CASE REPORT

Primary hyperaldosteronism: a case of unilateral adrenal hyperplasia with contralateral incidentaloma

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SUMMARY

Primary hyperaldosteronism is one of the most common causes of secondary hypertension but clear differentiation between its various subtypes can be a clinical challenge. We report the case of a 37-year-old African-American woman with refractory hypertension who was admitted to our hospital for palpitations, shortness of breath and headache. Her laboratory results showed hypokalaemia and an elevated aldosterone/renin ratio. An abdominal CT scan showed a nodule in the left adrenal gland but adrenal venous sampling showed elevated aldosterone/renin ratio from the right adrenal vein. The patient began a new medical regimen but declined any surgical options. We recommend clinicians to maintain a high level of suspicion to consider the less common subtypes of primary hyperaldosteronism, especially given the fact that the management greatly varies.

BACKGROUND

First reported in 1953 by Dr Litynski, primary aldosteronism (PA) involves an overproduction of the hormone aldosterone that results in the suppression of renin and influx of sodium and outflux of potassium, resulting in hypertension and hypokalaemia (and hypomagnesaemia).^{1–3} The diagnosis of each particular subtype of PA remains a clinical challenge because although the two most common subtypes are bilateral adrenal hyperplasia and aldosterone producing adenomas (APA), other rarer forms such as unilateral adrenal hyperplasia (UAH) and glucocorticoid responsive aldosteronism can manifest as well.⁴

The first case of UAH was presented in 1965. A prospective study in Japan showed a prevalence of 0.1% for UAH in over 1000 patients.^{5,6} By comparison, APA and bilateral adrenal hyperplasia were reported to have a prevalence of 4.9% and 1.2% respectively.⁶ UAH remains a rare subtype with infrequent case reports but this differentiation of subtypes is critical because it influences the type of treatment with medical and surgical options usually resulting in significant improvements in the patients' conditions.^{7–22} A review of the current literature yielded one case of UAH with coexisting contralateral incidentaloma.²³

CASE PRESENTATION

A 37-year-old African-American woman presented to the emergency room of Sisters of Charity Hospital reporting of palpitations, shortness of breath and headache. While all symptoms were sudden in onset, the patient had never experienced

palpitations or any difficulty breathing in the past. She was being managed in an outpatient setting for hypokalaemia and hypertension since 2009. She has been taking three antihypertensives (amlodipine, benazepril and labetalol) and supplemental potassium (2 tablets of 10 mEq three times a day) but was very recently switched to hydralazine, verapamil and doxazosin mesylate, and two potassium tablets of 20 mEq three times a day.

On physical examination, her heart rate was 110 bpm while the blood pressure was 170/110 mm Hg. Cardiac, abdominal, neurological and musculoskeletal examinations were unimpressive with no signs of clubbing or oedema. Initial investigations revealed normal haematological and renal parameters but showed sodium 135 mmol/L and potassium 2.5 mmol/L. Urinalysis returned negative for leucocyte esterase and nitrites. A chest X-ray and EKG performed at the time of admission were unremarkable as well.

After the patient was admitted for refractory hypokalaemia, oral and intravenous potassium supplementation was started. However, the patient's potassium remained at 2.9 mmol/L. Further studies yielded spot urine sodium 42 mEq/L, potassium 23 mEq/L, chloride 51 mEq/L and urine osmolality 209 mOsm/kg. There was no spot urine creatinine sample and the urine studies could not be adequately interpreted. In addition, serum aldosterone and renin levels were 97 ng/dL and 0.19 ng/mL/hour, respectively, and cortisol level was 11.7 Ag/dL. The aldosterone/renin ratio was calculated to be 510 ng/dL per ng/(mL/hour). A CT scan of the abdomen and pelvis with contrast showed an enhancing nodule of 87 HU measuring 1.1×1.2 cm in the lateral limb of the left adrenal gland (figure 1).

Figure 1 Transverse CT scan of the abdomen and pelvis showing an enhanced nodule measuring 1.1×1.2 cm in the lateral limb of left adrenal gland.

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Figure 2 Transverse MRI of the abdomen showing single dropout compatible with the left adrenal adenoma measuring 11 mm.

Unfortunately, adrenal protocol was not followed hence washout phase of the CT scan was unavailable. A MRI of the abdomen further showed signal dropout that was compatible with a probable left adrenal adenoma measuring 11 mm (figures 2 and 3).

A selective adrenal venous sampling (AVS) with adrenocorticotrophic hormone stimulation was also performed. While the aldosterone and cortisol levels in the left adrenal vein were 97 ng/dL and >120 µg/dL, the levels in the right adrenal vein were 4086 ng/mL and >120 µg/dL, suggesting a diagnosis of UAH. The full results are shown in table 1.

The patient was initially treated with oral spironolactone and oral potassium chloride during her hospital stay. By the fifth day of hospitalisation, her electrolytes and blood pressure had corrected and she was subsequently discharged on verapamil, hydralazine, doxazosin and spironolactone. The possibility of undergoing a right adrenalectomy has been discussed with the patient but she professed her desires to hold off on such an operation until after she has spoken to her primary care physician.

Figure 3 Coronal MRI of the abdomen showing single dropout compatible with the left adrenal adenoma measuring 11 mm.

Table 1 Selective adrenal venous sampling results

	Aldosterone (ng/dL)	Cortisol (µg/dL)
Right adrenal vein	4086	>120
Left adrenal vein	97	>120
Inferior vena cava	34	11.7

INVESTIGATIONS

- ▶ Complete metabolic panel;
- ▶ Plasma aldosterone concentration (PAC);
- ▶ Plasma renin concentration;
- ▶ CT scan of the abdomen with and without contrast;
- ▶ MRI of the abdomen;
- ▶ AVS.

DIFFERENTIAL DIAGNOSIS

- ▶ Conditions with true hyperaldosteronism;
 - Bilateral adrenal hyperplasia;
 - Conn's syndrome;
 - Renal artery stenosis;
- ▶ Conditions with mineralocorticoid affect;
 - Excessive licorice ingestion;
 - Cushing's syndrome;
 - Glucocorticoid-remediable aldosteronism;
 - Liddle's syndrome;
- ▶ Conditions with apparent mineralocorticoid excess;
 - 11 β Hydroxysteroid dehydrogenase deficiency.

TREATMENT

Unilateral laparoscopic adrenalectomy is used in patients with unilateral PA because blood pressure and serum potassium concentrations improve in nearly 100% of patients postoperatively. Although surgery is recommended for UAH, our patient refused to undergo surgery and was managed medically with spironolactone, verapamil, hydrazine and doxazosin.

Medical therapy with spironolactone is the treatment of choice for non-surgical PA or in patients who refuse surgery. Amiloride and triamterene can be used as first line in those who are not tolerant to spironolactone/eplerenone. Potassium supplementation is not routinely indicated. Thiazide diuretics, calcium channel blockers, and ACE inhibitors/angiotensin II receptor blockers are the second-line agents to control blood pressure.

OUTCOME AND FOLLOW-UP

Follow-up after 9 months was uneventful.

DISCUSSION

We report a case of PA due to UAH on the right side with coincidental left-sided adrenal incidentaloma. PA is a common diagnosis in cases of secondary hypertension and patients usually present with resistant hypertension and normokalemia and possible hypomagnesaemia, muscle weakness, muscle cramps and headache. It is important to note that normokalemia is more common than hypokalaemia and studies showed the prevalence of hypokalaemia to be <50% in patients with PA.⁷ The most common causes of PA are bilateral adrenal hyperplasia and unilateral adrenal adenoma but UAH only consists of 1–2% of all PA cases.²⁴

While bilateral adrenal hyperplasia with incidentalomas (especially microadenomas) is not uncommon, it is rare to have UAH with contralateral incidental macroadenoma. A literature review

revealed that only one other similar case has been published before our report. As mentioned in that initial presentation, these cases should serve as a warning for clinicians to tread cautiously in cases of apparent PA as a misdiagnosis would lead to surgical removal of a functional adrenal gland with no improvement of the patient's condition.²³

According to the Endocrine Society's Clinical Guidelines, if the plasma aldosterone/renin ratio is >20 , the next step is to perform any one of four confirmatory tests: oral and intravenous salt loading test, the fludrocortisone suppression and the captopril challenge test.²⁵ The confirmatory tests need not be performed if the PAC is >30 ng/dL with undetectable plasma renin in the setting of spontaneous hypokalaemia—such as in our case. Hence, we bypassed the confirmatory testing and proceeded with abdomen imaging instead.

CT of the abdomen and pelvis using the adrenal protocol (adrenal CT) tells us about the Hounsfield units and the per cent of contrast washout in the washout phase of the CT scan. Although CT abdomen and pelvis with contrast using the adrenal protocol can be useful in identifying masses that can be a potential APA, AVS remains the gold standard and the most accurate way to differentiate between the unilateral and bilateral categories of PA as benign non-functional adrenal nodules are extraordinarily common. More specifically, the analysis of an aldosterone/cortisol ratio from the sampling procedure can be the most reliable method of diagnosing unilateral PA.^{26–28} In this case, AVS revealed that the patient had high aldosterone output from the right adrenal gland which was apparently completely normal on performing CT and MRI of the abdomen. The left adrenal gland has an aldosterone output that was within normal limits. The data pointed towards the conclusion that patient had UAH on the right side and that the mass on left adrenal gland was an incidentaloma. The sensitivity and specificity of AVS (95% and 100%, respectively) for detecting

unilateral aldosterone excess are superior to that of adrenal CT (78% and 75%, respectively).^{26–29} Bilateral adrenal hyperplasia with unilateral non-functioning adrenal adenomas are fairly common and CT scan has the potential to mislead in such cases leading to unnecessary surgery.

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Learning points

- ▶ Measuring potassium excretion in a 24 hour urine sample collection is the best way to assess renal potassium excretion. If a 24 hour urine sample was collected, then an appropriate renal response to the hypokalaemia would be total K <15 mmol/day. However, if a spot sample was sent, a better indication of urine K wasting is the ratio of K:Cr. This ratio should be <1.5 if the kidneys were responding appropriately to hypokalaemia.
- ▶ An initial step is to obtain midmorning plasma aldosterone concentration (PAC) and plasma renin activity (PRA). The test is positive if PAC is >15 ng/dL and the PAC/PRA ratio is >20 .
- ▶ Since the PAC/PRA ratio has high false positive rate, one of the four confirmatory tests need to be performed before proceeding to imaging studies. Verapamil, hydralazine and doxazosin are the three common drugs which do not interfere with the PAC/PRA ratio.
- ▶ Imaging studies should be carried out using the adrenal protocol and are carried out to rule out large masses like adrenocortical carcinomas. However, AVS is the best way to lateralise the source of PA since imaging cannot distinguish functioning versus non-functioning adenomas.
- ▶ Treatment of choice for bilateral adrenal hyperplasia is medical therapy whereas for aldosterone producing adenoma and UAH it is unilateral adrenalectomy.

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