

## CORRESPONDENCE

# Cure for a resistant hypertension case that required seven drugs for blood pressure control

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Primary aldosteronism (PA) is characterized by an autonomous overproduction of aldosterone that is not suppressible after saline overload.<sup>1</sup> Prospective studies have estimated the incidence of PA in patients with resistant hypertension to be between 14 and 23%. This is far more common than in people with non-resistant hypertension,<sup>2</sup> although a high prevalence of PA has also been reported among prehypertensive and stage 1 hypertensive Japanese patients.<sup>3</sup> The first step in screening for PA is measurement of the aldosterone-to-renin ratio (ARR); a combined evaluation of ARR with the serum sodium to urinary sodium divided by the serum potassium<sup>2</sup> to urinary potassium ratio (ARR×SUSPPUP) seems to be the most reliable screening test, with a sensitivity of 92.3% and a specificity of 93.9%.<sup>4</sup> Surgery is an option in patients with unilateral adrenal disease. Adrenalectomy can ‘cure’ hypertension in an estimated 44–65% of patients; one of the greatest predictors of success is the number of drugs needed to control blood pressure (BP) before adrenalectomy.<sup>5</sup>

Here we present the unusual case of a patient who needed seven antihypertensive drugs to control her BP and then, following adrenalectomy, became normotensive without drugs.

This 26-year-old female patient was referred to us with a 2-year history of hypertension that was uncontrolled with Atenolol 100 mg once daily and Amlodipine 10 mg once daily. She had no family history of hypertension in first-degree relatives. She had a previous pregnancy, 5 years earlier, without hypertension. On physical examination, she had a body mass index (BMI) of 32.5 kg m<sup>-2</sup> and BP values of 180/110 mm Hg. Complementary examinations revealed hypokalemia (3.1 mEq l<sup>-1</sup>), elevated insulin (38.7 mU l<sup>-1</sup>), normal serum creatinine (0.79 mg dl<sup>-1</sup>), a glomerular filtration

rate of 125 cc min<sup>-1</sup>, and normal urinary catecholamine excretion. Urinary excretion of cortisol (234 nmol/24 h) and plasma levels of cortisol (416.0 nmol l<sup>-1</sup>) and corticotropin (42.2 pg ml<sup>-1</sup>) were also normal. Doppler ultrasonography showed normal renal arteries; the left ventricular mass was normal, measured using an Acuson Aspen echocardiograph (Acuson Corporation, Mountain View, CA, USA), and the relationship between E and A waves on Doppler-pulsed analysis were also normal. The treatment was replaced for 2 weeks by Doxazosine 8 mg per day and verapamil 240 mg per day, to measure plasma aldosterone and plasma renin activity. The ARR (aldosterone/plasma renin activity) after 2 h standing/walking was determined to be high (12.435 pmol l<sup>-1</sup> per ng ml<sup>-1</sup> h<sup>-1</sup>). Next, a saline suppression test was performed and absence of suppression was documented (baseline: 456 pmol l<sup>-1</sup>; after saline overload: 422 pmol l<sup>-1</sup>). Then, Spironolactone 100 mg daily was added to Atenolol and Amlodipine, but BP remained elevated. Computed tomography showed a 12-mm nodular image in the left adrenal gland, suggestive of adenoma. Finally, central venous sampling performed without stimulation of corticotropin showed that the aldosterone/cortisol ratio in the left adrenal vein was 7.4 times higher than that in the right adrenal vein.

An ambulatory BP monitoring (ABPM) record showed a 24-h mean BP of 161/104 mm Hg with the following treatment: Atenolol 100 mg, Amlodipine 10 mg, Spironolactone 100 mg, Hydrochlorothiazide 50 mg and Amiloride 5 mg, each taken once daily. Therefore, it was necessary to increase the Spironolactone dose to 150 mg daily, and add Enalapril 20 mg twice daily and Doxazosine 8 mg once daily to the therapeutic regimen. Only with these seven drugs was good BP control achieved. Analysis of a second blood sample showed that plasma

levels of potassium increased to 4.3 mEq l<sup>-1</sup>, and plasma levels of creatinine and insulin remained unchanged (respectively, 0.80 mg dl<sup>-1</sup> and 38.2 mU l<sup>-1</sup>). The patient's BMI at this visit was 32.3 kg m<sup>-2</sup>.

An adrenalectomy was performed by laparoscopic technique; after the surgical procedure, all drugs were progressively eliminated. The tumor was resected and the pathological findings were informed as follows. The macroscopic description indicated that it was a well-demarcated yellowing tumour, measuring 1.8×1.4 cm, which appeared to be related to adrenal cortex. The cut showed a homogeneous yellow surface without other features, and no areas of necrosis or hemorrhage were observed. The microscopic description stated that the tumor was an adrenal cortical adenoma.

After adrenalectomy and without drugs, BP values measured during two subsequent office visits were 114/78 and 117/85 mm Hg. One year after surgery, the patient's BMI was 32.1 kg m<sup>-2</sup> and plasma levels of potassium, creatinine and insulin, respectively, were 4.1 mEq l<sup>-1</sup>, 0.78 mg dl<sup>-1</sup> and 37.5 mU l<sup>-1</sup>. A second ABPM record proved that BP values remained normal (mean of 24 h: 105/66 mm Hg). This was surprising because, *a priori*, the high number of drugs needed for BP control, the BMI (indicative of obesity grade II) and the existence of hyperinsulinemia made successful treatment seem unlikely for this patient.

To our knowledge, this is the first report of a patient with RH requiring seven drugs for BP control, who became normotensive after a correct diagnosis and subsequent adrenalectomy. Moreover, this case illustrates that the possibility of PA should be considered in all patients with RH, and emphasizes that a screening test for PA should be performed in all such cases. Finally, there can be no doubt of the financial savings given the

reduction in for this 26-year-old woman, or the benefits of stopping the well-known deleterious effects of aldosterone excess on the cardiovascular system.<sup>6–9</sup>

#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

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