

A Misleading Presentation of Pheochromocytoma in Pregnancy: A Case Report

Gebelikte Feokromositomun Yanlış Sunumu: Bir Olgu Sunumu

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ABSTRACT

Pheochromocytoma is a catecholamine-secreting adrenal tumor and also a rare cause of secondary hypertension in pregnancy. Its low prevalence, nonspecific clinical presentation, and symptoms similar to preeclampsia generate a diagnostic challenge during pregnancy. A 23-year-old hypertensive pregnant woman at 36th gestational week of her first pregnancy was admitted with severe hypertension (210/150 mmHg), headache and proteinuria that made us presume the case as severe preeclampsia. In spite of starting with maximum doses of antihypertensive medications like IV labetalol, and oral nifedipine, loading dose of an anticonvulsant drug, and IV magnesium sulphate, her symptoms persisted. Keeping in view the risks involved to mother and fetus, we delivered the baby by emergency cesarean section. In the postoperative period, along with severe uncontrolled hypertension, she developed tremors, palpitation, and sweating that all led us to further diagnostic workup for secondary causes of hypertension. Eventually, a diagnosis of pheochromocytoma was confirmed by abdominopelvic contrast-enhanced computed tomography and by increased 24-hour urine metanephrine, normetanephrine, and vanillylmandelic acid levels. Subsequently, adrenal suppression was achieved by a multidisciplinary approach, and then she underwent laparoscopic adrenalectomy. This case highlights the importance of maintaining a high index of suspicion and multidisciplinary approach while investigating secondary causes of hypertension in young women, thereby differentiating it from preeclampsia.

Keywords: Pheochromocytoma, pregnancy, secondary hypertension

ÖZ

Feokromositoma, katekolamin salgılayan adrenal bir tümördür ve ayrıca gebelikte nadiren görülen ikincil hipertansiyonun nedenidir. Düşük prevalans, özgül olmayan klinik görünüm ve preeklampsiye benzer semptomlar, gebelik sırasında tanınan bir zorluk meydana getirmektedir. Hipertansif gebe bir kadın, 23 yaşındaki ilk gebeliğinde 36. haftada 210/150 mmHg tansiyon kaydı, baş ağrısı ve ağır preeklampsiyi düşündüren proteinüri ile ağır hipertansiyon belirtileriyle başvurmuştur. Enjeksiyon labetalol, tablet nifedipin gibi antihipertansif ilaçların maksimum dozları ve antikonvulsan ilaç, enjeksiyon magnezyum sülfat yükleme dozu ile tedaviye başlanmasına rağmen belirtileri devam etmiştir. Anneye ve fetüse ilişkin riskler göz önünde bulundurularak, bebeğin acil sezaryen ile doğumu gerçekleştirilmiştir. Postoperatif dönemde, şiddetli kontrolsüz hipertansiyon ile birlikte titreme, çarpıntı ve terleme gelişmiştir; bu da bizi ikincil hipertansiyonun nedenleri için daha fazla tanınan araştırmaya yönlendirmiştir. Sonunda konulan feokromositoma teşhisi, abdominopelvik kontrastlı bilgisayarlı tomografi ve 24 saatlik artan idrar metanefrin, normetanefrin, vanililmandelik asit seviyesi bulguları ile doğrulanmıştır. Ardından, multidisipliner bir yaklaşımla adrenal supresyon sağlanmıştır ve laparoskopik adrenalectomi yapılmıştır. Bu olgu, genç kadınlarda ikincil hipertansiyonun nedenleri araştırılırken yüksek bir şüphe indeksi ve multidisipliner yaklaşımın sürdürülmesinin önemini vurgulayarak, onu preeklampside ayırmaktadır.

Anahtar kelimeler: Feokromositoma, gebelik, ikincil hipertansiyon

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INTRODUCTION

Pheochromocytoma is a dangerous catecholamine producing endocrine tumor which occurs in adrenal glands (85%) or in the sympathetic ganglia (15%), and its prevalence in patients with hypertension is only between 0.1-0.6 percent¹. During pregnancy, the occurrence of pheochromocytoma is rare and majority of the cases are benign and sporadic. Only about 10% of tumors are familial which are associated with multiple endocrine neoplasia like MEN 2A or MEN 2B². Clinical presentation typically depends on the catecholamines released by the tumor.

The combination of its low prevalence and non-specific clinical presentation causes a diagnostic challenge in 20% of the cases during pregnancy. This diagnostic difficulty is more pronounced when pheochromocytomas mimic other conditions of pregnancy like preeclampsia. If untreated during pregnancy, it raises the maternal and fetal mortality rates up to 50% whereas early diagnosis and appropriate treatment reduces maternal mortality rates to less than 5% and fetal mortality rates to below 15% respectively^{3,4}.

Herein, we present a case diagnosed with and treated for preeclampsia till postpartum period and subsequently pheochromocytoma became evident due to paroxysmal hypertension, headache, sweating, and palpitations. Fortunately, she had an uneventful perioperative and postnatal period, and she was operated for pheochromocytoma during follow-up.

CASE REPORT

A 23-year-old primigravida at 36th week of gestation with singleton pregnancy was referred to our institute with severe hypertension, headache, and dizziness for past two days. She was hospitalized and diagnosed with severe preeclampsia, with a blood pressure of 210/150 mmHg on admission. However, there was no history of blur-

ring of vision, vomiting or epigastric pain. Her antenatal checkups were irregular though she took iron and calcium tablets in the last fourth month of gestation but had neither undergone screening for aneuploidy nor any anomaly. During her late second trimester she was started with oral labetalol 100 mg tablets twice daily after the diagnosis of gestational hypertension was made. The patient had no personal or family history of hypertension. Her past medical information before gestation showed that she was healthy and without any similar symptoms. All her blood tests like liver enzymes, creatinine, and platelet counts were in normal range except for urine sample which showed proteinuria. The combination of proteinuria with hypertension on admission made the diagnosis of severe preeclampsia overt, so she was started with intravenous labetalol with gradual escalation of doses. Magnesium sulphate as per Pritchard regimen and analgesic for headache were added to her regimen. Even with these measures, her blood pressure continued to be at a higher level so we added calcium channel blocker to her treatment. Keeping in view the risks involved to mother and fetus, a decision for termination of pregnancy was taken and she delivered a live healthy baby weighing 2200 grams by emergency cesarean section under regional anesthesia.

We were surprised to notice the development of tremors, palpitation, and sweating with uncontrolled hypertension on seventh postoperative day which directed us to rethink other possible causes. Hence, we decided to go for further evaluation of the patient. On further investigations, her 2D echo test was unremarkable, thereby ruling out any hypertension of cardiogenic origin. However, her abdominopelvic ultrasound revealed a solid mass with fine cystic components of size 7.9x6.8x4.2 cm above her right kidney with a high suspicion of a tumor of adrenal origin (Figure 1a). With these findings, we proceeded with an abdominopelvic contrast-enhanced computed tomography which showed an

arterial phase hyperenhancing lesion with dimensions of 5.4x6.3x6.4 cm in the right suprarenal location suggestive of pheochromocytoma (Figure 1b). We sought for the endocrinologist's opinion who advised for evaluation of a 24-hour urine metanephrine, normetanephrine, and vanillylmandelic acid levels which were raised beyond the normal range which was highly suggestive of pheochromocytoma (Table 1). Results of endocrinology and surgical oncology consultations were obtained for optimization of the treatment before surgery, and she was started on an alpha -blocker followed by a beta blocker for adrenal suppression. After two weeks of adrenal suppression with controlled hypertension and with the help of multidisciplinary team comprising of surgeons, anesthesiologist, and endocrinologist, she underwent an uncomplicated laparoscopic adrenalectomy (Figure 1c). Her hemodynamic condition was monitored in the intensive care unit for 24 hours and remained stable. Histologically, the tumor was confirmed to be a pheochromocytoma (Figure 2). During the follow-up, her urinary normetanephrine excretion remained normal as well as her vital signs.

Table 1. The results of 24-hour urinary metanephrines, normetanephrines and vanillylmandelic acid tests.

	Results	Reference values
Metanephrine	640.69	<530 (mcg/day)
Normetanephrine	8352.5	< 600 (mcg/day)
Vanillylmandelic acid	6.7	1.4-6.5 (mg/day)
Urine volume in 24 hours	3250 ml	

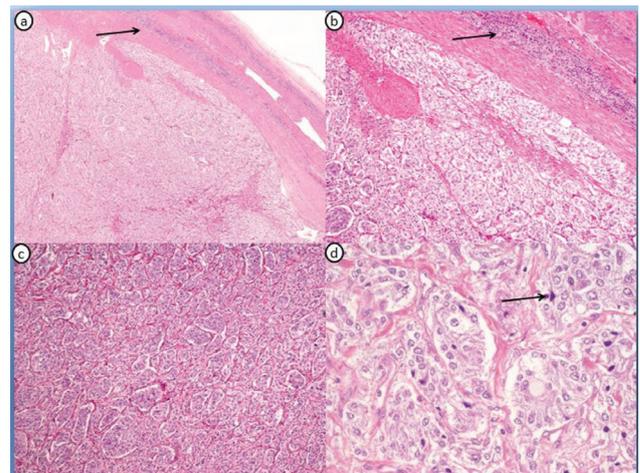


Figure 2a: H&E, 40x, Well circumscribed tumor with compressed peripheral adrenal parenchyma (black arrow). **2b:** H&E, 100x, Nests of tumor cells with circumscribed margin and adjacent normal adrenal parenchyma (black arrow). **2c:** H&E 100x Nests and trabecular pattern of tumor cells, separated by thin fibrovascular septae. **2d:** H&E, 400x, Tumor cells having moderate amount of granular eosinophilic cytoplasm, centrally placed round nucleus with fine granular chromatin and inconspicuous nucleoli. Scattered sustentacular cells (black arrow) are also noted.

DISCUSSION

Pheochromocytoma is a catecholamine-producing tumor of chromaffin cells of the adrenal medulla or the sympathetic ganglia and the most common adrenal tumor seen during pregnancy. Pheochromocytoma sometimes becomes clinically overt during pregnancy, and numerous reasons have been hypothesized like increased vascularity of the tumor, pressure from the enlarging uterus, fetal movements, uterine contractions, abdominal palpation, process of delivery, and also general anesthesia which often induces a surge of catecholamines and activates the pheochromocytoma. Inadequately managed pheochromocytoma leads to disastrous maternal out-

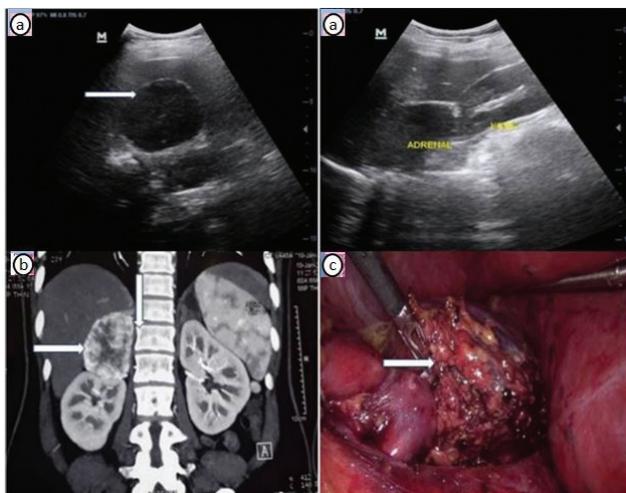


Figure 1a: Ultrasonography showing a 6.8x3.9 cm heterogeneous lesion on right adrenal suggestive of an adrenal neoplasm. **1b:** Contrast-enhanced computed tomography showing the arterial phase hyperenhancing lesion with dimensions of 5.4x6.3x6.4 cm in right suprarenal location suggestive of pheochromocytoma. **1c:** Showing the intraoperative images of pheochromocytoma.

comes like fatal arrhythmia, stroke, heart failure, death, and dangerous fetal outcomes like uteroplacental insufficiency, placental abruption, and fetal demise as a result of uncontrolled hypertension⁵.

Headache, diaphoresis and palpitations which are seen in 90% of patients with pheochromocytoma are often described as classical symptoms. Hypertensive crisis can cause pallor, dizziness, dyspnea, and polyuria whereas adrenergic crisis can mimic abdominal emergencies, presenting with features of nausea, vomiting, and acute abdominal pain⁴. However, diagnosis of pheochromocytoma in pregnant women is elusive as the presence of hypertension can be mistaken for the common hypertensive disorders of pregnancy such as preeclampsia. The onset of preeclampsia occurs after 20 weeks of gestation in contrast to pheochromocytoma which may be conspicuous at any time of pregnancy, presenting with paroxysmal hypertensive episodes.

Patients with preeclampsia present with edema, weight gain, abdominal pain, deranged liver function, oliguria, and thrombocytopenia. On the other hand, patients with pheochromocytoma present with flushing, headache, palpitations, cardiomyopathy, and most importantly hyperglycemia. Presence of café-au-lait spots, freckles, and fibromas are specific phenotypic features suggestive of pheochromocytoma and neurofibromatosis. In the current case, the antenatal diagnosis of pheochromocytoma was missed due to poor compliance of the patient during pregnancy. Presence of the overlapping symptoms of hypertension, proteinuria, headache, and absence of classical symptoms of pheochromocytoma misled us into diagnosing the case as severe preeclampsia.

The hallmark of successful diagnosis depends on biochemical tests like measurement of 24 hour-plasma and urinary metanephrine and nor-metanephrine levels, and tumor localization by appro-

prate imaging. Magnetic resonance imaging and ultrasonography are the preferred modalities during pregnancy keeping in view the safety of the fetus although computed tomography is generally seen to have a diagnostic sensitivity of 98%, and specificity of 92%⁶. After the diagnosis is established, other familial disorders associated with pheochromocytoma should be ruled out and involvement of specialists from the fields of endocrinology, anesthesiology, and surgery in the decision making process is necessary.

Preoperative optimization is essential as the blood pressure, heart rate, and intravascular volume needs to be corrected to prevent any intraoperative adverse events. The delicate balance of the hemodynamic status is managed initially with α -adrenoceptor antagonists followed by β -adrenergic blockers. This sequence is followed to prevent precipitation of pulmonary edema which may be caused by α -blockers⁷. As a useful adjunct in the management, both calcium channel blockers and magnesium sulphate can be used for the treatment of pre-eclampsia as well as pheochromocytoma. Magnesium sulphate acts by inhibiting catecholamine release and also blocking the receptors⁷.

Pheochromocytoma once diagnosed, becomes an indication for surgery, however if associated with pregnancy, the timing of surgery remains debatable. Factors which have a bearing on management are the gestation period, preoperative medical optimization, tumor accessibility, and fetal condition. Maternal and fetal outcomes are seen to be favorable if surgical intervention is done before the 24th week of gestation as pointed out by Kalra et al.⁸. Beyond this period, the uterus size may act as a deterrent to proper tumor assessment and removal. So, it becomes imperative to wait till fetal maturity for proper disease control and cesarean delivery followed by tumor removal. Cesarean section is the favored mode of delivery though some controversies do exist as successful vaginal deliveries

have also been reported. The proponents of cesarean delivery claim that the uterine contraction and fetal movements aggravate the disease by release of catecholamines during vaginal delivery⁸⁻¹⁰. However, a painless and stress-free instrument aided vaginal delivery under epidural analgesia has been reported in the literature. High mortality rate up to 31% has also been reported with vaginal delivery vis-a-vis cesarean section (19%)¹¹.

There is lack of consensus as to the preferred route of delivery in pregnant women as of date possibly due to the rarity of the disease and paucity of evidence, wherein patients are managed on a case-to-case basis. In this case, the maternal and fetal outcomes were unaffected even though the patient was harboring the tumor, but this cannot be generalized^{10,12}. Antenatal diagnosis of pheochromocytoma can have a positive impact on both maternal and fetal outcomes. If diagnosed antenatally, a fall in mortality rates from 29% to 0%, and also from 29% to 12% have been reported for mother and fetus, respectively^{10,12}. Fortunately, our patient had an uneventful perioperative and postnatal period until pheochromocytoma became evident. The usage of labetalol, calcium channel blocker, and magnesium sulfate in our case was the key for controlling hypertension perioperatively. Another factors which might have played roles were administration of epidural anesthesia and conduction of appropriately timed cesarean delivery. The diagnostic evaluation of the patient was geared up when we realized that the hypertension was unrelated to pregnancy, and very soon a multidisciplinary approach was undertaken when the features of pheochromocytoma were revealed by imaging. With these measures, the patient underwent uneventful laparoscopic adrenalectomy, and we could finally achieve a good maternal outcome. Consideration of varied possibilities while sticking to the correct diagnostic hints can pave way towards successful management.

CONCLUSION

Diligent history taking and proper awareness is of the paramount importance for disease identification. The meagre incidence of pheochromocytoma coupled with a fair amount of overlapping symptoms with hypertension in pregnancy is quite intriguing. The value of timely diagnosis, pretreatment, delivery route, and timing of surgery cannot be overemphasized. Evidence-based guidelines are still lacking so a case-to-case approach appears suitable. The myriad presentation of the disease often leads to misdiagnosis, but a vigilant approach with a devoted team can work wonders for both mother and baby.

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