Use of partial data from failed adrenal venous sampling to guide surgical management in primary aldosteronism; a case report and review of literature

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Abstract

Primary aldosteronism is associated with increased morbidity, mortality, and poor quality of life. Attempts should be made to diagnose, establish subtype classification, and offer the most appropriate diagnosis depending on the subtype. Adrenal venous sampling is the gold standard method in subtype classification. However, failure to cannulate the right adrenal vein is commonly encountered. A 55-year-old male with hypertension for 21 years, presented with generalized body aches, paraesthesia, and cramps for three months. His blood pressure was controlled on telmisartan and amlodipine. Serum potassium was 2.9 mmol/L. Serum aldosterone was elevated with suppressed plasma renin concentration. Magnetic resonance imaging of the abdomen showed a well-defined round 1.4 cm×1.3 cm isointense lesion in the right suprarenal gland and multiple bilateral renal cysts. During bilateral adrenal vein sampling, the right adrenal vein was not cannulated. Aldosterone: cortisol ratio of the left adrenal vein and inferior vena cava were 0.0264 and 0.0699, respectively. Left adrenal vein/ inferior vena cava index was 0.377, suggesting contralateral aldosterone excess. He underwent laparoscopic right adrenalectomy, which resulted in the resolution of hypertension and hypokalaemia. Careful analysis of partial data from 'failed' adrenal vein sampling can support management decisions avoiding unnecessary repetition of invasive procedures.

Introduction

Primary aldosteronism is the commonest secondary cause of hypertension (1). In addition to complications of hypertension, it is associated with aldosterone-specific cardiovascular and renal morbidity and mortality. poor quality of life. Therefore, diagnosis and optimal management of this condition would improve patient outcomes beyond blood pressure control. Improvement of hypertension and hypokalaemia is likely to occur in most patients with appropriate management, though cure of hypertension is seen only in 30-60% of the patients (1).

In the management of primary aldosteronism, one of the most important steps is the subtype classification between unilateral aldosterone-producing adenoma (APA) and bilateral idiopathic hyperaldosteronism (IHA). Unilateral APA is treated by ad-

renalectomy, whereas bilateral IHA is treated medically using mineralocorticoid receptor antagonists. Adrenal imaging using computed tomography (CT) and magnetic resonance imaging (MRI) performs poorly in differentiating between two main subtypes (2, 3). Except in individuals younger than 35 years, this helps localization in less than 60% of the patients. As a result, bilateral adrenal venous sampling (AVS) has become the mainstay of subtype classification.

Table 1 Summary of investigations at the time of the presentation		
Investigation	**Result**	**Reference range**
Haemoglobin (g/dL)	13.9	11-16
Mean corpuscular volume (fl)	87.1	80-96
White cell count ($\times 10^9$/L)	8.2	4-11
Platelet count ($\times 10^9$/L)	375	150-450
Urinalysis	Normal	
Serum creatinine (mg/dL)	1.02	0.7-1.2
Sodium (mmol/L)	140	135-145
Potassium (mmol/L)	2.9	3.5-5.1
Spot urinary potassium (mmol/L)	22.5	> 20 suggestive of renal loss
Plasma bicarbonate (mEq/L)	35	22-28
Aspartate transaminase (U/L)	19	<40
Alanine transaminase (U/L)	34	<40
Bilirubin (mg/dL)	0.7	0.5-1.1
HbA1c	5.6%	<5.7%
Thyroid-stimulating hormone (mIU/l)	0.87	0.5-4.7
Twenty-four-hour urinary metanephrine (µg/dL)	217	<350
Aldosterone (ng/dL)	37	1.76-23.2
Plasma renin concentration (mIU/mL)	1.98	2.8-39.9
Aldosterone: renin ratio	18.64	<3.7

Successful cannulation of both adrenal veins is technically demanding and requires a high degree of expertise. Cannulation of the right adrenal vein is particularly difficult. Though experienced centers have reported successful cannulation rates of both sides in up to 96% (3), failure to cannulate the right side can be seen in more than 30% in low volume centers (4, 5). Therefore, failure to cannulate one side can limit the benefit of this invasive procedure. Repeat testing would increase the cost, radiation exposure, and contrast agents.

Therefore, it is imperative to try and interpret partial data from these 'failed' procedures while maintaining the accuracy of the clinical decision.

Though the cannulation of the right side was not successful in our patient described below, careful assessment of the data allowed successful surgery for primary aldosteronism.

Case Report

A 55-year-old lawyer presented with generalized body aches, paraesthesia, and cramps for three months. Symptoms were slowly progressing over time without associated fever, muscle weakness, or loss of weight or appetite.

He was diagnosed with hypertension 21 years back. Since then, blood pressure control was satisfactory with two antihypertensive agents. At the time of the presentation, he was on telmisartan and amlodipine. Over the last few months, blood pressure control had not been achieved. There were no other co-morbidities. He had undergone left meniscectomy 25 years back and tonsillectomy five years back. At the time of tonsillectomy, serum potassium was 3.4 mmol/L. This had not been further pursued at that time. He has never smoked, and he is a teetotaller.

While being evaluated, he was found to have hypokalaemia (2.9 mmol/L). He was not on any other drugs in addition to the above antihypertensive agents. There was no polyuria, altered bowel habits, or diarrhea. He was started on oral potassium chloride. Potassium normalized to 3.9 mmol/L. Results of the laboratory investigations performed during the presentation are summarised in Table 1.

In the presence of hypertension, hypokalaemia, and metabolic alkalosis, a presumptive diagnosis of primary aldosteronism was made.

Aldosterone renin ratio was performed while on telmisartan, amlodipine, and oral KCL. Though

Figure 1 Isointense lesion in the right suprarenal gland
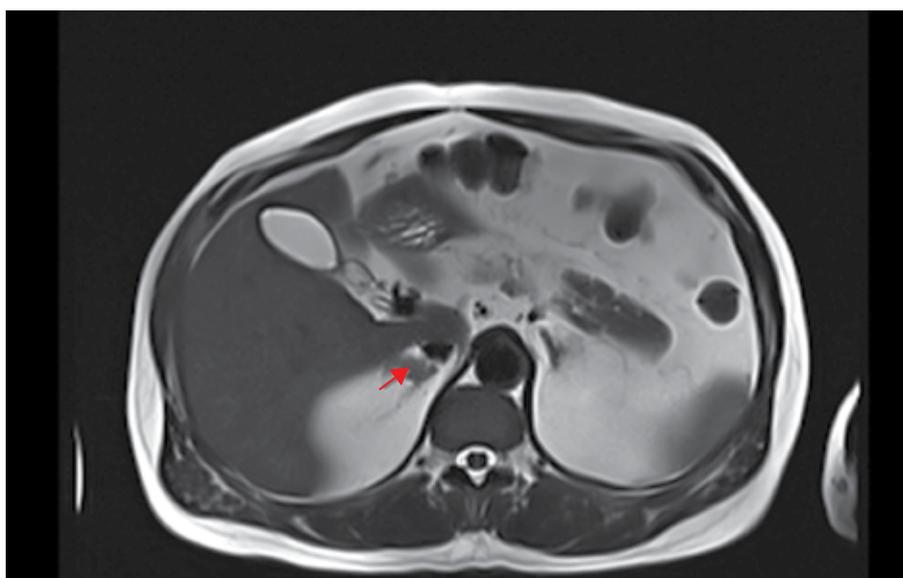
T2 weighted axial MRI of the abdomen showing a well-defined iso-intense lesion in the right adrenal gland measuring 1.4 × 1.3 cm. There is a clear signal drop-out in the out of phase imaging indicating fat within the lesion. There are no calcifications. The left adrenal gland appears normal.

telmisartan can potentially produce false-negative results, it was not discontinued due to persistent hypokalaemia while taking it. Due to the presence of aldosterone level > 20 ng/dL, renin lower than the reference range, and spontaneous hypokalaemia, it was considered that he does not need confirmatory testing (6, 7).

The diagnosis of primary aldosteronism was made. Magnetic resonance imaging of the abdomen showed a well-defined rounded 1.4 cm×1.3 cm iso-intense lesion in the right suprarenal gland. The left adrenal gland appeared normal (Figure 1).

There were multiple bilateral renal cysts. Renal cysts are known to occur in patients with primary aldosteronism (8).

He underwent unstimulated AVS after changing medicines to extended-release prazosin and sustained-release verapamil.

Images acquired during the procedure are shown in figure 2. The results of the study are shown in Table 2.

Findings were suggestive of a lack of successful cannulation of the right adrenal vein. But following calculation was performed using the available data.
Aldosterone/ cortisol ratio of left adrenal vein (LAV) = 0.0264
Aldosterone/ cortisol ratio of inferior vena cava (IVC) = 0.0699
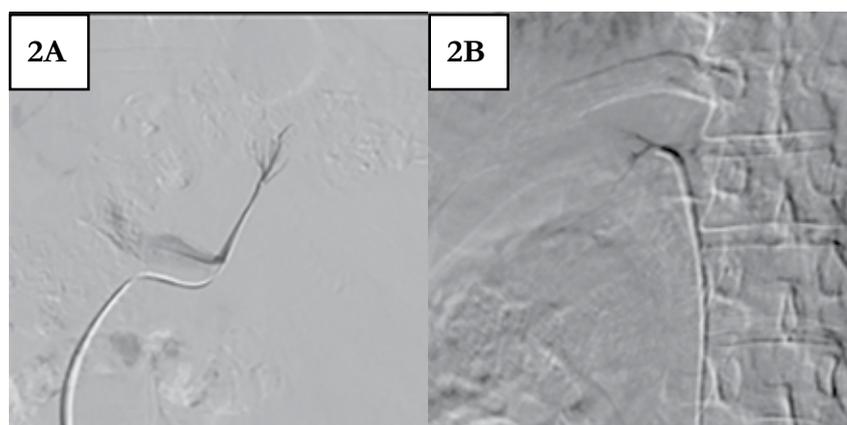LAV/IVC index: 0.0264/0.0699 = 0.377

Figure 2 Fluoroscopic images were acquired during catheterization of the left (Figure 2A) and presumed right (Figure 2B) adrenal veins

Table 2 Results of bilateral adrenal vein sampling

Site	Cortisol (nmol/L)	Aldosterone (ng/dL)	Selectivity index (adrenal vein cortisol/ IVC cortisol)
Left adrenal vein	905	23.9	3
Right adrenal vein	291	22.7	0.98
Inferior vena cava	296	20.7	N/A

*IVC- inferior vena cava

Since AV/IVC index <0.5 suggests unilateral disease from the opposite side, he underwent laparoscopic right adrenalectomy (9). Aldosterone dropped to 2.59 ng/dL one day after surgery. Within two weeks, blood pressure became normal without any antihypertensive agent. One week after surgery, serum potassium was 4.2 mmol/L without replacement.

One month after surgery, serum creatinine was 1.8 mg/dL with an eGFR of 41.7 ml/min/1.73m2. This decline in eGFR after surgery is likely due to relative hyperfiltration seen in primary aldosteronism (10). Serum creatinine stabilized thereafter with no further increase. Histology confirmed completely resected 10 mm right adrenal cortical adenoma. Currently, the patient is asymptomatic and feels well.

Discussion

Bilateral AVS is the gold standard method of subtype classification in primary aldosteronism. In the Sri Lankan setting, sequential catheterization of left and right adrenal veins was performed. Samples are obtained for cortisol and aldosterone levels. Same samples are obtained from the inferior vena cave or femoral vein as well. Successful cannulation is defined using the selectivity index. An unstimulated AVS selectivity index of ≥ 2 suggests successful cannulation of the given adrenal vein (5). When both sides are cannulated, the lateralization index is calculated by dividing the aldosterone/ cortisol ratio of the higher side from that of the lower side. Value ≥ 4 is commonly used to define unilateral APA (11).

The major limitation of interpreting AVS data is the failure to cannulate the right side. Failed right side cannulation is a common occurrence, particularly in low volume centers (4, 5). This is due to multiple reasons, including the short length, small caliber, and angulation at the origin of the right adrenal vein. In addition, it can arise in conjunction with hepatic vein branches, and it can be confused with small hepatic vein branches which lie nearby (11). The lateralization index cannot be calculated when one side is not calculated. As a result, traditionally, these patients had to undergo repeat AVS increase cost, radiation, and contrast agent exposure.

In such a scenario use of partial data from the successful left side can be evaluated carefully to guide management. Some studies have shown that suppressed cortisol corrected aldosterone levels in the cannulated adrenal vein compared to that of the IVC indicates contralateral APA (12). This had been systematically studied using 36 patients in the derivation cohort and 26 patients in the validation cohort. They have concluded that LAV/IVC aldosterone: cortisol ratio (AV/IVC index) <0.5 would reliably confirm contralateral aldosterone success. Similarly, a value >5.5 would reliably suggest ipsilateral disease (9). Values in between would require repeat AVS. Using their data, authors have indicated that this approach would prevent 50% repeat AVS procedures.

This was re-examined using simulated unilateral data from 150 patients who had successful bilateral AVS (13). By comparing unilateral data with the final diagnosis, they have confirmed that AV/IVC index <0.5 confirms contralateral unilateral disease. Using this cut-off will not lead to any inappropriate adrenalectomies though some contralateral disease will be missed. However, according to their data, it was shown that using AV/IVC index >5.5 would lead to inappropriate adrenalectomies in 18% since those patients have had bilateral disease. One limitation in applying the data from the above two studies to our patient is the lack of cosyntropin stimulation in him. Both studies have defined cut-offs using data from patients who received cosyntropin stimulation. Due to the lack of high-quality data on such patient populations, we had to depend on the assumption that markedly suppressed aldosterone in the contralateral adrenal vein would reliably exclude bilateral disease irrespective of cosyntropin stimulation. A successful outcome in our patient, confirmed biochemically and by resolution of hypertension and hypokalaemia despite long-standing disease, strengthens our approach.

Conclusions

While it is well established that an experienced interventionist must perform AVS to improve the results of the procedure, it should be interpreted by

an experienced clinician who can utilize data from even 'failed AVS' minimizing unnecessary repeat procedures and adrenalectomies.

List of abbreviations

APA- aldosterone-producing adenoma
AV- adrenal vein
AVS- adrenal venous sampling
CT- Computed tomography
eGFR- estimated glomerular filtration rate
IHA- Idiopathic hyperaldosteronism
IVC- inferior vena cava
MRI- Magnetic resonance imaging

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