Rhabdomyolysis in Celiac Disease

Vildan Ertekin[1], Mukadder Ayşe Selimoğlu[1], Hüseyin Tan[2], and Buket Kılıçaslan[1]

Atatürk University, Faculty of Medicine, Departments of [1]Pediatric Gastroenterology and Nutrition, [2]Pediatric Neurology, Erzurum, Turkey.

A 12-year-old female presented with chronic diarrhea, fatigue, failure to thrive, sudden weakness of her upper and lower extremities and inability to walk. On neurological examination, atrophy was found of the lower extremity muscles, coupled with muscle weakness. Hypokalemia and a high creatine kinase (CK) level were detected. Antigliadin IgA, IgG and antiendomysial antibodies were positive. A duodenal biopsy revealed the classical findings of celiac disease. To our knowledge this is the first childhood case of celiac disease presenting with rhabdomyolysis.

Key Words: Celiac disease, hypokalemia, rhabdomyolysis

INTRODUCTION

The term 'rhabdomyolysis' refers to the disintegration of striated muscle, resulting in the release, and circulation, of muscular cell constituents into the extracellular fluid.[1]

Hypokalemia, hypocalcemia, hypophosphatemia, hyponatremia, hypernatremia and hyperosmotic conditions have all been associated with rhabdomyolysis. Malnutrition and severe illness can also cause electrolyte disturbances that induce rhabdomyolysis.[1]

Hypokalemia alters the function of several organs, most predominantly affecting the cardiovascular, and neurological systems, the muscles and kidneys. Neuromuscular manifestations include muscle weakness and cramps, as well as increasing the incidences of rhabdomyolysis.[2]

Although muscle wasting and loss of muscular power, with hypotonia, may be present in celiac disease, rhabdomyolysis is an unusual presentation.[3] Only one case, a 60-year old, of celiac disease presented with rhabdomyolysis due to hypokalemia has been reported in the literature.[4] In this report, we present the first childhood case of celiac disease with this unusual presentation.

CASE REPORT

A 12-year-old female was admitted to the pediatrics clinic with fatigue and sudden weakness of her upper and lower extremities and with an inability to walk. Although she also had had a failure to thrive and chronic diarrhea for years, she had not been investigated for these complaints.

On physical examination her anthropometrical measurement revealed a failure to thrive. Her height and weight were both below the 3rd percentile (-5.4 S.D. and -3.9 S.D., respectively). Her blood pressure, heart rate and temperature were normal. She was cachectic; i.e. clubbing of her fingers was detected. Neurological examination was normal, with the exception of atrophy of the lower extremity muscles coupled with muscle weakness, which was more severe in lower extremities.

From laboratory investigations her urinalysis was normal; i.e. myoglobulinuria was not detected. Her hemoglobin, white blood cell (WBC) and platelet counts were 8.1 g/dl, 18×10^9/l, and 581×10^9/l, respectively. Her mean corpuscular volume (MCV) and red cell distribution wide (RDW) were 66.4 fl and 32.4, respectively, - with normal limits of serum glucose, urea, and creati-

nine. Her serum concentrations of sodium, potassium, calcium, magnesium and phosphate were 134 mEq/l, 1.2 mEq/l, 4.9 mg/dl, 2 mg/dl and 2.2 mg/dl, respectively. The corrected calcium level based on the serum albumin was 6.7 mg/dl. Serum alkaline phosphatase (ALP), aspartat aminotransferase (AST) and alanine aminotransferase (ALT) were 505 U/l, 321 U/l, and 168 U/l, respectively, with a creatine kinase (CK) of 6199 U/l. She had hypoproteinemia and hypoalbuminemia (total protein=4.7 g/dl and albumin=2.2 g/dl). The prothrombin time (PT), activated partial thromboplastin time (aPTT) and international normalized ratio (INR) were 15.9 seconds, 28.6 seconds and 1.3, respectively. A prominent U wave, prolonged Q-T interval and T wave inversion were detected in the ECG. She had steatorrhea, and the antigliadin IgA, IgG and antiendomysial antibodies were positive. After intravenous replacement of potassium, the ECG abnormalities disappeared; progressively she started to walk, and even run. On the third day of hospitalization she had no neurological abnormalities. An upper gastrointestinal endoscopy was performed, and a duodenal biopsy revealed total villous atrophy, crypt hyperplasia and increased intraepithelial lymphocytes; consistent with celiac disease. A gluten-free diet was started. Her serum CK, AST and ALT levels returned to the normal levels on the ninth day of hospitalization. And her PT and INR values responded to vitamin K administration.

DISCUSSION

Rhabdomyolysis is a common disorder, occurring as a primary disease or as a complication of a broad spectrum of other diseases. While some cases are caused by hereditary metabolic or structural abnormalities of the skeletal muscle cells, others occur in healthy persons as a result of exhaustive exercise, infections, intoxications, deficiency states, or trauma.[5]

Severe rhabdomyolysis (CK > or=5000 U/l) has been detected in 0.074% of the population of patients admitted to a large university hospital over a 7-year study period.[6]

Although the causes of rhabdomyolysis are diverse, current evidence suggests there may be a common final pathway mediating cellular injury. Hypokalemia, like hypophosphatemia, has been shown experimentally to reduce the muscle cell transmembrane voltage and to cause muscle cell damage.[7] Injury to the cells causes the efflux of cellular components into the circulation. The ability to identify some of these components, such as myoglobin or creatine kinase, facilitates the clinical recognition of rhabdomyolysis.

Since the occurrence of rhabdomyolysis may elevate the serum concentration of potassium, hypokalemia as a cause of rhabdomyolysis often goes unrecognized in many instances.[1]

In a study performed on 120 patients with hypokalemia, it was reported that 38 patients (31.7%) showed biochemical evidence of rhabdomyolysis (serum CK greater than 244 IU/l). The clinical and biochemical characteristics of patients with, or without, rhabdomyolysis were no different, with the exception of the mean serum osmolality, AST and creatinine and sodium levels, which were higher in patients with rhabdomyolysis.[8]

During rhabdomyolysis, extreme quantities of CK are released, with peak concentrations of 100,000 IU/ml, or more, not being unusual. Because the overall degradation and removal are slow, the concentration of CK remains elevated much longer, and more consistently than that of myoglobin. Consequently, CK is more reliable than myoglobin in assessing the presence, and the intensity, of damage to muscles.[1] In our case, although the CK level was high, no myoblobulinuria was detected. Myoglobinuria does not occur without rhabdomyolysis, but rhabdomyolysis does not necessarily result in visible myoglobinuria. Myoglobin causes discoloration of the urine, but not of the plasma. Urinary myoglobin causes a reddish-brown color, even in the absence of hematuria. Myoglobin is rapidly eliminated by the hepatic metabolism; therefore, tests for myoglobin in plasma or urine are not a sensitive diagnostic procedure.[1] Furthermore myoglobinuria may be sporadic or resolve early in the course of rhabdomyolysis. Since urine dipstick findings are positive in only 50% of patients with rhabdomyolysis, with a normal urine dipstick test result rhabdomyolysis cannot be ruled out.

Rhabdomyolysis can sometimes cause acute renal failure (ARF). If more than 100-g of skeletal muscle is damaged, the serum haptoglobin binding capacity becomes saturated; the circulating myoglobin becomes free, and is filtered by the kidneys. Myoglobin in the renal glomerular filtrate can precipitate causing renal tubular obstruction, and lead to renal damage.[9] In a study of 20 adult patients with rhabdomyolysis, seven patients (35%) were observed to develop ARF during hospitalization.[10] Another study reported 19% developing ARF; but in this study, with the exception of the initial serum creatinine, the clinical factors and laboratory tests were found not to be reliable predictors for its development.[11]

In the study of Veenstra et al.,[6] 51% of patients developed ARF. In a review by Ward[12] he states that there is a loose predictive correlation between CK levels and the development of ARF, where levels exceeding 16000 U/l are more likely to be associated with ARF. Other predictors for the development of ARF include: dehydration, sepsis, hyperkalemia or hyperphosphatemia on admission, and the presence of hypoalbuminemia. ARF had also been found to occasionally develop in patients with peak CK as low as 2000 IU/L.[12] In our case, no myoglobulinuria or ARF were detected even though the patient had hypoalbuminemia. Veenstra et al.[6] also reported the incidences of ARF and electrolyte disturbances were higher in patients with CK levels exceeding 15000 U/l.

While hyperkalemia, hypocalcemia, hepatic inflammation, cardiac arrhythmia, and cardiac arrest, are early complications of rhabdomyolysis; those of ARF and diffuse intravascular coagulation occur later. Hypocalcemia can be potentiated by the release of large amounts of phosphate from lysed muscle cells.[9] Hypocalcaemia was detected in 41% of patients with rhabdomyolysis.[6] In our case, the corrected calcium level, based on serum albumin, was 6.7 mg/dl, but returned to a normal level without calcium supplementation, suggestive of an early complication of rhabdomyolysis.

The treatment of rhabdomyolysis is primarily directed at preserving renal function. Intravenous hydration must be initiated as early as possible and should be used at least until the CK level

decreases to 1000 U/l. Initial hypocalcemia should only be corrected when a patient is symptomatic.[9] It is important to avoid further aggravating the hypercalcemia commonly developing during the recovery phase of rhabdomyolysis, when calcium deposited in the injured muscles is mobilized back to the extracellular space.[13]

This unusual presentation of celiac disease in childhood should raise the awareness of celiac disease as a potential cause of hypokalemic rhabdomyolysis, especially if the patient also has a failure to thrive.

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