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Managing Pheochromocytoma And Paraganglioma In Pregnancy: Lessons From A Clinical Case

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Abstract
Pheochromocytomas and paragangliomas (PPGLs) are rare neuroendocrine tumors that produce excessive catecholamines, posing significant risks during pregnancy. This case study follows a 24-year-old woman with untreated hypertension and Ménard's triad symptoms, initially managed without detailed investigation. Elevated plasma metanephrine levels and imaging confirmed a pheochromocytoma, and though the patient was lost to follow-up for a year, she was readmitted at 13 weeks of gestation. A pre-pregnancy CT scan identified a large hypervascular left adrenal mass. Following normal genetic testing and a multidisciplinary approach, she underwent a successful laparotomy with left adrenalectomy, with no complications in the ongoing pregnancy. This case underscores the importance of early diagnosis and appropriate management of PPGLs to prevent adverse maternal and fetal outcomes, highlighting the need for careful monitoring and surgical intervention when necessary.

Keywords: *Pheochromocytoma, Pregnancy, Multidisciplinary Management, Genetic Testing, Surgical Intervention*

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I. Introduction

Pheochromocytomas and paragangliomas (PPGLs) are tumors originating from the adrenal medulla and paraganglia, respectively. These tumors often secrete catecholamines, which can lead to potentially fatal hypertensive crises [1]. Although PPGLs are rare during pregnancy, failure to recognize them, due to the rarity of this association and their similarity to gestational hypertension, can significantly increase the risk of maternal and/or fetal mortality.

The primary challenge lies in diagnosing PPGLs, which represent a rare but potentially fatal cause of hypertension during pregnancy. Early and accurate diagnosis, combined with appropriate multidisciplinary management before delivery, is now generally associated with favorable outcomes for both the mother and the fetus [2,3].

Currently, the available data on the monitoring and management of these tumors during pregnancy are limited to case reports and literature reviews. Our objective is to present a to present a clinical case and discuss the appropriate management strategy for our patient during pregnancy.

II. Case Report

The patient, OE, a 24-year-old woman with no significant medical history, is the mother of one child born vaginally without complications. For the past year, she had been experiencing grade 3 hypertension, accompanied by Ménard's triad (headaches, palpitations, and sweating). She was treated without further investigations. She later presented to our department for evaluation and management.

On clinical examination, the patient was conscious, normocardiac, and hypertensive (grade 2), without orthostatic hypotension or blood pressure asymmetry. Her body mass index (BMI) was normal, and the urine dipstick test was negative. The physical examination did not reveal any particular abnormalities.

The electrocardiogram revealed a regular sinus rhythm with signs of left ventricular hypertrophy. The biological tests confirmed a pheochromocytoma with elevated plasma levels of methoxy derivatives (normetanephrine: 53.09 nmol/L < 1.07, i.e., 16.5 times the normal value; metanephrine: 1.15 nmol < 0.33, i.e., 3.48 times the normal value).

A topographic and functional assessment was requested, and the patient was started on alpha-blockers and calcium channel blockers.

She was lost to follow-up for a year and was then readmitted to our department at 13 weeks of gestation (WG) with a singleton pregnancy. Her blood pressure and heart rate were well controlled with nicardipine and alpha-methyldopa.

She provided a pre-pregnancy CT scan (CTAP) that displayed a large, hypervascular mass in the left adrenal gland, measuring 69 x 60 x 60 mm, suggestive of a pheochromocytoma. No other significant abnormalities were noted (Figure 1).

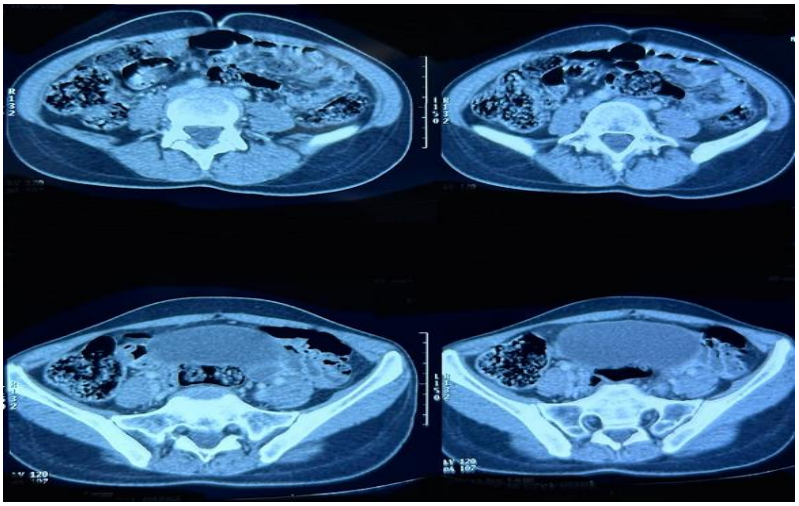

Figure 1: A Large, Hypervascular Mass In The Left Adrenal Gland, Measuring 69 X 60 X 60 Mm, Suggestive Of A Pheochromocytoma.

Genetic testing has been requested, and the syndromic evaluation revealed no abnormalities. The obstetrical examination was normal, with no signs of fetal growth restriction.

Following a multidisciplinary consultation, the patient underwent a laparotomy with left adrenalectomy. The procedure lasted 3 hours and 30 minutes and was characterized by well-managed hemodynamic fluctuations. The immediate postoperative recovery was uneventful.

Histological and immunohistochemical analysis confirmed the diagnosis of pheochromocytoma with a PASS score of 4, without capsular or vascular invasion.

The clinical symptoms resolved, and the pregnancy progressed without complications. Follow-up testing for plasma catecholamine metabolites was negative.

III. Discussion

Pheochromocytoma and paraganglioma (PPGL) are rare neuroendocrine tumors responsible for excessive catecholamine production [4]. These tumors are classified into two categories: adrenal pheochromocytomas (77%) and extra-adrenal paragangliomas (23%) [3,5].

The incidence of PPGL during pregnancy varies significantly, ranging from 1 in 15,000 to 1 in 300,000 pregnancies [4,6]. Most PPGL cases during pregnancy occur in primiparous women [2]. However, in our case, the patient had previously delivered vaginally without any complications.

The clinical presentation of PPGL during pregnancy is similar to what is observed outside of pregnancy. Hypertension is common and represents the initial manifestation in approximately 20% of PPGL cases during pregnancy [3]. This hypertension can be either sustained, paroxysmal, or a combination of both [7], with occasional episodes of hypotension. Other symptoms include paroxysmal headaches, palpitations, and sweating (Ménard's triad).

These conditions may also present as sinus tachycardia, arrhythmias, acute adrenergic cardiomyopathy, or even cardiogenic shock. During pregnancy, several factors can contribute to cardiogenic shock, such as tumor compression by the gravid uterus, abdominal palpation, uterine contractions, stress, anesthesia, and certain medications. It is, therefore, essential to take precautions and avoid specific products. In our case, the patient had sustained hypertension without orthostatic hypotension.

Around 30% of PPGL cases are not diagnosed during pregnancy, and in half of the detected cases, the diagnosis is made in the third trimester [2,3]. However, in our case, the diagnosis had already been established before pregnancy, which allowed for proactive management and reduced the risks often associated with a late diagnosis.

When PPGL is clinically suspected during pregnancy, urinary or plasma measurements of metanephrine derivatives (normetanephrine, metanephrine, and 3-methoxytyramine) should be conducted [8,9]. It is important to note that normal reference ranges for pregnant women have not yet been clearly established [7]. In our case, plasma metanephrine levels were elevated well before pregnancy; however, the patient was lost to follow-up.

According to the literature, catecholamine or metanephrine levels that exceed ten times the upper limit of normal are associated with poor maternal-fetal outcomes [2]. In our case, the normetanephrine level was 16.5 times the normal value, and the metanephrine level was 3.48 times the normal value.

Once biochemical confirmation of PPGL is obtained, MRI without gadolinium is the preferred imaging modality during pregnancy [7,10]. Functional imaging with MIBG or PET is contraindicated in pregnant patients [7,10]. Unilateral pheochromocytomas represent 60-70% of PPGLs during pregnancy, bilateral pheochromocytomas account for 8%, solitary paragangliomas constitute 18%, and multiple paragangliomas occur in 2.5-5% of cases [2,3]. Metastatic PPGL during pregnancy remains rare.

In our patient's case, a cervico-abdominopelvic CT scan performed prior to pregnancy revealed a large, hypervascular left adrenal mass measuring 69 x 60 x 60 mm, suggestive of pheochromocytoma.

The presence of PPGL during pregnancy significantly increases the risk of both maternal and fetal morbidity and mortality.

The maternal mortality rate is estimated at 9%, while fetal mortality is approximately 14% [3]. Maternal morbidity includes cardiovascular and neurological events, and fetal morbidity is characterized by intrauterine growth restriction (IUGR) [2,7]. Factors associated with adverse outcomes include undiagnosed PPGL during pregnancy, very high catecholamine levels, abdominal or pelvic tumor location, and the absence of alpha-blockade [2]. In our case, the early diagnosis allowed for timely treatment, the anticipation of complications, and the prevention of maternal mortality and fetal morbidity.

Once diagnosed, the optimal therapeutic strategy should be discussed in a multidisciplinary team meeting [11]. Medical management involves the initiation of alpha-receptor blockers for at least two weeks to improve outcomes [2,12,13]. Beta-blockers can be added to control tachycardia after adequate alpha-blockade has been achieved, usually for a short duration. Calcium channel blockers may also be necessary in some cases [10]. Our patient was stabilized with nicardipine and a centrally acting antihypertensive.

The definitive treatment for PPGL is surgical. The timing of surgery during pregnancy remains controversial and should be decided on a case-by-case basis [2,3]. Surgery is generally recommended if PPGL is diagnosed before 24 weeks of gestation, while it may be deferred until the postpartum period if diagnosed in the third trimester [7]. In our case, the pregnancy was at 13 weeks, and the surgery was performed without postoperative complications.

Historically, cesarean section was the preferred mode of delivery due to the higher mortality rate associated with vaginal delivery (33% compared to 19% for cesarean) [14]. However, more recent studies suggests that vaginal delivery is not necessarily associated with adverse outcomes [2,3,15]. The timing of delivery is generally determined by fetal well-being and the control of maternal hypertension [3]. As the pregnancy is ongoing in our case, the specific mode and timing of delivery will be decided at a later point. Women diagnosed with PPGL during pregnancy should be referred for genetic counseling and a syndromic evaluation to explore potential hereditary PPGL syndromes. In this instance, the syndromic evaluation was normal, and genetic testing is still being conducted.

IV. Conclusion

Pheochromocytomas and paragangliomas (PPGLs) during pregnancy, although rare, present significant diagnostic and management challenges. Early recognition and accurate diagnosis are crucial to mitigate the associated risks and improve maternal and fetal outcomes. The case presented underscores the importance of a multidisciplinary approach to management, including early biochemical diagnosis, appropriate imaging, and timely surgical intervention.

In our patient's case, early diagnosis facilitated effective management and prevented complications. Despite the inherent risks, a proactive approach allowed for the successful treatment of the PPGL and a favorable outcome for both mother and fetus. Continuous monitoring and adherence to a multidisciplinary management strategy remain essential in optimizing outcomes in such complex cases.

Future research and data collection on PPGLs during pregnancy are needed to further refine treatment protocols and improve predictive models for maternal and fetal outcomes. Enhanced understanding and guidelines will contribute to better management strategies and improved prognoses for affected individuals.

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