

## Cerebrovascular disease as an initial manifestation of conn's syndrome.

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### Abstract

**Primary Aldosteronism is the commonest cause of secondary arterial hypertension and is due to uncontrollable aldosterone secretion by a series of adrenal disorders. We describe a case of a 51-year-old male patient with uncontrollable hypertensive peaks in whom initial manifestation was ischemic stroke; he was diagnosed with Primary Aldosteronism (biochemically) and left adrenal gland mass measured 20×11×13 mm. The patient underwent a left laparoscopic adrenalectomy. The patient was discharged home with well-controlled blood pressure and normokalemia. No clinical symptoms were reported in follow-up. In the present article, we describe the pathophysiology, diagnosis and treatment of the disease.**

**Keywords:** Cerebrovascular disease, Conn's syndrome, hypertension.

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### Background

Primary aldosteronism, which refers to the autonomous excess production of aldosterone, was once considered to be a rare disease. Now, with advances in diagnostic methods, Primary aldosteronism has been identified as the most common cause of secondary hypertension [1], with a prevalence ranging from 5% to 15% in hypertension patients [2], and an even higher prevalence in patients with resistant hypertension [3]. Compared with essential hypertension patients, patients with primary aldosteronism are associated with an increased risk of cardiovascular comorbidities, including stroke, myocardial infarction, and atrial fibrillation, which are independent of blood pressure [4,5]. Several studies reported that the rate of stroke was significantly higher in patients with primary aldosteronism than in patients with essential hypertension (12.9% vs 3.4%) [6]. Most importantly, these complications can be reduced by medical and surgical treatment. Studies have shown that for the majority of patients with benign surgical adrenal disease, laparoscopic surgery is now the gold standard treatment [7]. The effectiveness of adrenalectomy has to be done with a fall of blood pressure or allowing the withdrawal of all antihypertensive medications [8].

### Case Report

O.G. a 51-year-old male, cameraman, was admitted to ER in Bite Medica Hospital, complaining with sudden loss of muscle strength in left pelvic and thoracic limbs with fall of his own height.

The patient has history of systemic arterial hypertension on treatment with prazosin, amlodipine and candesartan with hydrochlorothiazide, and type 2 Diabetes Mellitus in treatment with metformin and glimepiride. His father has died of acute

myocardial infarction. The mother has arterial hypertension systemic.

Physical examination showed alert, conscious, oriented in three spheres, mental functions preserved, cranial pairs without neurologic alterations, isometric, normo-reflective pupils, muscular force 4/5 in left thoracic and pelvic limbs with inability to walk without other focal data. Neck without IY, carotid pulse of normal amplitude, without murmurs. Anterior thorax rhythmic heart sounds, tip crash in 5 LMC IBD, rhythmic heart sounds, first and second normal sounds, no murmurs, no rubbing. Spontaneous ventilation, without data of respiratory difficulty, saturation by pulse oximetry 91% to ambient air, without pleuropulmonary syndrome. Abdomen globose at the expense of abdominal distension, tympanic, normal peristalsis is palpated descending colon and sigmoid dissected, without data of peritoneal irritation.

At admission the blood pressure was 240/130 mmHg, capilar glucose 27.75 mmol/L, with temperature, hearth and respiratory rate normal. The blood analysis showed a central glucose 26.7 mmol/L, potassium 2.9 mmol/L, sodium 134 mmol/L, Chloride 95 mmol/L, pH 7.47, HCO<sub>3</sub> 20.6 mmol/L. He was taken to a head simple tomography without the evidence of a hemorrhagic type cerebral vascular event. X-ray showed an enlargement of left ventricle. An electrocardiogram revealed hypertrophy of left ventricle. Antihypertensive treatment with intravenous nitroprusside was started with goals that allowed the maintenance of cerebral perfusion pressure and was admitted for close neurological surveillance and strict control of blood pressure to the intensive care unit. At his arrival, he also highlighted the presence of hypokalemia and metabolic alkalosis.

The approach was performed with negative carotid Doppler ultrasound extension studies for significant plaques, renal ultrasound in which a left adrenal tumor was evident,

transthoracic echocardiogram without evidence of intracavitary thrombi, normal left ventricular function, cerebral magnetic resonance that corroborated an event right thalamic cerebral vascular, suprarenal nuclear magnetic resonance compatible with adenoma. Coronary angiography was performed, which was negative for significant lesions.

He had been maintained with difficulty for hypertension control, requiring intravenous antihypertensives for 6 days and oral antihypertensives in the number of 6 at maximum dose to achieve removal of sodium nitroprusside. The results of the biochemical studies performed showed elevated aldosterone levels, 715 pg/ml, (normal maximum of 164 pg/ml), plasma and urinary metanephrines, plasma renin activity and cortisol within normal limits; Renin levels were low due to the use of beta blockers. Glycemic control was achieved with Lantus insulin, metformin and dapagliflozin. As a finding, a solid right renal mass was found. Adrenal tumor resection was performed laparoscopically on day 03.28.2019 without complications.

## Discussion

We report an unusual case of middle age patient with history of resistant hypertension, who presented in emergency department with very high blood pressure and ischemic cerebrovascular event, manifestation of aldosterone excess. We suspected secondary causes of hypertension because blood pressure control was difficult; the patient needed maximal dose of all antihypertensive groups, associate with hypokalemia and metabolic alkalosis. To rule out secondary causes we made an abdominal tomography that showed adrenal incidentaloma.

The association between hyperaldosteronism and vascular disease has been well recognized, this patient had a higher incidence of stroke 7(7.4%), ischemic heart disease (2.1%) and heart failure (0.6%) [1]. In TAIPAI database, the incidence of stroke in PA patients was 35 cases per 1,000 person-years [2]. Much higher than the general population (3.4 to 5.2 cases per 1,000 person-years) [3].

Another analysis showed that the excess risk of cardiovascular events and related mortality was only present in primary aldosteronism patients with suppressed renin ( $1 \leq \text{mcg/L/hr}$ ) [4]. Aldosterone generates oxidative stress which causes endothelial dysfunction and collagen remodeling leading to increased fibrosis of vessel walls [5]. Increased stiffness due to aldosterone can be reversed by adrenalectomy [6]. or the specific aldosterone antagonist eplerenone in an animal model [7].

Pathophysiology, clinical suspicion, diagnostic approach and treatment of Conn syndrome requires an ordered protocol. Suspect the diagnosis in all patients with, adrenal incidentaloma, refractory hypertension, hypokalemia not explained or with low doses of diuretic and metabolic alkalosis.

Adrenal computed tomography (CT) should be the initial study to determine subtype (adenoma versus hyperplasia) and exclude adrenal carcinoma. In imaging adrenal glands, CT has superior spatial resolution compared with magnetic

resonance imaging (MRI). The CT scan may be done without intravenous contrast; however, if an adrenal mass is detected, contrast administration provides additional imaging information. Somatic mutations in *KCNJ5*, *ATP1A1*, *ATP2B3*, *CTNNB1*, and *CACNA1D* are found in more than 50 percent of resected aldosterone-producing adenomas APAs [8-9].

In the approach, it is necessary to measure the plasma renin activity (PRA) (or plasma renin concentration [PRC]) and plasma aldosterone concentration (PAC) in the morning in a seated ambulatory patient.

Calculate a PAC/PRA ratio as part of the case detection strategy, but we prefer to use the paired random PAC and PRA (or PRC). The mean value for the PAC/PRA ratio in normal subjects and patients with primary hypertension (formerly called "essential" hypertension) is 4 to 10, compared with more than 30 to 50 in most patients with primary aldosteronism [10-11]. PRA and PRC are low in a significant number of patients with primary hypertension, but a high PAC (typically  $>15 \text{ ng/dL}$  [ $416 \text{ pmol/L}$ ]) and a truly abnormal ratio are uncommon. A PAC/PRA ratio greater than 20 is considered suspicious for primary aldosteronism, although others use a cutoff criterion of 30.

In general, APA patients have higher aldosterone secretion rates, resulting in more severe hypertension, more severe hypokalemia ( $<3.2 \text{ mmol/L}$ ), and higher plasma ( $>25 \text{ ng/dL}$ ) and urinary ( $>30 \text{ mcg/24 hour}$ ) levels of aldosterone; these patients are also younger ( $<50$  years) than those with IHA [12]. In one study, a plasma aldosterone concentration/plasma renin activity (PAC/PRA) ratio of  $>32$  had a sensitivity of 100 percent and specificity of 61 percent for an APA [13].

That study compared the cardiometabolic outcomes between medically treated PA patients and EH patients, and showed a higher incidence of cardiovascular events (myocardial infarction, coronary revascularization, admission for congestive heart failure or stroke) higher mortality risk, diabetes and atrial fibrillation in MRA-treated PA patients than in EH patients. Further analysis showed that the increased risk of cardiovascular events and related mortality was only present in PA patients with suppressed renin [4]. Clinical suspicion and the appropriate diagnostic approach are important for prevention of vascular events in patients with refractory hypertension.

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