Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Associated with Rhabdomyolysis and Acute Kidney Injury (AKI)

Dear Editor:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus is the known cause of coronavirus disease 2019 (COVID-19). SARS-CoV-2 has resulted in the ongoing 2019–2020 coronavirus pandemic since it was first recognized in December 2019 in Wuhan, China. The prevalence of acute kidney injury (AKI) in SARS-CoV-2 is 15%.[1] A study of 701 SARS-CoV-2 patients by Cheng and colleagues demonstrated that in-hospital mortality increased by almost three-fold in those who had AKI.[2] We report a patient with SARS-CoV-2 who developed AKI likely secondary to rhabdomyolysis and discuss the possible association between cytokine storm as the etiology.

A 37-year-old male without any medical history presented with a 2-day history of dyspnea and fatigue. He was diagnosed with SARS-CoV-2 confirmed by real-time reverse transcription-polymerase chain reaction (RT-PCR) nasopharyngeal swab. Physical examination revealed no evidence of swelling or tenderness of his extremities. He was subsequently intubated for acute hypoxic respiratory failure (AHRF) secondary to SARS-CoV-2 pneumonia. His-pertinent labs are summarized in Table 1. His-creatine kinase (CK) on admission was 17,000 and peaked at 35,000 IU/L. Inflammatory markers, such as lactate dehydrogenase (LDH), white blood cell count (WBC), and C-reactive protein (CRP), were markedly elevated since his admission. He was diagnosed with rhabdomyolysis and hydrated aggressively with intravenous fluids. He required renal replacement therapy (RRT) on day five of hospitalization due to poor urine output and worsening AHRF. No other predisposing factors for rhabdomyolysis were identified, such as drugs, toxins, electrolyte abnormalities, or other infections. He died 12-days later despite therapies involving hydroxychloroquine, azithromycin, dexamethasone, tocilizumab, and convalescent plasma.

SARS-CoV-2 belongs to the same family of coronavirus that caused the severe acute respiratory syndrome coronavirus (SARS-CoV) 2003 epidemic. A case series of SARS-CoV-related rhabdomyolysis showed the development of AKI with peak CK levels ranging from 7500 to 340,000 IU/L.[3] Jin and colleagues were the first to describe a 60-year-old man who was admitted with RT-PCR confirmed SARS-CoV-2 pneumonia and developed rhabdomyolysis on day 9th of hospital admission. His-renal function was within normal limits, and his peak laboratory values of CK, LDH, and CRP were markedly elevated at 12,000 IU/L, 2347 IU/L, and 206 mg/L, respectively.[4] He did not develop AKI and improved with hydration and supportive care. Peak CK has been shown to have a poor correlation with the incidence of AKI, where a retrospective study on influenza-related rhabdomyolysis showed 82% of patients developed AKI with peak CK 20,000 IU/L and less.[5] Rhabdomyolysis can be the initial presentation or occur at any time during the SARS-CoV-2 disease course. Clinicians should be aware that although aggressive fluid administration has been frequently applied to prevent AKI in rhabdomyolysis, SARS-CoV-2 patients are at risk of developing worsening ARHF from fluid overload, especially in the setting of AKI with oliguria.

Generalized muscle pain and fatigue are common presenting symptoms in SARS-CoV-2. However, this can be difficult to assess in critically ill patients, especially when they are intubated and sedated on a mechanical ventilator. Unlike other inflammatory markers[6] (white blood cell count, platelet count, LDH, CRP, and D-dimer) used for prognostication of SARS-Cov-2, CK levels are rarely monitored. Therefore, rhabdomyolysis can be easily misdiagnosed. A retrospective study of 171 SARS-CoV-2 patients showed that CK of more than 185 IU/L, AKI, and requirement of RRT was associated with an increase in mortality.[1] In the same cohort of patients who had elevated CK and developed AKI, they were more likely to have elevated inflammatory markers of LDH, D-dimer, ferritin, and procalcitonin. This may suggest a connection between excessive immune cytokine response leading to rhabdomyolysis and AKI. We postulate that the possible etiologies of SARS-CoV-2-related rhabdomyolysis could be 1) direct viral

TABLE 1. Pertinent laboratory data.

Day of admission	1	2	3	4	5
WBC (10×3/uL)	16	18	25	23	24
Platelet (10×3/uL)	300	350	400	370	390
BUN (mg/dL)	30	45	50	48	80
Creatinine (mg/dL)	2	2.4	2.5	2.8	5
CK (IU/L)	17,000	22,000	25,000	35,000	30,000
CRP (mg/L)	60	70	80	150	180
LDH (IU/L)	1300	2100	3200	4500	7600
Ferritin (ng/mL)	1100	2000	1500	3000	2700
D-Dimer (mg/L)	54	55	61	50	54

Abbreviations: BUN, blood urea nitrogen; CK, creatine kinase; CRP, c-reactive protein; LDH, lactate dehydrogenase; WBC, white blood cell count.

invasion of muscles, 2) release of viral-toxins causing myositis, or 3) overwhelming immune response to the virus leading to cytokine storm with resulting myositis.[2]

ACKNOWLEDGMENT

WC had full access to the data. WC and BS were involved in writing the manuscript.

Woon H. Chong, MD[1,*]
Biplab Saha, MD[2]
[1]Department of Pulmonary and Critical Care Medicine, Albany Medical Center, 16 New Scotland Avenue, Albany, NY
[2]Department of Pulmonary and Critical Care, Ozarks Medical Center, West Plains, MO
*E-mail: chongw@amc.edu
Funding Source: None.
Conflict of Interest: No author has a conflict of interest to disclose.

REFERENCES

1. **Zhou F, Yu T, Du R, et al.** Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054–1062. https://doi.org/10.1016/S0140-6736(20)30566-3.
2. **Cheng Y, Luo R, Wang K, et al.** Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int*. 2020;97(5):829–838. https://doi.org/10.1016/j.kint.2020.03.005.
3. **Wang J-L, Wang J-T, Yu C-J, et al.** Rhabdomyolysis associated with probable SARS. *Am J Med*. 2003;115(5):421–422. https://doi.org/10.1016/s0002-9343(03)00448-0.
4. **Jin Min, Tong Qiaoxia.** Rhabdomyolysis as potential late complication associated with COVID-19. *Emerg Infect Dis J*. 2020;26(7). https://doi.org/10.3201/eid2607.200445.
5. **Singh U, Scheld WM.** Infectious etiologies of rhabdomyolysis: three case reports and review. *Clin Infect Dis*. 1996;22(4):642–649. https://doi.org/10.1093/clinids/22.4.642.
6. **Jin Y-H, Cai L, et al.** A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res*. 2020;7(1):4. https://doi.org/10.1186/s40779-020-0233-6.