









Caso clínico

Rhabdomyolysis caused by exercise

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Resumen

Introducción: la rabdomiólisis es un síndrome clínico y paraclínico caracterizado por la presencia de necrosis del músculo esquelético que lleva a la liberación de componentes musculares intracelulares, con una presentación clínica variable y complicaciones que ponen en riesgo la vida, como la insuficiencia renal aguda.

Métodos: presentamos un caso clínico de un paciente con rabdomiólisis con elevación severa de enzimas musculares y lesión renal aguda secundaria que posteriormente se documentó (CK Total inicial 189.000 u/L) luego de actividad física extrema (CrossFit), quien desarrolló múltiples complicaciones y la necesidad de apoyo en la Unidad de Cuidados Intensivos (UCI) con evolución satisfactoria.

Resultados: Paciente con insuficiencia renal, que recibe terapia renal con una evolución favorable y supervivencia al egreso de la unidad de cuidados intensivos de un hospital de tercer nivel de la ciudad de Pereira, Risaralda, Colombia.

Conclusiones: La rabdomiólisis es un síndrome clínico y paraclínico caracterizado por la presencia de necrosis del músculo esquelético. La causa principal son las lesiones traumáticas directas severas o las lesiones por aplastamiento; sin embargo, otras condiciones como las infecciones, la intoxicación, la isquemia muscular, el síndrome neuroléptico maligno, la hipertermia maligna, los trastornos metabólicos y las patologías genéticas también pueden causarla, y en particular, el reposo prolongado, la inmovilización o el ejercicio extenuante. La presentación clínica y las complicaciones son variables.

Palabras clave: rabdomiólisis, fallo renal agudo, ejercicio, cuidados críticos.

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Rhabdomyolysis caused by exercise

Abstract

Introduction: rhabdomyolysis is a clinical and paraclinical syndrome characterized by the presence of skeletal muscle necrosis that leads to the consequent release of intracellular muscle components with a variable clinical presentation and complications that put life at risk such as acute kidney injury.

Methods: we present a case report of a patient with rhabdomyolysis with severe elevation of muscle enzymes and secondary acute kidney injury who was subsequently documented (initial Total CK 189,000 u/L) after extreme physical activity (CrossFit), who developed multiple complications and the need for support in the Intensive Care Unit (ICU) with satisfactory outcome.

Results: Patient with kidney failure, receiving renal therapy with a favorable evolution and survival at discharge from the intensive care unit of a third-level hospital in the city of Pereira, Risaralda, Colombia.

Conclusions: Rhabdomyolysis is a clinical and paraclinical syndrome characterized by the presence of skeletal muscle necrosis. The main cause is severe direct traumatic injury or crushes injuries; however, other conditions such as infections, intoxication, muscle ischemia, neuroleptic malignant syndrome, malignant hyperthermia, metabolic disorders, and genetic pathologies can also cause it, and particularly, extended rest, immobilization or strenuous exercise. The clinical presentation and complications are variable.

Keywords: rhabdomyolysis, acute renal injury, exercise, critical care.

Introduction

Rhabdomyolysis is a clinical and paraclinical syndrome characterized by the presence of skeletal muscle necrosis that leads to the consequent release of intracellular muscle components (myoglobin, creatinine kinase (CK), aldolase, lactate dehydrogenase, and electrolytes) into the systemic circulation [1]. Clinically, it has a variable presentation, ranging from the spectrum of asymptomatic elevation of creatinine kinase levels, myalgia, marked elevation of enzyme markers, myoglobinuria, macroscopic pigmenturia without hematuria, to severe complications that put life at risk such as acute kidney injury, electrolyte imbalance, arrhythmias, myocardial or liver dysfunction, disseminated intravascular coagulation (DIC) and even death [2–5]. The main cause is a severe direct traumatic injury or crushes injuries; however, other conditions such as infections, intoxication, muscle ischemia, neuroleptic malignant syndrome, malignant hyperthermia, metabolic disorders, and genetic pathologies can also cause it, and particularly the extended rest or immobilization [1–3, 6] or strenuous exercise as one of the etiologies that can cause it [7–9]. Rhabdomyolysis secondary to strenuous exercise is defined as the presence of some of the diagnostic criteria described, namely

1. An elevation of CK 12 to 36 hours after exercise, with a maximum at 3-4 days, followed by normalization within several weeks of rest
2. The increase in CK is preceded by exercise, generally beyond the limits of fatigue, also known as “unaccustomed physical exertion” or “involuntary exertion”
3. Symptomatic CK elevation with any of the following: myalgia (muscle pain or tenderness; rhabdomyolysis is generally very painful), swelling and/or weakness
4. The presence of myoglobinemia and/or myoglobinuria: either by inspection (pigmenturia) or by laboratory tests. Since the blood or urine myoglobin test is not widely available, many experts consider the combination of the first three diagnostic features to define exercise rhabdomyolysis [8,9]. This condition may be the first manifestation of a genetic muscle disease that reduces the exercise threshold to develop muscle rupture and this possibility should be considered in the event of recurrent episodes (high creatine kinase (CK) levels ($>50 \times$ upper limits of normal) or persistent hyperCKaemia; absence of unaccustomed exercise; absence of drugs (recreational or medical); or positive family history of rhabdomyolysis or other symptoms of exertion). [9]

Case report

In this case report, we present a patient with a picture of rhabdomyolysis with severe elevation of muscle enzymes and secondary acute kidney injury who was subsequently documented.

Our case is a 32-year-old man, with no relevant history, who consulted for symptoms of abdominal, lumbar, and thigh region pain, associated with changes in color in the urine of several hours of evolution. During the interrogation, as additional data, he reported that he had performed extreme physical activity (CrossFit) 2 days earlier with intense work on the lower limbs, which he was not familiar with, given that he had not performed a physical activity of this intensity for a long time.

He did not report the consumption of nutritional supplements. In the clinical evaluation at admission, he was hemodynamically stable, with mild pain on palpation of the abdominal flanks, without signs of acute abdomen, negative renal percussion, and pain in the thigh region. Blood and urine tests revealed: hemogram with normal cell count, hemoglobin 15.2 g/dL, hematocrit 42 %, normal volumes, urinalysis: density: 1.005, pH: 5, proteins 150 mg/dL, blood 250 Ery/c, normal glucose, negative ketone bodies. Creatinine 1.56 mg/dL, urea nitrogen (BUN) 12.6 mg/dL, GRF 57.9 mL/min/1.73m² (CKD-EPI). Rhabdomyolysis was suspected,

thus, hydration with intravenous fluids was initiated and requested complementary tests showed: total CK 189,000 U/L, AST 3,185 U/L, ALT 589 U/L, PT 10.6 sec, INR 1.04, PTT 29 sec, potassium: 4.2 mmol/L, ionic calcium 1.18 mmol, total bilirubin 0.42 mg/dL, direct 0.26 mg/dL, abdominal ultrasonography and chest X-ray within normal limits.

After the assessment by the internal medicine service with diagnoses of rhabdomyolysis, AKIN 2 acute kidney injury, and liver injury, a decision was made to transfer to the intensive care service (ICU). Management of intravenous water therapy was adjusted, bicarbonate was added, and control tests were requested (Table 1). The nephrology service identified acute kidney injury AKIN 3 and ordered an increase in venous fluids for a target diuresis between 200-300 mL/h. During his stay in the ICU, the patient had a favorable evolution, diuresis within the proposed limits, with no need to initiate renal support therapy, and a gradual decrease in creatinine and transaminase values. Hospital discharge was given with an outpatient follow-up order by the nephrology service.

Table 1. Follow-up of laboratory tests

Laboratory	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Creatinine (mg/dL)	2.29	3.3	3.22	3.1	2.97	2.76	2.53	2.46
BUN (mg/dL)	16.9	18.8	20.3	20.8	19.9	18.6	18.4	17.3
Total CK (U/L)	189.000	113.505	75.43 1	33.560	-	12.37 7	8.003	4.668
Potassium (mmol/L)	4.22	4.62	4.06	4.34	-	4.17	-	4.11
Sodium (mmol/L)	135.6	136	136.5	140	-	-	-	-

Source: own.

Discussion

One of the biggest challenges in diagnosing exertional rhabdomyolysis is the fact that serum CK levels will normally rise naturally after strenuous exercise, potentially up to 10 times the upper limit of normal [9]. Increased CK levels also vary widely among patients [10], and exposure to high temperatures and humidity during exercise may also play a role in higher rates of rhabdomyolysis according to reports in the literature [11]. A retrospective cohort study published in 2010 reported 22.2 cases of exertional rhabdomyolysis per 100,000 military personnel per year, with a low incidence and risk of exertional recurrence among young people [12].

The genetic disorders most frequently described in this clinical setting are disorders of glycolysis or glycogenolysis, including McArdle's disease, Tarui disease, LDH deficiency, and debranching enzyme, lipid metabolism disorders, including deficiency of CPT I and II, long-chain acyl-coenzyme A DH deficiency, medium-chain acyl-coenzyme A DH deficiency and thiolase deficiency, increased susceptibility to malignant hyperthermia, including familial malignant hyperthermia, Duchenne and Becker muscular dystrophies and myotonic dystrophy. Other genetic conditions include Krebs cycle disorders, mitochondrial respiratory chain disorders, G6PDH deficiency, and myoadenylate deaminase deficiency [1].

Clinically, it is manifested by a triad of symptoms: myalgia, weakness, and myoglobinuria. However, this rigid description of symptoms is only present in <10 % of patients [13]. The hallmark of rhabdomyolysis is the presence of elevated CK levels (these are usually at least five times the upper limit of normal, but range from approximately 1,500 to more than 100,000 international units/L). Levels begin to rise 2 to 12 hours after the onset of muscle injury and peak within 24 to 72 hours. Typically, a decrease is seen within three to five days after the muscle injury ceases. CK has a serum half-life of about 1.5 days and decreases at a relatively constant rate of about 40 to 50 % of the previous day's value [3]. Elevated CK levels are the most sensitive laboratory test to assess muscle injury [9, 13]. In patients whose CK does not decrease as expected, there may be ongoing muscle injury or the development of compartment syndrome [1-3].

The other characteristic finding is the reddish-brown urine of myoglobinuria, but since this can be observed in only half of the cases, its absence does not exclude the diagnosis. [9, 14] Myoglobin is rapidly excreted in the urine when the plasma concentration exceeds 1.5 mg/dL. Visible changes in urine only occur once urine levels exceed approximately 100 to 300 mg/dL, although they can be detected with the urine test strip (orthotolidine) at concentrations as low as 0.5 to 1 mg/dL [15]. Myoglobin has a half-life of only two to three hours, much shorter than that of CK. Due to its rapid excretion and metabolism to bilirubin, serum levels can return to normal within six to eight hours. Therefore, it is not uncommon for CK levels to remain elevated in the absence of myoglobinuria [1, 2]. In rhabdomyolysis, myoglobin appears in the plasma before the elevation of CK occurs and disappears while CK is still elevated or increasing [1]. Routine urine tests for myoglobin by urine dipstick evaluation may be negative in up to half of the patients with rhabdomyolysis [1-3]. It is estimated that 10 %-40 % of patients with rhabdomyolysis develop acute kidney injury [9, 13, 14, 16].

Routine laboratory tests, including complete blood count (CBC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), kidney function and urinary sediment

vary greatly depending on the underlying cause of rhabdomyolysis and its severity [1, 2, 9]. Elevation of serum aminotransferases is common at the expense of aspartate aminotransferase (AST) in cases of rhabdomyolysis in which CK was greater than or equal to 1000 units/L [17]. Electrolyte imbalance may be present, especially severe hyperkalemia that leads to the development of arrhythmias, putting the patient's life at risk [1-3].

Hyperphosphatemia, hypocalcemia, high anion gap metabolic acidosis, and the development of severe hyperuricemia are other manifestations that can be found. Later complications (intracompartmental include acute pressure is > kidney 30 injury, mmHg), compartment and, rarely, syndrome disseminated intravascular coagulation [1-4, 18, 19].

Acute kidney injury is a common complication of rhabdomyolysis, it is the result of the accumulation of myoglobin, which is nephrotoxic in the kidney, and its presentation varies between 15% and 50% [4]. The risk of AKI is greater when CK levels are in the greater range of 15 to 20,000 units/L, there is the presence of coke or dehydration, sepsis, and acidosis [3, 4]. The management of rhabdomyolysis aims to avoid acute kidney injury, since this condition leads to an increase in adverse clinical outcomes [4], through early hydration with crystalloids at a rate of 1.5 L/h [20], to maintain urinary output of 200 ml/h, urinary pH > 6.5 and drink reaches a plasma pH < 7.5 [1]. Alkalinization of urine with sodium bicarbonate has no conclusive evidence [21]. Early recognition of rhabdomyolysis is required, as well as an adequate differential diagnosis and timely treatment of the specific causes, including the intervention of complications to positively impact the results [1].

We present a case report of a patient with a rhabdomyolysis with a severe elevation of muscle enzymes and secondary acute kidney injury who was subsequently documented (initial Total CK 189,000 u/L) after extreme physical activity (CrossFit), who developed multiple complications and the need for support in the Intensive Care Unit (ICU) with satisfactory outcome.

Conflict of interest

No conflicts of interest for all authors.

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Author's contribution

Study concept and design: Ávila-Reyes D, Cruz-Echeverry EJ, Echeverry- Piedrahita DR, Gómez-González JF; Acquisition, analysis and interpretation of data: Ávila-Reyes D, Cruz-Echeverry EJ, Echeverry-Piedrahita DR, Gómez- González JF; Drafting of the manuscript: Ávila-Reyes D, Cruz-Echeverry EJ, Aguirre-Flórez M; Critical revision of the manuscript for important intellectual content: Ávila-Reyes D, Cruz-Echeverry EJ, Echeverry-Piedrahita DR, Gómez- González JF; Administrative, technical, and material support: Ávila-Reyes D, Cruz- Echeverry EJ, Echeverry-Piedrahita DR, Gómez-González JF, Aguirre-Flórez M; Study supervision: Ávila-Reyes D, Cruz-Echeverry EJ, Echeverry-Piedrahita DR, Gómez-González JF.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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