastrous hypertensive disorder, pheochromocytoma, a catecholamine producing tumor, with a reported incidence of <0.2 per 10,000 pregnancies. Despite its rarity, untreated pheochromocytomas carry a risk of mortality for both mother and fetus, as high as 58%. This may be attributed to several factors, such as the failure to detect the condition because of its extreme rarity, the tendency of these tumors to have varied presentations, and the fact that pregnancy may preclude certain imaging modalities and radioisotope testing. The enlarging uterus may also trigger tumor activity, in addition to the tendency for gravidas to undergo operative procedures on short notice. Thus, it is imperative that physicians who manage patients with pheochromocytoma familiarize themselves with special considerations in relation to pheochromocytoma during pregnancy. Focus should be directed toward understanding the indications of when women with chronic or de novo hypertension during gestation should undergo the special tests used to diagnose pheochromocytoma and how to manage the disease once diagnosed. This report surveys 6 pheochromocytomas managed at our institution, reviews the literature of pheochromocytomas, and presents recommendations on how to better suspect, detect, and manage these disorders in pregnant populations.

Case Reviews
We reviewed 6 cases of pheochromocytoma managed at the University of Chicago Medical Center between 1984 and 2009. Table 1 briefly summarizes their presentation and management. Two of these cases (cases 1 and 4) were published previously in detail but are presented to provide a more complete spectrum of presentation.

Case 1
A 31-year-old black woman presented during gestational week 21 with a blood pressure of 220/140 mm Hg. She was hypertensive for 7 years and was initially treated with atenolol. She had a history of 2 abortions and symptoms of severe headaches, palpitations, dizziness, and intermittent diaphoresis. Her blood pressure readings varied between highs of 210/120 mm Hg and as low as 80/50 mm Hg when standing. She also had new onset of arrhythmias. Biochemical and imaging testing was positive for an extra adrenal pheochromocytoma and was one of the first cases to use MRI in gestation. She was prescribed 40 mg/d of phenoxybenzamine and 40 mg/d of propanolol. She maintained acceptable blood pressures until gestational week 37, when she underwent cesarean section and an exploratory laparotomy resulting in a successful pregnancy outcome and removal of the tumor.

Case 2
A 21-year-old black female presented to the emergency department with uncontrolled hypertension and elevated blood sugar levels during her 16th week of gestation. She was known to have chronic hypertension and had been treated with labetalol with blood pressures ranging from 160 to 170/80 to 100 mm Hg. She was admitted with an initial diagnosis of preeclampsia. Ultrasound revealed a right adrenal mass measuring 5×4 cm, suggesting the possibility of a pheochromocytoma. Urinary metanephrines measured 4602 μg/24 hours (normal [N]: <900) and normetanephrines 4464 μg/24 hours (N: <600). She was treated with phenoxybenzamine and labetalol as a preoperative blockade. Laparoscopic adrenalectomy was performed during gestational week 18, and a healthy neonate was delivered by elective cesarean section during week 36 of gestation. She remained hypertensive; however, despite removal of the tumor and normalization of catecholamine excretion and required 25 mg/d of hydrochlorothiazide, 600 mg of labetalol twice daily, and 40 mg/d of lisinopril to control her blood pressure.

Case 3
A 28-year-old Hispanic female, initially diagnosed with gestational diabetes and preeclampsia, was noted to be mildly hypertensive at 21 weeks of gestation. Her hypertension failed to respond to treatment with methyldopa, and she was...
noted to exhibit orthostatic decreases in blood pressure combined with tachycardia. A 24-hour urine collection showed markedly elevated norepinephrine at 1453.1 μg (N: 15 to 80 μg), vanillylmandelic acid (VMA) at 17.6 mg (N: 15 to 80 μg), and metanephrines at 2.2 mg (N: 0.3 to 0.9 mg). An MRI performed during her 22nd gestational week revealed a 3.0-cm extra adrenal mass at the hilum of the left kidney. She was treated with phenoxybenzamine and subsequently prescribed propanolol for tachycardia. Obstetric ultrasound revealed placenta previa. She was hospitalized during gestational week 31 with poorly controlled hypertension and signs of placental abruption. She suffered intrauterine fetal demise. Her hospital course was complicated by the appearance of disseminated intravascular coagulation, renal failure, and hypertensive encephalopathy. After the resolution of these acute problems, she underwent excision of the pheochromocytoma. One month postoperatively, she was normotensive with normal blood chemistry including catecholamine metabolites.

**Case 4**

A 25-year–old Mexican woman was rushed to the emergency department because of acute onset of chest pain, shortness of breath, neck pain, nausea, and vomiting during the 38th gestational week. Pertinent past medical history included medullary thyroid carcinoma at age 21 y, history of missed abortion, hypertension, chest pains, and light-headedness. A 25-year-old Mexican woman was rushed to the emergency department during the 38th gestational week. Pertinent past medical history included medullary thyroid carcinoma at age 21 y, history of missed abortion, hypertension, chest pains, and light-headedness. She was hospitalized during gestational week 31 with poorly controlled hypertension and signs of placental abruption. She suffered intrauterine fetal demise. Her hospital course was complicated by the appearance of disseminated intravascular coagulation, renal failure, and hypertensive encephalopathy. After the resolution of these acute problems, she underwent excision of the pheochromocytoma. One month postoperatively, she was normotensive with normal blood chemistry including catecholamine metabolites.

**Table 1. Summary of Cases**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Case 1⁷</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4⁸</th>
<th>Case 5</th>
<th>Case 6</th>
</tr>
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<tbody>
<tr>
<td>Age, y</td>
<td>31</td>
<td>21</td>
<td>28</td>
<td>25</td>
<td>33</td>
<td>36</td>
</tr>
<tr>
<td>Race</td>
<td>Black</td>
<td>Black</td>
<td>Hispanic</td>
<td>Hispanic</td>
<td>Black</td>
<td>White</td>
</tr>
<tr>
<td>Obstetric score</td>
<td>G3P0 (0-2-2-0)</td>
<td>G1P0</td>
<td>G3P2 (2-0-0-2)</td>
<td>G2P1 (0-1-1-0)</td>
<td>G3P2 (1-0-1-1)</td>
<td>G2P2 (2-0-0-2)</td>
</tr>
<tr>
<td>Time of presentation, wk gestation</td>
<td>21</td>
<td>16</td>
<td>21</td>
<td>38</td>
<td>26</td>
<td>Postpartum</td>
</tr>
<tr>
<td>Presenting symptoms</td>
<td>Hypertension, severe headaches, palpitations, orthostasis, dizziness, diaphoresis</td>
<td>Hypertension, elevated sugar levels</td>
<td>Hypertension, orthostasis, tachycardia</td>
<td>Acute onset chest pain, shortness of breath, neck pain, nausea, vomiting</td>
<td>Hypertension, light-headedness, dizziness, emesis</td>
<td>Hypertension, chest pains, nausea, headaches</td>
</tr>
<tr>
<td>Weight gain*</td>
<td>Not available</td>
<td>None</td>
<td>Not available</td>
<td>None</td>
<td>Not available</td>
<td>None</td>
</tr>
<tr>
<td>Pertinent medical history</td>
<td>History of 2 abortions, hypertensive for 7 y</td>
<td>Hypertensive and diabetic for 10 y, initially treated as preeclampsia</td>
<td>Diagnosed with gestational diabetes</td>
<td>Medullary thyroid carcinoma at age 21 y, history of missed abortion</td>
<td>History of pheochromocytoma during first pregnancy</td>
<td>None</td>
</tr>
<tr>
<td>Biochemical results</td>
<td>Elevated plasma norepinephrine and epinephrine</td>
<td>Elevated urine metanephrine and normetanephrine</td>
<td>Elevated urine metanephrine, VMA, and normetanephrine</td>
<td>Elevated urine norepinephrine, epinephrine, metanephrine, and normetanephrine</td>
<td>Elevated urine norepinephrine, and metanephrine</td>
<td>Elevated urine VMA and metanephrine</td>
</tr>
<tr>
<td>Glucose</td>
<td>Normal</td>
<td>Elevated (136 mg/dL)</td>
<td>Elevated (150 mg/dL)</td>
<td>Elevated (155 mg/dL)</td>
<td>Normal</td>
<td>Elevated (116 mg/dL)</td>
</tr>
<tr>
<td>Imaging</td>
<td>MRI, 2 cm above the aortic bifurcation</td>
<td>Abdominal ultrasound, right adrenal mass 5×4 cm</td>
<td>MRI, 3 cm extra adrenal mass at the hilum of left kidney</td>
<td>MRI, left 3.7 cm adrenal mass; MIBG scan, increase activity in the left suprarenal region</td>
<td>First mass, 5.0×4.5 cm—mass between aorta and vena cava; second mass, 4×3×4-cm right adrenal mass</td>
<td>MRI, 2.6×2.6×3.1 cm right adrenal mass</td>
</tr>
<tr>
<td>Preoperative blockade</td>
<td>Phenoxybenzamine and propanolol</td>
<td>Phenoxybenzamine and labelol</td>
<td>Phenoxybenzamine and propanolol</td>
<td>Phenoxybenzamine</td>
<td>Phenoxbenzamine and atenolol</td>
<td>Phenoxbenzamine</td>
</tr>
<tr>
<td>Operative management</td>
<td>Cesarean section and exploratory laparotomy</td>
<td>Laparoscopic adrenalectomy</td>
<td>Adrenalectomy</td>
<td>Adrenalectomy</td>
<td>Cesarean section and exploratory laparotomy</td>
<td>Laparoscopic adrenalectomy</td>
</tr>
<tr>
<td>Maternal outcome</td>
<td>Resolution of symptoms</td>
<td>Still with elevated blood pressure</td>
<td>Resolution of symptoms</td>
<td>Peripartal cardiomyopathy, resolution of symptoms after surgery</td>
<td>Resolution of symptoms</td>
<td>Resolution of symptoms</td>
</tr>
<tr>
<td>Fetal outcome</td>
<td>Alive</td>
<td>Alive</td>
<td>Placental abruption with fetal demise</td>
<td>Alive</td>
<td>Alive</td>
<td>Alive</td>
</tr>
<tr>
<td>Comments</td>
<td>Extra adrenal pheochromocytoma</td>
<td>Extra adrenal pheochromocytoma</td>
<td>Diagnosed with MEN 2A; 4 siblings were found to have a mutation in the RET proto-oncogene</td>
<td>Recurrent pheochromocytoma</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MIBG indicates A¹⁴¹ meta-iodobenzylguanidine.

*“None” refers to no excess weight gain beyond what would be expected with a pregnancy.
formed shortly thereafter. Genetic evaluation was also performed for a possible multiple endocrine neoplasia 2A syndrome, and a mutation was identified in codon 634 of the RET proto-oncogene. Four of her 6 siblings were found to have the same mutation.

Case 5
A 33-year-old black woman was admitted during her 26th gestational week of her fourth pregnancy with symptoms of lightheadedness, dizziness, emesis, and a blood pressure of 195/64 mm Hg. She was examined initially at the University of Chicago Hospital 10 years earlier and documented to have episodes of headaches, palpitations, sweating, and chest pains. Her previous pregnancy was complicated by hypertension and preeclampsia, as well as a spontaneous preterm delivery. Her blood pressure remained elevated postpartum, as did the recurrent episodes of headaches, prompting the standard evaluation for secondary hypertension. Urinary norepinephrine of 406 μg/24 hours (N: <80) and normetanephrine of 1703 μg/h (N: <500) were elevated, whereas imaging studies revealed a right adrenal mass that measured 4.5 × 4.0 × 5.0 cm. A131 Meta-iodobenzylguanidine scan demonstrated uptake in the adrenal mass. She was treated with 20 mg of phenoxybenzamine twice daily and 20 mg/d of atenolol. She underwent exploratory laparotomy with excision of the right adrenal mass.

The current admission was a referral to rule out the possibility of pheochromocytoma recurrence. Results of the 24-hour urine collection were as follows: 290 μg of norepinephrine per 24 hours, 1.9 mg of metanephrine per 24 hours, and 6.1 mg of VMA per 24 hours. MRI revealed a 2.6 × 1.0 × 2.5-cm mass in the right adrenal bed consistent with local recurrence of her pheochromocytoma. She was treated with 20 mg of phenoxybenzamine twice daily and readmitted at gestational week 36 for cesarean delivery and a right adrenalectomy. The mother and infant had uneventful postoperative courses and were discharged 1 week later.

Case 6
A 36-year-old pregnant white female presented with a history of paroxysmal palpitations, chest pains, nausea, and headaches over a span of 3 years. Elevated blood pressures, as high as 200 mm Hg systolic, were noted as early as gestational week 25, and 2 weeks later, she was admitted with a diagnosis of “possible preeclampsia.” She was treated with magnesium sulfate, but because of her persistently elevated blood pressures, she underwent an emergent cesarean section. The patient experienced paroxysmal elevation of blood pressures, headaches, nausea, vomiting, and facial flushing postpartum. A 24-hour urine sample demonstrated elevated VMA (10.2 mg/24 hours) and metanephrine (4684 μg/24 hours) levels. An MRI revealed a 2.6 × 2.6 × 3.1-cm mildly T2 hyperintense enhancing right adrenal mass. She was treated with 20 mg of phenoxybenzamine twice a day for preoperative α blockade and underwent a laparoscopic right adrenalectomy. Her blood pressure remained stable during the procedure, and no additional problems were noted postoperatively.

Discussion
Pheochromocytomas and parangliomas are neuroendocrine tumors derived, respectively, from adrenal chromaffin cells and extra-adrenal paranglia, and these tumors can cause secondary hypertension.9 Sympathetic nervous system activity is enhanced and its function integral to the maintenance of elevated blood pressure. The excess release and high levels of catecholamines (norepinephrine, epinephrine, and, to a lesser extent, dopamine), account for the typical presentation of pheochromocytoma. Stimulation of α receptors induces vasoconstriction, whereas β2 receptors induce vasodilation and β1 receptors are associated with an increase in the rate of contraction myocardial and contractile force.10 Presynaptic α2-receptors inhibit release of neuronal norepinephrine, resulting in enhanced release of neuronal norepinephrine.

Many adrenal tumors produce both norepinephrine and epinephrine or are predominantly epinephrine-secreting tumors, whereas most (90%) extra-adrenal tumors produce predominantly norepinephrine.12 As a circulating hormone, epinephrine acts potently on β2 adrenergic receptors causing vasodilation and is an agonist at postsynaptic α2 receptors. Norepinephrine is released locally from sympathetic nerve endings within the vasculature and causes α1 adrenoreceptor-mediated vasoconstriction.13 Norepinephrine increases peripheral vascular resistance with a consequent increase in both systolic and diastolic blood pressures. Epinephrine increases cardiac output and systolic blood pressure, whereas it decreases or has no effect on diastolic blood pressure.11 Thus, epinephrine-secreting pheochromocytomas produce episodic symptoms and signs, such as palpitations, lightheadedness or syncope, anxiety, and hyperglycemia, more frequently, whereas norepinephrine-producing tumors are more often associated with continuous symptoms and signs, including hypertension, sweating and headaches.12,14

The diagnosis in pregnant patients is often missed because these tumors have the ability to produce signs and symptoms that mimic other forms of hypertension, including the new-onset hypertensive syndromes in pregnancy, gestational hypertension, and preeclampsia. In fact, the appearance of hypertension can be insidious, and the patient may even appear asymptomatic until delivery. Table 2 compares preeclampsia with pheochromocytoma in pregnancy. In fact, all of our patients were initially managed as having preeclampsia. Both of these diseases are characterized by hypertension, but preeclampsia is usually the first disease that the clinician considers when it appears de novo or accelerates rapidly. However, it is usually accompanied by proteinuria and, often, sudden weight gain and edema, as well as liver and coagulation abnormalities.5 Obesity and overweight contribute to the risk of both preterm preeclampsia and severe preeclampsia, with several studies revealing that women with high prepregnancy body mass index were more likely to develop severe preeclampsia.15–17 With pheochromocytoma, excessive urinary protein excretion and liver or coagulation abnormalities occur rarely, and sudden weight gain and edema are unusual. We could only gather data on weight in 3 of our patients, and no sudden weight gain was noted.

The difficulty in diagnosing pheochromocytoma in pregnancy is demonstrated in a recent case report of a pregnant
Table 2. Differentiating Features Between Preeclampsia and Pheochromocytoma

<table>
<thead>
<tr>
<th>Features</th>
<th>Preeclampsia</th>
<th>Pheochromocytoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs and symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time of presentation*</td>
<td>&gt;20 wk of gestation</td>
<td>Anytime during pregnancy</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Usually sustained</td>
<td>Paroxysmal</td>
</tr>
<tr>
<td>Orthostatic hypotension*</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Bipedal edema*</td>
<td>May be present</td>
<td>Absent</td>
</tr>
<tr>
<td>Headaches</td>
<td>Usually in more severe preeclampsia</td>
<td>Present</td>
</tr>
<tr>
<td>Flushing</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Palpitations</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Weight gain</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Laboratory findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteinuria*</td>
<td>Present</td>
<td>Often absent</td>
</tr>
<tr>
<td>Glucose</td>
<td>Normal</td>
<td>Elevated</td>
</tr>
<tr>
<td>Liver transaminases</td>
<td>Elevated</td>
<td>Normal</td>
</tr>
<tr>
<td>Catecholamines*</td>
<td>Normal</td>
<td>Elevated</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>May be present</td>
<td>Normal</td>
</tr>
</tbody>
</table>

*Data show common clinic and laboratory features to distinguish diseases states.

woman who presented with sudden onset of headaches and shortness of breath.19 The inability of the medical team to include pheochromocytoma as a differential diagnosis led to inadequate treatment of the patient and the eventual demise of the fetus. Clinical clues, such as labile hypertension, headaches, and the failure to respond to conventional treatment, should prompt physicians in the possibility of this condition in pregnant patients.

Several mechanisms can trigger clinically overt pheochromocytoma in pregnancy. These include increases in intra-abdominal pressure, fetal movement, uterine contraction, process of delivery, an abdominal surgical intervention, and even general anesthesia.22 In our small series, only 1 patient presented with “typical” presentation features of the disorder, which is paroxysmal hypertension, associated with headaches, sweating, and tachycardia. Two patients were diagnosed initially with gestational diabetes, which, in these cases, may have been explained by the effect of the excess catecholamines on glucose metabolism by inhibition of insulin secretion or by induction or aggravation of insulin resistance.19,20 Diabetes has been reported in ∼1 in 3 hypertensive patients with pheochromocytoma but not previously as an isolated finding.20,21 Three patients became symptomatic on standing, possibly explained by the relative hypovolemia associated with pheochromocytomas. The development of orthostasis may serve as a clue for suspecting pheochromocytoma in pregnant patients.22 Other symptoms seen in our patients included light-headedness, dizziness, diaphoresis, nausea, and vomiting. Although nausea and vomiting is observed with preeclampsia, abdominal pain, often over the liver, is also present in preeclampsia but not with pheochromocytoma. Other notable symptoms described in the literature include nervousness, pallor, fever, and cardiovascular manifestations, such as arrhythmias, angina pectoris, dilated cardiomyopathy, acute heart failure, and even cardiogenic shock.5,23 One of our patients presented with acute heart failure and was managed accordingly.

Pheochromocytoma-induced cardiomyopathy has been described in <10 cases.24,25 The specific mechanism is still unknown, but it has been suggested that excess catecholamines may cause myocardial necrosis, vasoconstriction leading to myocarditis, or both. Another possibility may be downregulation of the receptors, an occurrence described when terbutaline was administered for tocolysis. The reversibility of the cardiomyopathy in pheochromocytoma indicates that it is catecholamine induced, and removal of the adrenal mass can lead to resolution of the cardiomyopathy.8 The effects of catecholamines in pregnancy were demonstrated when dobutamine, a sympathomimetic agent, produced a reduction of contractile cardiac reserve and suboptimal response to hemodynamic stresses.26 This study demonstrated that patients with previous cardiomyopathy during pregnancy and seemingly normal cardiac function after delivery showed decreased cardiac reserve when treated with an amount of dobutamine that normally would mimic the increased cardiac output of pregnancy. Two types of responses are described; those with the best outcome have almost complete recovery, mimicking what happens after a pheochromocytoma is removed with subsequent downregulation of receptors. The second group of responders who did not recover probably had an organic etiology of heart failure, that is, viral or other causes.

Three of the 6 pregnant patients are black. Little is known in the epidemiology of blacks with pheochromocytoma. In the Rochester Epidemiology Project, the overall incidence of pheochromocytoma was 0.8 per 100 000 patients during 30 years of follow-up, and all were white.27 There are no such series in blacks. Thus, blacks who have paroxysmal episodes or resistant hypertension should be screened for pheochromocytoma.

Diagnosis

Pregnancy occurs in an age range where vigilance to detect secondary hypertension should always be emphasized. Thus, the question has been posed as to whether all gravidas with chronic hypertension who have not been evaluated for secondary causes should be screened for pheochromocytoma. The arguments given are that this condition is a great imitator, and maternal mortality can occur when a woman with unsuspected pheochromocytoma undergoes an operative delivery. On the other hand, given the very low incidence of the disease, the false-positive rate that would occur with almost universal screening of all chronic hypertensive pregnant patients might lead to unnecessary morbidity. In accordance with these issues, we offer the following guidelines.

Only when there is persistence of symptoms and a failure to lower blood pressure despite multidrug maximal therapy should screening be considered. Certainly, the incidental finding of an adrenal mass should raise suspicion. Added to this are the “classic” signs and symptoms (ie, sweating, hyperglycemia, paroxysmal changes in pulse and pressure,
The Figure is a proposed scheme on the management of pheochromocytoma in pregnancy. The 24-hour urinary catecholamines are highly recommended in pregnant patients because pregnancy does not elevate urinary catecholamine levels into the diagnostic range for pheochromocytoma. Some advocate the use of plasma metanephrines as a screening test for pheochromocytoma, but the specificity is poor at 85% to 89% and has a false-positive rate of 11% to 15%; thus, it lacks the necessary specificity to be recommended as a first-line test. MRI is the preferred imaging modality, because it locates adrenal and extra adrenal masses and requires no radiation, which is safe for the fetus. An abdominal ultrasound may also be used as an imaging modality, but the enlarging uterus makes visualization difficult, especially during the third trimester. Nonpregnant or postpartum patients may take advantage of the meta-iodobenzylguanidine scan, which may detect tumors not seen by the MRI.

Management
The primary goal for management is to prevent hypertensive crisis that may lead to both maternal and fetal demise. Medical treatment with α blockade should be started as soon as diagnosis is established and should be given for 10 to 14 days. The drug of choice is phenoxybenzamine (pregnancy class C) and may be prescribed in pregnancy, especially for such potentially life-threatening indications. The drug crosses the placenta and may cause perinatal depression in the mother and transient hypotension in the neonate. Other selective α1 blockers, such as doxazosin, have been used in these types of cases; however, as a competitive antagonist, it can be displaced by high levels of endogenous catecholamines. Three of our patients received β-blockers for control of tachycardia. This class of drugs should never be prescribed before α blockade, because β blockade alone can cause dramatic blood pressure elevations attributed to unopposed α-adrenergic effects by catecholamines, especially in patients with epinephrine-secreting tumors. α-Methyl-parathyrosine, a tyrosine hydroxylase inhibitor, has been used in patients who cannot tolerate combined α and β blockade, but we could locate no reports of its use in pregnancy. Methyldopa is not recommended, because it may worsen the symptoms of pheochromocytoma.

Surgery is the definitive treatment for pheochromocytoma. The timing remains a challenging and controversial issue, depending on the gestational age, clinical response to treatment, the accessibility of the tumor, and the presence or absence of fetal distress. Some investigators have recommended tumor removal early in pregnancy after adequate medical treatment, and laparoscopic adrenalectomy is recommended if tumor mass is <7 cm, but after 24 weeks of gestation, surgical removal is recommended after an elective cesarean
section.22,34 Vaginal delivery carries a higher mortality rate of 31% as compared with cesarean section (19%).35,36 In our limited experience with case reports presented, the mortality rate was higher in women who delivered vaginally compared with those undergoing surgical delivery. The anesthetic approach is also of extreme importance, because anesthetics can trigger a hypertensive crisis. As a rule, general anesthesia is safest for the fetus during the second trimester. General anesthesia is recommended, because most anesthetic gases can trigger a hypertensive crisis. As a rule, general anesthesia is also of extreme importance, because anesthetics may lead to severe hypoxia, causing fetal demise. It is important to maintain a balance during treatment of the hypertension to maintain adequate uterine perfusion. The uteroplacental circulation is also responsive to α-adrenergic stimulation and is subject to vasoconstriction because of elevated catecholamine levels.4,37

We have to remember that we are dealing with 2 patients: the mother and the infant. Pediatricians should be included in the management in these types of cases; the pediatrician should be aware of the risks early on, be a part of the management, be in constant communication with the obstetrician and the other doctors of the team, and be prepared for the outcomes that the pregnancy may bring to the infant. In cases of fetal distress, measures should be done to deliver the fetus as soon as possible,18 and an emergency cesarean section is warranted.

Maternal Outcomes

Improvement in maternal outcomes has been attributed to early recognition of the disease. Maternal deaths without treatment described mainly anecdotally in the older literature were as high as 48%, but with more rapid diagnosis and presurgical preparation mortality the number has decreased to ≈2%.4,38

Genetic Screening

It is important to screen patients with hereditary causes of pheochromocytoma, such as multiple endocrine neoplasia 2A and von Hippel-Lindau syndromes. The clinician should consider genetic testing for patients with a suspicious family history of pheochromocytoma, paraganglioma, or any signs that suggest a genetic cause.29,40 Our fourth patient presented with a history of thyroid carcinoma and a strong family history of thyroid cancer and hypertension. Genetic workup revealed a mutation in codon 634 of the RET proto-oncogene, indicating multiple endocrine neoplasia 2A.

Careful long-term postoperative follow-up is important because of the possibility of incomplete removal of tumor, recurrences that may develop for ≤20 years after removal of the mass, or metastasis of a malignant adrenal mass.39 This was also true in patient 5, who had tumor recurrence 10 years after treatment. Surgery is still the recommended treatment for these cases.

Conclusions

Pheochromocytoma is a rare but important cause of hypertension in pregnant patients because of its high morbidity and mortality to both mother and fetus. There are no official guidelines in the management of these cases, but it is recommended that an individualized approach to treatment be advocated. This disease (the great imitator) presents in many different ways, and in the second half of pregnancy, it may be mistaken for new-onset or superimposed preeclampsia. Management requires close collaboration among the obstetrician, hypertension specialist, endocrine surgeon, anesthesiologist, and pediatrician.

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Disclosures

None.

References


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Raymond Oliva, Peter Angelos, Edwin Kaplan and George Bakris

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