Rhabdomyolysis Secondary to Severe Hypokalemia: Case Report

Abstract
Primary hyperaldosteronism is an endocrine disorder characterized by an increased aldosterone excretion from the adrenal glands, which causes hypertension, hypokalemia, and suppressed plasma renin activity. It can be difficult to diagnose until hypokalemic manifestations, such as rhabdomyolysis, occur, and also these subjects may be treated as essential hypertensive patients. Here, we report a 51-year-old woman who presented with rhabdomyolysis caused by severe hypokalemia and was diagnosed with Conn's syndrome. Turk Jem 2010; 14: 100-2

Key words: Primary hyperaldosteronism, hypokalemia, rhabdomyolysis

Case Report
A 51-year-old woman was admitted to our hospital with severe weakness and muscle cramps. She had a history of hypertension for nine years and had been treated with indapamide for the last two years. Three months ago, her routine biochemical tests revealed hypokalemia and normal creatine phosphokinase (CPK) levels. At that time, she had no complaints and her examination was normal. The patient had been operated on for parathyroid adenoma in 2002. At admission, she was visibly unwell. The blood pressure was 150/80 mm/Hg, pulse rate was 76/min. Cardiovascular, pulmonary and abdominal examinations were unremarkable. She had paresthesia and muscle cramps, but musculoskeletal examination revealed normal muscle strength. Her neurological examination was normal. Initial laboratory tests showed severe hypokalemia (1.58 mmol/L, normal reference range: 3.6-5.1 mmol/L), extreme elevation of the serum CPK levels (22,230 IU/L, normal reference range: 29-200

Introduction
Primary hyperaldosteronism (PA) is characterized by hypertension, hypokalemia, metabolic alkalosis, suppressed plasma renin activity (PRA) and increased aldosterone excretion. With current screening methods, it appears that PA may be the most common form of secondary hypertension accounting for up to 5-10% of all hypertensives. The two major subtypes of primary hyperaldosteronism are bilateral idiopathic hyperaldosteronism and aldosterone-producing adenoma (APA) (1,2). It is has been recently recognized that most patients with PA are not hypokalemic. Plasma aldosterone concentration (PAC) to PRA ratio is currently the most reliable method of screening for PA (1-5). Clinically, hyperaldosteronism is mostly asymptomatic, but some patients may present with severe hypokalemia, muscle weakness, unusual sensations (paresthesias), muscle cramps, tetany, and in severe cases, transient paralysis. We present a patient with PA associated with severe rhabdomyolysis due to profound hypokalemia.
IU/L), and metabolic alkalosis (bicarbonate 29 mmol/L; normal reference range: 22-26 mmol/L). Other laboratory analysis showed: urea nitrogen 53 mg/dL (10-50 mg/dL); creatinine 1.5 (0.6-1.2 mg/dL); magnesium 1.9 mg/dL (1.7-2.3 mg/dL); uric acid 6.9 mg/dL. Electrocardiogram revealed a normal sinus rhythm with non-diagnostic T-wave changes consistent with hypokalemia. Complete blood count, urine examination and chest X-ray were normal. Electrocardiogram revealed a normal sinus rhythm with non-diagnostic T-wave changes consistent with hypokalemia. There was no history of crush injury, intense physical exercise, fever, seizures, diabetes mellitus, recent viral illness, alcohol and drug abuse or musculoskeletal disease, which can cause rhabdomyolysis. Based on these findings, the patient was diagnosed with hypokalemic rhabdomyolysis. Due to the possibility of drug-induced hypokalemia, indapamide was discontinued. Potassium and fluid replacement therapies were initiated. Two weeks later, the musculoskeletal symptoms resolved and the serum CPK levels, renal and hepatic function tests returned to normal ranges (Table 1). Because of the severe hypokalemia, the patient was screened for secondary causes of hypertension. The morning supine PAC was elevated at 38.6 ng/dL (supine normal range: 2.9-16.1). The simultaneous PRA was low at 0.16 ng/mL/h (supine normal range: 0.2-2.8), giving a calculated supine aldosterone-to-renin ratio (ARR) of 241.2. PAC was 33 ng/dL, remained high in response to a saline load, and ARR was calculated as 100. Abdominal computed tomography (CT) showed a low-density left adrenal mass measuring 2.5x1.5 cm in diameter (Figure 1). Also the laboratory analysis of thyroid function, urinary melanocortin, normetanephrine, vanilmandelic acid and cortisol levels, and renal Doppler ultrasound were normal. PA was suspected and the patient was referred to surgery service for laparoscopic adrenalectomy. A solitary adenoma was removed surgically and pathologic examination revealed a benign adrenocortical adenoma. After surgery, she had no complaints and did not need any antihypertensive medication or potassium replacement therapy.

Discussion

Here, we report the case of a patient with rhabdomyolysis who was admitted to our hospital with diffuse myalgia, cramps and weakness caused by severe diuretic-induced hypokalemia. There are a few reports of cases of PA complicated by hypokalemia and rhabdomyolysis [6,7]. The mechanism of the hypokalemia-induced rhabdomyolysis in PA is still not clear, but some reports suggest that the enhanced muscle sodium-potassium pump (ATPase) activity may cause an increased potassium entry into the cells. Hypokalemia may induce muscle injury or frank necrosis as a consequence of relative ischemia [3,7]. If hypokalemia is not treated early, it may lead to worsening of mild myalgia to tetraplegia or severe acute renal failure because of the release of intracellular muscle constituents such as CPK and myoglobin into the circulation [7]. PA should be suspected in a hypertensive patient with hypokalemia and metabolic alkalosis. However, hyperaldosteronism may also present with normokalemia, especially in the early phase of the disease, and after taking potassium-wasting diuretics, hypokalemia occurs, as seen in this case. Because of the severe hypokalemia, rhabdomyolysis, hypertension and metabolic alkalosis, the patient was screened for secondary causes of hypertension. There was no history of crush injury, intense physical exercise, fever, seizures, diabetes mellitus, recent viral illness, licorice, laxatives, alcohol and drug abuse or musculoskeletal disease, which are causes of rhabdomyolysis. Bartter syndrome and Gitelman syndrome were excluded, because the patient had a history of hypertension for nine years. Biochemical diagnosis of PA was made by measuring a high level of PAC (≥ 15 ng/dL) in the setting of low PRA (< 1 ng/mL/h). If the

| Table 1. Serum biochemistry profile of the patient on admission, on the third day, 1st week, 2nd week, 4th week (post-operative) |
|---------------|----------------|--------------|--------------|--------------|--------------|--------------|--------------|
|               | Reference range | Admission    | 3rd day      | 1st week     | 2nd week     | 4th week     | Post-op      |
| Sodium        | (136-144 mmol/L) | 145          | 145          | 143          | 137          | 143          |
| Potassium     | (3.6-5.1 mmol/L) | 1.58         | 3.6          | 4.1          | 4.6          | 3.8          |
| CPK           | (29-200 U/L)    | 22,230       | 1,8305       | 2,022        | 94           | 55           |
| Urea          | (10-50 mg/dL)   | 53           | 15           | 25           | 33           | 41           |
| Creatinine    | (0.6-1.2 mg/dL) | 1.5          | 1.2          | 1.2          | 1.2          | 1.2          |
| AST           | (15-41 U/L)     | 279          | 601          | 140          | 24           | 16           |
| ALT           | (10-40 U/L)     | 76           | 271          | 168          | 29           | 12           |
| Bicarbonate   | (22-26 mmol/L)  | 29.3         | -            | -            | 23.6         | 22.8         |

Figure 1. CT scan on admission showed a low-density left adrenal mass measuring 2.5x1.5 cm in diameter (arrow).
results are high (ARR ≥ 20 ng/dL per ng/mL per hour), then confirmation is required. These tests are available: [1] the saline suppression test, [2] the dietary sodium loading test, [3] the fludrocortisone suppression test, and [4] the captopril suppression test [1,2,4]. The most commonly used confirmatory test is the saline suppression test. Patient with inappropriate aldosterone secretion will not have a suppression of aldosterone [4,8,9]. The next step of the diagnosis is to perform a CT imaging. If there is an adrenal mass, adrenal vein sampling (AVS) should be tested. But, for cases, in which APA is identified with high prevalence (patients ≤ 40 years of age with marked PA, e.g. PAC ≥ 30 ng/dL and a well-defined hypodense adrenal mass), AVS can be bypassed and unilateral adrenalectomy can be performed [2,10]. In our case, biochemical and clinical evidence of aldosterone excess was clear. The presence of a left-sided adenoma (size > 1 cm, uniform, round, hypodense, e.g. Hounsfield unit score ≤ 10) was confirmed with CT imaging. Thus, AVS was not necessary.

Treatment for PA can be surgical or medical, which depends on the subtype of the disease. Most functional adrenal tumours are benign and surgery is the main treatment modality for Conn’s syndrome [2]. In the majority of patients with surgically managed APA, blood pressure and serum potassium levels improve [2,10]. PA is a common and potentially curable cause of secondary hypertension. This case showed us that PA may not be diagnosed until hypokalemic manifestations, such as rhabdomyolysis, occur. In hypertensive patients, the serum potassium concentration should be determined prior to the initiation of diuretic therapy.

Also, physicians should be aware of hypokalemia-induced rhabdomyolysis among patients with PA.

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Written consent for publication was obtained from the patient.

References