A case of acute psychotic episode at the onset of primary aldosteronism

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ABSTRACT

Primary aldosteronism (PA) is a common cause of secondary hypertension. Moreover, the spectrum of clinical manifestations of PA may involve a more extensive continuum and different clinical manifestations, including also neuropsychiatric symptoms. Until now, there have been only a few reports of psychiatric symptoms in patients with PA. Here, we describe a case of PA presenting with an acute psychotic episode. A 55-year-old Asian woman with no pathological history was admitted to the emergency room because of altered mental status with confusion and agitation, recurrent speech, and unmotivated laughter lasting for approximately 36 hours. The clinical manifestation was initially considered psychiatric and treated with olanzapine and lorazepam. She presented as hypertensive. The laboratory showed hypokalemia. PA was suspected and then confirmed by a saline infusion and captopril test. An abdominal computed tomography scan showed a left adrenal cortical adenoma. Significant left lateralization at adrenal vein sampling was obtained. We suggest considering PA in the differential diagnosis of hypertensive patients with psychiatric manifestations.

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Introduction

Primary aldosteronism (PA) is characterized by an autonomous secretion of aldosterone, independent of renin and sodium status, resulting in excessive activation of the mineralocorticoid receptor (MR) and in an increase of cardiovascular morbidity and mortality.[1] PA was usually investigated in patients with hypertension and hypokalemia. Accumulating evidence suggests that the prevalence of PA is much higher than commonly held and identifies PA as the most common cause of secondary hypertension. Moreover, the spectrum of clinical manifestations of PA may involve a more extensive continuum and different clinical manifestations, including neuropsychiatric symptoms. Until now, only a few studies have reported these symptoms in patients with PA.[2] Here, we describe a case of PA revealed by an acute psychotic episode.

Case Report

A 55-year-old Indian woman, living in Italy for a year and apparently without clinical history, was admitted to the emergency unit due to a confusional state with agitation, recurrent speech, and unmotivated laughter lasting for about 36 hours. Her relatives were unable to provide any information on previous laboratory tests or on the intake of medications or herbs. A similar episode occurred 6 months before and apparently disappeared without medical intervention; no blood pressure (BP) measurement was performed. In this episode, the clinical manifestation was initially considered as psychiatric and treated with olanzapine 10 mg daily and lorazepam 3 mg daily orally.

At admission to our unit, she presented with hypertension (BP 168/104 mmHg) with a normal physical examination. Amlodipine 10 mg once daily and subsequently doxazosin 4 mg twice daily were started. The laboratory showed hypokalemia (3.4 mmol/L, NV 3.5-5.0) while serum creatinine, sodium, calcium, thyroid function, urinary cortisol and urinary

metanephrines were normal. Brain computed tomography (CT) scan and electroencephalogram were normal, while brain nuclear magnetic resonance showed ischemic damage of the microcirculation. No atherosclerotic plaques were revealed on carotid ultrasound. Left ventricular hypertrophy was observed on the electrocardiogram. Fundoscopic examination revealed II-grade hypertensive retinopathy. Aldosterone and renin were 260 pg/mL and 0.3 ng/dL, respectively. A saline infusion and a captopril test confirmed PA (post-test aldosterone levels 98 pg/mL and 189 pg/mL, respectively). Abdominal CT scan showed a left adrenal cortical adenoma (9×9 mm) (Figure 1). Adrenal vein sampling, without cosyntropin stimulation, was performed. An optimal selectivity and a significant left lateralization were observed (Table 1). Therefore, canrenone 50 mg/day orally was started; the BP normalized (126/81 mmHg), and doxazosin was stopped. Left adrenalectomy was scheduled, and psychiatric symptoms were controlled despite discontinuation of olanzapine and lorazepam. The patient is still waiting for adrenalectomy.

Discussion

The organic etiologies of psychiatric pathologies are frequent but very underestimated. Due to clinical suspicion and a proactive attitude toward identification of secondary causes of hypertension can point to an organic etiology which, once treated, may avoid complications, relapses, and unnecessary psychoactive drug prescriptions.

Despite the high prevalence of psychiatric illnesses, it is always necessary to look for the organic causes that may be behind these pathologies, especially if they are in atypical forms.

Table 1. Adrenal vein sampling (no cosyntropin stimulation). Laterality index=8.5 left *vs.* right.

	Cortisol	Aldosterone
Right adrenal vein	28 g/dL	60 pg/mL
Left adrenal vein	31 g/dL	564 pg/mL
Inferior vena cava	7 g/dL	195 pg/mL

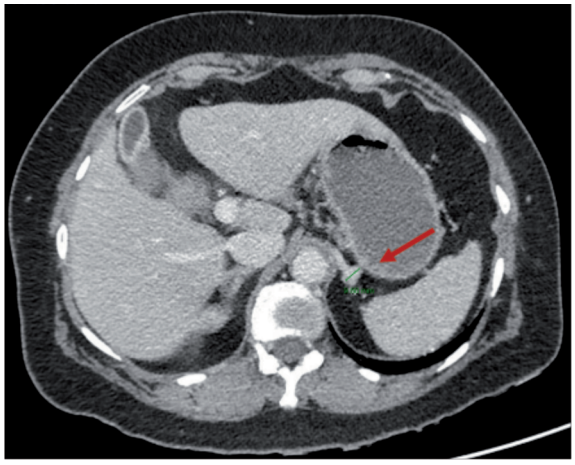

Figure 1. Contrast-enhanced abdominal computed tomography scan showing left adrenal cortical adenoma.

PA is the most common cause of secondary hypertension. It comes with an increased risk of cardiovascular, metabolic, and renal comorbidities compared with hypertensive patients of similar age, sex, and BP. Current guidelines recommend screening for PA in a few specific condition: patients with resistant or persistent hypertension, hypertensive patients themselves or first degree relatives who have early target organ damage, such as stroke and other disease, hypertensive patients with a history of PA in a first degree relatives, young onset hypertension (<40 years), hypertensive patients who also have hypokalemia (spontaneous or drug-induced) and all hypertensive patients with concurrent adrenal incidental tumors. However, PA may still be present in normotensive patients.[3] In a recent review, Huang *et al.* suggest screening for PA also in hypertensive patients with anxiety and other psychosomatic symptoms.[4]

The association between psychiatric manifestations and PA is widely reported. Generalized anxiety disorder was observed in 50-60% of cases, major depressive disorder in 8.7-25% of cases, persistent somatization in 8.7-20% of cases, obsessive compulsive disorder in 10-13%, and panic disorder in 10% of cases.[2-4] However, PA is not often investigated as a possible underlying condition of the psychiatric symptoms. A possible explanation for the underdetection of PA is that most doctors suspect PA only in hypertensive patients with hypokalemia, despite abundant evidence that hypokalemia is not a *sine qua non* condition for searching for PA.

Effects on mood in patients with PA could be mediated by several pathways. In many psychiatric studies, a dysregulation of the hypothalamus-pituitary-adrenocortical (HPA) system leading to hypercortisolism has been identified as a fundamental element in the pathogenesis of major depression and anxiety disorders.[5] But there are also findings which point to a disturbance of the renin-angiotensin-aldosterone system (RAAS) in depression and anxiety as well. Among structures being part of the HPA-system and RAAS, glucocorticoid receptors (GR) and MR could play a role in the pathophysiology of psychosis, depression, and anxiety. A disturbed expression of these structures, with a modified balance between GR and MR, can be mediated by the excessive aldosterone secretion responsible for PA. In addition, the MR, the main target of aldosterone, is supposed to be involved in the response to antidepressant treatment and in the mediation of anxiety. There is also evidence for the link between the HPA system and RAAS, as the aldosterone and renin secretion are partly driven by the ACTH concentration. In fact, elevated aldosterone concentrations caused by down-regulation of ACTH during depression and anxiety have been demonstrated.[5]

Conclusions

We are aware that our case is incomplete because no adrenalectomy has been performed yet. However, we believe that it underscores the widespread clinical evidence of the association between PA and psychiatric-related symptoms. In addition, it focuses on the importance of screening for PA in hypertensive patients with anxiety and/or other psychiatric manifestations but no meaningful hypokalemia. Diagnosing PA may allow a targeted drug or surgical treatment with good control of high BP, a more effective prevention of cardiovascular events, and improvement of quality of life.

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