

Case Report

Medical Management of Aldosterone-Producing Adenoma with Sequential Mineralocorticoid Receptor Antagonists: A Case Report

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Abstract: Primary aldosteronism (PA) is the most common cause of secondary hypertension, characterized by autonomous aldosterone overproduction leading to hypertension, hypokalemia, and increased cardiovascular risk. Mineralocorticoid receptor antagonists (MRAs) are the pharmacological cornerstone of treatment when surgery is not feasible. We describe a 34-year-old male with PA secondary to a right adrenal adenoma, who refused surgical treatment due to severe anxiety. After developing painful bilateral gynecomastia with spironolactone (50 mg/day), he was switched to eplerenone (50 mg twice daily), which normalized serum potassium (4.3 mEq/L), resolved gynecomastia, and maintained blood pressure control. Temporary replacement of eplerenone with finerenone because of drug unavailability resulted in recurrent hypokalemia, which resolved after eplerenone was resumed. Following psychotherapy, the patient subsequently underwent laparoscopic right adrenalectomy, achieving complete biochemical remission. This case highlights eplerenone as an effective, well-tolerated alternative MRA in patients who develop androgen-mediated adverse effects with spironolactone, reinforcing the importance of individualized therapeutic management in PA.

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1. Introduction

Primary aldosteronism (PA), or Conn's syndrome, results from excessive aldosterone production independent of renin and angiotensin II. This leads to increased tubular renal sodium reabsorption, potassium excretion, and blood volume expansion, culminating in systemic arterial hypertension (SAH) and hypokalemia [1]. PA is primarily represented by bilateral adrenal hyperplasia and unilateral aldosterone-producing adenoma (APA), but may also be caused by unilateral adrenal hyperplasia, adrenal carcinoma, extra-adrenal aldosterone-producing tumors, or genetic mutations [1]. It is one of the most common causes of secondary SAH [1].

Aldosterone acts on mineralocorticoid receptors (MRs), which are present in nephrons, colonic mucosa, sweat glands, and salivary glands, all ion-transporting tissues. Additionally, MRs are expressed in cardiac myocytes, endothelial cells, vascular smooth muscle, macrophages, brown adipose tissue cells, and neurons in several brain regions, including the hippocampus, hypothalamus, and brainstem [25]. Their principal physiological function is to regulate epithelial sodium transport and extracellular fluid volume. [1, 2]. Consequently, PA is associated with deleterious effects on the heart, vessels, brain, and kidneys, which are partially independent of aldosterone-induced blood pressure elevation. It is also associated with reduced insulin sensitivity and secretion, as well as a higher incidence of metabolic syndrome and type 2 diabetes mellitus [1]. The excess risk

of cardiovascular, cerebrovascular, and renal complications can be successfully reversed by specific treatment: adrenalectomy for unilateral APA and mineralocorticoid receptor antagonist (MRA) therapy for bilateral forms [1].

For APA, unilateral laparoscopic adrenalectomy is the preferred treatment, considered highly effective in reducing cardiovascular events and blood pressure [3, 4]. However, when the patient refuses surgery or when medical contraindications exist, MRAs, which competitively inhibit aldosterone binding to mineralocorticoid receptors, become therapeutic alternatives [1, 4]. Examples include spironolactone, eplerenone and finerenone (Table 1), which may be used alone or in combination with other antihypertensive agents [1, 3].

2. Case Report

A male patient, born on June 5, 1989, had been diagnosed with systemic arterial hypertension since the age of 19. He had been treated with olmesartan 40 mg/day, hydrochlorothiazide 25 mg/day, and amlodipine 5 mg/day. In September 2021, at the age of 32, investigation was initiated due to hypokalemia (serum potassium 2.6 mEq/L) that persisted even after discontinuation of the diuretic thiazide. Primary aldosteronism was diagnosed based on an aldosterone-to-renin ratio of 5.76 ng/dL per mIU/L (screening cutoff >3.7) and aldosterone level of 40.9 ng/dL. Computed tomography identified a 17-mm right adrenal nodule with lipid-rich density characteristic of a cortical adenoma, and the diagnosis of unilateral aldosterone-producing adenoma was established.

His medical history was significant for grade 3 obesity (BMI of 40.1 kg/m²), infertility (azoospermia), and generalized anxiety disorder treated with escitalopram 10 mg/day and psychotherapy. Transthoracic echocardiography revealed mild left ventricular hypertrophy, dilation of the left cardiac chambers, aortic root dilatation (39.4 mm), mild mitral regurgitation, left atrial enlargement (43 mm), and grade 1 left ventricular diastolic dysfunction. Holter monitoring identified frequent ventricular ectopic beats.

Following this diagnosis, the patient continued follow-up with his primary care physician, who discontinued hydrochlorothiazide. Although he was referred to an endocrinology clinic, he repeatedly postponed the appointment because of pronounced anxiety about receiving a diagnosis that might ultimately require surgery — a pattern consistent with reports that fear of surgery itself, independent of the severity of the underlying disease, can lead patients to postpone or remain indecisive about recommended procedures [20]. Consequently, 14 months elapsed between the initial diagnosis of PA and his first endocrinology visit, during which specific mineralocorticoid receptor antagonist therapy was not introduced.

In November 2022, at his first appointment with an endocrinologist, right adrenalectomy was recommended; however, the patient refused the procedure due to severe anxiety triggered by the prospect of any surgical intervention. Spironolactone was then started at 25 mg/day and subsequently increased to 50 mg/day. The patient soon reported painful bilateral gynecomastia. Serum potassium had risen from 2.6 mEq/L to 3.1 mEq/L. Owing to this adverse effect, spironolactone was replaced by eplerenone 50 mg twice daily. In March 2024, owing to a temporary shortage of eplerenone, treatment was switched to finerenone 20 mg/day. One month later, serum potassium had declined to 2.9 mEq/L. Eplerenone subsequently became available again, and the patient resumed the previous treatment. Table 1 summarizes the patient's clinical course. Through ongoing psychotherapy and escitalopram treatment, the patient ultimately agreed to undergo surgery. In April 2025, he underwent right laparoscopic adrenalectomy. Histopathological examination confirmed an adrenal cortical adenoma (2.5-cm partially encapsulated nodular formation; Weiss score 1). Biochemical cure was achieved, as demonstrated in Table 1.

In the immediate postoperative period, office blood pressure remained elevated (146/100 mmHg on postoperative day 12) despite normalization of serum potassium, without clinical or biochemical evidence of adrenal insufficiency. Reversal of aldosterone-induced vascular remodeling and arterial stiffness after adrenalectomy occurs gradually,

concentrated within the first 6 months rather than immediately after surgery [22]; together with perioperative pain, anxiety, and the patient's previously documented white-coat effect, this most plausibly accounts for the transient elevation, rather than recurrent or persistent hyperaldosteronism. Systematic home blood pressure monitoring performed one month after surgery, while the patient was taking olmesartan 20 mg/day, confirmed blood pressure readings in the target (below 130/80 mmHg).

Table 1. Serum potassium levels and side effects according to treatment employed for the patient.

	Sept, 2021	Nov, 2022	June, 2023	April, 2024	Sept, 2024	April, 2025	Aug, 2026
Office BP ^a	150x100 mmHg	140x100 mmHg	140x96 mmHg	140x90 mmHg	140x90 mmHg	146x100 mmHg	130x88 mmHg
Serum Potassium levels	2.6 mEq/L	3.1 mEq/L	4.1 mEq/L	2.9 mEq/L	3.5 mEq/L	4.3 mEq/L	4.8 mEq/L
Treatment with MRA	No	Spironolactone 50 mg/day	Eplerenone 50 mg twice daily	Finerenone 20 mg/day	Eplerenone 50 mg twice daily	No	No
Daily doses of other antihypertensive drugs	Olmesartan 40 mg, HCTZ 25 mg, amlodipine 5 mg	Olmesartan 40 mg, amlodipine 5 mg	Olmesartan 20 mg, amlodipine 5 mg	Olmesartan 20 mg, amlodipine 5 mg	Olmesartan 20 mg, amlodipine 5 mg, metoprolol 50 mg	Olmesartan 20 mg	Metoprolol 50 mg, amlodipine 5 mg
Side effects of MRA	N/A	Painful gynecomastia	No	No	No	N/A	N/A
Status of adrenalectomy	Preoperatively	Preoperatively	Preoperatively	Preoperatively	Preoperatively	12 days after adrenalectomy	18 months after adrenalectomy

BP, Blood Pressure; HCTZ, hydrochlorothiazide; MRA, mineralocorticoid receptor antagonist; N/A, not applicable. ^a Office blood pressure measurements were consistently higher than home blood pressure readings, consistent with a white-coat effect.

At reassessment approximately one year after adrenalectomy, by which time all antihypertensive medications had been discontinued, home blood pressure monitoring showed recurrent hypertension, and amlodipine and metoprolol were reintroduced, the latter because of bothersome frequent ventricular extrasystoles. At the most recent evaluation, in August 2026, the patient remained normokalemic (4.8 mEq/L) with blood pressure controlled on this two-drug regimen (Table 1). Given the patient's severe obesity (BMI 40.1 kg/m²), this trajectory is consistent with reports that obesity is associated with a substantially lower rate of hypertension cure after adrenalectomy for unilateral PA, despite comparable biochemical remission [21].

3. Discussion

3.1 Clinical Importance of Primary Aldosteronism

The estimated prevalence of PA was estimated to affect around 5% of patients with hypertension seen in primary care, 10% of patients in referral centers and more than 20% of those with treatment-resistant hypertension [4]. Factors associated with a high prevalence include treatment-resistant hypertension, hypertension with hypokalemia, adrenal incidentaloma, obstructive sleep apnea, family history of early-onset hypertension or cerebrovascular events at a young age (<40 years), and family history of PA [5]. Until recently,

PA screening was recommended only for these high-risk patients. The most recent Endocrine Society guideline now recommends that all patients with SAH be screened for PA, but the condition remains underdiagnosed and undertreated, contributing to significant cardiovascular morbidity and mortality [1].

The primary goals of PA treatment are normalization of blood pressure, correction of hypokalemia, and reduction of aldosterone excess-associated cardiovascular morbidity and mortality. Isolated blood pressure control without effective aldosterone blockade is insufficient for adequate disease management [1, 5].

3.2 Surgical Treatment

For patients with unilateral APA, videolaparoscopic adrenalectomy is the treatment of choice, offering high rates of biochemical and clinical cure, with improvement or resolution of SAH in more than 80% of cases, significant reduction in antihypertensive medication requirements, and improved quality of life [6]. The procedure carries low risk, requires a short hospital stay, and yields better outcomes when performed early. Even in resistant SAH, surgery may promote complete remission and regression of organ damage [6]. Complete adrenalectomy, preferably by laparoscopic or retroperitoneoscopic approach, is indicated for confirmed unilateral PA, with better prognosis in younger patients, women, those with lower body mass index, and those with greater initial hypertension severity [5].

Recent evidence suggests that in selected cases of bilateral adrenal hyperplasia with significant asymmetry, unilateral surgery may be beneficial, particularly in younger patients with associated renal or cardiovascular disease, or those receiving polypharmacy [7]. Percutaneous radiofrequency ablation has emerged as a minimally invasive alternative for patients who are not candidates for conventional surgery, with high biochemical remission rates in preliminary studies [5].

3.3 Medical Treatment

The Endocrine Society recommends that patients with a confirmed diagnosis of PA receive specific treatment, medical or surgical, according to individual characteristics [1]. Pharmacological therapy is indicated when surgical intervention is not desired or indicated, especially if the probability of lateralizing PA is low based on initial investigations. For intermediate probability of lateralization, aldosterone suppression testing and individualized evaluation are recommended to guide treatment decisions. When suppression testing is positive or the probability of lateralization is high, adrenal lateralization assessment with imaging and adrenal vein sampling should be performed before deciding on the therapeutic approach [1].

Patients with bilateral adrenal hyperplasia, contraindication to surgery, or surgical refusal should be treated with MRAs [1, 4]. Preoperative MRA treatment is recommended to optimize blood pressure control and correct electrolyte disturbances, thereby reducing perioperative risks [1, 4]. Table 2 summarizes the main differences of the available MRAs. Studies indicate that incomplete mineralocorticoid receptor blockade, reflected by persistently suppressed renin, is associated with greater cardiovascular risk, reinforcing the importance of adequate dose adjustment [6]. MRA prescription must be individualized according to each patient's clinical response.

3.3.1 Spironolactone

Spironolactone is generally considered the first-line option among MRAs due to its lower cost, wide availability, and competitive mineralocorticoid receptor blocking action [1, 5]. High doses may be required in some PA patients but also increase the risk of adverse effects, particularly due to sex hormone receptor interactions, resulting in gynecomastia, breast tenderness, reduced libido, or menstrual irregularities [1, 5].

Table 2. Comparison of the Pharmacological Characteristics of Available Mineralocorticoid Receptor Antagonists [1, 4, 18, 19].

	Spironolactone	Eplerenone	Finerenone
Structural properties	Steroidal [17]	Steroidal [17]	Nonsteroidal [17]
Potency to MR	High [18]	Low [18]	High [18]
Selectivity to MR	Low [18]	Moderate [18]	High [18]
Half-life ^a	Long (>12 h ^b /≥24 h ^c) [18]	Medium/short (3 h ^b /4–6 h ^c) [18]	Short (2–3 h) [18]
Metabolites	Multiple, active [18]	No active metabolites [18]	No active metabolites [18]
CNS penetration	Yes [19]	Yes [19]	No; based on preclinical data [19]
Sexual side effects	Yes (gynecomastia) [18]	Less than spironolactone [1,4]	No signal in phase 2 and 3 studies [1, 4, 19]
Tissue distribution	Kidney > heart (at least 6-fold) [18]	Kidney > heart (~3-fold) [18]	Balanced kidney:heart (1:1) [18]
Starting to maximum daily dose	25–200 mg [4]	25–100 mg [4]	10–20 mg [4]

^a Half-life of active compound/metabolites. ^b Healthy volunteers. ^c In rodents. CNS, central nervous system; MR, mineralocorticoid receptor; nsMRA, non-steroidal mineralocorticoid receptor antagonist.

3.3.2 Eplerenone

Eplerenone is a highly selective MRA chemically derived from spironolactone, with 50–75% of the potency of spironolactone [4, 8] and fewer adverse effects due to lower affinity for androgen and progesterone receptors. This selectivity results in a lower incidence of adverse effects such as gynecomastia and sexual dysfunction. It may be employed when antiandrogenic side effects emerge but requires at least twice-daily administration due to its shorter half-life [3, 7]. Eplerenone has demonstrated the ability to improve microvascular endothelial function, vascular smooth muscle function, and arterial stiffness in patients with idiopathic hyperaldosteronism [9].

A comparative study evaluating eplerenone and spironolactone demonstrated that both agents are effective in reducing blood pressure and correcting PA-associated hypokalemia, with eplerenone being better tolerated [10]. Another randomized study comparing the efficacy of eplerenone and spironolactone concluded that eplerenone appeared to reduce systolic blood pressure more rapidly than spironolactone in patients with idiopathic hyperaldosteronism; by the end of follow-up, blood pressure levels were similar between the two groups [11]. However, in another comparative study, spironolactone demonstrated a greater antihypertensive effect [12], albeit associated with a higher incidence of adverse effects. Thus, eplerenone, given its higher cost and possibly lower efficacy, should be primarily indicated for patients who develop adverse effects with spironolactone, as was the case in the present report.

3.3.3 Non-Steroidal MRAs

Non-steroidal MRAs have the advantage of not being associated with hormonal adverse effects, such as gynecomastia and mastalgia [13, 14]. Unlike steroidal MRAs, finerenone possesses a non-steroidal chemical structure and exhibits distinct pharmacological

effects on mineralocorticoid receptor-mediated transcriptional activity. While these mechanistic differences may confer biological advantages, clinical data in patients with PA remain scarce [4]. Unlike steroidal MRAs, which accumulate preferentially in renal tissue (approximately 3- to 6-fold higher than in the heart), finerenone shows a balanced, roughly equieffective distribution between the heart and kidney [18]. Because renal mineralocorticoid receptor blockade is the principal determinant of kalemic and antihypertensive control in PA, doses of finerenone established for cardiorenal indications (10–20 mg/day) may be pharmacologically insufficient to achieve the degree of renal blockade required to counteract the marked, autonomous aldosterone excess of a unilateral adenoma, a pharmacological mismatch rather than a simple therapeutic failure of the drug class.

In a randomized controlled trial including patients with mild PA, finerenone achieved blood pressure reductions comparable to those observed with spironolactone, while causing a significantly smaller increase in serum potassium concentrations [15]. Conversely, a real-world study evaluating patients who switched from spironolactone to finerenone because of drug intolerance or limited eplerenone availability demonstrated less pronounced blood pressure control, as well as reduced normalization of plasma renin activity and serum potassium [16]. These findings suggest that finerenone may be a reasonable therapeutic option for selected patients with milder forms of PA or for those with concomitant diabetic kidney disease, in whom its established cardiorenal benefits may provide additional advantages. However, its efficacy in more severe forms of PA remains uncertain, and comparative studies with adrenalectomy are still lacking [4].

Table 2 describes the main mechanistic properties of the three main MRAs currently available. Differences in potency, tissue distribution, and half-life among these drugs may account for different outcomes in PA treatment.

3.3.4 Epithelial Sodium Channels (ENaC) inhibitors

ENaC inhibitors, such as amiloride and triamterene, act downstream the mineralocorticoid receptor by directly blocking sodium reabsorption in the distal nephron, offering an alternative, MR-independent mechanism to counteract aldosterone excess. Small clinical studies and a recent network meta-analysis support their use as a reasonable second-line option for patients unable to tolerate MRAs [2, 4]. However, ENaC inhibitors are not commercially available as a standalone formulation in Brazil, only in fixed-dose combination with a thiazide diuretic, and, as ENaC inhibitors were not used in the present case, they are not discussed further here.

3.4 Clinical Implications of the Case

The clinical course of our patient closely reflects current evidence regarding the management of unilateral primary aldosteronism. The diagnosis of an aldosterone-producing adenoma was established without adrenal vein sampling (AVS), in accordance with the exception explicitly outlined in the current Endocrine Society guideline for patients younger than 35 years in whom unilateral disease is highly probable, specifically, marked PA with spontaneous hypokalemia and a unilateral adrenal adenoma >1.0 cm on CT [1]. Our patient, diagnosed at 32 years of age, fulfilled all of these criteria: a markedly elevated aldosterone level (40.9 ng/dL) with spontaneous hypokalemia (potassium = 2.6 mEq/L), and a well-defined 1.7-cm unilateral adenoma with lipid-rich density on CT, supporting a confident biochemical and radiological diagnosis of unilateral APA without the need for invasive lateralization testing.

Two baseline characteristics of our patient are relevant to his clinical course. First, grade 3 obesity (BMI 40.1 kg/m²) is a recognized contributor to aldosterone dysregulation: human adipocytes secrete mineralocorticoid-releasing factors that directly stimulate adrenocortical aldosterone production, and adipose-derived aldosterone excess may have aggravated the hemodynamic and metabolic phenotype of his underlying APA [23]. Obesity

is also independently associated with a substantially lower probability of hypertension cure after adrenalectomy despite comparable biochemical remission [21], consistent with the recurrent hypertension observed in our patient roughly one year after surgery (see below).

Second, the patient's baseline azoospermia suggests pre-existing dysfunction of the hypothalamic-pituitary-gonadal axis. Because gynecomastia results from an increased estrogen-to-androgen ratio at the breast tissue level, patients with baseline gonadal dysfunction or lower testosterone may be more susceptible to the antiandrogenic effects of steroidal MRAs such as spironolactone, which further suppresses androgen synthesis and displaces estradiol from sex hormone-binding globulin [24]. This may partly explain the prompt and pronounced gynecomastia observed in our patient at a comparatively modest spironolactone dose (50 mg/day).

Although adrenalectomy was recommended as definitive treatment, the patient's initial refusal required prolonged medical management. Spironolactone partially corrected hypokalemia but treatment was discontinued because of painful gynecomastia. This side effect precluded increasing spironolactone dose. Combining a lower spironolactone dose with a potassium-sparing ENaC inhibitor such as amiloride was considered as an alternative strategy to mitigate antiandrogenic effects while preserving mineralocorticoid receptor blockade; however, amiloride is not commercially available as a single agent in Brazil, only in fixed-dose combination with a thiazide diuretic, which precluded this option. Switching to eplerenone resulted in complete resolution of the adverse effect while maintaining normalization of serum potassium, illustrating its favorable tolerability profile.

By contrast, temporary replacement with finerenone 20 mg/day was associated with recurrent hypokalemia. Because finerenone exhibits a balanced, roughly equieffective kidney-heart tissue distribution rather than the renal-predominant distribution of steroidal MRAs [18], and because the dose used corresponds to regimens developed for cardiorenal indications, this recurrence more plausibly reflects pharmacological under-dosing relative to the marked, autonomous aldosterone excess of a unilateral adenoma than a true failure of the drug class [15,16]. Dose escalation beyond 20 mg/day was not attempted, owing to off-label prescribing restrictions and cost considerations.

These findings reinforce the importance of individualized titration of MRAs with regular monitoring of serum potassium, renal function, and plasma renin activity to optimize mineralocorticoid receptor blockade [5]. Although eplerenone provided effective biochemical control and served as an excellent bridge to surgery, adrenalectomy achieved durable biochemical remission, with normalization of serum potassium in the absence of MRA therapy. Blood pressure control proved more variable: early postoperative readings were favorable, but hypertension recurred approximately one year after surgery, once all antihypertensive medications had been discontinued, requiring reintroduction of amlodipine and metoprolol, a pattern consistent with the patient's severe obesity, a recognized predictor of incomplete blood pressure cure despite biochemical remission after adrenalectomy [21].

This case therefore highlights both the clinical value of eplerenone in patients who develop spironolactone-related adverse effects and the fact that, while adrenalectomy reliably corrects the biochemical abnormality in unilateral aldosterone-producing adenoma, blood pressure outcomes may still require adjunctive antihypertensive therapy, particularly in patients with substantial comorbid cardiometabolic risk.

4. Conclusion

PA is a frequent and underdiagnosed cause of secondary hypertension. This case supports eplerenone as an effective and well-tolerated alternative to spironolactone in patients with aldosterone-producing adenoma who develop antiandrogenic adverse effects while awaiting definitive surgical treatment.

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