

Unusual presentation of the Conn's syndrome: a case report

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Abstract

A 26-year-old woman presented with rhabdomyolysis secondary to severe hypokalemia. Hypertension and metabolic alkalosis could lead to the suspicion of primary aldosteronism, which was confirmed by a decreased plasma rennin, elevated plasma aldosterone levels and high aldosterone/rennin ratio additionally. Additionally adrenal computed tomography showed an adrenal tumour. Blood pressure and hypokalemia returned to the normal level after adrenalectomy was performed. This case report highlights the need to be alert to the possibility of primary aldosteronism incidence in a patient presenting with rhabdomyolysis and hypertension caused by severe hypokalemia.

Keywords: Conn's syndrome, hypokalemia, rhabdomyolysis.

Introduction

The primary aldosteronism (PA) resulting from an adrenocortical adenoma (Conn's syndrome) is a common and a curable cause of secondary hypertension [5]. The combination of hypertension, hypokalemia, and metabolic alkalosis is important for a diagnosis of PA. In few cases, hypokalemia caused by PA can be severe enough to cause rhabdomyolysis. Here we report a case of rhabdomyolysis caused by severe hypokalemia, which in turn was resulted in the PA. The patient was cured after performing adrenalectomy.

Case report

A 26-year-old-woman was admitted to the hospital because of five days history of generalized muscle weakness involving predominantly the lower limbs. That was associated with myalgia, muscle cramp and paresthesia. She had history of episodic

muscle weakness of the lower limbs over the past few months. There was no history of infection or trauma. She also had not experienced diarrhea or vomiting, and any use of diuretics, herbal supplements, liquorice, laxatives or other medications. She did not suffer from renal disease or hypertension and had no symptoms suggestive of thyroid disease. She had regular menstrual cycles.

On physical examination, her weight was 58Kg and height 160cm (BMI = 22.65), blood pressure 170/115 mmHg, body temperature 36.8 °C, pulse rate 70 beats/min, and respiratory rate 18/min. There was weakness of both lower limbs (4/5) with normal sensations. The power and sensation of both upper limbs were normal and normal cardiovascular and respiratory rates. The abdominal examination did not reveal hepatosplenomegaly or bruits on auscultation with no features of Cushing's syndrome.

Laboratory investigations were as follow: potassium 1.5 mEq/L [normal range (NR):

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3.6-5.1 mEq/L] pH7.53, PaO₂ 10.4 kPa, PCO₂ 5.27 kPa, HCO₃ 32.5 mEq/L, creatinine phosphokinase (CPK) 19395 IU/L [NR: 20-270 IU/L], creatinine 0.52 mg/dl [NR:0.599-1.09 mg/dl], sodium 141 mEq/L [NR: 134-144 mEq/L], corrected calcium 2.21 mEq/L [NR: 2.1-2.6 mEq/L], magnesium 0.91 mEq/L [NR: 0.4-2.88 mEq/L], and phosphate 0.57mEq/L [NR: 0.87 – 1.45 mEq/L]. The transaminases were slightly raised (AST 68 IU/L, ALT 109 IU/L). The bilirubin and coagulation indices and thyroid function test were normal (TSH 3.81 IU/mL). Urinary potassium was 33.5 mEq/24h [NR: 2-300 mEq]. The ECG showed presence of U waves and no hypertensive changes. She was treated with boluses of IV potassium chloride plus oral potassium supplements, for a total of 700 mmol over 4 days. Initially her hypertension was treated with Amlodipine 5mg once a day. In spite of repeated IV and oral potassium supplements, her potassium level remained low and the ECG showed changes of hypokalemia.

The PA was suspected because of persistent hypokalemia in association with hypertension and metabolic alkalosis. Therefore, after correction of her potassium level, she was examined for the plasma aldosterone concentration (PAC) and direct rennin concentration (DRC). Results revealed a low DRC level of 1.5 mUI/L (NR: 2.8-39.9 mUI/L), along with a very high PAC level of 2669 pmol/L (NR: 22-477 pmol/L). The aldosterone/rennin ratio was 1779. 24-hour urinary aldosterone excretion after 3 days of salt overload was 182.9 microg. (NR: 3.9-55.5 microg). The CT abdomen revealed a left adrenal gland mass measuring about 2.5x1.2 cm (Fig.1). The patient was on spironolactone treatment for three weeks pre-operatively, which improved her weakness and hypokalemia. Hence, she underwent a successful laparoscopic left adrenalectomy.

On gross examination, the mass was golden-yellow in colour without evidence of necrosis or hemorrhage (Fig.2). Histopathological examination of the mass showed features of adrenal adenoma, without necrosis,



Fig.1. CT scan of the adrenal gland.



Fig. 2 Gross appearance of the adrenal gland.

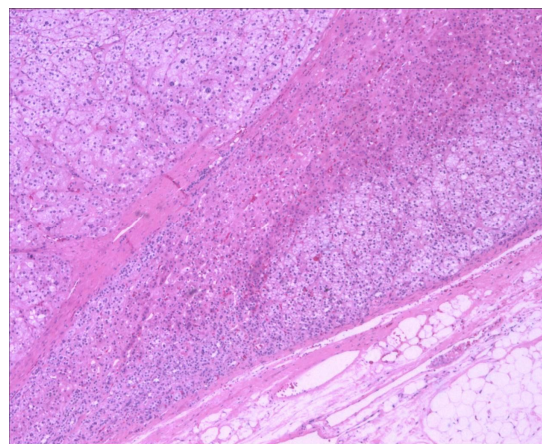


Fig. 3. histopathology of the adrenal gland.

vascular or capsular invasion (Fig.3). The findings were consistent with Conn's syndrome. Following surgery, the patient was normotensive, and the serum potassium was 3.7 mmol/L without antihypertensive medications. She was discharged without medication, and follow up continued at the outpatient clinic. She remained normotensive and normokalemic for the last 4-5 months after discharge.

Discussion

PA is a common cause of secondary hypertension, and characterised by hypertension, hypokalemia, suppressed plasma renin, and increased aldosterone excretion. The rhabdomyolysis as a presentation feature of primary aldosteronism is an extremely rare association. There are about sixteen related reported cases in the literature [1] and to the best of our knowledge this is the first reported case in Kuwait. The rhabdomyolysis is characterized by muscle necrosis and the release of its contents into the circulation, including myoglobin, potassium, phosphate, urate and creatinine kinase. There are many causes of rhabdomyolysis, including crush injury, excessive exercise, metabolic and endocrine disorders, infections, drugs, toxins like alcohol or statins, and excessive heat exposure [2]. Hypokalemia is a recognised cause of rhabdomyolysis. The symptoms of malaise, muscle weakness, fatigability, and myalgia occur when serum concentration of potassium is below 3 mEq/L. However, muscle enzyme elevations are usually seen when potassium concentrations fall below 2.5 mEq/L [2]. The important biochemical findings in rhabdomyolysis are hyperkalemia and a high anion gap acidosis as a consequence of the release of organic acids from necrotic muscles. In our case, hypokalemic metabolic alkalosis and hypertension raised the suspicion of primary aldosteronism.

The aldosterone-producing adenoma (APA) and bilateral idiopathic hyperaldosteronism (IHA) are the most common subtypes of PA. The APA is a small nodule (< 2cm) that mostly occurs in the left adrenal gland and commonly found in females, and usually present with severe hypertension and more profound hypokalemia. It is also more common in younger patients (between the ages of 30-50), with higher plasma and urinary levels of aldosterone [3].

Biochemical abnormalities of the APA include hypokalemia, metabolic alkalosis, and a relative hypernatremia. Although spontaneous hypokalemia in a patient with hyper-

tension is a strong indicator of aldosteronism, only a minority of patients (9-30%) have a potassium level that is in the low-normal range [4]. Therefore, hypokalemia is not the criterion used for diagnosis of the PA. It is recommended to test for the PA in the following groups: patients with hypertension and hypokalemia, treatment-resistant hypertension (i.e on 3 antihypertensive medications with poor control), severe hypertension (≥ 160 mmHg systolic or ≥ 100 mmHg diastolic), hypertension with adrenal incidentaloma, and the onset of hypertension under the age of 20 [5]. Screening is done by measuring the PAC level and PRC. When the PAC is greater than 15ng/mL, the PRC is less than 1ng/mL/h – as seen in this case – and the ratio of the two (PAC/PRC) is greater than 20, with the sensitivity and specificity of approximately 75%. This test is valid as long as a patient is not taking aldosterone antagonists, such as spironolactone, epleranone, or renin inhibitors [6].

The screening test is not a diagnostic tool, and PA must be confirmed by demonstrating inappropriate aldosterone secretion. Confirmatory testing can be done by any of the four procedures: oral sodium loading and measurement of urinary aldosterone, intravenous sodium chloride loading and measurement of PAC, fludrocortisone suppression, or captopril challenge [6]. In our case we used the oral sodium loading test which showed a non-suppressed urinary aldosterone excretion.

Once PA has been diagnosed biochemically, it is important to determine the subtype to help in directing the therapy. Unilateral adrenalectomy in patients with the APA or unilateral adrenal hyperplasia results in normalization of hypokalemia and hypertension, while in bilateral IHA, unilateral or bilateral adrenalectomy rarely corrects the hypertension [7], and medical therapy is therefore the treatment of choice.

Adrenal CT is not a correct choice in distinguishing between the APA and IHA. It cannot reliably visualize microadenomas or distinguish incidentalomas from the APAs, which makes the adrenal venous sampling

(AVS) to be the most accurate mean to differentiate between unilateral from bilateral forms of PA [8]. The AVS is essential for appropriate therapy in many patients with PA who have a high probability of having an APA and want to pursue surgical management [6], but it is expensive and invasive. The procedure itself has a relatively low success rate because of the difficulty in cannulating the right adrenal vein (which is smaller than the left and empties directly into the IVC rather than the renal vein) [8]. The most important factors that determine the successful characterization of both adrenal veins in a patient with PA are the experience, dedication and presence of repetition of the radiologist performing the procedure [9]. A more practical approach is the selective use of AVS as recommended by Young [5] which is based on patient preferences, age, adrenal morphologic appearance on CT, clinical comorbid conditions, and clinical probability of finding an APA. For patients younger than 40, in whom a solitary adenoma is >1cm with normal contralateral adrenal gland, a unilateral adrenalectomy may be done without venous sampling and in the absence of comorbid conditions. Therefore, the AVS was bypassed in our case based on these criteria.

The mainstays of therapy for the APA include surgical adrenalectomy, and alternatively the use of aldosterone antagonists, such as spironolactone. The efficacy of adrenalectomy has been confirmed in a study where the diagnosis of APA was established, and in which a fall of BP observed in all patients. Moreover, 82% of patients were either improved markedly or cured (32%), thereby allowing the withdrawal of all antihypertensive medications [10,11,12].

Conclusion

Rhabdomyolysis is uncommon in patients with the APA. We recommend considering the APA, when rhabdomyolysis occurs in a patient with severe hypokalemia and meta-

bolic alkalosis since the disease could be curable like in our case.

References

1. Martinez JJ et al. Rhabdomyolysis due to primary hyperaldosteronism. A case report. *Endocrinol Nutr.* 2009;56:431-4.
2. Allison RC, Bedsole DL. The other medical causes of rhabdomyolysis. *Am J Med Sci.* 2003; 326:79-88.
3. Stewart PM. Mineralocorticoid hypertension. *Lancet* 1999; 353:1341-7.
4. Mulatero P, Stowasser M, Loh KC, Fardella CE, Gordon RD, Mosso L, Gomezsanchez CE, Veglio F, Young WF, Jr: Increased diagnosis of primary aldosteronism, including surgically correctable forms, in centers from five continents. *J Clin Endocrinol Metab* 2004; 89:1045-50
5. Young WF. Primary aldosteronism: renaissance of a syndrome. *Clin Endocrinol (Oxf).* 2007; 66:607-18.
6. Funder JW, Carey RM, Fardella C, Gomez-Sanchez CE, Mantero F, Stowasser M, et al. Endocrine Society. Case detection, diagnosis, and treatment of patients with primary aldosteronism: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2008; 93:3266-81.
7. Myer, A., Brabant, G. & Behrend, M. Long-term follow-up after adrenalectomy for primary aldosteronism. *World Journal of Surgery* 2005; 29: 155-159.
8. Kempers MJ, Lenders JW, van Oudehousden L, van der Wilt GJ, Schultze Kool LJ, Hermus AR, et al. Systematic review. Diagnostic procedures to differentiate unilateral from bilateral adrenal abnormality in primary aldosteronism. *Ann Intern Med.* 2009; 151:329-37.
9. Young WF, Stanson AW. What are the keys to successful adrenal venous sampling (AVS) in patients with primary aldosteronism? *Clin Endocrinol (Oxf).* 2009;70:14-7.
10. Rossi GP, Bolognesi M, Rizzoni D, Seccia TM, Piva A, Porteri E, et al. Vascular remodelling and duration of hypertension predict outcome of adrenalectomy in primary aldosteronism patients. *Hypertension* 2008; 51:1366-1371.
11. Hari Kumar KV, Jha S, Jha R, Modi KD. Conn's Syndrome – Atypical Presentations. A report of two cases. *Saudi J Kidney Dis Transpl* 2009; 20(2):278-281.
12. Tien-Hua Chuang, Chin-Hsein Wang, Bo-Yuan Tseng, Yung-Hsiang Hsu, Jen-Pi Tsai, Bang-Gee Hsu, et al. Conn's Syndrome with an Unusual Presentation of Rhabdomyolysis Secondary to Severe Hypokalemia. A case report. *Tzu Chi Med J* 2008; 20(4):327-331.