

Conn Syndrome in postpartum, an easily overlooked diagnosis – case report

Síndrome de Conn no pós-parto, um diagnóstico facilmente esquecido – caso clínico

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Abstract

Primary aldosteronism (PA) is a difficult and an easily overlooked diagnosis in pregnancy and postpartum period, resulting in an underdiagnosed condition. We report a case of PA diagnosed in the postpartum period. A 31-year-old woman was presented with severe resistant hypertension at emergency room at 35 weeks pregnancy. After delivery, she maintained severe resistant hypertension and hypokalemia which led to a diagnosis of PA due to an adrenal adenoma. Secondary causes of hypertension should be considered in cases of resistant hypertension in order to prevent adverse maternal outcomes.

Keywords: Pregnancy, Hypertension, Primary aldosteronism, Preeclampsia.

Resumo

O hiperaldosteronismo primário (HAP) é um diagnóstico difícil e geralmente subdiagnosticado na gravidez e no pós-parto. Descreve-se um caso clínico de HAP diagnosticado no pós-parto numa mulher que recorreu ao Serviço de Urgência com quadro hipertensivo grave às 35 semanas de gestação. No pós-parto devido à manutenção de hipertensão e hipocaliémia refratárias à medicação, diagnosticou-se HAP resultante de adenoma da supra-renal. As causas secundárias de hipertensão devem ser consideradas na gravidez e no pós-parto, perante um quadro hipertensivo refratário ao tratamento.

Palavras-chave: Gravidez; Hipertensão; Hiperaldosteronismo primário; Pré-eclâmpsia.

INTRODUCTION

Primary aldosteronism (PA), also known as Conn's syndrome, was first reported by Conn et al., and is described as a clinical syndrome characterized by hypertension, hypokalemia and metabolic alkalosis, as a result of autonomous aldosterone production¹⁻³. PA is

commonly caused by an adrenal adenoma or by adrenal hyperplasia (unilateral or bilateral)⁴. With a prevalence between 3 and 10% in the hypertensive population^{5,6}, PA is one of the leading causes of secondary hypertension.

Hypertension affects 2-8% of pregnancies, and is associated with significant maternal-fetal morbidity⁷. Nevertheless, PA is a rare diagnosis in pregnant women^{1,2,8}, with an estimated incidence of 0,6-0,8% and is scarcely reported in postpartum⁹. However, that is likely significantly underestimated due to difficulty of establishing a diagnosis¹. Diagnosing PA during pregnancy or

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TABLE I. LABORATORY TEST RESULTS.

	Reference Range	At admission	One day after delivery	2 months after delivery*
Hemoglobin	12.0 – 16.0 g/dL	10.3 g/dL	7.0 g/dL	11.4 g/dL
Platelets	150-400 x10 ⁹ /L	200 x10 ⁹ /L	138 x10 ⁹ /L	194 x10 ⁹ /L
Protein-to-creatinine ratio		0.751		
Creatinine	0.55-1.02 mg/dL	0.68 mg/dL	0.68 mg/dL	0.72 mg/dL
Potassium	3.5-5.1 mmol/L		2.8 mmol/L	3.4 mmol/L
Sodium	136-146 mmol/L		138 mmol/L	140 mmol/L
AST	< 31 U/L	28 U/L	26 U/L	14 U/L
ALT	< 34 U/L	23 U/L	16 U/L	13 U/L
GGT (U/L)	< 38 U/L	7 U/L	4 U/L	8 U/L
Total Bilirubin	0.2-1.2 mg/dL	0.4 mg/dL	0.3 mg/dL	0.8 mg/dL
Active Renin	7-76 µU/mL		4.0 µU/mL	< 0.5 µU/mL
Aldosterone	40-310 pg/mL		843 pg/mL	1745 pg/mL
Cortisol	5-25 µ/dL		7.6 µ/dL	7.7 µ/dL
ACTH	9-52 pg/mL			66 pg/mL

*with triple anti-hypertensive medication: perindopril, spironolactone and nifedipine.

the postpartum period is challenging due to heterogeneity in clinical manifestations and to marked alterations in the renin angiotensin system in normal pregnancy⁸. Moreover, it remains uncertain which patients should be screened for PA in the postpartum period¹⁰.

Herein, we report a case of a pregnant woman with primary aldosteronism, diagnosed during the postpartum period.

Informed consent was obtained from the patient.

CASE REPORT

A healthy 31-year-old Caucasian GII/PI woman at 35 weeks of gestation was referred to our emergency department due to new onset of hypertension and mild headaches. The previous gestation, which occurred nine years earlier, was uneventful, with a normal tensional profile, with a vaginal term birth.

The initial evaluation reported high blood pressure (182/106 mmHg) and proteinuria, determined by the urine dipstick test 2+. Severe hypertension was documented following blood pressure re-evaluation. Laboratory tests (Table I) were normal with the exception of a protein-to-creatinine ratio in a random urine specimen of 0.751 mg/mg. Intravenous labetalol was introduced aiming to control blood pressure (duration of 6

hours, cumulative dose of 300 mg at a maximum infusion of 80 mg/h), according to local protocol. Preeclampsia with severity criteria was assumed due to uncontrolled severe blood pressure and labor was induced at 35 weeks of pregnancy, resulting in a vaginal delivery of a baby with 2645 g.

After delivery, despite antihypertensive treatment with intravenous labetalol (max 80 mL/h) and oral perindopril (5 mg per day), the patient blood pressure remained elevated (160/100 mmHg). Subsequent laboratory evaluation included the concentration of potassium (which remained low at 2.7-2.9 mmol/L despite intravenous supplementation), plasma aldosterone (843.0 pg/mL) and active renin (4.0 µU/mL) (Table I). According to these data, PA was diagnosed and the treatment readjusted. In order to control blood pressure, an extensive regimen was prescribed (perindopril 5 mg bid, spironolactone 50 mg id and nifedipine 60 mg id). The patient was discharged eight days after delivery with strict blood pressure control and with scheduled etiologic evaluation.

An abdominal CT scan three months after delivery revealed a 30 mm hypodense (9 HU) solid adrenal mass, which was consistent with adrenal adenoma. A right laparoscopic adrenalectomy was proposed and performed 13 months after birth. Following surgery, the patient discontinued all anti-hypertensive medica-



FIGURE 1. Abdominal computed tomography showing a hypodense solid adrenal mass in the right adrenal gland.

tions, achieving good blood pressure control and serum potassium returned to normal values. Pathologic evaluation of the adrenal gland revealed an aldosterone-secreting adrenal adenoma, which confirmed the medical imaging suspicion.

DISCUSSION

Hypertension is a common clinical complication of pregnancy, and preeclampsia complicates around 2-8% of pregnancies⁷. Secondary causes of hypertension affect 0.24% of pregnancies and pose a significant short and long-term risk of complications for both mother

and babies⁵. In this patient, resistant hypertension and hypokalemia during postpartum raised concern for a primary aldosteronism.

PA is a cause of secondary hypertension and one of the most potentially treatable⁵. This is relevant because PA is associated with adverse maternal-fetal outcomes such as severe hypertension, superimposed preeclampsia, placental abruption, and preterm delivery^{2,5}. In fact, the estimated risk of developing preeclampsia associated with primary aldosteronism in pregnancy can be up to 31%^{2,11}, which is higher than in women with primary chronic hypertension⁶.

As shown in this case, several factors contribute to the difficulty of diagnosing PA in pregnancy.

First new onset of severe hypertension in late pregnancy in a previous normotensive woman is generally interpreted as a hallmark of preeclampsia, potentially neglecting other causes of hypertension⁹. Secondly, distinguishing PA from preeclampsia is further complicated by the fact that proteinuria may be present in PA¹². Because of this, it is hard to understand whether there was a superimposed preeclampsia¹¹. Thirdly, the clinical manifestations of PA are heterogeneous, ranging from severe complications (hypertension, preterm delivery or even fetal loss) to little impact on pregnancies^{5,11}.

Additionally, during pregnancy there are profound alterations in the renin-angiotensin system^{4,6,13} including: 1) elevated renin concentrations due to extra-renal release from ovaries through estrogen stimulation and maternal decidua^{8,9} and 2) increased liver production of angiotensinogen, which elevates aldosterone and angiotensin II levels^{8,14}. There is also an increased aldosterone secretion because progesterone is a competitive inhibitor of aldosterone in the distal convoluted tubule⁸⁻¹⁰. The balance between progesterone and aldosterone leads to normal blood pressure in healthy pregnant women⁸. At the end of pregnancy, the reduction of circulating progesterone levels releases the action of aldosterone, triggering the peri-partum and postpartum presentation of hypertension in PA^{6,10}. This may explain why some cases of PA can have normal or mildly elevated blood pressures during pregnancy, but presented with severe postpartum hypertension.

Currently, the diagnostic criteria for PA in pregnancy is not well defined². Nonetheless, the most recent guidelines from the Endocrine Society for the diagnosis of PA recommend using the plasma aldosterone/renin ratio (ARR) to detect possible cases⁴. Confirmatory tests are not necessary in pregnant women with spontaneous hypokalemia, high aldosterone levels of more than 20 ng/dL (550 pmol/L) and a suppressed renin^{4,8}.

Some authors suggest that PA should be screened in select patients, especially those with severe resistant hypertension and/or spontaneous hypokalemia^{4,8}, or patients with hypertension at a young age¹².

An adrenal CT scan is suggested as the first study to determine the subtype of PA⁴. If a solitary, hypodense, unilateral macroadenoma is found and there is normal

contralateral adrenal morphology, an adrenal adenoma is the most probable diagnosis^{4,5}. Since during pregnancy CT scan is contraindicated, adrenal MRI could be the baseline exam^{8,9}.

When feasible, laparoscopic adrenalectomy is the treatment of choice, ideally performed in the second trimester^{5,13}. Following a conservative management during pregnancy can be challenging because spironolactone and angiotensin-converting enzyme inhibitors are contraindicated^{8,15}. After gestation, both spironolactone and angiotensin-converting enzyme inhibitors are considered safe for breastfeeding¹².

This case illustrates the difficulty of diagnosing primary aldosteronism in both pregnancy and the postpartum period, primary aldosteronism in pregnancy and the postpartum period, and the overlap of clinical manifestations between PA and preeclampsia. It also highlighted the importance of investigating secondary causes of hypertension, such as PA in women with severe and resistant hypertensive disorder. Hypertension and hypokalemia are unreliable markers of PA, and despite hypokalemia not being a sensitive tool for screening, potassium levels should be checked in all resistant hypertension.

Prompt diagnosis followed by surgical treatment led to the resolution of hypertension and hypokalemia, reducing the risk of downstream cardiovascular events.

REFERENCES

1. Corsello SM, Paragliola RM. Evaluation and Management of Endocrine Hypertension During Pregnancy. *Endocrinology and Metabolism Clinics of North America* 2019;48:829-42. <https://doi.org/10.1016/j.ecl.2019.08.011>.
2. Vidyasagar S, Kumar S, Morton A. Screening for primary aldosteronism in pregnancy. *Pregnancy Hypertension* 2021;25:171-4. <https://doi.org/10.1016/j.preghy.2021.06.005>.
3. Young WF. Adrenal causes of hypertension: Pheochromocytoma and primary aldosteronism. *Reviews in Endocrine and Metabolic Disorders* 2007;8:309-20. <https://doi.org/10.1007/s11154-007-9055-z>.
4. Funder JW, Carey RM, Mantero F, Murad MH, Reincke M, Shibata H, et al. The management of primary aldosteronism: Case detection, diagnosis, and treatment: An endocrine society clinical practice guideline. *Journal of Clinical Endocrinology and Metabolism* 2016;101:1889-916. <https://doi.org/10.1210/jc.2015-4061>.
5. Malha L, August P. Secondary Hypertension in Pregnancy. *Current Hypertension Reports* 2015;17. <https://doi.org/10.1007/s11906-015-0563-z>.

6. Zelinka T, Petrák O, Rosa J, Holaj R, Štrauch B, Widimský J. Primary Aldosteronism and Pregnancy. *Kidney and Blood Pressure Research* 2020;45:275-85. <https://doi.org/10.1159/000506287>.
7. Committee on Practice Bulletins – Obstetrics, Espinoza J, Vadaeff A, Pettker CM, Simhan H. ACOG Practice Bulletin No. 202- Gestational Hypertension and Preeclampsia. *Obstetrics and Gynecology* 2019;133.
8. Manoharan M, Sinha P, Sibtain S. Adrenal disorders in pregnancy, labour and postpartum—an overview. *Journal of Obstetrics and Gynaecology* 2020;40:749–58. <https://doi.org/10.1080/01443615.2019.1648395>.
9. Landau E, Amar L. Primary aldosteronism and pregnancy. *Annales d'Endocrinologie* 2016;77:148-60. <https://doi.org/10.1016/j.ando.2016.04.009>.
10. Kilmartin C, Opu T, Podymow T, Dayan N. Primary hyperaldosteronism presenting as persistent postpartum hypertension: Illustrative case and systematic review. *Obstetric Medicine* 2019;12:190-5. <https://doi.org/10.1177/1753495X18772999>.
11. Morton A. Primary aldosteronism and pregnancy. *Pregnancy Hypertension* 2015;5:259-62. <https://doi.org/10.1016/j.preg-hy.2015.08.003>.
12. Berberich AJ, Penava D, Sun D, MacDougall A, Lum A, van Uum S. High aldosterone, hypertension and adrenal adenoma in a 36-year-old pregnant patient: Is this primary aldosteronism? *Obstetric Medicine* 2020;13:88-91. <https://doi.org/10.1177/1753495X18786422>.
13. Eguchi K, Hoshide S, Nagashima S, Maekawa T, Sasano H, Kario K. An adverse pregnancy-associated outcome due to overlooked primary aldosteronism. *Internal Medicine* 2014;53:2499-504. <https://doi.org/10.2169/internalmedicine.53.2762>.
14. Okawa T, Asano K, Hashimoto T, Fujimori K, Yanagida K, Sato A. Diagnosis and Management of Primary Aldosteronism in Pregnancy: Case Report and Review of the Literature. vol. 19. 2002.
15. Quan A. Fetopathy associated with exposure to angiotensin converting enzyme inhibitors and angiotensin receptor antagonists. *Early Human Development* 2006;82:23-8. <https://doi.org/10.1016/j.earlhumdev.2005.11.001>.

AUTHOR CONTRIBUTION STATEMENT

Daniela Agostinho David: Conceptualization; Data curation; Investigation; Methodology; Resources; Visualization; Writing - review & editing. Rafaela Pires: Conceptualization; Data curation; Investigation; Methodology; Resources; Visualization; Writing - review & editing. Ana Filipa Marques: Supervision; Visualization; Writing - review & editing. Isabel Santos Silva: Supervision; Visualization; Writing - review & editing.

CONFLICT OF INTEREST

The authors have no conflicts of interest relevant to this article.

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RECEIVED: 11/07/2022

ACCEPTED: 20/03/2023