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CASE REPORT

Rhabdomyolysis and Acute Renal Failure in an Adolescent With Coronavirus Disease 2019

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There is growing appreciation of the wide range of clinical presentations seen in pediatric patients with coronavirus disease 2019 (COVID-19). Rhabdomyolysis appears to be a rare, but potentially serious, manifestation of COVID-19. Here, we report an adolescent with COVID-19-associated rhabdomyolysis who required hemodialysis due to acute kidney injury. Pediatric providers should consider rhabdomyolysis and the possibility of acute renal failure in children with COVID-19.

Key words. acute renal failure; adolescent; COVID-19; rhabdomyolysis; SARS-CoV-2.

As the number of individuals diagnosed with coronavirus disease 2019 (COVID-19) continues to increase, the array of clinical presentations that affected patients may present with has varied. Common symptoms noted in adults with COVID-19 include fever, cough, dyspnea, malaise, myalgias, diarrhea, and/or anosmia and ageusia [1]. Children typically are asymptomatic or have a mild course with symptoms such as fever, cough, fatigue, and/or diarrhea [2]. Few reports of COVID-19–associated rhabdomyolysis in adults and children have been published to date [1–4]. Herein, we describe an adolescent with COVID-19 without respiratory symptoms or abnormal chest radiography who presented with rhabdomyolysis and acute renal failure. To our knowledge, this constitutes the first published report of a pediatric patient with COVID-19–associated rhabdomyolysis requiring hemodialysis due to acute renal failure.

CASE PRESENTATION

A 16-year-old African American boy with obesity, hypertension, type 2 diabetes mellitus, and obstructive sleep apnea presented to the emergency department with a 3-day history of intermittent fever, sore throat, nonproductive cough, myalgia, and new onset of dark-colored urine that began on the day of presentation. His daily medications at home included lisinopril, hydrochlorothiazide, and metformin.

On examination, he had diffusely tender muscles in his upper and lower extremities but was afebrile and had no signs of respiratory distress. Initial laboratory tests demonstrated a white blood cell count of $4.3 \times 10^3/\mu L$ with 15% lymphocytes, hemoglobin of 15 g/dL, platelets of $241 \times 10^3/\mu L$, blood urea nitrogen of 9 mg/dL, and creatinine level of 1.6 mg/dL (baseline creatinine level approximately 9 months prior was 0.61 mg/dL). In addition, his alanine aminotransferase and aspartate aminotransferase levels were elevated to 107 U/L and 1316 U/L, respectively, and creatine kinase (CK) level was elevated to 274 664 U/L. Rapid influenza test was negative. The patient reported having recent exposure to family members with confirmed COVID-19 in the week leading up to his illness, including his mother, who had recently been hospitalized due to COVID-19, and his aunt, whom he had been caring for at home. Due to these exposures, a nasopharyngeal (NP) swab was obtained as part of his initial evaluation to test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA and was positive via real-time reverse-transcription polymerase chain reaction (RT-PCR). Chest radiography was unremarkable.

Despite fluid resuscitation, the patient became anuric and was transferred to a tertiary care children's hospital on the same day as his initial presentation for further management of rhabdomyolysis and acute kidney injury (AKI). He also enrolled in an institutional review board–approved natural history study of children with COVID-19, as part of which serial NP, nasal, and saliva swabs were collected and tested for SARS-CoV-2 RNA by RT-PCR and viral load was estimated based on cycle threshold (Ct) values. Upon admission, his creatinine level had increased to 2.08 mg/dL and his CK level exceeded the laboratory's upper limit of quantification of 426 700 U/L. Additional laboratory tests indicated a C-reactive protein of 7.17 mg/dL and erythrocyte sedimentation rate of 9 mm/hour. Physical examination continued to demonstrate diffusely tender upper and lower extremities with no signs of respiratory distress.

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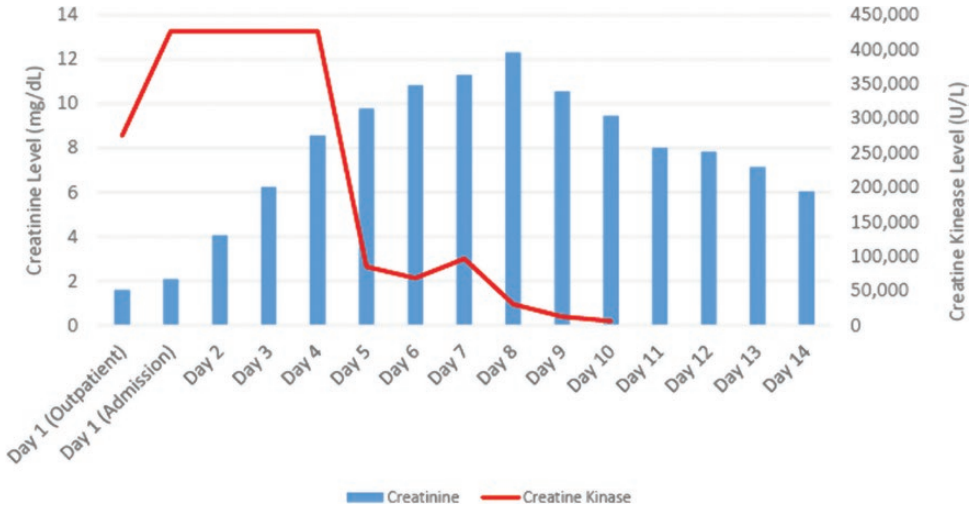

Figure 1. Trend in creatine kinase and creatinine levels during hospitalization. Creatine kinase levels were not obtained after hospital day 10.

Urine output was restored following administration of intravenous fluids and diuretics, with close monitoring of renal function and CK levels. Troponin I was obtained on hospital day 3 and was normal (0.02 ng/mL). By day 5 of hospitalization, the CK level began trending down (Figure 1), but his renal function continued to worsen with a peak creatinine level of 12.03 mg/dL on day 8 of hospitalization, at which time hemodialysis was initiated. Hemodialysis was discontinued after 5 days based on improving renal function, and he was closely monitored over the following 2 days to ensure he did not require additional dialysis. He was discharged home on hospital day 14 with plans for close nephrology follow-up.

Serial sampling for SARS-CoV-2 RNA by RT-PCR on NP and corresponding nasal and saliva samples were available on hospital days 4, 6, 9, and 12, whereas only nasal and saliva swabs were available from day 2 of hospitalization. The patient tested positive from nasal swab on day 2 of hospitalization (Ct value 37), with all other nasal and saliva swabs testing negative throughout his hospitalization. NP samples were positive for SARS-CoV-2 on hospital days 4 (Ct value 31), 6 (Ct value 31), and 12 (Ct value 37), and negative on day 9.

DISCUSSION

Rhabdomyolysis is characterized by skeletal muscle breakdown leading to the increase of cellular components such as creatine phosphokinase, phosphorous, potassium, and myoglobin into the plasma as a result of cellular death [5]. Patients rarely present with the classic triad of symptoms (myalgias, weakness, and dark urine), but rather are diagnosed based on CK level elevations >1000 U/L, or 5 times higher than the normal level of 200 U/L [2, 5]. The most common causes of rhabdomyolysis in children include viral myositis, trauma, strenuous exercise, seizures, connective tissue disorders, and drug overdose [2, 5]. Our patient had no history of trauma, strenuous exercise, seizure, connective tissue disorder, or drug overdose, and his daily medications are not known to be associated with rhabdomyolysis.

The most common viral etiology associated with rhabdomyolysis is influenza, but other possible causes include parainfluenza, human immunodeficiency virus, Epstein-Barr virus, herpes simplex virus, cytomegalovirus, and enteroviruses [1–3]. Other than influenza, our patient did not have additional testing to evaluate for other potential viral etiologies. The pathophysiology of viral-induced rhabdomyolysis is not well known, but hypothesized mechanisms include direct viral invasion into skeletal muscle cells, cytokine-induced immune response, and a viral toxin–mediated process [1, 2].

Few reports of COVID-19–associated rhabdomyolysis in adults have been published to date, predominantly in patients aged >60 years, with substantially lower CK levels than in our patient (2000–13 500 U/L) [1, 3, 4]. These patients also presented with respiratory distress or were noted to have abnormal chest radiography, with only one of these reports progressing to renal failure requiring hemodialysis due to rhabdomyolysis. In the pediatric population, there is one report of an adolescent with COVID-19–associated rhabdomyolysis [2]. Similar to our patient, this patient was obese and had a CK level >400 000 U/L. Unlike our patient, he had mild respiratory distress on presentation, his CK level rapidly declined with fluid management, and he never developed AKI. Similar to our patient, all documented cases of COVID-19–associated rhabdomyolysis occurred at or near time of presentation, suggesting rhabdomyolysis to be a finding in the acute setting of COVID-19. A known complication of rhabdomyolysis, AKI is thought to be the result of myoglobin cast

formation that leads to renal hypoperfusion, decreased glomerular filtration, and subsequent tubular dysfunction [5]. In this report, additional virological data provided by serial sampling for SARS-CoV-2 RNA by PCR documents continued viral shedding from the respiratory tract even after improvement of rhabdomyolysis and renal function.

CONCLUSIONS

Rhabdomyolysis appears to be a rare, but potentially serious, manifestation of COVID-19. To our knowledge, this is the first report of a pediatric patient with COVID-19–associated rhabdomyolysis requiring hemodialysis due to AKI. This report also demonstrates that complications such as rhabdomyolysis can occur with COVID-19 even in the setting of low viral burden (as determined by Ct values) and the absence of respiratory symptoms. Pediatric providers should consider rhabdomyolysis and the possibility of AKI in children with COVID-19. Providers should also keep SARS-CoV-2 on their differential as a cause of myalgia.

Notes

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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