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CASE REPORT: MULTIDISCIPLINARY MANAGEMENT OF PHEOCHROMOCYTOMA IN A PREGNANT WOMAN WITH HYPERTENSIVE EMERGENCY

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ABSTRACT

INTRODUCTION: Pheochromocytomas are rare tumors of the chromaffin cells of the sympathetic-adrenomedullary axis, which produce catecholamines and can cause severe, sustained, or paroxysmal arterial hypertension (Lenders et al., 2005; Neumann, Young, & Eng, 2019). Clinical manifestations typically occur between the third and fourth decades of life but can occur at any age and affect both sexes equally (Bravo & Tagle, 2003). The maximum incidence is between the third and fifth decades of life, with a mean age at diagnosis of 24.9 years in hereditary cases and 43.9 years in sporadic cases (Lucena et al., 2023).

Keywords: Pheochromocytoma. Hypertensive Emergency. Acute Pulmonary Edema. Pregnancy. Multidisciplinary Approach.

INTRODUCTION

Pheochromocytomas are rare tumors of the chromaffin cells of the sympathetic-adrenomedullary axis, which produce catecholamines and can cause severe, sustained, or paroxysmal arterial hypertension (Lenders et al., 2005; Neumann, Young, & Eng, 2019). Clinical manifestations typically occur between the third and fourth decades of life but can occur at any age and affect both sexes equally (Bravo & Tagle, 2003). The maximum incidence is between the third and fifth decades of life, with a mean age at diagnosis of 24.9 years in hereditary cases and 43.9 years in sporadic cases (Lucena et al., 2023). Approximately 90% of pheochromocytomas are adrenal, with a slight predominance in the right adrenal gland, and approximately 10% are located extra-adrenally, mainly intra-abdominally. Malignancy occurs in approximately 10% of cases, increasing to 20-40% in extra-adrenal locations (Favier, Amar, & Gimenez-Roqueplo, 2015). Pheochromocytomas may be associated with familial syndromes such as multiple endocrine neoplasia (MEN) type IIA (medullary thyroid carcinoma, hyperparathyroidism or parathyroid tumors and pheochromocytoma, with autosomal dominant inheritance) and type IIB (medullary thyroid carcinoma, intestinal and mucosal ganglioneuromatosis, pheochromocytoma and marfanoid habitus), neurofibromatosis and Von Hippel-Lindau disease (brain, renal, ocular, pancreatic and spinal cysts or tumors) (Pacak & Linehan, 2005; Lucena et al., 2023). Hypertension is the main manifestation, which may be intermittent or sustained, and hypertensive paroxysms can be triggered by various situations, such as stress, exercise, and medical procedures (Lenders et al., 2005). For diagnosis, laboratory tests are used to detect hypersecretion of catecholamines and their metabolites, such as epinephrine, norepinephrine, metanephrines, and normetanephrine, in addition to imaging tests such as magnetic resonance imaging (MRI) and metaiodobenzylguanidine (MIBG) scintigraphy (Neumann, Young, & Eng, 2019). The treatment of choice is the surgical removal of the tumor, preceded by rigorous clinical preparation with alpha-adrenergic blockers to control hypertension and reduce intraoperative risks (Bravo & Tagle, 2003). It is believed that preoperative blood pressure control is one of the main means of reducing mortality associated with pheochromocytoma removal. Therefore, the use of alpha-1-adrenergic blockers should precede surgery by at least two weeks (Lucena et al., 2023).

CASE REPORT

Patient DSB, 30 years old, in her fifth pregnancy, in the 28th week of pregnancy, hypertensive prior to pregnancy and with a history of preeclampsia in other pregnancies, presented to the emergency room complaining of dyspnea. She presented with orthopnea, diffuse pulmonary crackles, desaturation and severe arterial hypertension, and the diagnostic hypothesis was acute hypertensive pulmonary edema.

COMPLEMENTARY TESTS

- ECG: Regular sinus rhythm. Heart rate: 156 bpm. Normal PR interval. Narrow QRS. No evidence of bundle branch block or other significant abnormalities. - Transthoracic echocardiogram: Moderate left ventricular dilation, eccentric hypertrophy and severely decreased systolic function (ejection fraction of 22%). - Laboratory (06/20/2024):

- Hemoglobin: 12.2 g/dL
- Hematocrit: 37.6%
- Leukocytes: 13,180/mm³ (Rods 11.0%, Segmented 69.6%)
- Platelets: 434,000/mm³
- Creatinine: 0.90 mg/dL
- Proteinuria: 1,200 mg/24h
- Uric Acid: 8.1 mg/dL
- ALT: 20 U/L
- AST: 32 U/L
- LDH: 201 U/L
- CRP: 22 mg/L
- Total Bilirubin: 0.90 mg/dL (Direct: 0.50 mg/dL, Indirect: 0.40 mg/dL)
- X-ray Chest: Bilateral alveolar opacities predominantly in the hilar and perihilar regions, extending to the middle and lower zones of the lungs. Increased cardiothoracic index. Small amount of pleural fluid visible at the lung bases, more pronounced on the right. 2.2 PROPAEDEUTICS FOR PHEOCHROMOCYTOMA
- Fractionated Metanephrines in Blood:
- Metanephrine: 57.9 pg/mL (VR: < 200.0 pg/mL)
- Normetanephrine: 7,200.0 pg/mL (VR: < 200.0 pg/mL)
- Fractionated Metanephrines in 24-Hour Urine:

- Urinary volume: 3,250 mL
- Normetanephrine: > 4,260.0 mcg/24h (VR: up to 732.0 mcg/24h)
- Metanephrine: 330.2 mcg/24h (VR: up to 280.0 mcg/24h)
- Vanillylmandelic Acid (Urine 24h):
- Urinary volume: 3,250 mL
- Result: 24.2 mg/24h (VR: < 6.6 mg/24h)
- Aldosterone dosage:
- Result: 17.8 ng/dL (VR: 1.8 to 39.2 ng/dL)
- Plasma renin:
- Activity: > 48 ng/mL/h (VR: 0.60 to 4.18 ng/mL/h in orthostatic position; 0.32 to 1.84 ng/mL/h in supine position)

Magnetic resonance imaging (MRI) of the abdomen identified a heterogeneous expansile formation in the right adrenal gland, with no cleavage plane with the upper cortex of the right kidney and hepatic segment VI, suggesting primary adrenal injury (Figures 1-5).

Figure 1: Magnetic resonance imaging showing heterogeneous expansile formation in the right adrenal gland (Sagittal section).

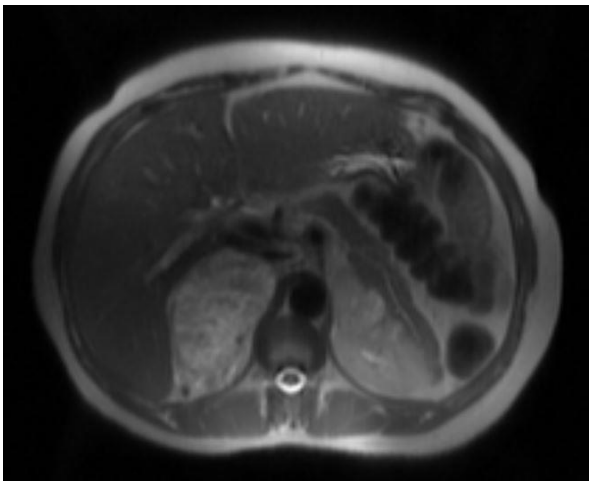


Figure 2: Magnetic resonance imaging showing heterogeneous expansile formation in the right adrenal gland (Coronal section)).

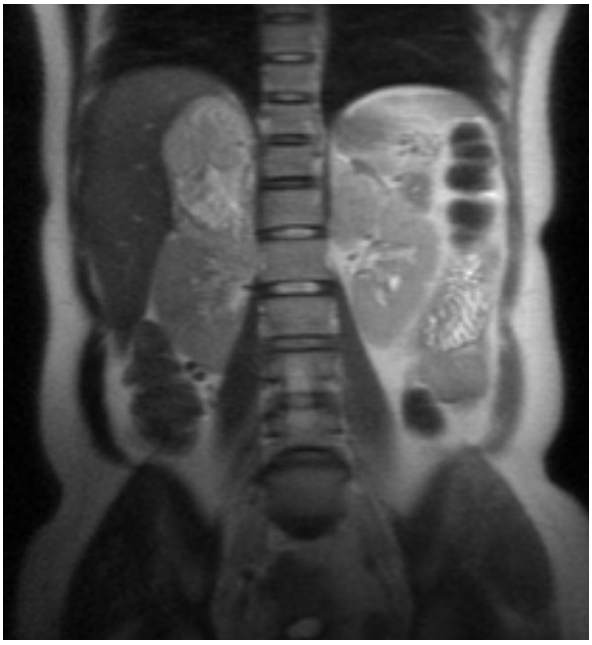


Figure 3: Magnetic Resonance Imaging showing heterogeneous expansile formation in the right adrenal gland (Axial Section)).

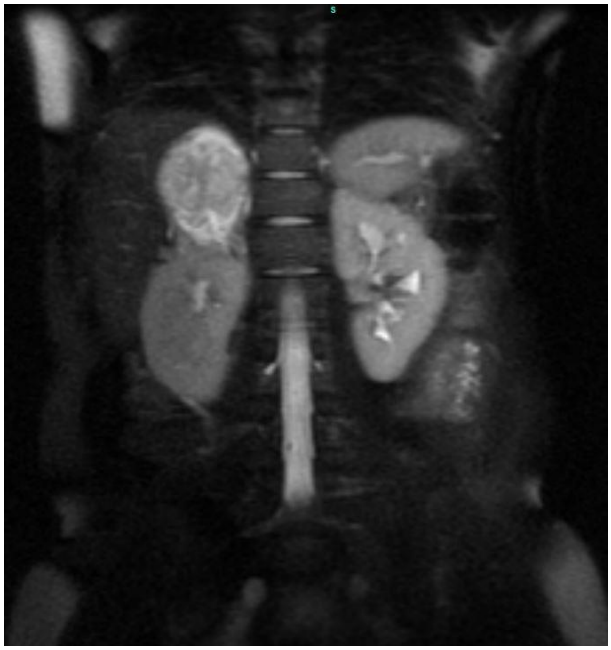


Figure 4: Magnetic resonance imaging showing heterogeneous expansile formation in the right adrenal gland (Oblique view))

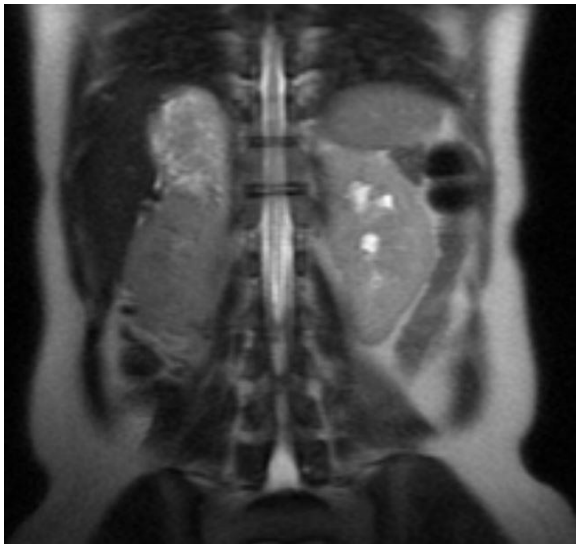
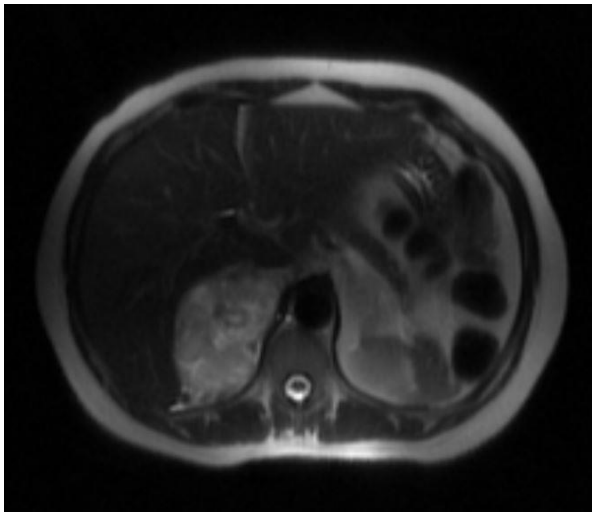


Figure 5: Magnetic resonance imaging showing heterogeneous expansile formation in the right adrenal gland with contrast enhancement



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Due to the severity of the condition and the imminent risk of maternal-fetal complications, the patient was admitted to the Intensive Care Unit (ICU). Alpha-adrenergic blockade with prazosin was initiated (initial dose of 1 mg/day, gradually increasing to 6 mg/day, if tolerable) and maintained with other oral antihypertensives already in use (hydralazine, metoprolol, methyldopa and amlodipine). The objective was to prolong the gestation to increase fetal viability.

However, the patient again presented uncontrolled blood pressure, worsening dyspnea, epigastric discomfort, platelet consumption, elevated uric acid and altered ALT.

- Hemoglobin: 11.1 g/dL (RR: 12.0 to 16.0 g/dL)

- Hematocrit: 34.0% (RR: 36.0 to 46.0%)
- Leukocytes: 17,630/mm³ (RR: 5,000 to 10,000/mm³)
- Segmented Neutrophils: 65.6% (11,570/mm³) (RR: 35 to 75%)
- Platelets: 97,000/mm³ (RR: 140,000 to 400,000/mm³)
- Uric Acid: 9.1 mg/dL (RR: 2.6 to 6.0 mg/dL)
- ALT: 48 U/L (RR: 5 to 52 U/L)
- TGO (AST): 59 U/L (VR: 4 to 36 U/L)
- LDH: 242 U/L (VR: 125 to 271 U/L)

The patient reported that in previous pregnancies she also had complications related to high blood pressure, which were resolved with termination of pregnancy by emergency cesarean section. She also reported that she had been aware of the existence of a "renal mass" that should be investigated since the previous pregnancy.

In view of the clinical picture and laboratory findings, the gynecology-obstetrics opinion suggested specific hypertensive disease of pregnancy (DHEG) with pre-eclampsia, and was then advised to undergo sulfation (attack with 5g of magnesium sulfate) and maintenance with 2g/h of magnesium sulfate, in addition to emergency cesarean section. Therefore, with less than two days of use of prazosin, the patient required emergency surgery.

Due to clinical decompensation, the patient was referred to the surgical center with assistance from the Obstetrics and Urology Oncology teams, and an emergency cesarean section was performed followed by right adrenalectomy. At the patient's request, tubal ligation was also performed.

In the immediate postoperative period, the patient presented hypovolemic shock (Hemoglobin 7.7 g/dL; Hematocrit 23.5%), requiring red blood cell transfusion (2 packed red blood cells) and vasopressor support with norepinephrine (0.1 µg/kg/min). Subsequently, the patient developed hemodynamic compensation, requiring antihypertensives again, initially sodium nitroprusside, followed by oral antihypertensives. With clinical improvement, she was discharged from the ICU (Intensive Care Unit) to the cardiology ward, where medication optimization continued for adequate blood pressure control.

The newborn was referred to the Neonatal Intensive Care Unit (NICU), where he progressed with clinical stabilization.

POST-ADRENALECTOMY HISTOPATHOLOGICAL ANALYSIS

The material received in formalin consisted of a nodular fragment of tissue, weighing 175.0 g and measuring 10.5 x 6.0 x 5.0 cm. The external surface was smooth and grayish. On sectioning, a solid, yellowish-brown, encapsulated and firm lesion was observed, measuring 10.5 x 6.0 cm and touching the surgical resection margin. In the adjacent adipose tissue, a light-brown, firm and elastic nodule was noted, measuring 1.9 x 0.8 cm.

MICROSCOPIC EXAMINATION AND CONCLUSION

Microscopic analysis revealed an adrenal gland neoplasm with the following characteristics:

- Type of Resection: Right Adrenalectomy.
- Size: 10.5 cm.
- Macroscopic Pattern: Solid.
- Nuclear Atypia: Marked.
- Presence of Areas of Tumor Coagulative Necrosis.
- Morphological Pattern: Rounded Nests ("Zellballen").
- Mitotic Index: No mitoses were observed.
- Encapsulation: Present, incomplete.
- Capsular Neoplastic Invasion: Present, focal.
- Angiolymphatic Neoplastic Infiltration: Present.
- Cellular Monotony, Solid-Confluent Cell Growth, Nuclear Hyperchromasia or Areas of Spindle Cells: Not detected.
- Surgical Margins: Free of neoplasia.
- Adjacent Adrenal Cortical Tissue: Within normal limits.
- Adjacent Connective-Adipose Tissue with Neural Ganglion: Within normal limits.

The present morphological picture is suggestive of adrenal gland pheochromocytoma. Immunohistochemical study is necessary for definitive diagnostic definition.

DISCUSSION

This case highlights the importance of early suspicion, with prompt diagnostic procedures and aggressive management of pheochromocytoma in pregnant women,

particularly in hypertensive emergencies and cardiac complications. Literature describes that most familial pheochromocytomas and paragangliomas are caused by mutations in the succinate dehydrogenase (SDH) subunit genes, and genetic tests are often performed after pathological confirmation (Pacak & Linehan, 2005).

Biochemical and imaging evaluation are crucial for diagnosis and surgical planning. Studies show high sensitivity and specificity for catecholamine measurements and their metabolites (Lenders et al., 2005; Neumann, Young, & Eng, 2019). The combination of resting plasma catecholamines [norepinephrine (NE) with epinephrine (E)] > 2000 pg/mL and urinary metanephrines > 1.8 mg/24h has diagnostic accuracy close to 98%. Provocative and suppressive tests may be necessary when baseline biochemical evaluation is inconclusive (Lucena et al., 2023).

Table 1: Sensitivity and Specificity of Diagnostic Tests

Test	Sensitivity %	Specificity %
Plasma NE + E	85	97
Urinary NE + E (24h)	85-100	72-99.5
Urinary NM + MN (24h)	97-100	84-98
Urinary VMA (24h)	64-90	87-98

Abbreviations: NE (norepinephrine), E (epinephrine), NM (normetanephrines), MN (metanephrines), VMA (vanillylmandelic acid).

Table 2: Sensitivity and Specificity of Imaging Methods

Imaging Method	Sensitivity %	Specificity %	Positive Predictive Value	Negative Predictive Value
CT Scan	98	67	70	69
MRI	100	98	100	100
MIBG	78	100	100	87

Abbreviations: MRI (magnetic resonance imaging), MIBG (metaiodobenzylguanidine scintigraphy).

The differential diagnosis of pheochromocytoma includes several clinical conditions, with the most common being: labile hypertension, tachyarrhythmias, angina, acute pulmonary edema, anxiety, panic syndrome, migraine, brain tumors, porphyria, dysautonomia, thyrotoxicosis, climacteric syndrome, eclampsia, hypoglycemia, diabetes mellitus, carcinoid syndrome, post-surgical hypertension, and hypertensive crisis associated with medications (Lucena et al., 2023).

Surgical treatment is the definitive therapeutic approach. In cases where surgery is not possible, medical treatment can reduce paroxysms and target organ damage, improving life expectancy. In multiple tumors, MIBG scintigraphy can identify tumor locations, providing conditions for surgical approach. In malignant pheochromocytomas

with unresectable metastases, in addition to antihypertensive control, chemotherapy, tumor embolization, radiotherapy, and analgesia are included (Neumann, Young, & Eng, 2019).

Clinical preparation is crucial. The use of alpha-1 adrenergic blockers should precede surgery for at least two weeks, reducing systemic vasoconstriction and postoperative risks. Prazosin is frequently used, starting with 1 mg at night and can increase to 20 mg/day (Lenders et al., 2005). Other antihypertensives can be used as adjuncts in blood pressure control, including beta-blockers, ACE inhibitors, calcium channel antagonists, and central sympatholytics.

Paroxysms are treated with intravenous sodium nitroprusside, and intravenous beta-blockers may be required for supraventricular tachyarrhythmias, while lidocaine is used for ventricular tachycardia (Bravo & Tagle, 2003).

CONCLUSION

The multidisciplinary management of pheochromocytoma in pregnant women, especially in hypertensive emergencies such as the acute pulmonary edema presented in this case, is essential to ensure favorable outcomes. This report highlights the importance of collaboration between different medical specialties, with coordinated clinical and surgical interventions, which favor a positive outcome for a complex situation. It is plausible that the patient had been harboring the pheochromocytoma for years, having gone through clinical decompensations in previous pregnancies, either due to the overlap of DHEG with preeclampsia or exacerbation of the pheochromocytoma itself.

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