Italian Journal of Medicine

https://www.italjmed.org/ijm

eISSN 1877-9352

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Please cite this article as:

Concistrè A, Caramazza C, D'Abbondanza M, Imperoli G. **Primary aldosteronism unmasked during pregnancy: a case report**. *Ital J Med* doi: 10.4081/itjm.2025.1949

Submitted: 13-02-2025
Accepted: 24-06-2025

Primary aldosteronism unmasked during pregnancy: a case report

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Key words: mineralocorticoid excess, adrenal adenoma, secondary hypertension, pregnancy, primary aldosteronism.

Contributions: AC, conceived the case report and wrote the first draft of the manuscript; CC, provided clinical care and contributed to data interpretation; MDA, performed clinical follow-up and contributed to manuscript revision; GI, supervised patient management and provided review of the manuscript content. All authors contributed to manuscript revision and approved the final version of the manuscript.

Conflict of interest: the authors declare no conflicts of interest.

Ethics approval and consent to participate: this case report was conducted in accordance with the Declaration of Helsinki.

Patient consent for publication: written informed consent was obtained from the patient for publication of this case report and accompanying images.

Availability of data and materials: data supporting the findings of this case report are available from the corresponding author upon reasonable request, within the limits of patient privacy.

Funding: the authors received no financial support for the research, authorship, and/or publication of this article.

Abstract
Primary aldosteronism during pregnancy is a rare but significant cause of secondary hypertension with potentially serious implications for maternal-fetal outcomes. This case adds to our understanding of how pregnancy can unmask previously compensated disease. A 37-year-old woman with pre-existing hypertension developed severe treatment-resistant hypertension at 36 weeks' gestation, despite normal pre-pregnancy aldosterone-to-renin screening. Emergency cesarean section was required. Postpartum evaluation revealed hypokalemia, elevated aldosterone, suppressed renin, and a left adrenal adenoma. Complete resolution followed laparoscopic adrenalectomy. This case demonstrates the importance of maintaining clinical suspicion for primary aldosteronism in pregnancy-associated resistant hypertension, regardless of pre-pregnancy screening results, and highlights the value of a comprehensive postpartum evaluation.

Introduction

Primary aldosteronism (PA) represents a diagnostic challenge during pregnancy. While the exact prevalence during pregnancy remains difficult to establish due to limited systematic screening studies, the available case series and cohort studies suggest an occurrence of less than 1% among pregnant women.[1] The physiological adaptations of pregnancy include substantial modifications in the renin-angiotensin-aldosterone system,[2,3] which can mask or exacerbate underlying pathology. Previous case series have demonstrated various presentations of PA during pregnancy,[4] but optimal diagnostic and management strategies remain debated.[5,6]

Case Report

Patient information

A 37-year-old woman presented to our secondary hypertension clinic following delivery with a history of severe hypertension during pregnancy. Her medical history was significant for hypertension diagnosed approximately one year before conception, with blood pressure consistently above 140/90 mmHg. The initial pre-pregnancy evaluation had included a complete workup for secondary hypertension, with aldosterone-to-renin ratio within normal limits. The patient had no other significant medical history and no family history of endocrine disorders or early-onset hypertension.

Clinical course

During pregnancy, antihypertensive therapy had been initiated with alpha-methyldopa 250 mg twice daily. Adequate blood pressure control was maintained throughout the first trimester. At 20 weeks' gestation, progressive blood pressure elevation required dose escalation to 500 mg three times daily. Despite maximum methyldopa dosing, persistent hypertension necessitated the addition of labetalol 100 mg twice daily at 24 weeks' gestation. This was subsequently increased to 200 mg twice daily at 28 weeks. At 32 weeks, extended-release nifedipine 30 mg once daily was introduced as third-line therapy due to inadequate blood pressure control with dual therapy. At 36 weeks' gestation, the patient developed severe hypertension with blood pressure readings of 180/110 mmHg associated with neurological symptoms including headache and visual impairment. Given the clinical presentation suggestive of preeclampsia and signs of fetal compromise, an emergency cesarean section was performed.

Diagnostic assessment

Postpartum evaluation revealed significant laboratory abnormalities characteristic of PA (Table 1). The patient demonstrated marked hypokalemia (2.8 mEq/L) despite no diuretic use, elevated plasma aldosterone (31.7 ng/dL), and suppressed direct renin concentration (0.9 μIU/mL), resulting in an elevated aldosterone-to-renin ratio of 35.22. Magnetic resonance imaging identified a 1-cm left adrenal nodule consistent with an aldosterone-producing adenoma (Figure 1). Adrenal vein sampling was not performed based on several factors. The patient presented with clear biochemical evidence of PA, including suppressed renin, elevated aldosterone, and marked hypokalemia. Imaging demonstrated a unilateral adrenal nodule. The patient's young age also supported direct surgical intervention. This approach follows current evidence supporting imaging-guided adrenalectomy in young patients with unilateral disease and confirmed biochemical diagnosis.[7] Recent data demonstrate that imaging-guided adrenalectomy in young patients achieves excellent cure rates comparable to those following adrenal vein sampling, while avoiding procedural risks.[7]

Therapeutic intervention and follow-up

Following delivery and the diagnosis of PA, treatment was initiated with spironolactone 25 mg once daily, gradually increased to 50 mg daily. Given the unilateral adrenal adenoma and the patient's young age, she underwent laparoscopic left adrenalectomy one year postpartum. The procedure was uncomplicated, and histopathological examination confirmed an aldosterone-producing adenoma. Following adrenalectomy, the patient experienced rapid normalization of blood pressure, allowing

discontinuation of all antihypertensive medications within two weeks. At 3-month follow-up, her blood pressure remained normal (average 118/75 mmHg), with normalized laboratory values including potassium (4.2 mEq/L), aldosterone (8.4 ng/dL), and direct renin concentration (15.2 μIU/mL).

Discussion

This case illustrates several critical features of PA in pregnancy and provides important insights into the pathophysiological mechanisms underlying this condition.

During normal pregnancy, the renin-angiotensin-aldosterone system undergoes significant physiological adaptations. The marked increase in plasma volume and cardiac output leads to activation of the renin-angiotensin system, with a consequent elevation of both renin and aldosterone levels.[2] In healthy pregnancies, this represents a compensatory mechanism to maintain adequate perfusion pressure despite peripheral vasodilation.[3] However, in patients with underlying subclinical PA, these same physiological changes may potentially unmask previously compensated disease.

The patient's clinical course, progressing from pre-gestational essential hypertension to severe, treatment-resistant hypertension during pregnancy, demonstrates how pregnancy's physiological adaptations can unmask previously compensated subclinical PA. The normal pre-pregnancy aldosterone-to-renin ratio, followed by the development of overt mineralocorticoid excess during pregnancy, highlights the diagnostic challenges inherent in this clinical scenario and emphasizes the importance of maintaining clinical suspicion throughout gestation.

In our case, the pre-pregnancy aldosterone-to-renin ratio was within normal limits, yet severe PA manifested during pregnancy. This suggests that the increased mineralocorticoid activity during gestation may have exceeded the compensatory capacity of normal physiological mechanisms, leading to sodium retention, plasma volume expansion, and severe hypertension. The development of marked hypokalemia postpartum, despite its absence pre-pregnancy, further supports this hypothesis.

The management of PA during pregnancy presents unique therapeutic challenges due to limited pharmacological options and the need to balance maternal and fetal safety. According to recent systematic reviews, PA during pregnancy is associated with increased maternal and perinatal morbidity, including preeclampsia, preterm delivery, and fetal growth restriction.[8] Early recognition and appropriate management are crucial for optimizing outcomes.

The therapeutic approach in pregnancy is primarily medical, with mineralocorticoid receptor antagonists being the preferred treatment. However, spironolactone use during pregnancy remains controversial due to potential anti-androgenic effects on male fetuses, while eplerenone has limited safety data. Consequently, calcium channel blockers and alpha-methyldopa remain first-line antihypertensive agents, as demonstrated in our case.[9,10]

Our patient's clinical course illustrates the diagnostic complexity of PA during pregnancy. The rapid deterioration of blood pressure control despite therapeutic escalation with multiple antihypertensive agents served as an important clinical indicator of secondary hypertension. The requirement for emergency cesarean section due to severe hypertension and fetal compromise underscores the potential serious consequences of unrecognized PA during pregnancy.

The diagnosis of PA during pregnancy is challenging due to physiological changes in the renin-angiotensin-aldosterone system.[11] Current guidelines suggest that biochemical screening should be performed in cases of resistant hypertension, even during pregnancy, though interpretation must account for gestational changes.[5,6] However, as demonstrated in our case, normal pre-pregnancy screening does not exclude the possibility of PA manifestation during gestation.

The systematic approach to postpartum evaluation proved crucial in establishing the correct diagnosis. The combination of severe hypokalemia, elevated aldosterone levels, suppressed renin activity, and imaging evidence of unilateral adrenal pathology provided clear diagnostic evidence for PA. This highlights the importance of comprehensive postpartum evaluation in all cases of pregnancy-associated resistant hypertension.[12]

The successful surgical outcome, with complete resolution of hypertension and normalization of biochemical parameters, confirms both the diagnosis and the curative potential of adrenalectomy in unilateral PA. The patient's excellent postoperative course emphasizes the value of timely diagnosis and appropriate treatment, particularly in young patients with unilateral disease.

This case has several important clinical implications. First, it demonstrates that normal pre-pregnancy aldosterone-to-renin screening does not exclude the possibility of PA manifestation during pregnancy. Second, it highlights the importance of maintaining clinical suspicion for secondary hypertension in cases of treatment-resistant hypertension during pregnancy. Third, it emphasizes the value of systematic postpartum evaluation, including comprehensive biochemical and imaging studies, in patients with pregnancy-associated resistant hypertension.

The excellent outcome following postpartum diagnosis and surgical treatment underscores the importance of appropriate follow-up care and the potential for complete cure in patients with unilateral PA. These findings support current recommendations for careful monitoring of hypertensive disorders during pregnancy and comprehensive evaluation in the postpartum period.[13]

Conclusions

This case demonstrates how pregnancy can unmask previously unrecognized PA and highlights the importance of maintaining clinical vigilance throughout gestation. The successful outcome following postpartum diagnosis and treatment emphasizes the value of comprehensive evaluation in cases of persistent hypertension. These findings support the need for careful monitoring of hypertensive disorders during pregnancy and appropriate follow-up in the postpartum period.

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Table 1. Laboratory parameters before pregnancy, postpartum, and after surgery.

Parameter	Pre-pregnancy	Postpartum (1 month)	Post-surgery	Reference range
Glucose (mg/dL)	68	94	90	70-99
Urea (mg/dL)	16	16	14	7-20
Creatinine (mg/dL)	0.79	0.65	0.68	0.6-1.2
Total cholesterol (mg/dl)	132	190	180	<200
HDL cholesterol (mg/ dL)	38	42	48	>50
LDL cholesterol (mg/ dL)	76	124	115	<100
Triglycerides (mg/ dL)	91	118	105	<150
Sodium (mEq/L)	145	143	138	135-145
Potassium (mEq/L)	4.3	2.8	4.2	3.5-5.0
Hb (g/ dL)	12.1	12.3	12.8	12-16
U-ALB/U-CREA ratio	5.4	6.67	4.8	<30
Plasma aldosterone (ng/ dL)	13.8	31.7	8.4	3-16
PRA (ng/mL/h)	0.9	-	-	0.2-2.8
DRC (µIU/mL)	-	0.9	15.2	4.4-46.1
ARR (ng/dl)/(ng/mL/h)	15.3	-	-	<30
ARR (pg/ml)/(µIU/mL)	-	35.22	0.55	<3.7
Plasma cortisol (µg/ dL)	13.3	9.8	9.5	6.2-19.4

Hb, hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; U-ALB/U-CREA, urine albumin-to-creatinine ratio; PRA, plasma renin activity; DRC, direct renin concentration; ARR, aldosterone-to-renin ratio.

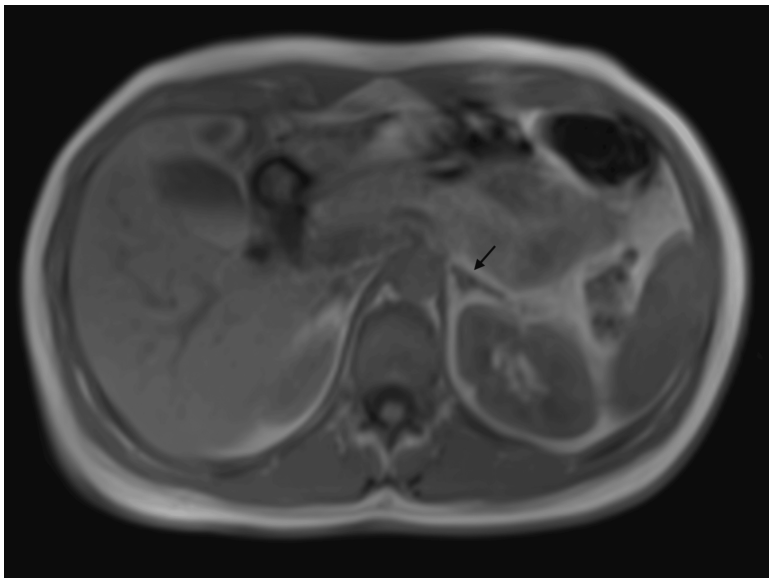

Figure 1. Abdominal magnetic resonance imaging showing a 1-cm aldosterone-producing left adrenal adenoma. T1-weighted magnetic resonance imaging showing a well-defined, 1-cm left adrenal nodule (arrow).