CLINICAL VIGNETTE

Rhabdomyolysis Due to SARS-CoV2-2 Infection

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Case Report

A 54-year-old female with a past medical history of diabetes, hypertension, and morbid obesity presented to the emergency department with two days of shortness of breath, cough, fevers, myalgias, and loss of smell and taste. She noted that her urine was darker and brown in color. She denied dysuria and urinary frequency. The patient denied any alcohol or drug use. Her medication list included metformin, glimepiride, and lisinopril. Her vitals on admission included temperature of 39.5 °C, heart rate of 90/bpm, blood pressure of 116/64 mm Hg, respiratory of 20/minute, and oxygen saturation of 93% on room air. Physical exam was notable for mild tachypnea but was otherwise unremarkable. Labs were pertinent for a potassium of 4.8 mmol/L, bicarbonate 25 mmol/L, creatinine of 0.9 mg/dL (baseline 0.8 mg/dL), calcium 8.2 mg/dL, phosphorous 2.4 mg/dL, creatine kinase (CK) 212,786 U/L, urinalysis dipstick showed a large amount of blood but only 6-10 red blood cells/high power field and 11-20 granular casts/lower power field, negative urine toxicology screen and positive SARS-CoV-2 PCR testing.

She was treated for rhabdomyolysis attributed to acute COVID-19 infection and did not receive COVID-19 therapy due to lack of persistent hypoxia. She recieved fluid resuscitation with two liters of normal saline (NS) and started on an infusion of NS at 150 mL/hour, which was later increased to 250 mL/hour. Her CK consistently improved while receiving IV fluids. By hospital day four, the patient's CK was 28,133 U/L and she was discharged to home.

Discussion

Since the beginning of the COVID-19 pandemic, many cases of rhabdomyolysis caused by SARS-CoV-2 have been reported. The exact mechanism of skeletal muscle injury from SARS-CoV-2 is unclear, but proposed mechanisms include direct viral myotoxicity and excessive cytokine-mediated inflammation.[1] The overall incidence of rhabdomyolysis, defined as a creatine kinase level above five times the upper limit of normal, in a retrospective study with 825 hospitalized COVID-19 patients was 16.9%.[2] In this study, median CK level on admission was 1,323 U/L and peak CK level was 2,209 U/L.

The clinical manifestations of rhabdomyolysis include muscle pain and swelling, weakness, reddish-brown-dark urine, malaise, nausea, vomiting, and fever.[3,4] The classic triad of symptoms are myalgia, weakness, and tea-colored urine, but this is seen in <10% of patients and >50% of patients do not have muscle symptoms.[5] Complications of rhabdomyolysis include acute kidney injury, compartment syndrome, hyperkalemia, hypocalcemia, hypovolemia, hyperuricemia, acidosis, liver injury, disseminated intravascular coagulation, arrhythmias, and cardiac arrest.[3-5]

A wide variety of viral and bacterial infections can cause rhabdomyolysis, including influenza, adenovirus, coxsackie, Epstein-Barr virus, HIV, streptococcus pyogenes, staphylococcus aureus, and clostridium.[3-5] Other non-infectious etiologies of rhabdomyolysis include medication-induced, such as HMG-CoA reductase inhibitors and fibrates, and toxins, such as alcohol, cocaine, amphetamines, and snake venom.[3,5] Traumatic causes include prolonged, immobilization, crush injuries, extensive 3rd degree burns, intense exercise, and status epilepticus.[3-5] Metabolic and endocrinologic causes include hypokalemia, hypophosphatemia, hypocalcemia, hypothyroidism, thyrotoxicosis, and diabetic ketoacidosis.[3] Other causes of rhabdomyolysis are heat stroke, malignant hyperthermia, neuroleptic malignant syndrome, limb ischemia, polymyositis, dermatomyositis, and genetic defects in glycolysis and lipid metabolism.[3,4]

There is no established cut-off for creatine kinase level to diagnose rhabdomyolysis, but a common practice is to use five times the upper limit of normal.[5] The diagnosis should be made by a combination of history and physical, identification of a cause, myoglobinuria, and elevated creatine kinase level. A muscle biopsy is generally not necessary for diagnosis, unless there is suspicion for an inflammatory myositis.

Treating rhabdomyolysis of any cause involves prevention of kidney injury, managing complications if present, and eliminating the precipitating cause if possible. Patients should be aggressively fluid resuscitated with isotonic saline between 200 mL to 1000 mL per hour depending on the severity to a goal urine output of 3 mL/kg/hour.[6] Basic metabolic panels should be checked regularly with attention to potassium, calcium, and creatine. Creatine kinase should be monitored in case an ongoing or new process is causes additional skeletal muscle destruction, suggested by a stable or rising CK level. Peak CK levels less than 5,000-10,000 U/L have a smaller likelihood of

developing AKI, while a peak CK level greater than 15,000 U/L has a higher incidence of acute renal failure and electrolyte disturbances.[7] CK levels will typically increase in the first 12 hours and peak within 3-5 days, and return to baseline in 6-10 days. However, it remains unclear at what CK level intravenous fluids can be discontinued.[8] Thus, urine output should be monitored closely to help with titration of the intravenous fluid rate and to monitor for anuria or oliguria in patients with acute kidney injury.

Hospitalized patients with COVID-19 who develop rhabdomyolysis, appear to be correlated with increased mortality and increased need for renal replacement therapy (RRT). A retrospective study of 140 patients with COVID-19 rhabdomyolysis, found that 17.1% of patients needed RRT, vs. 2.9% of patients without rhabdomyolysis and higher in-hospital mortality of 47.1% vs. 26.4% of patients without rhabdomyolysis.[2] Another smaller cohort of 22 hospitalized patients with rhabdomyolysis due to COVID-19, had mortality of 90.9%, vs. 3.2% in those without rhabdomyolysis.[9] Our patient with COVID-19 rhabdomyolysis and a peak CK level of 212,786 U/L did not develop acute renal failure or other complications and was managed successfully with normal saline hydration.

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