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CASE REPORT

Rhabdomyolysis and coeliac disease: A causal or casual association? A case report and review of literature

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KEYWORDS
Rhabdomyolysis;
Coeliac disease;
Hypokalemia

Summary
Background: Rhabdomyolysis is a rare, potentially life-threatening condition, caused by multiple disorders. The association with Coeliac Disease (CD) has been rarely reported and in these cases muscular damage was imputed to hypokalemia. Herein we describe a new case of severe rhabdomyolysis in a child subsequently diagnosed as affected by CD, and review previous reports.
Case presentation: A 3-year-old boy was referred for diarrhea, brown urine, muscular pain/weakness, and no history of muscular trauma. At entry, laboratory tests showed elevated levels of creatine kinase (CK) (x 100 unv) and aspartate aminotransferase (AST) (x 10 unv), alanine aminotrasferase (ALT) (x 5 unv); electrolytes were within the reference range. Twenty-four hours after admission serum CK peaked 115,000 U/L and transaminases increased up to 30 times unv. Hyperhydration treatment was started with renal function monitoring. Urine output decreased little, while serum creatinine and urea nitrogen stayed within the reference range. Serum potassium levels went down to 2.8 mEq/L at day 3, in spite of supplementation. The patient completely recovered at day 16. Main metabolic causes of rhabdomyolysis were ruled out by appropriate tests. Because of rarely reported cases of CD/rhabdomyolysis, anti-tissue transglutaminase (tTG) antibodies were measured and found positive (IgA 34 U/mL, unv <9). HLA typing was DQA1 05:02, DQB1 03:02. As jejunal biopsy showed patchy villous atrophy, gluten free diet (GFD) was prescribed. One year after starting GFD, histology was normal.
Review of literature: Literature (search engines: PUB MED and GOOGLE SCHOLAR) from 1980 to 2016 retrieved 8 cases (age range: 12 to 75 years old) previously described.

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Conclusion: The present case suggests to check for CD in children with severe rhabdomyolysis. Because severe rhabdomyolysis itself may elevate the serum potassium levels, hypokalemia might go unrecognized as the cause of muscular damage.

Introduction

Rhabdomyolysis is a clinical syndrome characterized by skeletal muscle breakdown with leakage of muscle tissue components, including electrolytes (potassium, phosphate and urate), myoglobin and other sarcoplasmic proteins [e.g. creatine kinase (CK), lactate dehydrogenase (LDH), alanine aminotransferase (AST), and aspartate aminotransferase (ALT)] into the circulation [1].

Classical clinical presentation comprises (sub)acute-onset myalgia, transient muscle weakness and pigmenturia, caused by an excessive amount of myoglobin in the urine. However, the complete triad is observed in less than 10% of the patients [2]. Correct diagnosis is mandatory to interrupt the offending mechanism of action.

In children the most common cause of rhabdomyolysis is infectious while autoimmunity is rare [2—4]. Although coeliac disease (CD) is not listed among the major causes of rhabdomyolysis, hyper-transaminasemia frequently observed in CD has been attributed not only to liver disease but partly also to muscle injury including subclinical rhabdomyolysis with muscular enzymes release [5]. In the few adolescent-adult described cases of CD with overt rhabdomyolysis the latter was constantly triggered by hypokaliemia secondary to CD-related chronic malabsorption [6,7].

Here we describe a case of severe rhabdomyolysis in a 3-year-old child with a concurrent challenging diagnosis of CD. Also, we reviewed literature regarding the association rhabdomyolysis/CD.

Case presentation

A previously healthy 3-year-old boy was referred for intermittent diarrhea during the last 2 weeks, brown urine, and muscular pain. Neurological examination showed muscle weakness in the lower extremities with reduced tendon reflexes. Heart rate was 120 per minute, respiratory rate 30 per minute, blood pressure 120/70 mmHg, oxygen saturation 99%, temperature 36.1 °C. No signs of dehydration were reported. Examination of the cardiovascular and respiratory systems and abdomen were found normal. Liver and spleen were not enlarged. There was no evidence of any other organ system involvement. No history of muscular trauma or strenuous exertion was referred. Anamnestic data excluded the use of drugs or herbal products. Clinical symptoms were not precipitated by fasting, cold, illness, or emotional stress. Patient's laboratory data are summarized in Table 1.

At admission blood tests showed markedly elevated CK and transaminases levels; electrolytes were within the reference range. Urine dipstick (Ames) showed 4+ hemoglobinuria. Microcytosis and polyglobulia, with normal ferritin level, were also detected suggesting a possible thalassemia trait (positive family history). Rhabdomyolysis was immediately treated with hydration (15 mL/Kg isotonic chloride solution bolus and continued at 2 times maintenance [8]), strictly monitoring renal function. Urine output was maintained at 2—4 mL/Kg/hour. Twenty-four hours after admission serum CK peaked 115,000 U/L; transaminases serum levels also increased. Furosemide (2 doses 0.6 mg/Kg) was administered on hospital day 2 because of signs of fluid overload (increasing weight and blood pressure). Serum creatinine and urea nitrogen constantly stayed within the reference range as well as coagulation tests. Unexpected hypokaliemia, with normal magnesemia, appeared in the follow-up and treated. Asymptomatic hypocalcemia required no treatment. Renal potassium loss and subsequent related conditions were excluded due to low fractional excretion of potassium, tested after furosemide withdrawal (1.2%). Subsequently, CK and transaminases serum levels gradually declined and urine color normalized.

Infectious and autoimmune causes of acute rhabdomyolysis were ruled out by appropriate tests (Table S1 — Online only). Metabolic tests (including blood glucose, blood gas, lactate, plasma acylcarnitines [9]) were found normal. Metabolic or respiratory alkalosis and hormonal disorders (hyperthyroidism, Cushing's syndrome) were also ruled out by appropriate laboratory tests.

The patient completely recovered, apart for persistent abdominal bloating, and was discharged on hospital day 16 with a follow-up program.

Based on previously reported cases of CD/rhabdomyolysis possible association, tissue-transglutaminase 2 (tTG2)-IgA antibodies were measured and found positive (IgA 24U/mL, reference range < 9 U/mL), while endomysial antibodies (EMA)-IgA tested negative. HLA typing showed a DQA1*05:02 (DQ2), DQB1*03:02(DQ8) Haplotype, which was consistent with a higher risk for coeliac disease.

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