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A case dilemma: When the IVC aldosterone cortisol ratio is higher than the adrenal vein ratio in a case of primary hyperaldosteronism

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Abstract

Primary aldosteronism (PA) is an underdiagnosed cause of resistant hypertension. The classic presentation is hypertension and hypokalemia. It is presented commonly as either bilateral or unilateral adrenal hyperplasia. The conformed test that has the ability to distinguish between them is Adrenal venous sampling (AVS) which has higher challenges in the right adrenal gland due to the anatomical course of the right adrenal vein that is supplied.

Therefore, AVS is crucial in the subtype classification of PA, as relying on imaging alone can miss small APA (false negative) or identify coincidental nonfunctioning adenomas (false positive). In our patient, the successfully performed AVS test based on cortisol levels showed paradoxically low aldosterone-cortisol ratios bilaterally. This would raise the possibility of ectopic aldosterone-producing adenoma or super selective cannulation of the right adrenal vein which was the situation of our patient.

Keywords: Adrenal venous sampling, Primary aldosteronism, ratio of aldosterone to cortisol

Introduction

Primary aldosteronism (PA) is a common cause of drug-resistant hypertension. It is estimated that PA may be diagnosed in 11% of patients referred to specialized hypertension centers [1]. Most patients with PA have either a unilateral aldosterone-producing adenoma (APA), that required laparoscopic adrenalectomy as definitive treatment [2], or bilateral adrenal hyperplasia, which is treated with mineralocorticoid receptor antagonists Such as (Spironolactone) [3]. Currently, Adrenal venous sampling (AVS) is the most precise test used for the measurement of aldosterone, If the sample was collected properly, by an experienced interventional radiologist it can distinguish between unilateral adenoma or bilateral hyperplasia, and cases of co-incidental nonfunctioning cortical adenomas, Hence, the therapeutic decision depends on the lateralization of aldosterone hypersecretion [3].

However, the situation will be more challenging when the cannulation is successful but the Inferior Vena Cava (IVC) Aldosterone Cortisol ratio is higher than both of the adrenal vein ratio. Under this issue, we share a case with this scenario.

Case presentation

A 44-year-old male patient who had been Hypertensive for 10 years was treated with amlodipine/valsartan 10/160 mg daily. He has a family history of essential hypertension. He has a history of persistent Spontaneous Hypokalemia with the lowest potassium concentration of 2.90 meq/L requiring admissions for intravenous potassium infusion and he was kept on oral potassium chloride 40 mEq TID. His blood pressure was poorly controlled with an average of 145/ 95 mmHg. He has hyperlipidemia treated with statin and he is a known case of primary hypothyroidism since 2012 treated with Levothyroxine 100 mcg daily. He was always clinically and biochemically euthyroid and had no symptoms or signs of Cushing's syndrome.

Investigations

The baseline laboratory test results are shown in Table 1. He has a plasma aldosterone concentration of 26.0 ng/dl and a direct renin concentration of less than the lower detectable limit (< 1 ng/dl). Post Dexamethasone Suppression Test was negative. The patient did not require a confirmatory test because he has spontaneous hypokalemia with plasma aldosterone concentration of more than 20 ng/dl.

Table 1: The baseline laboratory test

Test	Result	Reference Range
Potassium	2.9 mmol/L	3.5 – 5.1 mmol/L
TSH	1.9 mIU/l	0.35 – 4.94 mIU/l
Creatinine	90.9 umol/l	63.6 – 110.5 umol/l
Aldosterone	26.0 ng/dl	2.5-39.5 ng/dl
Aldosterone Renin Ratio	>260	<19
Renin	<1.0 ng/l	2.6-28.0 ng/l
Sodium	139 mmol/l	136-145 mmol/l

Adrenal Triphasic CT scan showed suspicious nodule of the right adrenal gland with coincidence finding of gallstones (Fig. 1).

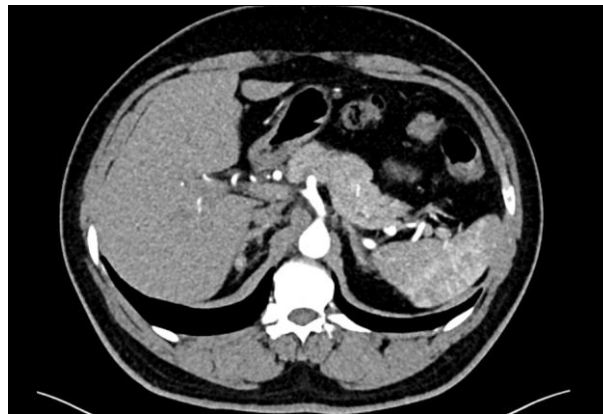


Fig 1: Adrenal Triphasic CT scan

The patient was keen to pursue surgical management (unilateral adrenalectomy) of his primary aldosteronism with the resolution of hypokalemia and cure or better control of his hypertension. So the next step, AVS was done by continuous cosyntropin

infusion protocol (50 mcg per hour) which is started 30 minutes before sequential sampling of the right adrenal vein, left adrenal vein, and IVC and was infusion continued throughout the procedure. All sampling was taken and measurements as showing in Table 2.

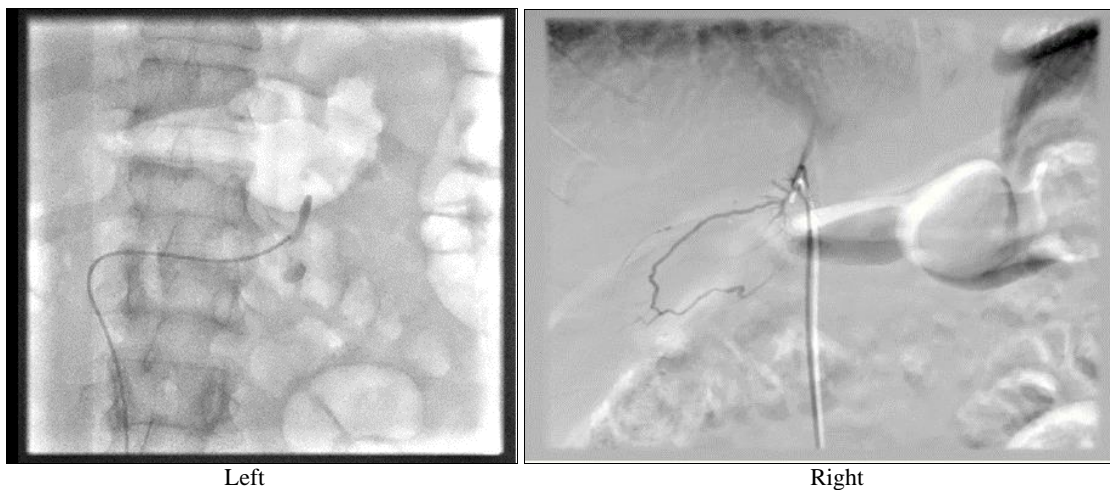


Table 2: Adrenal vein

	Right Adrenal Vein	Left Adrenal Vein	IVC
Aldosterone	798	66.5	38
Cortisol	31,562	14,832.9	815.5
Aldo/Cortisol Ratio	0.025	0.004	0.046
Aldo lateralization Ratio	Right : Left is 6.25		

Aldosterone in ng/dl. Cortisol in nmol/L

Hypersecretion and the aldosterone cortisol ratio on the left adrenal vein was significantly lower than the IVC which is called contralateral suppression. However, the aldosterone-cortisol ratio right adrenal veins were surprisingly lower than that from IVC. This patient has most likely right adrenal APA but the AVS did not prove it. This may be because the catheter was embedded too far into the Right adrenal vein and bypassed the APA.

In our patient, the cortisol-corrected aldosterone lateralization ratios between the right and left adrenal veins are greater than 4 which was suggestive of Right Unilateral

Treatment

The patient refused to repeat the AVS and after a thorough

discussion with the patient, he elected to go for surgery. He underwent a laparoscopic right adrenalectomy and cholecystectomy. The plasma aldosterone concentration the following day of surgery was 5.7 ng/dL and the potassium was 4.5 mmol/L. Treatment with potassium chloride and amlodipine/valsartan combination was discontinued. During his post-adrenalectomy hospitalization, he developed hypotension 1 day after surgery and his morning cortisol level was less than 27.6. He was started on stress dose hydrocortisone which was changed to oral prednisolone 10 mg po od upon discharge. The patient was advised to monitor his blood pressure and to repeat his potassium level after 1 week.

Histopathology

Right Adrenal gland weight was 12.70 g with adrenocortical adenoma (8 mm).

Follow up

The patient was normokalemic over the first month after surgery and his blood pressure has been cured. His Pituitary Adrenal Axis had recovered and the Glucocorticoids were discontinued Table 3. He continued to have normal potassium concentration and blood pressure over 1-year post-adrenalectomy.

Table 3: Post Adrenalectomy Laboratory

Post Adrenalectomy Laboratory Results	
Potassium	4.50 mmol/L
Aldosterone	5.7 ng/dl
Total Cortisol	- 226.60 nmol/l

Discussion

In the early years of AVS, Retrograde injection of contrast medium in the adrenal vein was done as a method to confirm the success of catheterization, and a venogram was taken to visualize the abnormal vascular tree that can be seen in case of aldosterone-producing adenoma (APA). In order to decrease the risk of adrenal vein rupture. With new imaging, the availability of CT and MRI, adrenal venography is no longer indicated. Nevertheless, confirmation of the proper position of the catheter tip via injection of a small amount of dye with gentle pressure is still done [1].

For the right AVS, the drainage right adrenal vein into the accessory hepatic vein need to be confirmed by injection of a very small amount of contrast on the tip of a suitable catheter should be performed just before and after blood extraction located in the right adrenal vein and not the hepatic venous tributaries. For the left AVS, the tip of the catheter should be placed beyond the orifice of the left inferior phrenic vein but including all the left adrenal tributaries [1].

When the displacement of the catheter during sample collection occurred, adrenal hormones concentration will be high in the blood taken from the inferior vena cava above the adrenal veins due to the laminar blood flow may prevent the complete dilution of blood coming from the adrenal veins. In the other hand, a low concentration of aldosterone coming from hepatic veins lying close to the adrenal veins may also be true [4].

As the data showed the number of AVS cannulation cases from 2005 to 2014 and the success rate by year [3].

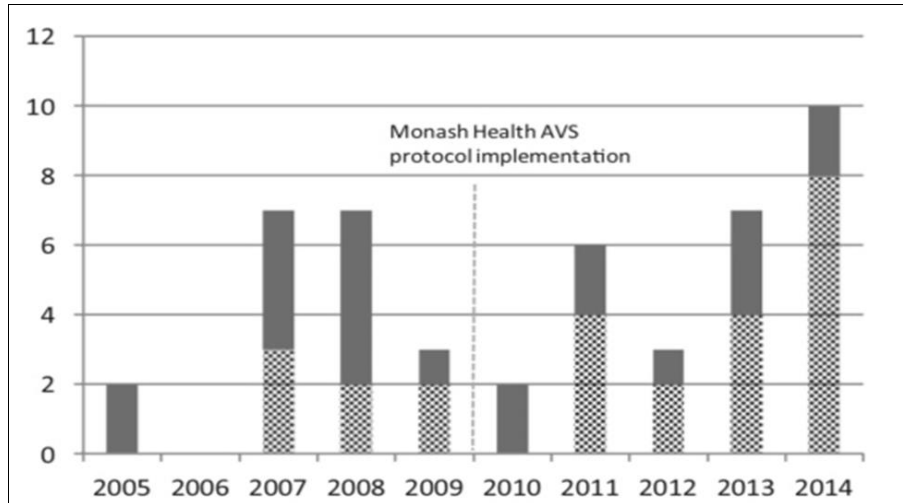


Fig 1: Number of adrenal vein sampling (AVS) cases and success rates by year. Total n= 19 AVS cases performed in 2005-2009 but results only available for n = 17; 7 cases had bilateral successful cannulation. Total n =28 AVS cases performed 2010-2014; 18 cases had bilateral successful cannulation (◐), Unsuccessful bilateral cannulation; (○), Successful bilateral cannulation.

The way to confirm the success of cannulation of adrenal vein sampling (AVS) is a measurement of the ratio of cortisol concentration in an adrenal vein and the infra-adrenal IVC (Cortisol adrenal /Cortisol IVC). The published criteria for appropriate adrenal vein sampling range from Cortisol adrenal /Cortisol IVC is $\geq 2-5$ with cosyntropin and from C adrenal /C IVC is $\geq 1.1-3$ without cosyntropin [4]. The use of the aldosterone to cortisol (AC) ratio as a parameter to compare both adrenals has a high value as it eliminates variable dilution of adrenal venous blood. The lateralization of aldosterone secretion is assessed by the

ratio AC dominant adrenal /AC nondominant adrenal, The reported criteria for abnormal lateralization of aldosterone secretion also vary significantly, with the ratio AC dominant adrenal /AC nondominant adrenal varying from ≥ 2 to ≥ 5 [4]. As here our patient, during the analysis of AVS sampling results showed the AC ratio confirmed the abnormal lateralization of the right adrenal gland which is patient clearly improved after the removal of the gland, but we noted the IVC AC Ratio concentration was higher than the right adrenal AC Ratio which is unexpected due to dilutional effect in IVC, The only hypothesize that may

explain is the unintentional deep cannulation in branches of the adrenal vein.

Conclusion

Primary aldosteronism (PA) is an underdiagnosed cause of resistant hypertension. The conformed test is Adrenal venous sampling (AVS) which has higher challenges in the right adrenal gland due to the anatomical course of the right adrenal vein that is supplied. So the technical challenge during cannulation is not uncommon which raises the possibility the catheter was embedded too far into the Right adrenal vein and bypassed the aldosterone-producing adenoma (APA) which may be explained why the Inferior Vena Cava (IVC) Aldosterone Cortisol ratio is higher than the adrenal vein ratio.

Conflict of Interest

Not available

Financial Support

Not available

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