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SARS-CoV-2 infection presenting as rhabdomyolysis: case report and review

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Abstract

Coronavirus disease 2019 (COVID-19) is the health crisis of our time and a great challenge we face, requiring the implementation of worldwide general containment. The symptoms and complications of COVID-19 are diverse, and rhabdomyolysis is an atypical manifestation. We report a case of a 63-year-old patient, admitted to the emergency room for myalgia and fever evolving over 5 days, in whom laboratory and other examinations indicated rhabdomyolysis complicated by renal insufficiency. During the diagnostic workup, the real-time polymerase chain reaction (RT-PCR) test result for COVID-19 was positive, revealing infection with sudden acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Although the severity of COVID-19 infection relates mainly to acute respiratory syndrome, other complications can be prognostic, and these complications make the management of this disease difficult. Rhabdomyolysis is one of the fatal complications; first, because the pathophysiological mechanism is not yet understood, and second, because rhabdomyolysis, itself, is usually complicated by acute renal failure. This complication makes the disease management difficult, especially in patients with SARS. Rhabdomyolysis during COVID-19 infection represents a significant challenge, given the few reported cases, and further research is required to develop a therapeutic consensus.

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Introduction

The emergence of a new strain of the beta-coronavirus family (severe acute respiratory syndrome coronavirus 2, SARS-CoV-2) has upset the world by causing coronavirus disease 2019 (COVID-19). This infection can be considered a general disease because of the possible attacks on multiple body systems, including muscular involvement, which is mainly represented by rhabdomyolysis, and which can occur acutely or late in the course of the infection.[1] We report the details of a patient admitted for rhabdomyolysis in whom COVID-19 infection was confirmed. This case shows the importance of fluid therapy in rhabdomyolysis to improve renal failure, contrasting with fluid restriction in respiratory distress, because there is no consensus on fluid therapy in the management of COVID-19-related respiratory distress.

Case presentation

We report the case of a 63-year-old patient, with no remarkable medical history, who was admitted to the emergency room for recently worsening myalgia associated with a fever of 38.8°C for 5 days. On admission, the patient was conscious and hemodynamically stable, with a heart rate of 110 bpm, blood pressure: 130/75 mmHg, oxygen saturation (SpO_2) on room air: 92%, respiratory rate: 20 breaths per minute, and no signs of respiratory distress. On presentation, the patient's temperature was 38.7°C, body weight was 91 kg, height was 177 cm, and the body mass index was 29.04 kg/m^2. The clinical examination revealed a myogenic syndrome predominantly in the distal muscles of the upper and lower limbs. Urine output was preserved, and the urine was concentrated.

Blood analysis showed the following: lymphocytes: 0.473 G/L (normal range: 1–4 G/L), creatinine: 229.89 µmol/L (normal range: 53–106 µmol/L), urea: 19.9 mmol/L (normal range: 6–9 mmol/L), lactate dehydrogenase (LDH): 839 IU/L (normal range: 125–143 IU/L), creatine kinase (CK): 7,098 IU/L (normal range: 20–200 IU/L), serum potassium: 5.8 mmol/L (normal range: 3–5 mmol/L), alanine aminotransferase (ALT): 68 IU/L (normal range: 0–55 IU/L), and aspartate aminotransferase (AST): 538 IU/L (normal range: 5–34 IU/L). Myoglobinuria was present, and a diagnosis of rhabdomyolysis was established. The patient did not report known toxin intake, medications, or recent trauma, and there was no report of prolonged bed rest. Considering the pandemic context, the lymphopenia, fever, rhabdomyolysis, and slightly low SpO_2, SARS-CoV-2 infection was suspected, and a real-time polymerase chain reaction (RT-PCR) COVID-19 test result was positive. Thoracic non-contrast-enhanced computed tomography (CT) (Figure 1) was performed and revealed typical ground-glass opacities in the periphery of both lungs, with an estimated parenchymal involvement of 25% to 50%.

The patient was admitted to the COVID-19 department, with the following

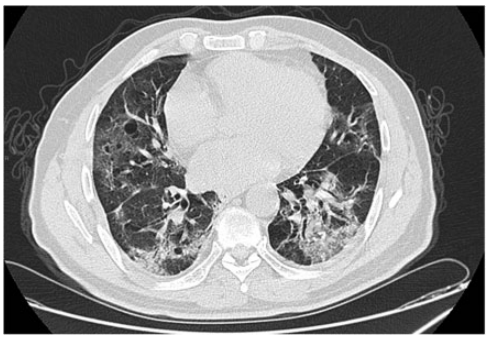

Figure 1. Axial nonenhanced chest computed tomography (CT) image (lung window) showing bilateral ground-glass opacities typical of sudden acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, with pulmonary involvement estimated between 25% and 50%.

protocol: vitamin C: 2 g/day, zinc: 45 mg per 12 hours, prophylactic dose of low-molecular-weight heparin (LMWH): 6000 IU/24 hours (adjusted for renal deficiency using the Modification of Diet in Renal Disease (MDRD) creatinine clearance equation; result: 32), and gastric protection using a proton pump-inhibitor (PPI): 20 mg/day. The rhabdomyolysis was treated with hyperhydration with a starting saline dose of 500 mL/2 hours with bicarbonate at a dose of 100 mL/day, to achieve a urinary pH >6.5. The patient's urine output was preserved, and there were no signs of pulmonary edema. Hyperkalemia was corrected after administering 500 mL of saline with 7 units of insulin. The potassium concentration decreased to 4.5 mmol/L after this therapy. We also started corticosteroid therapy with dexamethasone (6 mg/day), as the patient's oxygen saturation was 92%.

The patient improved clinically, and the creatinine and urea concentrations normalized on day 3 after admission, at which time, CK, ALT, and AST concentrations were decreasing (Figure 2).

On day 5 of hospitalization, the patient reported dyspnea associated with a room air SpO_2 of 80%. Contrast-enhanced thoracic CT (Figure 3) showed worsening of the lung lesions, with an estimated damage of more than 75%. Repeat blood laboratory testing showed a marked increase in the inflammatory markers, C-reactive protein (CRP): 241 mg/L (normal range: 0–6 mg/L), ferritin: 629 µg/L (normal range: 30–300 µg/L), and LDH: 769 IU/L (normal range: 125–143 IU/L). We decided to initiate oxygen therapy using a high-flow-oxygen face mask at a rate of 12 L/minute, with 16 hours/day in the prone position, to achieve a target SpO_2 of 92%. Remdesivir was not available, and we changed to therapeutic dosing of LMWH at 6000 IU/12 hours (creatinine had normalized at this point). The patient's progression was favorable, and on day 15 after admission, he was successfully weaned from oxygen therapy. The only persistent abnormality at that time was a slight increase in inflammatory marker concentrations. The patient was discharged home with a very good evolution.

Discussion

The new coronavirus (COVID-19) has put the world into a health crisis and is the first of its kind in the 21st century.[2] This virus of the beta-coronavirus family mainly uses the angiotensin-converting enzyme 2 (ACE-2) receptor as a pathway to enter cells.[3] The severity of the infection by this virus is explained by severe acute respiratory distress syndrome (ARDS), mainly secondary to cytokine release syndrome (CRS),[4] which is the first cause of mortality with COVID-19 infection. This pulmonary tropism of the infection is explained by the richness of the pulmonary system regarding the expression of the ACE-2 receptor.[5]

Apart from ARDS, thromboembolic events during COVID-19 infection are a significant problem because of the diversity of the systems that are attacked, which

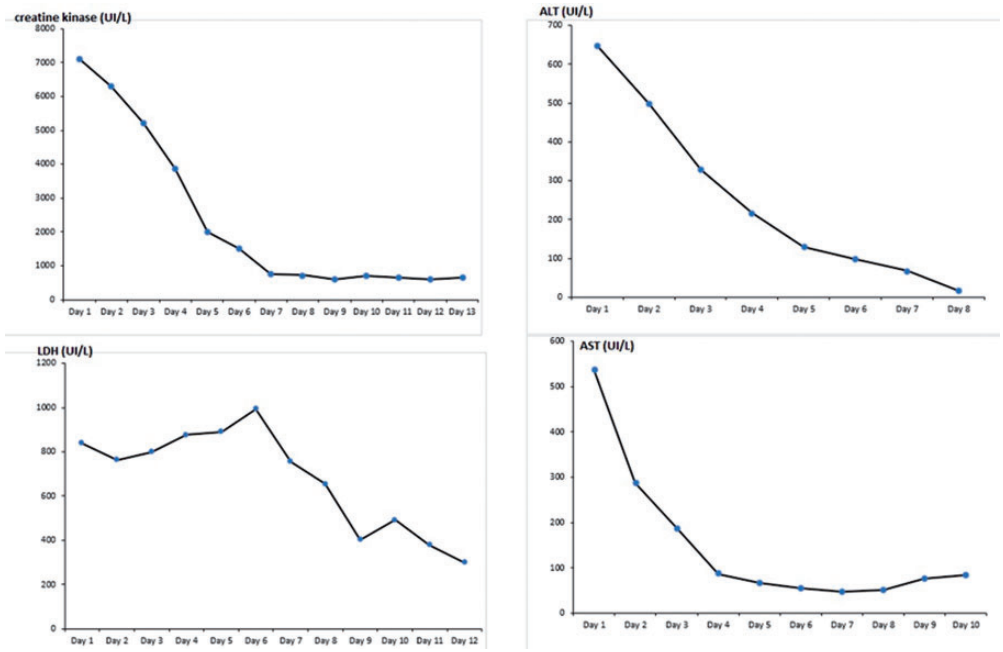

Figure 2. Progression of creatine kinase, lactate dehydrogenase, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) concentrations during hospitalization.

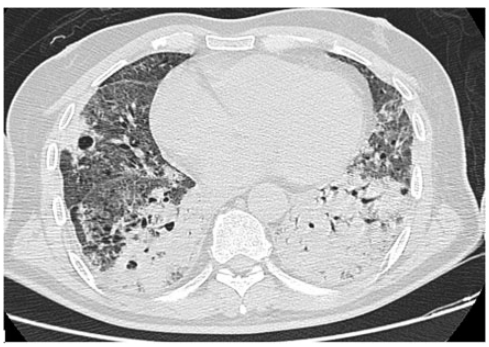

Figure 3. Axial contrast-enhanced chest computed tomography (CT) image (lung window) showing worsening of the lung lesions, with an estimated pulmonary involvement of more than 75%.

can be venous or arterial or both.[5] Extra-pulmonary involvement may involve the cardiac, digestive, and neurological systems.[1] Muscle involvement is possible and has been reported in several case series concerning the clinical characteristics of patients hospitalized with SARS-CoV-2 infection.[6] Muscle involvement in COVID-19 is represented by myalgia, myositis, and rhabdomyolysis.[6] The incidence of rhabdomyolysis during COVID-19 infection is low, with only a few cases reported. According to a series of 1099 patients hospitalized in China because of COVID-19 infection, only 0.2% developed rhabdomyolysis.[7] Rhabdomyolysis involves the release of myocyte contents into the general circulation, and the severity of this condition is represented by acute renal failure, which can be severe in some cases, requiring renal replacement therapy. The etiologies of rhabdomyolysis are varied: toxin intake, drug intake (mainly statins), trauma, and viral infections.[8] Several viral infections can be associated with rhabdomyolysis, namely infection by influenza A and B, Epstein–Barr, adenovirus, varicella, and herpes simplex virus.[9] Regarding the

beta-coronavirus family, 10% of patients with SARS and 14% of patients with Middle East respiratory syndrome (MERS) developed rhabdomyolysis, in one study.[10]

The exact pathophysiology of muscle destruction in rhabdomyolysis is not yet well understood, but two hypotheses are discussed. The first hypothesis describes muscle necrosis secondary to direct invasion of myocytes by the virus, and the second describes myocyte toxicity secondary to CRS.[11] The diagnosis of rhabdomyolysis is made according to the CK concentration. Although there is no consensus regarding the exact ck value to establish the diagnosis of rhabdomyolysis, an elevation of more than 10 times the normal concentration is widely used in current practice.[8] Another pathognomonic criterion is the detection of myoglobinuria.[11] This biological parameter is easy to detect, but plays a major role in the generation of acute renal failure in rhabdomyolysis. It should be noted that the mechanism of acute renal failure is acute tubular necrosis, which is secondary to mechanical obstruction of the renal tubules by myoglobin. Other mechanisms explaining this renal failure are intra-renal vasoconstriction or tubular ischemia.[8,9] Our patient also had elevated AST, which is not only of hepatic origin, but can also indicate muscular damage. The renal failure in our patient could have been caused by the COVID-19 infection; however, this possibility was eliminated with renal improvement after hyperhydration.

Apart from managing the COVID-19 infection, managing patients with rhabdomyolysis is based mainly on preserving renal function by hyperhydration, as well as correcting other disorders by alkalinizing the urine, and in some cases, using mannitol. In all cases, treating the cause of the rhabdomyolysis is important.[8]

The management of patients with COVID-19 and rhabdomyolysis is delicate because the exact pathophysiology of the muscle lysis is unknown; therefore, there are no specific therapies. Patients with severe SARS-CoV-2 infection must undergo restricted hydration as much as possible to prevent worsened gas exchange.[12] This fluid restriction, if applied, promotes renal failure, which is why the management of these patients is such a challenge. There is currently no international consensus on fluid management in patients with severe COVID-19 infection with rhabdomyolysis complicated by renal failure. Solis et al. proposed an algorithm for these patients involving hydration at 400 mL/hour with saline and with a diuresis goal of >200 mL/hour or 3 mL/Kg, while considering alkalinization with bicarbonate and mannitol according to the clinical and biological progression.[10]

This case is unique because the patient's COVID-19 disease presented as rhabdomyolysis, and despite worsening of the lung lesions during hospitalization, he was able to heal.

Conclusion

Rhabdomyolysis remains a possible complication of COVID-19 infection, and the severe outcome of this condition is acute renal failure, which makes patient management very difficult given the therapeutic divergence regarding hydration between SARS-CoV-2 and acute renal failure.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Ethics statement

Ethics committee approval was not required in our institution because this study is a case report. Written informed consent was obtained

from the patient for publication of this case report.

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