PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

# Rhabdomyolysis as the Initial Presentation of SARS-CoV-2 in an Adolescent

Shawnese Gilpin, MD, MPH, Michael Byers, MD, Allison Byrd, MD, MPH, Jennifer Cull, MD, Danielle Peterson, DO, Bettina Thomas, DO, Phillip Jacobson, MD

**DOI:** 10.1542/peds.2020-019273

**Journal:** *Pediatrics*

**Article Type:** Case Report

**Citation:** Gilpin S, Byers M, Byrd A, et al. Rhabdomyolysis as the initial presentation of SARS-CoV-2 in an adolescent. *Pediatrics.* 2020; doi: 10.1542/peds.2020-019273

# Rhabdomyolysis as the Initial Presentation of SARS-CoV-2 in an Adolescent

Shawnese Gilpin, MD, MPH[a], Michael Byers, MD[a], Allison Byrd, MD, MPH[a], Jennifer Cull, MD[b], Danielle Peterson, DO[b], Bettina Thomas, DO[a], Phillip Jacobson, MD[a,c]

**Affiliations:** [a] Department of Pediatrics, John H. Stroger Jr. Hospital of Cook County, Chicago, IL; [b] Department of Pediatrics, University of Illinois at Chicago, Chicago, IL; [c] Department of Pediatrics, Rush University Children's Hospital, Chicago, IL

**Corresponding Author:** Shawnese Gilpin, MD, MPH, Department of Pediatrics, John H. Stroger Jr. Hospital of Cook County, 1969 W. Ogden Avenue, Chicago, IL 60612 [slsgilpin@gmail.com]

**Funding Source:** No authors have relevant funding disclosures.

**Conflict of Interest:** The authors have no conflicts of interest to disclose.

**Abbreviations:** novel coronavirus disease 2019 (COVID-19); severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); creatinine kinase (CK); World Health Organization (WHO); emergency department (ED); complete metabolic panel (CMP); lactate dehydrogenase (LDH); aspartate aminotransferase (AST); alanine aminotransferase (ALT); reverse transcription polymerase chain reaction (RT-PCR); pediatric intensive care unit (PICU); hospital day (HD); intravenous fluids (IVF)

**Table of Contents Summary:** Rhabdomyolysis is a potential initial presentation of COVID-19. SARS-CoV-2 viral testing should be considered in persons presenting with rhabdomyolysis for appropriate triaging and isolation.

## Contributor's Statement Page

Drs. Gilpin, Byers, Byrd, Cull, Peterson, Thomas and Jacobson gave substantial contribution to conception and design, drafted the article, reviewed and revised the manuscript.

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

**Abstract**

The novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has created a global pandemic, with many cases affecting the elderly. However, children have been affected as well, with about 2.4-3.7% of cases reported. This case is the first published case of an adolescent presenting with rhabdomyolysis as the first sign of COVID-19, with extremely elevated creatinine kinase (CK) levels, approaching almost 400,000 U/L. This case adds to the growing body of literature of a variety of life-threatening manifestations associated with SARS-CoV-2 infection, and highlights the importance of how prompt recognition of these unique presentations of the disease is important to mitigate complications.

## Introduction

The novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has created a global pandemic unlike any seen in modern history. Originating from Wuhan, China in December 2019, there have now been 21,294,845 confirmed cases, 761,779 deaths, and 216 countries, areas, and territories reporting cases according to the World Health Organization (WHO) as of August 16th, 2020[1]. Many reported cases have affected the elderly; however, children have been affected as well, with about 2.4% of cases occurring in patients under 18 years of age worldwide, with a higher incidence in the United States up to 3.7% in ages 10-19 [2,3]. Some children remain asymptomatic during infection with the virus; nevertheless, the most common symptoms reported are fever, cough, chills, dyspnea, myalgias, sore throat, anosmia, ageusia, nausea, vomiting and diarrhea [4,5,6]. There have been no published cases of rhabdomyolysis as the primary sign of COVID-19 in children and adolescents. Herein, we discuss a case of COVID-19 presenting as rhabdomyolysis in an adolescent male.

## Clinical Presentation

A 16-year-old male with a history of asthma presented to the emergency department (ED) with 1 day of dark, black-colored urine and bilateral pain in his shoulders and thighs. He denied

any inciting factors such as strenuous exercise, recent injuries, new medications, illicit drug use, or known metabolic syndromes. He denied sick contacts and had been at home in quarantine per community stay at home orders. On presentation to the ED, his temperature was 37.7° C, he was hypertensive with a blood pressure measurement of 136/97 mmHg, tachycardic with a pulse of 136 beats per minute and normoxic with an oxygen saturation of 98% via pulse oximetry. His weight was 86 kg and his body mass index was 29.4 kg/m$^2$ (97$^{th}$ percentile). On physical examination, he had bilateral tenderness to palpation in his anterior shoulders and thighs. His physical examination was otherwise unremarkable. A chest radiograph revealed no evidence of pneumonia or other acute cardiopulmonary process.

Laboratory tests in the ED included a urinalysis, which revealed an amber and cloudy appearance, pH of 6.0, proteinuria measured at 100 mg/dL, and a large amount of blood, measuring greater than 4+ on urine dipstick, but less than 1 intact red blood cell on urine microscopy. A creatine kinase (CK) level was elevated at 116,640 U/L. A complete metabolic panel (CMP) revealed an elevated lactate dehydrogenase (LDH) of 7,389 U/L, and elevated hepatic enzymes, with an aspartate aminotransferase (AST) of 662 U/L and an alanine aminotransferase (ALT) of 131 U/L. The patient's BUN and creatinine were within normal range at 12 mg/dl and 0.8 mg/dl, respectively on presentation. A nasopharyngeal SARS-CoV-2 real-time reverse transcription polymerase chain reaction (RT-PCR) test was sent from the emergency department which detected the presence of the virus on day 2 of admission. A respiratory viral panel testing for additional viruses was not completed due to hospital protocol to preserve nasopharyngeal viral swabs. The patient was admitted to the pediatric intensive care unit (PICU), due to COVID-19 positive status per hospital protocol, for management of rhabdomyolysis.

**Hospital Course**

In the PICU, the patient had low-grade fevers on hospital days (HD) 1 and 2, with a peak temperature of 39.4 º C, and remained afebrile for the remainder of his hospitalization, without antipyretic therapy. Intravenous fluids (IVF) were initiated on HD 1 using 0.9% normal saline at two times the maintenance rate. Over the course of his hospital stay, IVF included a combination 0.9% normal saline and 0.45% normal saline with sodium bicarbonate. Fluids were titrated to achieve alkalinization of the urine with a goal urine pH of 8.0. The patient's CK levels continued to uptrend, with a maximum of 392,488 U/L on HD 3, and then began to downtrend with a nadir of 13,912 U/L prior to discharge. Additionally, his AST, ALT, and LDH began to uptrend until HD 2-3, and then steadily decreased until discharge (see Table 1). Due to concern over worsening rhabdomyolysis, leading to the potential for life threatening electrolyte abnormalities and renal injury, consideration was also given to the administration of remdesivir, which the hospital possessed exclusively for experimental use. After consultation with the infectious disease service, it was determined that the patient could only receive the medication in a compassionate use capacity. He did not qualify based upon his age and clinical status. Administration of glucocorticoids was also entertained, in order to suppress the inflammatory process. However, at that time, the general consensus among medical professionals was that this therapeutic modality was not recommended for infection with this virus. He exhibited myoglobinuria and proteinuria each day until HD 6, with daily improvement in urine color. The pain in his upper and lower extremities also improved, resolving completely on HD 7. His kidney function and electrolyte levels remained stable in normal range over the course of the hospitalization (see Table 1). The patient denied symptoms of shortness of breath, cough, sore throat, and chills throughout his hospital course. The patient was discharged on HD 9, with

follow up 8 days after discharge, at which point he remained asymptomatic. No additional labs were completed at this time.

**Discussion**

Rhabdomyolysis is "the dissolution of striated muscle", resulting in the release of muscle cell contents, including electrolytes (potassium and phosphates), enzymes (CK, LDH and AST) and proteins (myoglobin), as demonstrated in the laboratory abnormalities of our patient [7,8]. The underlying pathophysiology resulting in the lysis of myocytes involves increased intracellular calcium levels that increase calcium-dependent enzyme activity that subsequently destroys cell membrane proteins [8]. Rhabdomyolysis is commonly the result of congenital disorders or infections in children, with viral infections accounting for the majority of the pathogens [7,9,10].

Influenza A and B, enteroviruses, and human immunodeficiency virus have been most implicated in precipitating rhabdomyolysis. Less commonly, it can be triggered by herpesviruses, Chinkungunya, and norovirus [8,9,10,11,12]. Infection with another coronavirus, SARS-CoV-1, has also been associated with rhabdomyolysis, during the 2002-2004 outbreak, but few cases were reported in the literature[13]. Jin and Tong presented a case of rhabdomyolysis as a late onset of COVID-19 infection in a 60-year-old male in Wuhan China, Suwanwongse and Shabarek presented a case of an 88-year-old male with rhabdomyolysis as an initial presentation of COVID-19, and Valente-Acosta, et al., also presented a case of a 71-year-old male with rhabdomyolysis as an initial presentation of COVID-19[14,15,16]. In each case, the primary signs and symptoms were cough and fever. Rhabdomyolysis was an incidental finding and the peak CK of less than 14,000, hardly life threatening. In addition, a recent publication from the Critical Coronavirus and Kids Epidemiology (CAKE) Study collected data on 17 children less than 19 years old with critical COVID-19 requiring PICU management; findings also demonstrate that rhabdomyolysis is rare[17]. The exact pathogenesis that causes muscle

destruction from a viral etiology remains unclear as the presence of a virus in muscle is difficult to demonstrate. However, current working theories include direct invasion into muscle tissue by a viral agent and myotoxic cytokines released in response to a virus [17]. Our case reports the first pediatric patient with COVID-19, or other coronaviruses, whose presenting symptom was severe rhabdomyolysis with an extremely elevated CK, that peaked at almost 400,000. This case adds to the growing body of literature of a variety of life-threatening manifestations associated with SARS-CoV-2 infection. One limitation of this report is that there was no way to definitively rule out other viruses as a cause of this patient's disease, however, other viruses are less likely given the time of presentation in May, which is after the typical respiratory season. Pediatric patients with COVID-19 have increasingly started having unique presentations of this disease, including immune thrombocytopenia, respiratory failure, severe thrombocytopenia, multisystem inflammatory syndrome, and myocarditis, especially with those patients presenting with predominantly gastrointestinal symptoms [17, 18 19, 20]. Prompt recognition of these associations are important for proper testing, triage and isolation precautions. Furthermore, continuous monitoring and publications of novel presentations will be important for clinicians as this disease continues to manifest itself in various ways.

**Conclusion**

Rhabdomyolysis can be a presenting finding of COVID-19 in pediatric patients and high clinical suspicion must be held for any patient demonstrating signs or symptoms of rhabdomyolysis.

**Acknowledgments**

Thank you to the patient and his family for their willingness to share this case. Thank you to all the members of the healthcare team who contributed to the care of this patient. Thank you to Dr. Letitia Hillsman (pediatric resident), Dr. Norman Jacobs (Pediatric Infectious Disease),

Dr. Kenneth Soyemi (Pediatric Emergency Medicine) and Dr. Paul Severin (Pediatric Critical Care) for their review and feedback on this paper.

**References**

1. World Health Organization. Coronavirus disease 2019 (COVID-19): situation report- 209. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200816-covid-19-sitrep-209.pdf?sfvrsn=5dde1ca2_2 Accessed August, 21 2020.
2. Yi, J., Xiaoxia, L., Runming, J., et al. Novel coronavirus infections: Standard/protocol/guideline recommendations for the diagnosis, prevention and control of the 2019 novel coronavirus infection in children, second edition. *Cin J Appl Clin Pediatr.* 2020; 35(2):143-150. doi:10.3760/cma.j.issn.2095-428X.2020.02.012.
3. Stokes, E., Zambrano, L., Anderson, K., et al. Coronavirus disease 2019 case surveillance- United States, January 22-May 30, 2020. *Morbidity and Mortality Weekly Report*. 2020; 69: 759-765. doi: http://dx.doi.org/10.15585/mmwr.mm6924e2
4. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-10): Symptoms of coronavirus. https://www.cdc.gov/coronavirus/2019-ncov/symptoms- testing/symptoms.html. Accessed May 29, 2020.
5. Castagnoli, R., Votto, M., Licari, A., et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: A systematic review. *JAMA Pediatr*. 2020. doi: 10.1001/jamapediatrics.2020.1467.
6. Dong, Y., Mo, X., Hu, Y., et al. Epidemiology of COVID-19 among children in China. *Pediatrics*. 2020; 145(6):e20200702. doi: 10.1542/peds.2020-0702.
7. Zimmerman, J. & Shen, M. Rhabdomyolysis. *CHEST.* 2013; 144(3): 1058-1065.
8. Zutt, R., van der Kooi, A., Linthorst, G., et al. Rhabdomyolysis: Review of the literature. *Neuromuscular Disorders*. 2014; 24(8): 651-659. doi: 10.1016/j.nmd.2014.05.005.
9. Elsayed, E., & Reilly, R. Rhabdomyolysis: a review, with emphasis on the pediatric population. *Pediatr Nephrol.* 2010; 25(1): 7-18. doi: 10.1007/s00467-009-1223-9.
10. Mannix, R., Tan, M., Wright, R., et al. Acute pediatric rhabdomyolysis: Causes and rates of renal failure. *Pediatrics*. 2006; 118(5): 2119-2125. doi: 10.1542/peds.2006-1352.
11. Elfert, K., Abdelwahed, M., & Chi, G. Chikungunya virus infection-related rhabdomyolysis: A case report. *Cureus.* 2019; 11(2):e4036. doi: 10.7759/cureus.4036.
12. Nisho, T, Yonetani, R., Ito, E., et al. Development of rhabdomyolysis in a child after norovirus gastroenteritis. *BMC Pediatrics*. 2016; 16(176). doi: 10.1186/s12887-016-0720-9.
13. Chen, L., Hsu, C., Tian, Y., et al. Rhabdomyolysis associated with acute renal failure

in patients with severe acute respiratory syndrome. *Int J Clin Pract*. 2005; 59(10): 1162-1166. doi: 10.1111/ j.1368-5031.2005.00540.x.

14. Jin, M., & Tong, Q. Rhabdomyolysis as potential late complication associated with 2019 novel coronavirus disease. *Emerg Infect Dis*. 2020; 26(7). doi: 10.3201/eid2607.200445

15. Suwanwongse, K., & Shabarek, N. Rhabdomyolysis as a presentation of 2019 novel coronavirus disease. *Cureus*. 2020; 12(4): e7561. doi: 10.7759/cureus.7561.

16. Valente-Acosta, B., Moreno-Sanchez, F., Fueyo-Rodriguez, O., et al. Rhabdomyolysis as an initial presentation in a patient diagnosed with COVID-19. *BMJ Case Report*. 2020; 13(6): e236719. doi: 10.1136/bcr-2020-236719.

17. Gonzalez-Dambrauskas, S., Vasquez-Hoyos, P., Camporesi, A., et al. Pediatric critical care and COVID 19. *Pediatrics*. 2020; doi: 10.1542/peds.2020-1766.

18. Tsao, H., Chason, H., & Fearon, D. Immune thrombocytopenia (ITP) in a SARS-CoV-2 positive pediatric patient. *Pediatrics*. 2020; doi: 10.1542/peds.2020-1419

19. Patel, P., Chandrakasan, S., Mickells, G., et al. Severe pediatric COVID-19 presenting with respiratory failure and severe thrombocytopenia. *Pediatrics*. 2020; doi: 10.1542/peds.2020-1437.

20. Centers for Disease Control and Prevention. Emergency Preparedness and Response. Health Alert Network. Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19). https://emergency.cdc.gov/han/2020/han00432.asp. Accessed May 29, 2020

**Table 1: CK, AST, ALT, LDH, potassium, phosphate, and calcium by hospital day**

| Hospital Day | CK (U/L) | AST (U/L) | ALT (U/L) | LDH (U/L) | Potassium mEq/L | Phosphate mg/dL | Calcium mg/dL |
|---|---|---|---|---|---|---|---|
| 0 | 116,640 | 662 | 131 | 7,389 | 4.0 | 4.8 | 9.1 |
| 1 | 196,341 | 991 | 185 | 10,728 | 4.0 | 4.2 | 8.7 |
| 2 | 268,326 | 1,291 | 261 | 10,774 | 4.4 | 4.3 | 8.4 |
| 3 | 392,488 | 2,055 | 385 | 13,942 | 4.7 | 4.2 | 8.5 |
| 4 | 160,975 | 1639 | 426 | 6059 | 4.4 | 3.9 | 8.4 |
| 5 | - | 1,053 | 381 | 2,214 | 4.2 | 3.9 | 8.4 |
| 6 | 28,965 | 556 | 342 | 583 | 4.1 | 3.9 | 8.6 |
| 7 | 13,912 | 230 | 263 | - | 4.2 | 4.4 | 9.2 |

**Rhabdomyolysis as the Initial Presentation of SARS-CoV-2 in an Adolescent**

Shawnese Gilpin, Michael Byers, Allison Byrd, Jennifer Cull, Danielle Peterson, Bettina Thomas and Phillip Jacobson

*Pediatrics* originally published online October 9, 2020;

**Rhabdomyolysis as the Initial Presentation of SARS-CoV-2 in an Adolescent**

Shawnese Gilpin, Michael Byers, Allison Byrd, Jennifer Cull, Danielle Peterson, Bettina Thomas and Phillip Jacobson

*Pediatrics* originally published online October 9, 2020;