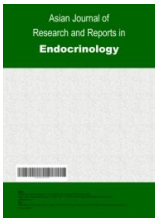

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Atypical Presentation of Conn's Syndrome

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Authors' contributions

This work was carried out in collaboration among all authors. Authors FH and MAM designed the study. Authors KB and HB wrote the first draft of the manuscript. Authors FH, OK and IM managed the analyses of the study. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Primary Aldosteronism (PA) is a common cause of secondary hypertension, arising from aldosterone-producing adenomas.
It mostly presents with resistant hypertension, hypokalemia and metabolic alkalosis, secondary to excess secretion of aldosterone and a suppressed plasma renin activity (PRA).
Hypokalemia typically presents with myalgia, cramps and muscle weakness. Rhabdomyolysis associated with hypokalemia. Paralysis represent an uncommon presentation of PA, described in few cases in medical literature.
Herein, we report a 41-year-old male with an initial presentation of an acute onset paraplegia and malignant hypertension.
The biochemical evaluation revealed rhabdomyolysis potentially due to severe hypokalemia. Then, investigations for primary hyperaldosteronism showed an elevated aldosterone-renin ratio (ARR).
Preoperative localization study with contrast-enhanced computed tomography (CT) scan revealed a left adrenal adenoma.
Laparoscopic adrenalectomy resulted in a complete clinical resolution, normalization of kalemia, muscle enzymes and ARR.

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Keywords: Hypokalemia; rhabdomyolysis; primary aldosteronism; adrenalectomy.

1. INTRODUCTION

Primary aldosteronism (PA) related to an adrenocortical adenoma (Conn's syndrome) is an endocrine disorder caused by excessive aldosterone secretion.

PA is a frequent and remediable cause of endocrine hypertension, with an incidence rate ranging from 6% in patients with high blood pressure to 20% of malignant arterial hypertension [1,2].

Hypokalemia occurs in 30-40% of cases of primary aldosternism.

Clinical manifestations resulting from hypokalemia in Conn's syndrome are most often moderate and potentially reversible [3].

Patients suffer rarely from neuromuscular symptoms, including mild muscle weakness, uncontrolled contractions and paresthesias. In rare cases, hypokalemia caused by PA may be profound enough to induce rhabdomylosis [4,5].

Here, we report an uncommon presentation of Conn's syndrome revealed by metabolic myopathy with rhabdomyolysis, potentially due to severe hypokalemia.

2. CASE PRESENTATION

A 41-year-old man presented to emergency department of our institution with sudden onset paraplegia, diffuse myalgia and dark urine.

He additionally complained of loss of appetite, vomiting and headaches for several weeks.

His relatives reported history of recurrent muscle fatigue of lower limbs over the past few months, frequently requiring assistance.

There was no history of neuropathy or trauma. He also denied any drug use including corticosteroids, laxatives or statins.

The family history was positive for hypertension, but there were no symptoms to suggest kalemia disorders.

On admission, his blood pressure was 220/110 mmHg, but his other vital signs were within normal range.

Neurological examination demonstrated grade 3 muscle strength in upper and lower extremities, without associated pyramidal signs or vesico-sphincter dysfunction.

The electrocardiogram (ECG) showed prolongation of PR interval and flattened T waves.

Laboratory investigations showed profound hypokalemia of 1,8 mmol/L (reference ranges of 3,5 – 5,1 mmol/L) with an elevated twenty- four-hour urinary potassium excretion of 63,2 mmol/ 24 hours.

The creatine phosphokinase (CPK) level was significantly elevated to 6525 IU/L (reference ranges of 20–170 IU/L), and the lactate dehydrogenase (LDH) level was 867 IU/L (reference ranges of 98-192 IU/L). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were 210 IU/L (15-34IU/L) and 89 IU/L (14-45 IU/L), respectively.

Arterial blood gas analysis revealed metabolic alkalosis (pH 7,53, $p0_2$ 56,3 mmHg, pCO_2 38,2 mmHg, HCO3 29,1 mmol/L).

The patient had normal renal parameters: urea 7,3 mmol/L (3-8 mmol/L), creatinine 74 µmol/L (30 -115 µmol/L). Thyroid hormone levels were normal.

In view of severe hypokalemia, neuromuscular manifestations were related to rhabdomyolysis.

The patient was initially managed with generous hydration and intravenous potassium supplementation.

Neuromuscular symptoms were remarkably ameliorated and muscle strength returned to normal. ECG abnormalities disappeared.

Both potassium and muscle enzymes gradually normalized.

As combined hypokalemia and markedly elevated blood pressure, endocrine hypertension was strongly considered and investigated.

Moreover, spectral analysis of renal arteries on Doppler ultrasonography didn't detect any stenosis.

Laboratory findings showed also normal serum metanephrines and normetanephrines.

The overnight 1 mg dexamethasone screening test for Cushing's syndrome revealed suppressible plasma cortisol level of 12 ng/ml.

Plasma rennin activity (PRA) was suppressed while plasma aldosterone concentration (PAC) and the ratio of PAC /PRA were elevated, which confirmed the diagnosis of PA (Table 1).

An adrenal computed tomography (CT) scan was then performed and revealed a nodular lesion, measuring 40 x 28 mm in size, with homogenous enhancement, involving the left adrenal gland (Fig. 1).

The association of hypertension with hypokalemia, high plasma aldosterone level, elevated ARR ratio and unilateral adrenal adenoma pointed to the diagnosis of Conn's syndrome.

The patient was treated by spironolactone in a daily dose of 75 mg for six weeks preoperatively with oral potassium replacement, which provided an excellent improvement in his blood pressure.

The patient underwent a laparoscpic left adrenalectomy (Fig. 2).

The resected mass showed a typical –yellow appearance, and the results of histological analysis were consistent with adrenal adenoma with no cytologic features of malignancy (Fig. 3).

Post operatively, patient had complete recovery of neuromuscular symptoms. However, his blood pressure ranged between a maximum of 160/90 mmHg and a minimum of 120/70 mmHg.

He was discharged on the third day after surgery, with normal serum potassium level and blood pressure of 130/60 mmHg on Amlodipine 10 mg/day.

The patient's serum potassium remained normal during the following 4 months with a well-controlled blood pressure.

Plasma aldosterone and renin levels markedly declined 3 months after surgery with normal ARR.

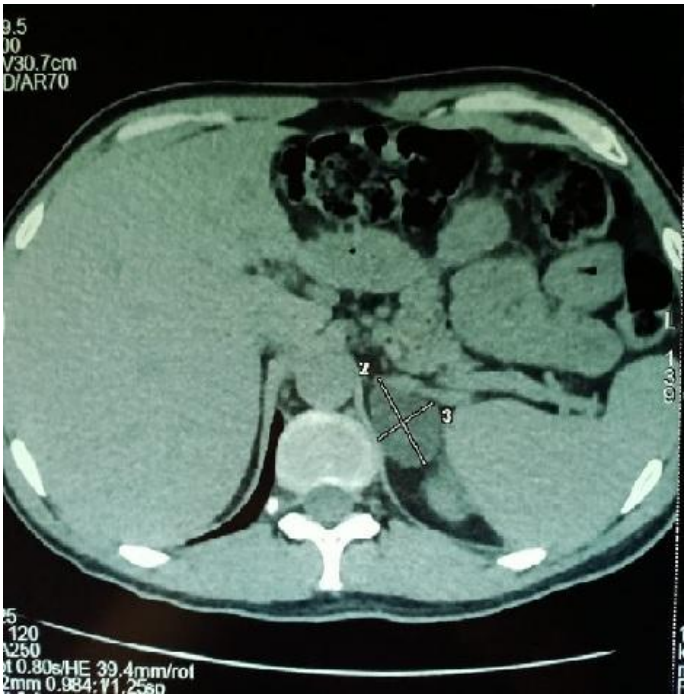

Fig. 1. Contrast enhanced CT scan showed a nodular mass measuring 40 x 28 mm with intact capsule located in the left adrenal gland

Table 1. The laboratory results of the hormone levels

Test	Patient's result	Normal range
Metanephrines (mmol/L)	0.24	<0.37
Normetanephrines (mmol/L)	0.4	<0.93
Plasma renin activity (PRA) (mIU/L)	<0.5	2.8-39.9
Plasma aldosterone (PA) (pmol/L)	686	32.5-655
PAC /PRA	137	<64

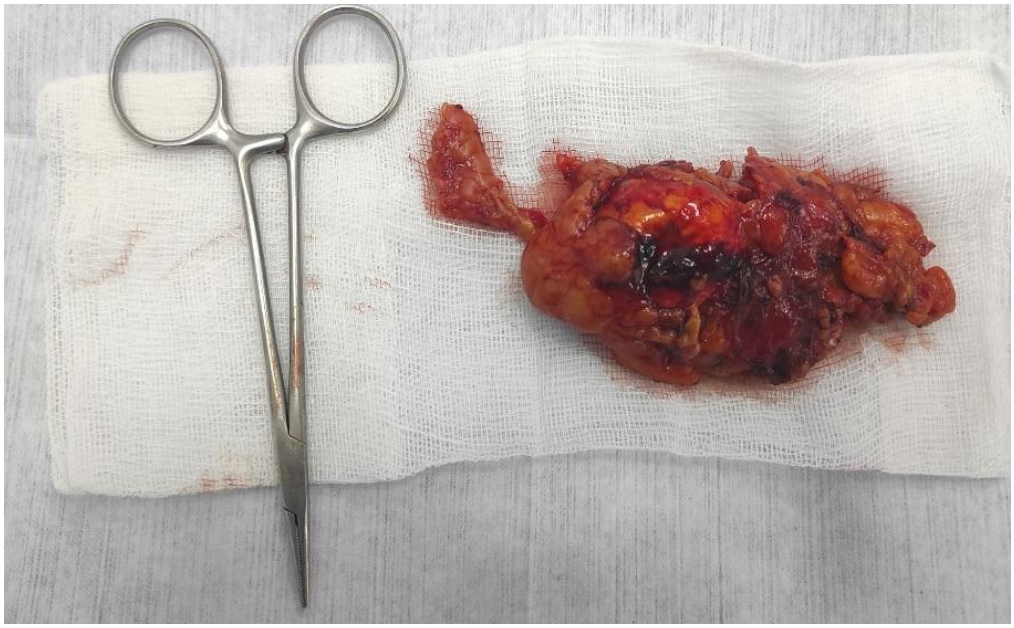

Fig. 2. Biopsy specimen of the left adrenal gland

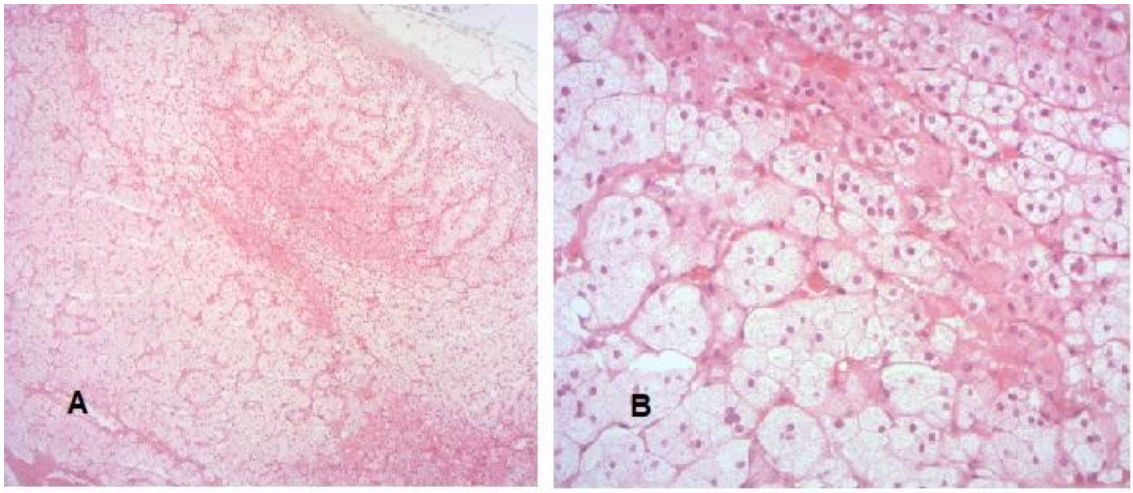

Fig. 3. (A): Tumor proliferation with nested architecture separated by vascular stroma. The capsule was intact (HEx50). (B): Tumor cells with abundant clear vacuolated or eosinophilic cytoplasm. The nuclei were small and monomorphic without mitotic figures (HEx200)

3. DISCUSSION

Primary aldosteronism (PA) is a common cause of secondary hypertension arising from autonomous over-secretion of aldosterone and a suppressed plasma renin activity [6].

In the majority of cases, clinical features of PA are variable and non-specific. Thus, it is usually underrecognized and identified as an essential hypertension.

Although spontaneous hypokalemia (less than 3,5 mmol/L)is not frequently alarming for clinicians, it may aid in the early diagnosis of PA [3].

Recent studies have reported the prevalence of hypokalemia in PA, ranging from 9% to 37% [7,8].

The hypokalemia secondary to PA is commonly moderate and asymptomatic [9].

Hypokalemic patients typically present with muscle weakness and extremity paresthesias. Thus, chronic hypokalemia is frequently well endured and patients may not manifest serious complaints.

Nevertheless, in cases where hypokalemia becomes significant, it may result in rhabdomyolysis [10].

Muscle enzyme elevation usually occur when serum potassium concentration drop below 2,5 mmol/l [11].

In our clinical case, we describe an uncommon presentation when severe rhabdomyolysis was the primary presenting feature of PA.

The patient presented with neuromuscular symptoms and findings of rhabdomyolysis due to profound hypokalemia.

Indeed, rhabdomyolysis is life-threatening emergency as it can lead to potential complications including acute renal failure, irregular heart beat and disseminated intravascular coagulation. There are multiple causes of rhabdomyolysis, including alcoholism, some drugs such as lipid-lowering agents, infections, and trauma and crush injuries.

Nevertheless, rhabdomyolysis related to Conn's syndrome is uncommon and there are few reported cases in the literature [12,13].

To the best of our knowledge, this is the first reported case in Tunisia.

The mechanisms by which rhabdomyolysis may occur are many. As reported by several studies, hypokalemia results in dysfunction of the sodium-potassium adenosine triphosphate (Na/K-ATPase) pump, leading to an increase of sodium permeability and calcium influx via the sodium –calcium pump [13].

Consequently, excess intracellular calcium activates signaling to stimulate intracellular proteolytic enzymes which lead to muscle necrosis [13].

Similarly, hypokalemia induces insufficient vasodilatation of arterioles and capillaries that perfuse muscles, resulting in ischemia and necrosis of myocytes.

Clinically, rhabdomyolysis may include muscle weakness, myalgia and myoglobinuria which is responsible of the tea-colored urine, despite the fact that some patients are totally asymptomatic [14].

The gold standard for laboratory investigation is the determination of plasma CK level. Despite no absolute cut -off value can be established, a serum concentration at least 5 times the upper limit of normal (1000 IU/L) is usually considered in clinical practice [15].

The management of neuromuscular symptoms and rhabdomyolysis required potassium replacement therapy associated with generous intravenous hydration [14]. But, the treatment of the underlying etiology is imperative to prevent rhabomyolysis's recurrence.

In our case, rhabdomyolysis was the leading symptom of an aldosterone- producing adenoma. Once diagnosed, adrenalectomy represents the gold standard treatment for patients with unilateral primary aldosteronism variants [16].

Laparoscopic adrenalectomy, using transperitoneal or retroperitoneal approaches, is currently the preferred strategy.

Laparoscopically treated patients experienced markedly less complications after surgery and are similarly likely to enhance blood pressure control and correct hypokalemia, when compared to patients who underwent an open approach [17]. Thus, laparoscopic partial (sparing)

adrenalectomy has newly featured as an increasing approach in patients with unilateral PA [17,18].

Benefit-risk balance should be carefully considered before selecting the surgical approach.

In fact, adrenalectomy is considerably successful in curing the Conn 's syndrome ,with improvement of hypokalemia in almost all patients, resolution of hypertension in about 50% of cases, and a significant improvement in control of blood pressure in patients who remain hypertensive [19,20].

In many recent studies, the outcomes of adrenalectomy have focused mainly on blood pressure control and the normalization of serum potassium concentration, as markers for recovery of primary aldosternism.

Yet, the aim of surgical treatment is the normalization of aldosterone, as high levels of this hormone can induce cardiovascular diseases and renal failure, independently of controlled blood pressure. Consequently, we absolutely recommend the requirement of considering the normalization of aldosterone-renin ratio (ARR) after surgery as the leading biological marker for identifying outcomes of PA.

Moreover, recent onset-hypertension and the preoperative blood pressure response to spironolactone are considered as predictors of clinical success after surgery.

4. CONCLUSION

The presenting case underlines that Conn's syndrome can have a varied clinical spectrum and the diagnosis should be established at earliest, as it is remediable.

We reported an unusual situation of PA which is manifested not only by severe hypertension but also complicated with metabolic myopathy and rhabdomyolysis.

Therefore, when evaluating patients with hypokalemia induced myopathy, clinicians should bring PA into consideration.

For this reason, plasma aldosterone and renin levels should be evaluated.

Underlying causes of secondary hypertension is potentially crucial, which can lead to certain recovery with optimal surgical treatment.

CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this case report and accompanying images.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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