CASE REPORTS

COVID-19-induced rhabdomyolysis in an adolescent: A rare presentation

Rabdomiólise induzida por COVID-19 num adolescente: Uma apresentação rara

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ABSTRACT

Viral infections are a well-known cause of myositis. The clinical presentation may vary from mild myalgia to severe muscle injury. Coronavirus disease 2019 (COVID-19), a viral respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can be a cause of myositis and of rhabdomyolysis, a rare and severe complication.

A previously healthy 11-year-old female adolescent with COVID-19 presented to the Emergency Department with lower limb pain and inability to walk. The initial laboratory study revealed a marked elevation of muscular enzymes, particularly creatine kinase (13046 UI/L; reference value 149 UI/L). Urine dipstick test reacted positively for hemoglobinuria. The patient started treatment with aggressive intravenous hydration, with progressive clinical and analytical improvement.

Musculoskeletal symptoms associated with COVID-19 are a frequent complaint, with potentially severe complications, such as rhabdomyolysis. A proper and timely diagnosis can prevent further clinical deterioration and enable adequate treatment and follow-up.

Keywords: COVID-19; muscle; myositis; rhabdomyolysis

RESUMO

As infeções víricas são uma causa conhecida de miosite. A apresentação clínica pode variar desde mialgias ligeiras a lesões musculares graves. A COVID-19, uma infeção respiratória viral provocada pelo coronavírus da síndrome respiratória aguda grave 2 (SARS-CoV-2), pode ser uma causa de miosite e de rabdomiólise, uma complicação muscular rara e grave.

Uma adolescente de 11 anos, previamente saudável, positiva para COVID-19, recorreu ao Serviço de Urgência por dor nos membros inferiores e incapacidade para a marcha. O estudo analítico inicial revelou uma elevação das enzimas musculares, nomeadamente da creatina fosfocinase (13046 UI/L; valor de referência 149 UI/L). A tira teste urinária reagiu positivamente para hemoglobina. A doente iniciou tratamento com fluidoterapia endovenosa, com melhoria clínica e analítica progressiva.

Os sintomas músculo-esqueléticos associados à COVID-19 são uma queixa frequente, com potencial para complicações graves, como a rabdomiólise. Um diagnóstico adequado e atempado permite prevenir o agravamento clínico e instituir um tratamento e seguimento adequados.

Palavras-chave: COVID-19; miosite; músculo; rabdomiólise

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INTRODUCTION

Viral infections are a well-known cause of myositis, being influenza A and B and enteroviruses the most commonly reported viral agents.[1-4] The clinical presentation may vary from mild myalgia to severe muscle injury.[4]

Despite its rapid onset, myositis following acute viral infections is a usually benign and self-limited clinical condition. Rhabdomyolysis, resulting from a breakdown of muscle tissue that leads to the release of muscle fiber content into blood, is an infrequent but possible complication that should be considered.[5]

Coronavirus disease 2019 (COVID-19) is a multisystemic disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with a variety of possible manifestations.[5] Most pediatric patients are asymptomatic or present mild manifestations.[6,7] Fever, headache, myalgia, cough, and dyspnea are the most common symptoms in this age group.[6]

COVID-19-induced myositis can be one of the disease manifestations, with rhabdomyolysis representing a rare and potentially severe complication.[4,5]

CASE DESCRIPTION

Herein is described the case of a previously healthy 11-year-old female adolescent, who presented to the Emergency Department (ED) with fever with 48 hours of evolution associated with occasional dry cough and odynophagia. The nasopharyngeal swab for detection of SARS-CoV-2 viral RNA through polymerase chain reaction (PCR) was positive. The girl was treated at home with supportive care and isolation measures.

Three days later, she was admitted to the ED due to lower limb pain beginning that same day, with inability to walk. She was apyretic for 24 hours and denied other symptoms, such as urine or skin alterations and arthralgia. No history of trauma or heavy exercise was reported, as well as no personal or family history of muscle diseases. On clinical examination, the girl mentioned pain on palpation of the gastrocnemius bilaterally. No skin color alterations, venous or lymphatic vessel alterations, limb edema, or articular pain were observed. The neurologic exam was unremarkable, with preserved strength, reflexes, and sensitivity.

The initial laboratory study revealed normal hemoglobin, leucocyte count, and platelet count. The patient presented an important elevation of creatine kinase (CK) (13046 UI/L; reference value 149 UI/L) and myoglobin (3562 ng/mL; reference value 65.8 ng/mL). Aspartate aminotransferase (AST 275 UI/L; reference value <47 UI/L) and alanine aminotransferase (ALT 60 UI/L; reference value <39 UI/L) were also elevated. Ions and renal function were normal and the urine dipstick test reacted positively for hemoglobin. C-reactive protein (CRP) was negative and venous blood gas analysis was normal. These biochemical abnormalities were compatible with severe muscle injury and rhabdomyolysis, and a presumptive diagnosis of myositis with rhabdomyolysis caused by SARS-CoV-2 was established.

The patient was started on treatment with intravenous hydration (10% glucose solution + 0.9% saline solution), providing 150% of baseline needs, and was admitted to the pediatric ward to continue treatment and for surveillance, with cardiac and diuresis monitoring.

Organic acid and acylcarnitine profile was performed before the beginning of fluid therapy, showing no alterations suggestive of metabolic diseases.

During hospitalization, the girl remained hemodynamically stable and showed progressive muscular pain resolution and walking improvement. Diuresis remained within normal values. Twenty-four hours after treatment start, blood workout revealed an elevation of CK (14,740 UI/L), AST (371 UI/L), ALT (98 UI/L), and lactate dehydrogenase (DHL 538 UI/L; reference value <300 UI/L). Myoglobin levels decreased to 1,575 ng/mL. The urine analysis was normal at this time. The patient maintained the previously established treatment, with progressive reduction of CK and AST levels over the next days (**Table 1**). She was discharged with pain relief medication as needed and surveillance, with a follow-up appointment scheduled for analytical reassessment.

Table 1 - Patient's blood workup over time

Day	CK (UI/L)	AST (UI/L)	ALT (UI/L)	Myoglobin (ng/mL)	LDH (UI/L)	Creatinine (mg/dL)	Urea (mg/dL)	K+ (mmol/L)	CRP (mg/L)
1	13,046	275	60	3 562	-	0.55	17	4.3	<5
2	14,740	371	98	1 575	538	0.54	14	4.4	<5
3	11,215	423	180	517	579	0.55	13	4.1	<5
6	1,195	169	285	-	-	0.54	13	4.1	<5
73 (follow-up)	217	21	13	18	164	0.62	27	4.3	-

ALT – Alanine Aminotransferase; AST – Aspartate Aminotransferase; CK – Creatine Kinase; CRP – C-reactive protein; K+ - Potassium; LDH - Lactate Dehydrogenase

DISCUSSION/CONCLUSIONS

Musculoskeletal symptoms associated with COVID-19 are a frequent complaint, both in mild and severe cases of the disease.[8,9] Being one of the most commonly reported symptoms, myalgia is present in approximately half of COVID-19-infected patients.[5,8,9] This myopathy might be accompanied by elevation of muscular enzymes, particularly CK, ranging from mild elevation to extensive rhabdomyolysis.[8,10]

The pathogenic mechanisms by which SARS-CoV-2 cause muscular damage are still under investigation, with some major mechanisms already established.[5] One of those is viral tropism, by which the virus enters muscle tissue cells by binding to the angiotensin-converting enzyme 2 (ACE2) receptor using the surface spike protein. This mechanism is thought to explain the invasion process in other affected body tissues, potentially explaining the multisystemic manifestations of the disease observed.[5,7] On the other hand, the significant immune activation, with production of inflammatory cytokines, that characterizes the disease also seems to play a relevant role in the pathogenesis of the considered muscle conditions.[5,7,8]

Other mechanisms potentially contributing to muscle injury still under investigation include the presence of a hyperinflammatory state with increase of TNF-alpha and interleukin, and an antibody attack to myocytes as a result of cross reactivity, with antibodies initially produced to attack the virus.[5]

The treatment focus in acute viral myositis is symptom relief and prevention of complications. Outpatient management is possible in most patients with mild presentation.[1]

Patients with rhabdomyolysis induced by viral infections require additional therapy, particularly aggressive fluid therapy, and screening and treatment of complications, if present, especially acute kidney injury.[1,11]

In the present case, muscle symptoms appeared suddenly but had a significant impact on the adolescent's wellbeing and walking ability. The patient experienced an elevation of muscular enzymes compatible with rhabdomyolysis, with no evidence of other complications. This biochemical alteration required prompt treatment and adequate follow-up.

A limitation of this case report is the fact that some frequent causes of rhabdomyolysis were not excluded, such as exposure to toxins, other common infections, or auto-immune diseases. A presumptive correlation between SARS-CoV-2 infection and muscular symptoms was assumed, in view of the timing of clinical findings and resolution of the clinical condition with the instituted treatment. Besides SARS-CoV-2 infection, only metabolic disorders were investigated. Of note, the occurrence of other episodes of myositis during patients' follow-up should prompt further study of other causes.

As only few cases of COVID-19-induced rhabdomyolyses have been reported in children and adolescents, further studies are required to better understand the impact of this condition in the pediatric population with SARS-CoV-2 infection. Furthermore, a high index of suspicion should be kept for COVID-19-positive patients with significant muscular pain, who should be tested for an elevation of muscular enzymes to establish the diagnosis of myositis and rhabdomyolysis.[7,11] Although rare, these conditions carry potentially severe complications,[7,11] and proper and timely diagnosis can prevent further clinical deterioration and enable adequate treatment and follow-up.

AUTHORSHIP

Rita Calejo – Conceptualization; Bibliographic research; Writing – original draft; Writing – review & editing

Joana Queirós - Writing – original draft; Writing – review & editing

Carla Brandão – Validation; Writing – review & editing

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