CASE REPORT

A Case Report: Discordant Imaging and Adrenal Venous Sampling in Primary Aldosteronism

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ABSTRACT

Accurate diagnosis and subtype classification are essential for determining the most appropriate treatment approach for primary aldosteronism (PA). While imaging methods such as adrenal computed tomography (CT) can identify structural abnormalities in the adrenal glands, adrenal venous sampling (AVS) remains the gold standard for localising aldosterone hypersecretion. We report a case of a 57-year-old-man with longstanding hypertension and noted to have hypokalaemia, elevated plasma aldosterone concentration and an increased aldosterone-to-renin ratio. Although adrenal CT suggested bilateral adrenal hyperplasia, AVS showed a lateralisation index ≥4, indicating right-sided unilateral aldosterone hypersecretion. He subsequently underwent a right retroperitoneoscopic adrenalectomy resulting in normalisation of potassium levels and improved blood pressure control. This case emphasises the crucial role of AVS in distinguishing between unilateral and bilateral aldosterone hypersecretion to ensure optimal patient management and improved clinical outcomes.

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INTRODUCTION

Primary aldosteronism (PA) poses significant cardiovascular and metabolic risks if left untreated. It accounts for 5-10% of all hypertension cases and up to 20% of resistant hypertension (1). Despite its clinical importance and potential for cure, PA is often underdiagnosed due to limited screening and the complexity and cost of confirmatory testing (2). There is also a significant risk of subtype misclassification, especially when diagnosis relies solely on imaging with studies showing a 22–28% discrepancy between imaging and adrenal venous sampling (AVS) (3). This report describes a 57-year-old man with resistant hypertension and biochemical evidence of PA. AVS confirmed unilateral aldosterone hypersecretion, prompting timely surgical intervention that resulted in the normalisation of biochemical markers and significant clinical improvement.

CASE REPORT

A 57-year-old man with a two-decade history of hypertension, diabetes mellitus and dyslipidaemia had regular follow-ups at a health clinic. Despite being on perindopril 8 mg and bisoprolol 10 mg daily, his blood pressure (BP) remained elevated resulting in multiple hospital admissions for hypertensive crises. In 2016, he presented to the emergency department (ED) at Ministry of Health (MOH) Hospital I with dizziness. His BP was 175/113 mmHg and he had left-sided weakness with muscle strength graded at 4/5. A computed tomography (CT) brain scan showed no infarction or haemorrhage. He was diagnosed with a hypertensive emergency and transient ischaemic attack and amlodipine 10 mg was

added. Serum potassium was 2.8 mmol/L, but no further investigations were done. He was discharged without neurological deficits. In 2022, he returned to the same hospital with a persistent headache and a BP of 202/127 mmHg. Hypokalaemia was noted but no additional investigations were performed. He was treated for hypertensive urgency with a STAT dose of captopril 25 mg and monitored in ED before being discharged with his usual antihypertensives (perindopril, bisoprolol, amlodipine).

Table I: Baseline routine blood investigations

Serum	Results from MOH Hospital I		Reference interval
	February 2016	March 2022	
Urea (mmol/L)	3.4	3.5	3.2 – 8.2
Creatinine (µmol/L)	83	109	62 – 115
Sodium (mmol/L)	143	138	136 – 145
Potassium (mmol/L)	2.8	3.3	3.4 – 4.5
Chloride (mmol/L)	100	100	98 – 107
Phosphate (mmol/L)	0.80	0.83	0.78 – 1.65
Magnesium (mmol/L)	0.89	0.90	0.66 – 1.07

In October 2023, the patient presented to a private hospital with lower limb swelling. His early-onset hypertension and hypokalaemia (Table I), previously uninvestigated, prompted evaluation for hyperaldosteronism. Prior to this, potassium supplements were prescribed, normalising his potassium levels. The assessment revealed classic signs of PA, including hypertension with elevated plasma aldosterone, an increased aldosterone-to-renin ratio (ARR) and high urinary potassium excretion (Table II). Adrenal CT showed bilateral adrenal hyperplasia, more pronounced on the left (Table II).

He was referred to MOH Hospital II for further management where he was seen in the endocrine clinic and scheduled for AVS. Amlodipine was changed to felodipine 5 mg daily due to bilateral pedal oedema. To optimise AVS accuracy and maintain BP control, perindopril was replaced with prazosin 1 mg twice daily, while bisoprolol was continued. The AVS results showed a selectivity index (SI) >5, confirming successful cannulation of both adrenal veins. At 0 and 5 minutes, the lateralisation index (LI) was ≥4, indicating unilateral hypersecretion from the right adrenal gland (Table III).

Based on the AVS results, the patient was scheduled for a right retroperitoneoscopic adrenalectomy.

Table II: Investigation workup for Primary Aldosteronism (October 2023)

Serum	Results October 2023	Reference interval
Urea (mmol/L)	3.9	3.2 – 8.0
Creatinine (µmol/L)	80	44 –132
eGFR (ml/min/1.73m^2)	86	>60
Sodium (mmol/L)	139	137 – 150
Potassium (mmol/L)	3.7	3.5 – 5.3
Chloride (mmol/L)	104	99 – 111
Plasma		
Aldosterone (pmol/L)	917.0	61.2 – 977.8 (Upright) 32.4 – 653.7 (Supine)
Renin direct (mU/L)	5.7	4.4 – 46.1 (Upright) 2.8 – 39.9 (Supine)
Aldosterone/Renin ratio (pmol/IU)	160.9	<36
Urine		
Urine potassium (mmol/L)	24.6	>15
CT scan of adrenal gland	Left adrenal gland: Medial limb of left adrenal gland is thickened with mild nodular outline and homogenous enhancement, measures 1 cm in thickness. The apparent nodular thickening at medial limb shows absolute constrast washout >60 % (HU on plain study: +14.9HU portovenous phase: 93.5HU, and delayed 15 minute: +36.7HU). Right adrenal gland: Lateral limb of right adrenal gland is mildly thickened with homogenous enhancement, measures 0.7 cm in thickness. No definite focal enhancing adrenal nodules. Conclusion: Suggestive for bilateral adrenal hyperplasia (more conspicuous on the left).	

eGFR estimated glomerular filtration rate; CT computed tomography; HU Houndsfield unit

Preoperatively, his BP was optimised. Intraoperatively, adrenal tissue biopsy confirmed adrenal hyperplasia without malignancy. Based on these findings, the final diagnosis was PA secondary to right adrenal hyperplasia. Postoperatively, all antihypertensive medications were withheld and the patient remained normotensive before discharge. One month after the surgery, his potassium level was 4.4 mmol/L and his BP was well-controlled on felodipine 10 mg once daily.

Table III: Results of Cosyntropin-Stimulated Adrenal Venous Sampling (AVS) at MOH Hospital II

Duration	Site	Aldosterone (pmol/L)	Cortisol (nmol/L)	Cortisol AV:P	A/C	LI
0 min	Left AV 1	1,769	9634	8	0.2	0.1
	Peripheral 1	523	1199		0.4	-
5 min	Left AV 2	2,980	14359	13	0.2	0.2
	Peripheral 2	493	1127		0.4	-
10 min	Left AV 3	7,360	16729	15	0.4	0.3
	Peripheral 3	526	1144		0.5	-
0 min	Right AV 1	15653	11264	10	1.4	8
	Peripheral AV 1	554	1134		0.5	-
5 min	Right AV 2	15,918	15513	14	1.0	5
	Peripheral AV 2	553	1125		0.5	-
10 min	Right AV 3	18413	12956	11	1.4	3
	Peripheral AV 3	575	1204		0.5	-

AV Adrenal vein, P – peripheral, A-Aldosterone, C-Cortisol, LI -Lateralisation index

DISCUSSION

How do we screen and diagnose PA?

a) *Screening and diagnosis*

The ARR is the most reliable screening test for PA. Laboratory reports should include plasma aldosterone concentration, plasma renin activity or direct renin concentration and ARR (1). An ARR <25 is negative (PA unlikely), 25–35 is indeterminate and >35 is positive (high PA likelihood). PA can be ruled out if plasma aldosterone is <170 pmol/L (6 ng/dL) (4). Screening is recommended for individuals who meet any of the criteria in Table IV (2). This patient met at least three criteria, including poorly controlled BP >150/100 mmHg despite multiple antihypertensives and spontaneous hypokalaemia. Based on these factors, the patient's case aligns with the Endocrine Society guidelines, supporting further testing and adrenalectomy for definitive management (2). The patient's ARR was 160.9 pmol/IU, and plasma aldosterone was 917.0 pmol/L (approximately 33 ng/dL), both well above their respective diagnostic thresholds, confirming a high likelihood of PA. These results indicate a positive screening for PA.

b) *Confirmatory test*

Patients with a positive ARR usually need confirmatory testing for PA, except those with spontaneous hypokalaemia, undetectable renin and aldosterone >550 pmol/L, where PA is likely and testing is skipped (2). This patient met these criteria, so imaging was performed instead.

Table IV: Recommendation for PA screening (2)

Screening for PA is advised for individuals who meet any of the following criteria:

- Subjects with sustained BP above 150/100 mm Hg on each of three measurements obtained on different days;
- Subjects with hypertension (BP>140/90 mm Hg) resistant to three conventional anti-hypertensive drugs (including a diuretic);
- Subjects with controlled BP (<140/9 mm Hg) on four or more anti-hypertensive drugs;
- Subjects with hypertension and spontaneous or diuretic-induced hypokalaemia;
- Subjects with hypertension and adrenal incidentaloma;
- Subjects with hypertension and sleep apnoea;
- Subjects with hypertension and a family history of early onset hypertension or cerebrovascular accident at a young age (<40 years);
- All hypertensive first-degree relatives of patients with PA.

PA, primary aldosteronism; BP, blood pressure

c) *Subtype evaluation*

Once PA is confirmed, subtype evaluation is performed, including a CT scan of the adrenal glands and possibly AVS. This helps determine whether PA is due to an adenoma or hyperplasia, guiding the choice between adrenalectomy and mineralocorticoid receptor antagonist therapy (1).

i. Adrenal CT

Adrenal CT is recommended as the first step in subtype testing for all PA patients to exclude large masses suggestive of adrenocortical carcinoma and to assist interventional radiologists and surgeons when necessary (2). In this case, the adrenal CT findings (Table II) suggested bilateral adrenal hyperplasia, more pronounced on the left side with no definite focal enhancement of adrenal nodules observed on the right side.

ii. AVS

If surgical treatment is feasible and desired by the patient, AVS should be performed by an experienced radiologist. As the gold standard test, AVS distinguishes unilateral adrenal disease [such as an aldosterone-producing adenoma (APA) or unilateral adrenal hyperplasia (UAH)] from bilateral disease such as idiopathic adrenal hyperplasia in patients with PA (2). Unilateral aldosterone excess is usually treated with adrenalectomy while bilateral overproduction is managed medically with mineralocorticoid receptor antagonists and if needed, potassium-sparing diuretics like amiloride (2, 5).

A pre-procedure consultation with the interventionalist is recommended to ensure proper medication management, including the discontinuation of renin-angiotensin aldosterone system (RAAS)-interfering medications such as ACE inhibitors, angiotensin receptor

blockers, and mineralocorticoid receptor antagonists. These medications can falsely lower lateralisation rates by increasing renin levels and stimulating adrenal cortices. Serum potassium should also be checked and corrected as hypokalaemia can suppress aldosterone and affect results (5). In this patient, perindopril (ACE inhibitor) was stopped and replaced with prazosin while felodipine and bisoprolol were continued. Prazosin, an alpha-blocker, does not affect the RAAS, making it a suitable alternative to optimise BP. The patient was also prescribed potassium supplements to maintain normal levels before the procedure.

AVS has superior diagnostic accuracy for unilateral aldosterone excess with 95% sensitivity and 100% specificity compared to adrenal CT's 78% sensitivity and 75% specificity (2). CT suggested bilateral adrenal hyperplasia, predominantly on the left, but AVS confirmed unilateral hypersecretion from the right adrenal gland indicating unilateral disease. This highlights AVS's superior accuracy in localising aldosterone overproduction and guiding management.

Cosyntropin, a synthetic form of adrenocorticotropic hormone (ACTH), is administered during AVS to reduce stress-related aldosterone fluctuations, increase the cortisol gradient between adrenal vein and inferior vena cava (IVC) samples and stimulate aldosterone secretion from a unilateral adenoma. Cannulation is typically done through transfemoral access with blood samples taken from the right and left adrenal veins as well as from peripheral or IVC blood. This patient's samples for plasma aldosterone and cortisol were collected in pre-labelled bottles (4).

In this patient, adrenal cortisol levels increased significantly after ACTH stimulation while peripheral cortisol remained stable. This emphasises ACTH's role in improving the cortisol gradient resulting in a higher SI that confirms successful adrenal vein cannulation. The SI (ratio of adrenal to peripheral cortisol) indicates catheter placement adequacy. An SI ≥5 with cosyntropin confirms successful cannulation while SI ≥2 without cosyntropin is sufficient and SI <2 indicates failed cannulation (4). SI values >5 at 0, 5, and 10 minutes bilaterally in this patient confirmed successful cannulation.

LI, the aldosterone to cortisol ratio (A/C) between the dominant and non-dominant adrenal glands assesses aldosterone lateralisation (4). An LI ≥4.0 with ACTH stimulation or ≥2.0 without ACTH stimulation indicates unilateral aldosterone hypersecretion (APA or UAH) (2). In this patient AVS at 0 and 5 minutes showed an LI ≥4, indicating right-sided aldosterone access.

Although AVS is clinically valuable, its limited availability at specialised centres makes it relatively inaccessible. Concerns about procedural risks such as venous rupture and adrenal infarction with early studies reporting complication rates of up to 10% have contributed to its underuse (5).

CONCLUSION

AVS is considered the gold standard for aldosterone secretion lateralisation and for distinguishing between unilateral and bilateral forms of PA. If PA had been considered earlier, the patient could have been spared years of poorly controlled hypertension and its associated complications. This case underscores the critical need for heightened clinical awareness and timely evaluation of PA in patients with resistant hypertension and hypokalaemia to ensure accurate diagnosis and effective, targeted treatment.

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