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Primary Hyperaldosteronism Caused by Bilateral Adrenal Hyperplasia and a Unilateral Adrenal Adenoma: A Diagnostic and Therapeutic Challenge (Case Report)

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Case Report

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Abstract

Background

Primary aldosteronism (PA) is the most common endocrine cause of secondary hypertension. Accurate diagnosis is essential, especially in patients with refractory hypertension and hypokalemia. Differentiating between aldosterone-producing adenoma (APA) and bilateral adrenal hyperplasia (BAH) is critical to guide management, however the coexistence of both is extremely rare but clinically significant.

Case presentation:

We report the case of a 49-year-old woman with poorly controlled hypertension and recurrent episodes of hypokalemia and hypocalcemia, leading to multiple hospital admissions. Computed tomography (CT) revealed a right adrenal hypodense lesion consistent with an adenoma. However, adrenal venous sampling (AVS) indicated dominant aldosterone secretion from the left adrenal gland, and biopsy confirmed left-sided hyperplasia. This discordance between imaging and hormonal function posed a diagnostic and therapeutic challenge.

Intervention and outcomes:

Based on biochemical lateralization and after multidisciplinary evaluation, a left unilateral adrenalectomy was performed. The patient had no surgical complications. At six-month follow-up, blood pressure was controlled with only two antihypertensive agents and no additional complications. Hormonal re-evaluation showed biochemical improvement.

Conclusion

This case illustrates the limitations of relying solely on imaging in PA. The coexistence of a non-functioning adrenal adenoma and contralateral functional hyperplasia is rare but clinically significant. AVS remains the gold standard for lateralization and should guide surgical decisions. An individualized approach, prioritizing biochemical over radiological findings, can improve outcomes even in complex or bilateral secretion scenarios.

Introduction

Primary aldosteronism (PA) is the most common endocrine cause of secondary hypertension, with a prevalence between 5% and 15% in the general hypertensive population, and up to 20% in patients with resistant or refractory hypertension [1–5]. Early recognition is essential, as it is associated with a higher risk of cardiovascular events, target organ damage, and severe hypokalemia [6–8]. The two most common causes of PA are aldosterone-producing adenoma (APA), usually unilateral and more frequent in women, and bilateral adrenal hyperplasia (BAH), which tends to be more common in men [8].

The coexistence of a unilateral aldosterone-producing adenoma (APA) and bilateral adrenal hyperplasia (BAH) is rare and sparsely documented in the literature. This scenario poses a significant diagnostic and therapeutic challenge because it can lead to bilateral aldosterone secretion with a dominant focus in a single gland, complicating the interpretation of both imaging and functional studies. Radiological findings often fail to accurately distinguish between hyperplasia and non-functioning incidentalomas; therefore, **adrenal vein sampling (AVS)** remains the diagnostic gold standard for determining hormonal lateralization [6, 9–11].

Case presentation

We present the case of a 49-year-old woman with arterial hypertension diagnosed at age 35, who showed poor response to pharmacological therapy, with no other significant past medical history. Over the past two years she experienced multiple hypertensive crises characterized by stable angina, headache with red-flag features, and muscle weakness in the setting of documented severe hypokalemia. These clinical manifestations led to twelve hospital admissions during that time. Blood-pressure readings during the crises were persistently elevated, reaching 160/118 mmHg (mean arterial pressure [MAP] 123 mmHg) and decreasing only partially with treatment to 138/84 mmHg (MAP 102 mmHg). Simultaneously, during the hospitalization she presented with critically low serum potassium levels that required urgent replacement.

Hormonal testing showed elevated plasma aldosterone levels, yielding a high aldosterone-to-renin ratio (Table 1). The persistence of symptoms despite the concomitant use of multiple antihypertensive drugs from different classes raised suspicion of a secondary cause of hypertension.

Table 1. Hormonal profile of the patient, including evaluation of cortisol secretion, renin–aldosterone axis parameters, and plasma metanephrines obtained during the diagnostic workup

An abdominal computed tomography (CT) scan with an adrenal-specific protocol (Figure 1) revealed a 23 × 17 mm hypodense lesion in the right adrenal gland with an attenuation value of 4 Hounsfield units (HU), consistent with a right adrenal adenoma.

Subsequently, adrenal venous sampling under pharmacological preparation (Table 2) demonstrated higher aldosterone production from the left adrenal gland, with a lateralization index of 1.62. This lateralized secretion pattern, discordant with the right-sided adenoma seen on imaging, prompted a biopsy that confirmed hyperplasia of the left adrenal gland.

Table 2. Biochemical Study of Adrenal Venous sampling

Because of the patient's refractory hypertension, established target-organ involvement, as evidenced by nephrotic range proteinuria in a 24-hour urine sample, age, and biochemical findings indicating bilateral secretion with lateralization, the multidisciplinary surgical board decided to perform a left unilateral adrenalectomy. The procedure was completed without complications.

Upon discharge, the patient was receiving prazosin 3 mg every 6 hours, nifedipine 30 mg every 8 hours, irbesartan 300 mg every 24 hours, minoxidil 5 mg every 12 hours, carvedilol 12.5 mg every 12 hours, and spironolactone 100 mg every 24 hours. At the one- and two-month follow-ups, there was a notable improvement in blood pressure control and normalization of serum potassium with oral supplementation. Antihypertensive therapy was reduced to prazosin 1 mg every 12 hours, nifedipine 30 mg every 12 hours, and carvedilol 12.5 mg every 24 hours. Blood pressure remained within normal ranges since adrenalectomy, with regular hormonal follow-up by endocrinology and internal medicine with no hospital readmissions to date. Adherence and tolerability were adequate with no adverse events reported in the follow-up with endocrinology.

Discussion

Primary aldosteronism (PA) should be diagnosed in a structured, stepwise manner. The two most common etiologies are bilateral adrenal hyperplasia (BAH), which is more prevalent in men (4:1 ratio), and aldosterone-producing adenomas (APA), typically unilateral and more frequent in women in a 2:1 ratio [8, 12]. Although PA lacks specific clinical manifestations, the coexistence of arterial hypertension and hypokalemia may raise its prevalence to as high as 28% [2, 12].

In such cases, once refractory hypertension with hypokalemia is confirmed, the renin-aldosterone axis must be evaluated. An elevated aldosterone-to-renin ratio, characterized by suppressed renin and elevated aldosterone, is highly suggestive of PA, particularly when persistent hypokalemia is also present [8, 11]. In our patient, renin levels < 0.3 pg/mL and aldosterone > 80 ng/dL, along with imaging findings, were sufficient to confirm the diagnosis and determine the etiology.

Regarding treatment, computed tomography (CT) revealed a hypodense lesion suggestive of an adenoma in the right adrenal gland. However, adrenal venous sampling (AVS) demonstrated dominant functional secretion from the left adrenal gland, and biopsy confirmed hyperplasia on that side. This mismatch between imaging and hormonal function represents one of the main complexities of this case, being an atypical presentation in clinical practice.

Two diagnostic possibilities were considered: firstly, a non-functioning adenoma in the right gland with secretory hyperplasia in the left and secondly, bilateral secretion with left-sided predominance. The patient experienced multiple hospitalizations due to hypertensive crises, hypokalemic paralysis, and target-organ damage, prompting the need for a definitive therapeutic intervention. Therefore, following interdisciplinary board discussion, a left adrenalectomy was performed based on functional secretion patterns rather than imaging findings.

In such scenarios, the literature indicates that available noninvasive methods, such as adrenal computed tomography (CT), magnetic resonance imaging (MRI), and adrenal scintigraphy are often insufficient to accurately identify the source of hormonal overproduction [8–10]. Therefore, in patients with medically refractory hypertension or virilization, unilateral adrenalectomy has been employed, as in the present case. This approach aims to improve disease control by reducing overall hormonal output, even when

bilateral activity is present. In our patient, this intervention significantly lowered hormonal production and allowed for improved blood pressure control with reduced pharmacological requirements.

This case highlights the limitations of isolated imaging studies. Non-functioning adrenal incidentalomas are common in the adult population and interpreting them without functional testing can lead to diagnostic errors [10]. In our case, had a right adrenalectomy been performed based solely on the imaging findings, the clinical outcome would likely have been unfavorable. Additionally, no genetic or molecular studies were performed to investigate potential mutations explaining this atypical phenotype, such as KCNJ5, CACNA1D, CACNA1H, ATP1A1, ATP2B3, or germline variants associated with familial hyperaldosteronism subtypes (e.g., *CYP11B1/CYP11B2* chimeric gene in FH-I, KCNJ5 germline mutations in FH-III) [7, 9]. These mutations have been implicated in the pathogenesis of aldosterone-producing adenomas and bilateral adrenal hyperplasia, influencing both clinical presentation and prognosis [7, 8, 9]. Nevertheless, considering the clinical context and hormonal findings, this limitation did not compromise the therapeutic decision-making process.

The coexistence of a non-functioning unilateral adrenal adenoma with contralateral functional hyperplasia is extremely rare. Few such cases have been reported in the literature, and in most, the diagnosis was only achievable through adrenal venous sampling (AVS), as in our case. This scenario is particularly challenging, as it requires clinical decision-making based on discordant morphological and functional findings.

This case serves as a paradigmatic example of how biochemical lateralization should take precedence over imaging findings in the management of PA. It also shows that surgical treatment can be effective even in the context of bilateral secretion, provided a dominant functional focus is clearly identified. Finally, it reinforces the importance of considering primary aldosteronism in any patient with refractory hypertension, hypokalemia, and recurrent clinical crises, even when imaging findings are ambiguous or contradictory.

Conclusion

This case highlights the importance of considering primary aldosteronism in young patients with refractory hypertension and hypokalemia. The coexistence of a non-functioning adrenal adenoma with contralateral functional hyperplasia represents an uncommon diagnostic scenario, in which adrenal venous sampling was critical for guiding surgical management. The decision to perform unilateral adrenalectomy in the context of bilateral secretion illustrates how an individualized approach can improve clinical outcomes without causing chronic adrenal insufficiency.

Declarations

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This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Interests:
The authors declare no conflicts of interest.

Clinical trial number: Not applicable.

Ethics, Consent to Participate, and Consent to Publish declarations: not applicable.

Consent for publication

The patient provided written informed consent for the publication of this case report. The study was submitted to the Ethics Committee of Fundación Cardioinfantil, where it was reviewed and approved.

Author Contributions and Acknowledgments

NTA: Case history summary, literature search and manuscript drafting.

MJAG: Case history summary, literature search and manuscript drafting.

JAAB: Case history summary, literature search and manuscript drafting.

AMS: Case history summary, literature search and manuscript drafting.

LV: treating physician of the patient, obtaining informed consent, case history summary, literature search, and manuscript drafting.

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Tables

Table 1 and 2 are available in the Supplementary Files section.

Figures

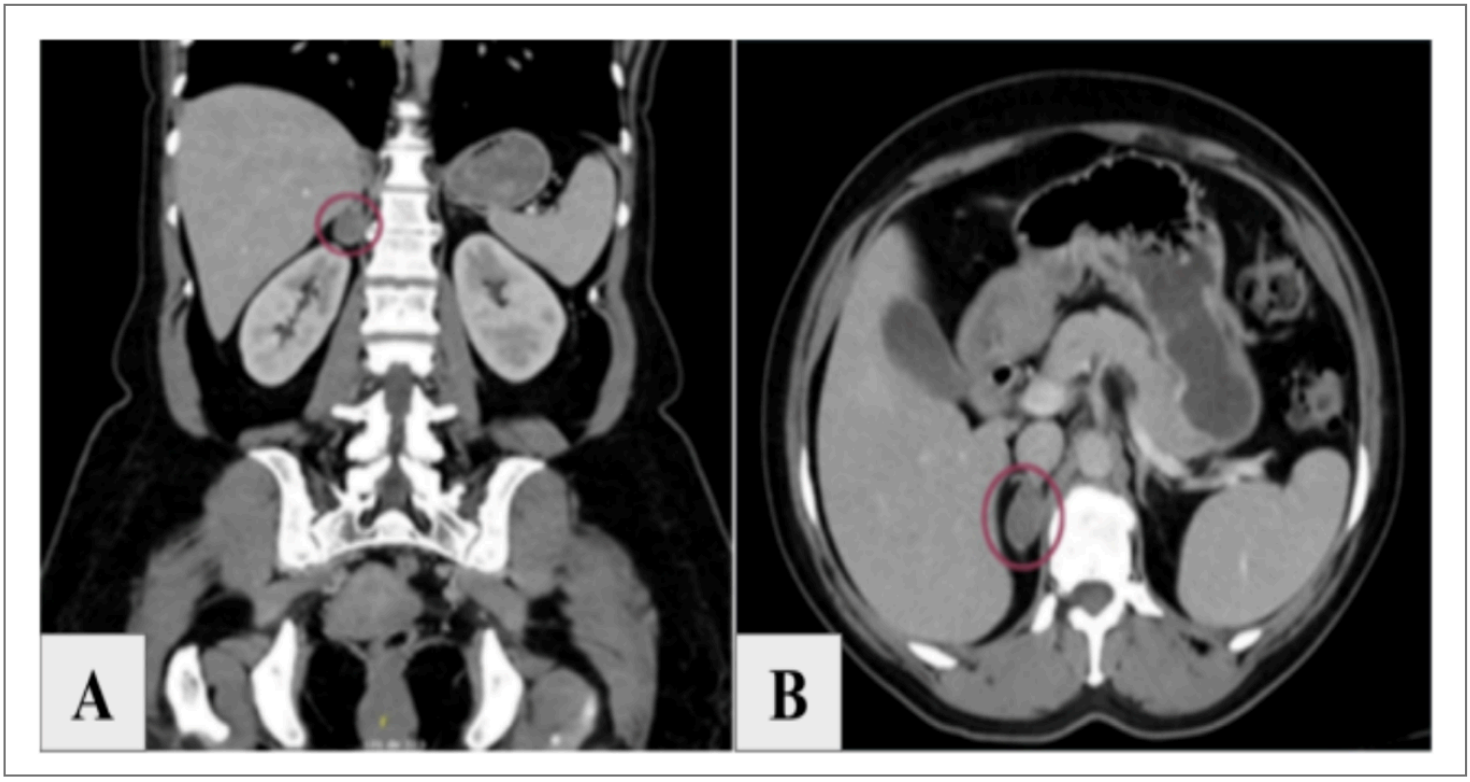


Figure 1

Adrenal computed tomography (CT)
A) Coronal view of the right adrenal gland (red circle) compatible with an adenoma.
B)Transverse view of the right adrenal lesion (red circle) compatible with an adenoma.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1and2.docx