

Normotensive Primary Aldosteronism: A Case Report

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Citation

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Abstract

We report the case of 35 year-old woman referred to endocrine department for hypokaliemia revealed by cardiac and neuromuscular symptoms. Clinical and ambulatory blood pressure measurements were normal (respectively: 120 / 80 mmHg and $122 \pm 13.5 / 79 \pm 13.4$ mmHg). Biological findings: Hypokaliemia (2.1 to 2.5 mmol/l), metabolic alkalosis, inappropriate kaliuresis (42 mmol/24h), high plasma aldosterone (523 ng/l) and suppressed renin activity (<2.5 ng/l). Computerized tomodensitometry showed a well-circumscribed homogenous mass, 12 mm in diameter, in the inner arm of the left adrenal gland.

After surgical removal of the adenoma, blood pressure level decreased by about 20 mmHg, and biological and hormonal status were normalized. Spontaneous low baseline blood pressure level may explain lack of hypertension in this patient. In hypokaliemic patients, lack of hypertension should not exclude primary aldosteronism. Protective mechanisms against hypertension in such patients should be more studied and used in hypertension treatment research.

INTRODUCTION

Primary aldosteronism is the most common cause of endocrine hypertension. In recent studies, using aldosterone to renin ratio as diagnostic tool, 5 to 15% of hypertensive patients had primary aldosteronism [1,2]. In Several studies primary aldosteronism was associated with increased risk of heart and kidney damage independently of blood pressure levels [3,4,5]. Its typical hallmarks are hypertension associated with hypokaliemia, increased aldosterone level and suppressed plasma renin activity or increased plasma aldosterone/renin ratio [3,6]. Although many patients with primary aldosteronism may not have hypokaliemia [2], those with normal blood pressure levels are scarce. Only 18 cases were reported in the literature until 2004 [7,8,9,10,11,12,13,14,15,16,17,18,19,20] and 10 French cases collected over a period of 12 years were recently reported by Medeau et al [21]. In this paper we report a case of normotensive primary aldosteronism revealed by hypokaliemia with cardiac and neuromuscular manifestations.

was treated with amiodarone and chloride potassium supplementation. Under this treatment, cardiac arrhythmia resumed, but kaliemia still at under ranges. She was then referred to the endocrinologist.

At admission in Endocrinology department, physical examination was normal. Her weight and height were respectively 47 kg and 1.59 m. Blood pressure was 120 / 80 mmHg, heart rate was 72 beats per minute and regular. There was neither facio-truncular obesity nor hirsutism. The thyroid was not enlarged. Neurological examination showed no abnormalities. EKG showed long QT interval of 450 ms.

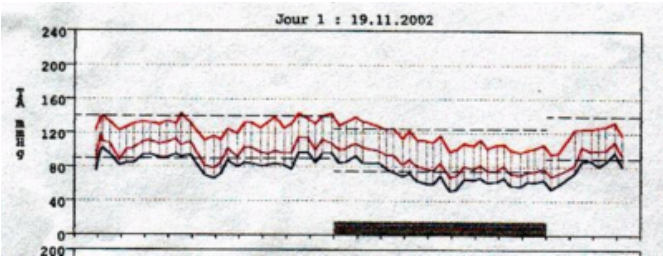
Twenty four hours ambulatory blood pressure measurements (ABPM) were normal [figure-1]: mean 24 hours SBP 122 ± 13.5 mmHg [95 – 143] and mean DBP 79 ± 13.4 mmHg [52 – 102].

CASE REPORT

A 35 year-old Tunisian woman was admitted to the Endocrinology department for hypokaliemia. Two months before she started to have weakness, numbness in her hands and feet, cramps and constipation. She did not look for medical care until she developed lipothymia. Diagnosis of cardiac arrhythmia and hypokaliemia were then retained. She

Figure 1

Figure 1: Twenty four hours ambulatory blood pressure measurements before surgery



Laboratory findings were hypokaliemia (fluctuating between 2.1 and 2.5 mmol/l) with inappropriate kaliuresis and metabolic alkalosis [table-1]. Hormonal analysis showed increased plasma aldosterone level with suppressed renin activity [table-1].

Abdominal computered tomodensitometry showed a well-circumscribed homogenous mass, 12 mm in diameter, in the inner arm of the left adrenal gland [figure-2].

After correction of hypokaliemia with spironolactone 100 mg a day, patient underwent left adrenalectomy. Macroscopic examination of the extracted adrenal found an encapsulated 20 x 15 mm golden yellow nodule. Microscopic examination concluded to the adenomatous nature of this adrenocortical nodule without malignancy signs.

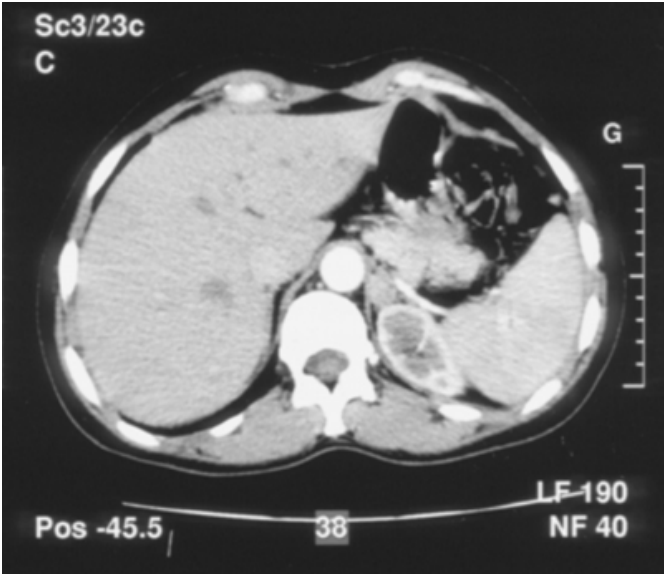
Figure 2

Table 1: Laboratory findings before and after surgery

	Before surgery	After surgery
Potassium		
Blood (mmol/l)	2.5	4.3
Urine (mmol/24h)	42	
Sodium		
Blood (mmol/l)	140	134
Urine (mmol/24h)	108	
Chloride (mmol/l)	106	103
Bicarbonates (mmo/l)	30.3	27
Creatinine (mg/l)	9.8	
Glucose (g/l)	0.70	
Protide	72	
Aldosterone (ng/l)		
Supine [NR: <154]	523	109
Orthostatism [NR: 39 – 308]	757	162
Renine (ng/l)		
Supine [NR:3 – 16]	< 2.5	5.7
Orthostatism [NR: 3 – 33]	< 2.5	18.5

Figure 3

Figure 2: Abdominal computered tomodensitometry showing a well-circumscribed homogenous mass, 12 mm in diameter, in the inner arm of the left adrenal gland

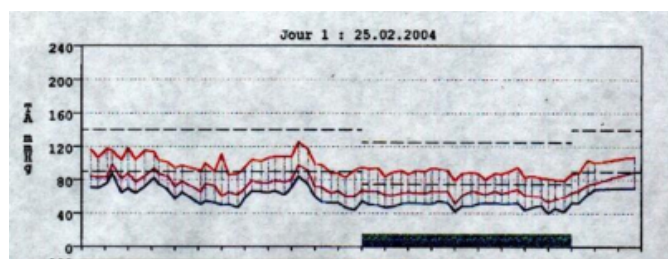


After Surgical treatment and withdrawal of spironolactone, biological abnormalities (hypokaliemia and metabolic

alkalosis) and hormonal status (plasma aldosterone and renin activity) were normalized [table-1]. Blood pressure levels were about 20 mmHg lower than preoperative state, as shown by multiple conventional blood pressure measurements and by ABPM [figure-3]. Four years later, she was not taking any treatment and her blood pressure and kaliemia were within the normal ranges (respectively 115/70 mmHg, and 4.6 mmol/l).

Figure 4

Figure 3: Twenty four hours ambulatory blood pressure measurements after surgery



DISCUSSION

Primary aldosteronism was confirmed in this patient by high plasma aldosterone level contrasting with suppressed plasma renin activity. This primary aldosteronism was due to aldosterone producing adenoma as shown by computed tomography and confirmed by histological examination. In this case, hypokaliemia and its clinical neuromuscular consequences were the main manifestations of hyperaldosteronism. Lack of hypertension was its main particularity and had lead to postponed diagnosis.

Normotensive primary aldosteronism is scarcely reported. In the 18 reported cases [7,8,9,10,11,12,13,14,15,16,17,18,19,20], 55% were Asian, especially Japanese and 67% were female. They were aged between 23 and 55 years. No familial cases were reported. Neuromuscular signs and symptoms (i.e. paresthesia, muscular weakness and paralysis) were the main clinical characteristics. Biological manifestations were typically those of primary aldosteronism. Hypokaliemia was present in all patients ranging from 1.4 to 3.5 mmol/l. All patients had increased aldosterone and suppressed renin secretion. Adrenocortical adenoma was found in 17 patients and only one had bilateral adrenocortical hyperplasia. Comparing their 10 normotensive primary aldosteronism cases to hypertensive cases, Medeau et al [21] found that the former had lower body mass index, deeper hypokaliemia but similar levels of aldosterone and renine and greater adenoma size.

Primary aldosteronism results in sodium and fluid retention

which lead to extracellular volume expansion. Hypervolemia results in hypertension and suppressed renin secretion[22]. Other effects of aldosterone may contribute to increased blood pressure levels in primary aldosteronism. In fact, Aldosterone promotes the vascular action of angiotensin II [23], impairs endothelial function [24], alters vascular compliance [25] and activates sympathetic ways in central nervous system mechanisms [26].

Different mechanisms leading to maintained normal blood pressure levels in primary aldosteronism were advanced:

Precocious diagnosis of the disease before the development of defined hypertension may explain lack of hypertension in some patients. Nishimiya found that diagnostic delay of his case of normotensive primary aldosteronism was shorter than in his 13 cases of hypertensive primary aldosteronism [13]. However, in other cases of normotensive primary aldosteronism delayed diagnosis, within 3 years, and experimental aldosterone injection in normotensive healthy subjects increased blood pressure and decreased kaliemia in a few minutes did not sustain this hypothesis [10,19].

Blood pressure level is the product of cardiac output and vascular resistance. Vascular resistance is the resultant of two opposite systems: the vasoconstrictor system which tend to increase blood pressure and the vasodilator system which tend to lower it [27]. Patients with normotensive primary aldosteronism may have lower level of vasoconstrictor system or higher level of vasodilator system.

Lower level of vasoconstrictor system may result from lower secretion of, or decreased responses to vasoconstrictor factors, such as angiotensin II and catecholamines. In their respective patients, Kono and Shiroto found that vasopressive responses to angiotensin II or to noradrenalin perfusions were lower in normotensive primary aldosteronism than in hypertensive primary aldosteronism [9,10]. In a large epidemiological population study, a gain in β_1 subunit function of the calcium sensitive potassium channel was associated with protection against diastolic hypertension in humans [28]. In animal studies, overexpression of catalase in mice reduced pressure response to vasoconstriction effects of norepinephrine and angiotensine II [29].

High level of vasodilator system may result from higher secretion of vasoconstrictor factors, such as Prostaglandin E, Kallikreins and nitric oxid, or increased responses to these factors [27]. Excessive urinary kallikrein excretion was found in a patient with normotensive primary aldosteronism [11].

However, responses to these substances were not studied.

Individuals in the low normal ranges of blood pressure have wider intervals to reach hypertension defined values. Thus, in hypertensive circumstances, like primary aldosteronism, they may increase their blood pressure by more than 30 mmHg but still in normal ranges and are considered normotensive. In Our patient and many others [19], decreased blood pressure after surgical removal of the adenoma sustained this hypothesis. Blood pressure in patient with hypokaliemia should be compared to its previous level when available.

CONCLUSION

Lack of hypertension in hypokaliemic patients should not exclude primary aldosteronism. Blood pressure level in hypokaliemic normotensive patients should be compared to their previous levels to detect an increase of blood pressure without reaching defined hypertension values.

In extrapolation of this conclusion, definition of hypertension should take in account previous values of individual blood pressure to diagnosis an increase in blood pressure.

Mechanisms maintaining blood pressure in normal values in hyperaldosteronism should be more studied and might be useful in hypertension treatment.

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