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Teen Athlete with Recurrent Rhabdomyolysis: A Case Report

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Abstract

Background: Rhabdomyolysis is a frequent disorder in the pediatric emergency room, and it can result from various acquired and inherited causes.Case presentation: We report the case of a 15-year-old female triathlon athlete with recurrent exertional rhabdomyolysis. The clinical severity alerted for a subjacent cause, and further investigation was taken, leading to the diagnosis of very long-chain acyl-CoA dehydrogenase (VLCAD)deficiency.
Conclusion:Exertional rhabdomyolysis may be the first manifestation of a metabolic myopathy, like VLCAD deficiency. VLCAD deficiency has a broad clinical spectrum, and the most common is the late-onset, which presents mainly with episodic symptoms, with predominant muscular involvement and exercise-induced rhabdomyolysis.

Index terms— adolescent medicine, exertional rhabdomyolysis, sports medicine, metabolic myopathy, VLCAD deficiency.

1 Introduction

habdomyolysis is a relatively common condition, however the actual incidence of this clinical syndrome is unknown, and many mild cases probably go unrecognized. (1) This pathologyis defined by elevated serum creatine kinase (CK) activity by at least ten times the normal range followed by a fast decline. It results from the rapid breakdown of skeletal muscle fibers, leading to leakage of potentially toxic cellular contents into the bloodstream. (2) The leading causes for rhabdomyolysis are trauma, intense exercise, infection, drugs, and toxins, although it can result from a range of acquired and inherited causes. (3,4)Although many situations are selflimited and benign, the possibility of endocrine, metabolic, or neuromuscular disease should also be contemplated primary causes or contributing factors for the episode. (4) The authors describe a case of a teen athlete with recurrent severe episodes of exertional rhabdomyolysis.

2 II.

3 Case Report

A15 year-old-girl, a triathlon athlete with daily trainings was admitted to the pediatric emergency room with a history of generalized myalgia and tea-colored urine following a triathlon training. She had an irrelevant family history with no consanguinity, had adequate weight and height, and a complete vaccination schedule for the age.

The patient revealed a similar episode one year before, following an intense effort, in which she didn't consult a doctor. The symptoms spontaneously resolved in 2 to 3 days. The patient denied consumption of drugs, fever, dysuria, asthenia, and other constitutional symptoms.

On examination, she had pale skin, dry tongue, tense, and swollen muscles of the upper and lower limbs with palpation-inducedmyalgia.

The blood diagnostic tests (Table 1) showed myoglobin >1.200 ng/L, creatine kinase (CK) > 85.340 IU/L, aspartate aminotransferase 4756 IU/L; alanine aminotransferase 564 IU/L; LDH >1.995 IU/L. Urinalysis showed false haematuria with no erythrocytes in the urine sediment. There were no changes in blood counts, infectious parameters, or kidney function.

The patient was admitted to the Pediatric Department to diagnose for exertional rhabdomyolysis and started aggressive hydration with intravenous fluids. She was hospitalized for five days with clinical and analytical (Table2) improvement, being referenced for an out-patient follow-up.

During this follow-up, we realized that CK values decreased during the rest periods but increased to a thousand values after mild efforts (less intense training). She had no complaints suggestive of inflammatory myopathies. The endocrinological study was also negative.

In the course of the etiological investigation (Table **??**), the metabolic study showed an acylcarnitine profile compatible with very-long-chain fatty acid acyl-CoA dehydrogenase (VLCAD) deficiency. The genetic analysis confirmed the findings, identifying the variants p.Gly140Glu (c.419>A) and p.Gly442Ala (c.1322G>C) in heterozygosity in acyl-CoA dehydrogenase, very longchain (ACADVL) gene. Thus, establishing the diagnosis of VLCAD.

4 Discussion

Exertional rhabdomyolysis (ER) happens in reaction to excessive, prolonged, repetitive exercise, or normal exercise under extreme circumstances. Well described among athletes, it is presented by severe muscle pain, muscle swelling and muscular weakness within 24h to 72h after the exercise, and can be associated with myoglobinuria. (5) When assessing a patient diagnosed with rhabdomyolysis, it is essential to obtain a thorough history regarding the onset, location, quality of the muscle discomfort, and the temporal relationship to metabolically stressful triggers such as strenuous activity, fasting, fever, infection, cold exposure, and medications. Physicians should question about altered urine coloration, previous similar episodes, and if any family members are similarly affected. As many metabolic myopathies have an autosomal recessive inheritance, consanguinity in the family should be stated. (3) Even though the ER frequently represents a 'physiological' response to extreme physical exercise, the physician should be aware of the characteristics that may alert for an underlying cause. (**??**)Some of those clinical indicators are female patients; recurrent episodes of exertional rhabdomyolysis; persistent elevation of CK or weakness four weeks after the event; rhabdomyolysis in the course of regular exercise; CK more than fifty times the upper limit of normal range; family history of similar episodes. (2,6,7) In these circumstances, the differential diagnosis must consider metabolic myopathies, heterogeneous group of genetically defined syndromes that may appear at any age. They characterized by defects in the biochemical pathways of storage, mobilization, and utilization of the substrates of muscle energy production. A detailed clinical approach will help distinguish between the three major disorders (glycogenosis, lipid-related disorders, or mitochondrial diseases). (8,9) The most important energy source of the muscle depends on the intensity and duration of the exercise, which can provide clues to the specific condition. Fatty acids are the primary energy source at rest, when fasting, or during endurance activities. (3) Very long-chain acyl-CoA dehydrogenase (VLCAD) catalyzes the first step of the fatty acid ?oxidation spiral, and its deficiency results in the reduced capacity to utilize fat. Depending on the severity of the enzymatic deficiency and other individual factors there is a continuum of clinical severity of VLCAD deficiency, divided into three phenotypes. The severest form with early-onset cardiac and multiorgan failure typically arrives in the first months of life with hypertrophic or dilated cardiomyopathy, pericardial effusion, and arrhythmias, as well as hypotonia, hepatomegaly, and intermittent hypoglycemia. An infantile form with hypoketotic hypoglycemia and hepatomegaly, but without cardiomyopathy, is typically presented during early childhood. The most common form is the lateonset and milder type that poses with intermittent rhabdomyolysis provoked by exercise with or without myoglobinuria, muscle cramps and pain, and exercise intolerance. Cardiomyopathy and liver dysfunction do not usually appear in late-onset VLCAD deficiency. (8,(10)(11)(12) VLCAD deficiency is the second most common disorder of fatty acid oxidation in Europe and shows an autosomal recessive inheritance pattern. (13)The diagnosis is based on the assessment of a metabolic profile, indicating abnormal elevation of long-chain acylcarnitine.(**??**4)It also can be performed by other methods, including molecular analysis (which may be inconclusive in cases of novel mutations or genetic variants), enzyme testing in fibroblasts and lymphocytes as well as flux studies in fibroblasts. (13)The genetic basis is complex, caused by a variety of pathogenic variants in the ACADVL gene, the most common of which is c.848T>C (p.V283A), which retains 11-12% residual enzymatic activity in homozygotes. (11) The inheritance is recessive autosomal, with homozygous or compound heterozygous mutations. (12) In general, treatment aims to prevent acute episodes. Regular, frequent meals rich in carbohydrates and low in long-chain fats is advised. Medium-chain triglycerides may also be helpful. (3) It is imperative to notice that rhabdomyolysis is a significant complication in VLCAD deficiency that may lead to kidney damage and even renal failure and can be triggered by prolonged or intense exercise, prolonged fasting, and fever or illness. (15) The prognosis of the late-onset form is usually good, but the outcome isn't completely obvious, so careful management is desirable. (10) IV.

5 Conclusion

Exertional rhabdomyolysis may be the first expression of a genetic muscle disease that which lowers the exercise threshold for developing muscle breakdown. (6) The patient presented was a teen athlete accustomed to regular high intensity exercise with no complaints of effort intolerance.

Nonetheless, the severely elevated CK and the history of recurrent rhabdomyolysis took us to the clue of a subjacent cause and guided the ambulatory workup.

Although this case report stated a typical clinical presentation, the differential diagnosis of severe rhabdomyolysis is broad, and a high suspicion is needed to undergo further investigation.

The identification of an underlying genetic disorder is essential for acute management and, most importantly for subsequent counselling.

On the genetic analysis, the variants p.Gly140Glu (c.419>A) and p.Gly442Ala (c.1322G>C) were identified, the first not yet described in the literature and the second without obvious pathogenicity. Bioinformatics predictors of these variants are suggestive of pathogenicity.

1

Hemoglobin (g/L)	147
White blood cell and differential count (x10 9 /L)	
Leukocytes	13.6
Neutrophils	11.6
Lymphocytes	1.2
Monocytes	0.8
Eosinophils	0.0
Basophils	0.1
Platelets (x10 9 /L)	334
Prothrombin time (sec)	15.2
aPTT (sec)	26.1
Myoglobin (ng/L)	>1200
Glucose (mg/dL)	84
Aspartatetransaminase (AST) (UI/L)	4756
Alanine transaminase (ALT) (UI/L)	564
Creatine kinase (CK) (IU/L)	>85340
LacticAcidDehydrogenase (LDH)(UI/L)	>1995
Na + (mmol/L)	137
K + (mmol/L)	4.3
Cl + (mmol/L)	107
Ca 2+ (mg/dL)	8.6
P (mg/dL)	5.1
Blood urea nitrogen (BUN) (mg/dL)	22
Creatinine (mg/dL)	0.7
C-Reactive Protein (CRP) (mg/dL)	18
Urinalysis	+++ Blood

Tabela 2: Evolution during hospitalization

	Day 1	Day 2	Day 3	Day 4	Day 5
AST (UI/L)	4756	5364	4633	-	1222
ALT (UI/L)	564	888	1234	-	899
CK (UI/L)	>85340	36049	19054	19446	8939
BUN (mg/dL)	22	12	10	9	8
Creatinine (mg/dL)	0.7	0.7	0.5	0.6	0.5

Tabela 3: Etiological investigation

Thyroid-Stimulating Hormone (TSH) (µIU/mL)	1.17
UricAcid (mg/dL)	2.9
Erythrocyte sedimentation rate (mm/h)	8
Haptoglobin (mg/dL)	93
Angiotensin Converting Enzyme (UI/L)	416
C3 (g/L)	1.08
C4 (g/L)	0.254
ANA	Negative
dsDNA	Negative
Thyroglobulin Antibody	Negative
Thyroid peroxidase	Negative
Metabolic study for GLUT diseases	Negative
Global metabolicstudy	Acylcarnitine deficiency in very long-ch

Figure 1: Tabela 1 :

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