Rhabdomyolysis may be secondary to trauma, excessive muscle activity, hereditary muscle enzyme defects and other medical causes. Primary hyperaldosteronism is characterised by hypertension, hypokalemia, suppressed plasma renin activity, and increased aldosterone excretion. Rhabdomyolysis is not common in primary hyperaldosteronism. We report here a 42-year-old woman presenting with rhabdomyolysis as heralding symptom of primary hyperaldosteronism. We also carried out a search of the literature to identify all cases of rhabdomyolysis as the first-recognized expression of a primary hyperaldosteronism. Sixteen cases met the criteria for inclusion. When rhabdomyolysis occurs in a patient with hypokalemia and metabolic alkalosis, primary hyperaldosteronism has to be suspected: if confirmed, an aldosterone-producing adenoma is the most probable cause.

Key words: Rhabdomyolysis. Hyperaldosteronism. Adrenal adenoma.

INTRODUCTION

The word rhabdomyolysis is generally used to include the clinical and laboratory syndrome resulting from muscle injury and release of potentially dangerous substances into the circulation\(^1\). Rhabdomyolysis may be secondary to trauma, excessive muscle activity, hereditary muscle enzyme defects and other medical causes including drugs, metabolic disorders (such as hypokalemia, hypophosphatemia, hypernatremia and hyperosmolar state) and endocrine diseases (such us hypothyroidism, hyperthyroidism, diabetic ketoacidosis, and pheochromocytoma)\(^1\).

Primary hyperaldosteronism (PA) was reported by Conn more than fifty years ago\(^2\), and hypertension, hypokalemia, suppressed plasma renin activity (PRA), and increased aldosterone excretion characterise classically this syndrome\(^3\).

Although the first reports of primary hyperaldosteronism included weakness among the symptoms of this syndrome\(^4\), and myopathy related to hyperaldosteronism have been reported in several cases, rhabdomyolysis is not common in primary hyperaldosteronism. Here we report a new case of rhabdomyolysis due to primary hyperaldosteronism and review the patients reported in the literature that showed rhabdomyolysis as the opening manifestation of the syndrome.

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Los autores declaran no tener ningún conflicto de intereses.

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Manuscrito recibido el 29-7-2009 y aceptado para su publicación el 14-9-2009.
CASE REPORT

A 42-year old woman was admitted to hospital because she complained of generalized weakness and muscular pain. She had not been diagnosed of hypertension, although she said she had had elevated blood pressure sometimes in the past. She did not take any medical or herbal treatment, and she denied to take any kind of liquorice. She had had 3 progressive weakness since one month prior to admission although she had suffered similar symptoms several times in the past. Physical examination revealed a well orientated, alert patient, a blood pressure of 166/108 mm Hg, and flaccid quadripareisis with hyporeflexia.

Laboratory data included the following serum values: sodium 138 mEq/L [normal range (NR): 135-145], bicarbonate 38.8 mEq/L [NR: 20-24], potassium 1.3 mEq/L [NR: 3.5-5], pH 7.536 [NR: 7.350-7.450], creatinine 0.9 mg/dL [NR: 0.5-0.9], creatine phosphokinase (CPK) 21000 IU/L [NR: 26-140], calcium 7.4 mg/dL [NR: 8.6-10.2], and magnesium 1.8 mEq/L [NR: 1.58-2.55]. An electrocardiogram (ECG) showed plain T waves. Urinary potassium at admission was 9.3 mEq/L.

The patient was treated with intravenous potassium, and muscular strenght and CPK gradually normalised, and blood pressure remained high.

Endocrinologic investigation showed intact parathyroid hormone (PTH) 184 pg/mL [NR: 10-65]; 25-OH-vitamin D 47.7 ng/mL [NR: 12-80]; cortisol after 1 mg of dexametasone 0.2 μg/dL; resting aldosterone 96.6 ng/dL [NR: 1-10.5]; PRA undetectable [NR: 0.4-1.9 ng/mL/h]; 24-hour urinary aldosterone excretion after 3 days salt overload 23.73 μg; aldosterone before infusion of 2 litres of normal saline 52.4 ng/dL [NR: 1-10.5], and after the infusion 116.4 ng/dL, resting aldosterone before 4 hours upright 77.6 ng/dL [NR: 1-10.5], and after being upright 32.2 ng/dL. An abdominal computed tomography (CT) showed a 20×10 mm mass located in the right adrenal gland. Bilateral adrenal venous sampling localized aldosterone production in the right adrenal gland (right adrenal aldosterone/cortisol quotient 98; left adrenal aldosterone/cortisol quotient 3.76; peripheral vein aldosterone/cortisol quotient 13.9) and confirmed the diagnosis of Conn’s syndrome. Patient was on spironolactone treatment until a laparoscopic right adrenalectomy was performed. Pathological examination of the gland confirmed a 20 mm adrenal adenoma. Postoperatively the patient was normokaliemic without spironolactone, resting PRA was 0.52 ng/mL/h and aldosterone was 1.3 ng/dL, although hypertension persisted.

DISCUSSION

PA is characterised by hypertension, hypokalemia, suppressed PRA, and increased aldosterone excretion. Bilateral idiopathic hyperaldosteronism (IHA) and aldosterone producing adenoma (APA) are the most common subtypes of primary aldosteronism.

Unilateral hyperplasia and familial hyperaldosteronism are much less common. The first description of PA included muscular symptoms such as spams, weakness and paralysis and one of the first series of primary hyperaldosteronism, that included 103 patients, reported muscle weakness in 73% of patients, intermittent paralysis in 21%, tetany in 21% and muscle discomfort in 16%.

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<table>
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<th>Patient [reference]</th>
<th>Sex</th>
<th>Age</th>
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<th>Diameter (mm)</th>
<th>Serum potassium (mEq/l)</th>
<th>CPK (IU/l)</th>
<th>Anti-hypertensive treatment</th>
<th>Diuretics</th>
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ACE: angiotensin converting enzyme; AF with RVR: atrial fibrillation with rapid ventricular response; CPK: creatine phosphokinase; ECG: electrocardiogram; (p.c): present case.

Hypokalemia may potentially cause rhabdomyolysis. Frank rhabdomyolysis with myoglobinuria is usually observed only when serum potassium values are below 2 mEq/L. When serum potassium concentrations fall below 2.5 mEq/L, frank rhabdomyolysis may be mediated by release of intracellular potassium into the extracellular space caused by 3 mechanisms. First, increased blood flow to the exercising muscle may cause hypokalemia to lower the cell membrane potential to a point where excitability is increased, so that premature ventricular contractions occur. Second, hypokalemia may cause the muscle cell membrane potential to be more negative, leading to a decreased calcium influx. Third, hypokalemia may decrease the activity of certain enzymes, including aldosterone, which are involved in the production of aldosterone. Hypokalemia is a recognized cause of rhabdomyolysis.
nous potassium supplements resolved rhabdomyolysis normalising CPK values, before hyperaldosteronism was treated with spironolactone or surgery. This support that the main cause of rhabdomyolysis was hypokalemia and not the direct effect of aldosterone. Gender and age characteristics of patients with rhabdomyolysis and primary hyperaldosteronism are similar to the ones of a recent report of primary hyperaldosteronism in hypertensive patients, although we have found a difference in the age of presentation of rhabdomyolysis between men and women. All patients with rhabdomyolysis and primary hyperaldosteronism in whom the aetiology was reported had a APA. In contrast, one series of primary hyperaldosteronism showed an APA as the cause of PA in 42.8%, and IHA in the remaining 57.2% of patients. Another study reported 20% of surgically confirmed APA and 8% of probable APA, while the remainder 72% were considered to have probable or confirmed IHA. This finding is compatible with the fact that patients with APAs have more frequent hypokalemia, and higher concentrations of aldosterone, than those with IHA. Half of the patients with rhabdomyolysis and primary hyperaldosteronism were treated with diuretics, and this could aggravate hypokalemia, precipitating rhabdomyolysis. This underlines the importance of measuring potassium levels before treating a hypertensive patient with diuretics.

Although rhabdomyolysis is not a common entity in patients with primary hyperaldosteronism, we think that CPK levels have to be determined in these patients, especially when serum potassium is lower than 2.5 mEq/L. When rhabdomyolysis occurs in a patient with hypokalemia and metabolic alkalosis, PA has to be suspected: if confirmed, an APA is the most probable cause.

REFERENCES