sciendo Internal Medicine 2025 vol. XXII No. 1 - www.srmi.ro 95
10.2478/inmed-2025-0322

PRIMARY ALDOSTERONISM IN A YOUNG WOMAN: DIAGNOSTIC AND THERAPEUTIC CHALLENGES

Brînză Paula[1], Radu Sebastian Gavril[1,2], Florin Mitu[1,2,3,4]
[1] Department of Medical Specialties I, Faculty of Medicine, University of Medicine and Pharmacy "Grigore T. Popa", 700115 Iași, Romania
[2] Department of Cardiovascular Rehabilitation, Clinical Rehabilitation Hospital, 700661 Iași, Romania
[3] Academy of Romanian Scientists, 700050 Iași, Romania
[4] Academy of Medical Sciences, 030167 Bucharest, Romania
Corresponding author: Radu Sebastian Gavril
E-mail: rgavril87@yahoo.com

Abstract:
Primary aldosteronism is a frequently overlooked cause of secondary hypertension, despite its association with significant cardiovascular morbidity. Spontaneous or diuretic-induced hypokalemia can serve as an important clinical clue, particularly in younger individuals with resistant hypertension. This case report describes a 39-year-old female who was admitted with high blood pressure (160–180/100 mmHg) and severe hypokalemia (serum potassium: 2.4 mmol/L), requiring frequent potassium supplementation. Biochemical evaluation revealed suppressed renin levels and significantly elevated plasma aldosterone concentration, with an aldosterone-to-renin ratio diagnostic for primary aldosteronism. Adrenal computed tomography identified an unilateral adrenal nodule consistent with an aldosterone-producing adenoma. The patient underwent laparoscopic adrenalectomy, with histopathological confirmation of a benign aldosterone-producing adenoma. After surgery, her blood pressure improved significantly, hypokalemia was corrected, and her antihypertensive medication requirements decreased. Early recognition and targeted treatment, including adrenalectomy for unilateral lesions, can lead to improved long-term outcomes by reducing hypertension severity, cardiovascular risk, and medication burden. This case underscores the need for increased awareness and systematic screening in hypertensive patients, particularly those with hypokalemia or resistant hypertension, to ensure timely diagnosis and optimal management.
Keywords: *Primary aldosteronism, secondary hypertension, resistant hypertension, hypokalemia, laparoscopic adrenalectomy.*

INTERNAL MEDICINE

Clinical Cases

Rezumat:
Aldosteronismul primar este o cauză frecvent neglijată a hipertensiunii secundare, desi acesta este asociat unei morbiditati cardiovasculare semnificativă. Hipokaliemia spontană sau indusă de diuretice poate reprezenta un indiciu clinic important, în special la persoanele tinere cu hipertensiune rezistentă. Prezentul articol relateaza cazul unei paciente de sex feminin, in varsta de 39 de ani internată cu valori tensionale crescute (160–180/100 mmHg) și hipokaliemie severă (potasiu seric: 2,4 mmol/L), necesitând suplimentare frecventă de potasiu. Evaluarea biochimică a evidențiat nivel scăzut al reninei și o concentrație plasmatică semnificativ crescută de aldosteron, cu un raport aldosteron-renină sugestivă pentru aldosteronism primar. Tomografia computerizată a identificat un nodul suprarenalian unilateral sugestiv pentru un adenom secretant de aldosteron. Pacienta a fost supusă unei adrenalectomii laparoscopice, cu confirmare histopatologică a unui adenom benign secretant de aldosteron. Postoperator, tensiunea arterială s-a îmbunătățit semnificativ, hipokaliemia s-a corectat, iar necesarul de medicație antihipertensivă s-a redus. Recunoașterea precoce și tratamentul țintit, inclusiv adrenalectomia pentru leziunile unilaterale, pot duce la îmbunătățirea rezultatelor pe termen lung prin reducerea severității hipertensiunii, a riscului cardiovascular și a necesarului de medicamente. Acest caz subliniază necesitatea creșterii gradului de conștientizare și a screeningului sistematic la pacienții hipertensivi, în special la cei cu hipokaliemie sau hipertensiune rezistentă, pentru a asigura un diagnostic precoce.
Cuvinte-cheie: *Aldosteronism primar, hipertensiune secundară, hipertensiune rezistentă, hipokaliemie, adrenalectomie laparoscopică.*

Introduction

Primary aldosteronism (PA) is the most common cause of endocrine hypertension, accounting for approximately 5–10% of hypertensive patients in referral settings and an even higher prevalence among those with resistant hypertension[1]. Characterized by autonomous aldosterone secretion leading to sodium retention, potassium wasting, and suppressed renin levels, PA is associated with increased cardiovascular morbidity and mortality, independent of blood pressure levels. Early recognition and targeted treatment of PA are essential to prevent complications such as atrial fibrillation, left ventricular hypertrophy and stroke, and chronic kidney disease[1,2].

Historically considered a rare condition primarily diagnosed in patients with hypokalemia, current evidence suggests that most cases are normokalemic, contributing to

underdiagnosis [1, 3, 4]. Hypokalemia, however, remains a useful clinical clue, particularly in younger patients with resistant hypertension or those with adrenal incidentalomas. The aldosterone-to-renin ratio (ARR) is the preferred screening test for PA, with further confirmatory testing required in most cases. Imaging with adrenal computed tomography (CT) is recommended for subtype classification, while adrenal venous sampling (AVS) remains the gold standard for distinguishing unilateral adenomas from bilateral adrenal hyperplasia (BAH). However, in younger patients with severe biochemical abnormalities and unilateral adrenal lesions on imaging, AVS may not always be necessary before surgical intervention[2,5-8].

Laparoscopic adrenalectomy is the treatment of choice for unilateral aldosterone-producing adenomas, often leading to improved blood pressure control, resolution of hypokalemia, and reduced cardiovascular risk. Patients with bilateral disease or those ineligible for surgery are managed with mineralocorticoid receptor antagonists (MRAs), such as spironolactone or eplerenone[2,4,8,9].

This case report presents the case of a 39-year-old female with resistant hypertension and spontaneous hypokalemia, ultimately diagnosed with unilateral aldosterone-producing adenoma. The case highlights the diagnostic and therapeutic challenges associated with PA, emphasizing the importance of early recognition, appropriate diagnostic workup, and individualized treatment strategies to optimize patient outcomes.

Case presentation

A 39-year-old female, residing in a rural area, presented with persistent headaches, muscle cramps, and palpitations. She had been experiencing poorly controlled hypertension for over a year, despite treatment with lercanidipine (10 mg/day). On presentation to the endocrinology clinic, she reported fatigue, generalized weakness, and polyuria, which had progressively worsened.

Medical and family history

The patient had no prior hospitalizations or significant medical conditions aside hypertension. She denied a history of diabetes mellitus, cardiovascular disease, or renal disease. Her menstrual cycles were regular, with no signs of hirsutism or menstrual abnormalities suggestive of other endocrinological disorders. She denied chronic alcohol consumption, tobacco use, or illicit drug use. Her family history was significant for hypertension, with her father being diagnosed at an early age and later developing type 2 diabetes mellitus. There was no known history of stroke, early cardiovascular events, or endocrine tumors in her relatives.

Clinical examination

On clinical examination, the patient appeared alert and in no acute distress. Her blood pressure was 165/105 mmHg on the right arm, measured in a seated position after five minutes of rest. Repeated measurements confirmed persistent hypertension despite the use of antihypertensive medication. Her heart rate was 92 bpm, regular, and peripheral pulses were palpable bilaterally with no evidence of bruits.

The cardiovascular examination revealed no murmurs, gallops, or peripheral edema. On auscultation of the lungs, breath sounds were normal, with no signs of pulmonary congestion. The abdominal examination showed no palpable masses or tenderness, and no audible bruits were detected over the renal arteries. Neurological examination was

normal, with no focal deficits or signs of encephalopathy. Notably, there were no stigmata of secondary hypertension, such as skin changes or specific physical findings suggestive of Cushing syndrome or pheochromocytoma.

Initial clinical presentation and laboratory findings

At the time of admission, the patient's blood pressure was 160/110 mmHg, measured on multiple occasions despite being on antihypertensive therapy. Her heart rate was 90 bpm, and she had no signs of heart failure (no peripheral edema, jugular venous distension, or pulmonary rales). Neurological and fundoscopic examinations did not show any pathological findings.

A basic serum electrolyte panel revealed:

- potassium (K^+): 2.4 mmol/L (normal range: 3.5–5.0 mmol/L)
- sodium (Na^+): 141 mmol/L (normal range: 135–145 mmol/L)
- chloride (Cl^-): 98 mmol/L
- serum bicarbonate: 30.2 mmol/L (mild metabolic alkalosis).

Renal function was normal, with a serum creatinine of 0.52 mg/dL and estimated glomerular filtration rate (eGFR) of 105 mL/min/1.73m².

Further testing revealed markedly suppressed plasma renin activity (PRA) and elevated aldosterone levels, with an aldosterone-to-renin ratio (ARR) diagnostic for primary aldosteronism: a) plasma aldosterone concentration (PAC): 31,500 pg/mL (normal: 1,170–23,600 pg/mL); b) plasma renin activity (PRA): <0.5 µIU/mL (normal: 2.8–39.9 µIU/mL); c) ARR: 63 (cut off for PA diagnosis: >30).

Further 24-hour urinary potassium and sodium excretion revealed urinary potassium of 53.2 mmol/24h (suggesting excessive renal K^+ loss) and urinary sodium of 158 mmol/24h. A morning cortisol level was within normal limits, ruling out Cushing's syndrome. Additionally, metanephrines and normetanephrines were normal, findings which excluded pheochromocytoma.

Diagnostic workup, imaging and confirmation of diagnosis

An electrocardiogram was performed as part of the initial workup. It revealed sinus rhythm at 88 bpm with a normal axis, but with signs of left ventricular hypertrophy (LVH). There were no significant ST-segment or T-wave abnormalities suggestive of ischemia. The corrected QT interval was within normal limits. These findings were consistent with chronic hypertension leading to cardiac remodeling, which is commonly observed in patients with long-standing primary aldosteronism.

A transthoracic echocardiography was performed to assess structural and functional

cardiac abnormalities secondary to chronic hypertension. This investigation showed left ventricular hypertrophy, with an interventricular septal thickness of 13 mm and posterior wall thickness of 12 mm, confirming concentric hypertrophy.

The left ventricular ejection fraction was preserved (LVEF, 60%), with no evidence of segmental wall motion abnormalities. Diastolic function was mildly impaired, indicated by an E/A ratio of 0.8 and increased deceleration time, consistent with grade 1 diastolic dysfunction. There were no signs of valvular disease, pericardial effusion, or pulmonary hypertension.

These findings reinforced the presence of target organ damage secondary to uncontrolled hypertension, a hallmark of undiagnosed or poorly managed primary aldosteronism.

In line with current diagnostic guidelines, the investigation proceeded without confirmatory testing given the patient's spontaneous hypokalemia, a plasma aldosterone concentration exceeding 20 ng/dL, and a significantly elevated ARR. Imaging studies were performed to subtype the condition.

A contrast-enhanced abdominal CT scan revealed a 15 mm hypodense nodule in the left adrenal gland with a negative spontaneous density and washout values of 65% absolute and 60% relative, findings highly suggestive of an aldosterone-producing adenoma. The right adrenal gland was unremarkable, and no evidence of hyperplasia or mass was noted. Additionally, the imaging identified uterine leiomyomas, while the other abdominal organs, including the kidneys, appeared normal.

Given the clear biochemical and radiological findings, a decision was made not to perform adrenal venous sampling (AVS), as the patient met the criteria for direct surgical intervention (age <40 years, spontaneous hypokalemia, markedly elevated aldosterone, and a solitary adrenal lesion on CT).

Surgery and management

The patient was prepared for surgery with a regimen of spironolactone at a dose of 100 mg/day to mitigate the effects of excess aldosterone and potassium chloride supplementation to correct hypokalemia. Within weeks, her serum potassium normalized to 3.9 mmol/L, and her blood pressure showed mild improvement.

She underwent laparoscopic left adrenalectomy without intraoperative complications. She was extubated immediately postoperatively and transferred to the surgical ward for monitoring. Histopathological examination confirmed a well-circumscribed aldosterone-producing adenoma and no evidence of necrosis, vascular invasion, or malignancy.

Postoperative course and follow-up

Three days post-surgery, the patient's blood pressure was 140/90 mmHg without antihypertensive medication. Her potassium remained stable at 4.0 mmol/L, and she was discharged on a low-dose beta-blocker (carvedilol 12.5 mg/day) and lercanidipine (10 mg/day) to control residual hypertension.

During her three-month follow-up, spironolactone treatment was stopped, and her blood pressure stabilized at 130/85 mmHg with minimal medication.

Her renin levels increased postoperatively, confirming resolution of autonomous aldosterone production. By six months postoperatively, she no longer required antihypertensive medications, her serum potassium remained normal, and her cardiovascular risk profile had improved significantly. A genetic evaluation for familial hyperaldosteronism type II was considered but deferred due to lack of family history of PA.

Internal Medicine

Clinical Cases

Discussion

Primary aldosteronism, once considered a rare cause of secondary hypertension, is now recognized as a leading contributor to resistant hypertension and associated cardiovascular complications[1,10-12]. This case of a 39-year-old female with spontaneous hypokalemia and severe hypertension illustrates the diagnostic and therapeutic challenges inherent in managing PA, as well as the importance of timely detection and intervention.

The diagnosis of PA relies on demonstrating autonomous aldosterone secretion, typically characterized by suppressed renin levels and elevated aldosterone concentrations[13-15]. Guidelines from the Endocrine Society recommend screening patients with resistant hypertension, spontaneous or diuretic-induced hypokalemia, or adrenal incidentalomas. In this case, the markedly elevated plasma aldosterone concentration (31,500 pg/mL), suppressed plasma renin activity (<0.5 µIU/mL), and aldosterone-to-renin ratio (ARR) of 63 provided definitive biochemical evidence of PA. The ARR remains the cornerstone of screening, with thresholds varying between >20 and >30 depending on the assay and laboratory calibration[1].

Confirmatory testing, such as the saline infusion test or captopril challenge, is often recommended to verify the diagnosis [1, 16-18]. However, these tests were deemed unnecessary in this case due to the presence of spontaneous hypokalemia, a plasma aldosterone concentration exceeding 20 ng/dL, and an elevated ARR, all of which fulfill diagnostic criteria for PA. This approach aligns with the British and Irish Hypertension Society's practical guidelines, which allow confirmatory testing to be bypassed in cases of high pretest probability[1,9].

Imaging studies, particularly adrenal computed tomography (CT), play a major role in subtype classification of PA, distinguishing unilateral aldosterone-producing adenomas (APA) from bilateral adrenal hyperplasia (BAH) [1,10,19]. In this case, a 15 mm hypodense nodule with negative spontaneous density and washout values (60% relative, 65% absolute) on CT was highly suggestive of an PA. These imaging features are well-documented in guidelines, which emphasize the reliability of washout criteria in identifying adenomas.

Adrenal venous sampling (AVS) is the gold standard for lateralizing PA and is generally required to confirm the source of aldosterone hypersecretion [1, 5, 20-22]. However, the AVIS-2 study and recent guidelines highlight specific scenarios where AVS may be omitted, such as in younger patients with clear biochemical and radiologic evidence of unilateral disease. In this case, the decision to forgo AVS was based on the patient's age (<40 years), marked aldosterone elevation, and CT findings

consistent with APA. This approach expedited treatment while adhering to guideline recommendations, demonstrating the importance of individualized management strategies[1,23].

Management of PA is driven by the underlying subtype. Unilateral disease, such as an APA, is best treated surgically with adrenalectomy, whereas bilateral disease requires medical management with mineralocorticoid receptor antagonists (MRAs)[1].

Laparoscopic adrenalectomy is the preferred surgical approach for unilateral PA due to its minimally invasive nature, shorter recovery times, and low complication rates [24-26]. In this patient, adrenalectomy resulted in significant clinical and biochemical impro-vements, with normalization of blood pressure and potassium levels within six months postoperatively. This aligns with evidence from Rossi et al., which demonstrates that surgery leads to complete remission of hypertension in 30–50% of cases and partial improvement in up to 90% of the cases. Moreover, surgical intervention reduces long-term cardiovascular risks, including stroke, myocardial infarction, and atrial fibrillation, by addressing the root cause of aldosterone excess[1,2].

For patients with bilateral disease or those who are not surgical candidates, MRAs such as spironolactone or eplerenone are the cornerstone of medical therapy [2]. These agents counteract the effects of aldosterone on the cardiovascular and renal systems, improving blood pressure control and reducing potassium wasting. However, MRAs do not address the underlying pathology and require lifelong administration, with close monitoring for potential side effects such as hyperkalemia and gynecomastia. When compared, surgical treatment offers a more definitive resolution but is limited to patients with unilateral disease[1,9]. PA is associated with significant cardiovascular and renal morbidity due to the chronic effects of aldosterone-mediated hypertension, vascular remodeling, and end-organ damage [27-29]. Studies indicate that patients with untreated PA have a higher prevalence of left ventricular hypertrophy, atrial fibrillation, chronic kidney disease, and stroke compared to patients with essential hypertension. Early diagnosis and treatment are critical to mitigate these risks. In this case, the normalization of blood pressure and resolution of hypokalemia post-adrena-lectomy likely contributed to the prevention of further cardiovascular complications[27,28,30].

Outcomes vary depending on the way of treatment choice [1, 9]. Surgical intervention in unilateral disease has been shown to reduce left ventricular mass, improve diastolic function, and decrease the incidence of atrial fibrillation. Medical therapy with MRAs, while effective in improving symptoms and preventing progression of target organ damage, may not fully reverse established cardiovascular changes.

Thus, timely intervention is essential to optimize outcomes[1,9].

Conclusion

This case underscores the importance of systematic screening, early diagnosis, and tailored management of primary aldosteronism. The analysis of biochemical testing, imaging, and guideline-based decision-making generated timely surgical intervention, resulting in significant clinical improvement. Adrenalectomy offers a definitive cure for unilateral PA, while medical therapy remains a viable alternative for bilateral disease or nonsurgical candidates. Long-term follow-up is essential to monitor for residual hypertension and optimize cardiovascular risk management. The case

Internal Medicine

Clinical Cases

highlights the need for heightened awareness of PA in patients with resistant hypertension and hypokalemia to improve diagnostic rates and outcomes.

References:

1. Funder, J.W., et al., The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab, 2016. 101(5): p. 1889-916.

2. Rossi, G.P., et al., Clinical management of primary aldosteronism: an update. Hypertension, 2024. 81(9): p. 1845-1856.

3. Hundemer, G.L. and A. Vaidya, Primary aldosteronism diagnosis and management: a clinical approach. Endocrinology and Metabolism Clinics, 2019. 48(4): p. 681-700.

4. Utsumi, T., et al., Laparoscopic adrenalectomy for adrenal tumors with endocrine activity: perioperative management pathways for reduced complications and improved outcomes. International Journal of Urology, 2023. 30(10): p. 818-826.

5. Buffolo, F., et al., Subtype diagnosis of primary aldosteronism: is adrenal vein sampling always necessary? International journal of molecular sciences, 2017. 18(4): p. 848.

6. Lenders, J.W., G. Eisenhofer, and M. Reincke, Subtyping of patients with primary aldosteronism: an update. Hormone and Metabolic Research, 2017. 49(12): p. 922-928.

7. Zhang, M., et al., Assessment of biochemical outcomes in patients with primary aldosteronism after adrenalectomy based on CT scan diagnosis of unilateral adenoma without adrenal vein sampling. Frontiers in Oncology, 2022. 12: p. 944035.

8. Ahmed, S. and G.L. Hundemer, Benefits of surgical over medical treatment for unilateral primary aldosteronism. Frontiers in Endocrinology, 2022. 13: p. 861581.

9. Faconti, L., et al., Diagnosis and management of primary hyperaldosteronism in patients with hypertension: a practical approach endorsed by the British and Irish Hypertension Society. Journal of Human Hypertension, 2024. 38(1): p. 8-18.

10. Kline, G.A., et al., Primary aldosteronism: a common cause of resistant hypertension. Cmaj, 2017. 189(22): p. E773-E778.

11. Charles, L., J. Triscott, and B. Dobbs, Secondary hypertension: discovering the underlying cause. American family physician, 2017. 96(7): p. 453-461.

12. Mulatero, P., et al., Subtype diagnosis, treatment, complications and outcomes of primary aldosteronism and future direction of research: a position statement and consensus of the Working Group on Endocrine Hypertension of the European Society of Hypertension∗. Journal of hypertension, 2020. 38(10): p. 1929-1936.

13. Byrd, J.B., A.F. Turcu, and R.J. Auchus, Primary aldosteronism: practical approach to diagnosis and management. Circulation, 2018. 138(8): p. 823-835.

14. O'Shea, P.M., et al., The aldosterone to renin ratio in the diagnosis of primary aldosteronism: promises and challenges. International journal of clinical practice, 2019. 73(7): p. e13353.

15. Young Jr, W., Diagnosis and treatment of primary aldosteronism: practical clinical perspectives. Journal of internal medicine, 2019. 285(2): p. 126-148.

16. Lin, C., et al., A combination of captopril challenge test after saline infusion test improves diagnostic accuracy for primary aldosteronism. Clinical Endocrinology, 2020. 92(2): p. 131-137.

17. Leung, A.A., et al., Performance of confirmatory tests for diagnosing primary aldosteronism: a systematic review and meta-analysis. Hypertension, 2022. 79(8): p. 1835-1844.

18. Liu, B., et al., Seated saline suppression test is comparable with captopril challenge test for the diagnosis of primary aldosteronism: a prospective study. Endocrine Practice, 2021. 27(4): p. 326-333.

19. Grytaas, M.A., Primary aldosteronism in Western

Norway. Studies of diagnostic approach and treatment outcome. 2018.

20. Campbell, R.A., et al., Influence of adrenal venous sampling on management in patients with primary aldosteronism independent of lateralization on cross-sectional imaging. Journal of the American College of Surgeons, 2019. 229(1): p. 116-124.

21. Betz, M.J. and C.J. Zech, Adrenal venous sampling in the diagnostic workup of primary aldosteronism. The British Journal of Radiology, 2022. 95(1129): p. 20210311.

22. Rossi, G.P., New concepts in adrenal vein sampling for aldosterone in the diagnosis of primary aldosteronism. Current hypertension reports, 2007. 9(2): p. 90-97.

23. Rossitto, G., et al., Subtyping of Primary Aldosteronism in the AVIS-2 Study: Assessment of Selectivity and Lateralization. J Clin Endocrinol Metab, 2020. 105(6).

24. Uludağ, M., N. Aygün, and A. İşgör, Surgical indications and techniques for adrenalectomy. Şişli Etfal Hastanesi Tip Bülteni, 2020. 54(1): p. 8-22.

25. Heger, P., et al., Evaluation of open and minimally invasive adrenalectomy: a systematic review and network meta-analysis. World Journal of surgery, 2017. 41: p. 2746-2757.

26. Li, K.-p., et al., Partial versus total adrenalectomy for the treatment of unilateral aldosterone-producing adenoma: a systematic review and meta-analysis. Updates in Surgery, 2021. 73(6): p. 2301-2313.

27. Lin, X., et al., Cerebro-cardiovascular risk, target organ damage, and treatment outcomes in primary aldosteronism. Frontiers in cardiovascular medicine, 2022. 8: p. 798364.

28. Buffolo, F., et al., Aldosterone as a mediator of cardiovascular damage. Hypertension, 2022. 79(9): p. 1899-1911.

29. Bioletto, F., et al., Primary aldosteronism and resistant hypertension: a pathophysiological insight. International Journal of Molecular Sciences, 2022. 23(9): p. 4803.

30. Ferreira, N.S., et al., Aldosterone, inflammation, immune system, and hypertension. American journal of hypertension, 2021. 34(1): p. 15-27.