



# An Atypical Case of COVID-19 induced Rhabdomyolysis and Acute Kidney Injury

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## Introduction

Since early 2020, SARS-CoV-2 called coronavirus disease 2019 (COVID-19), a viral infection, has been spreading throughout the world [1]. The symptoms vary from asymptomatic disease to pneumonia to life-threatening complications. Fever, cough, myalgia, sore throat, dyspnea, and fatigue are the most common symptoms of COVID-19. However, there have been multiple reports which show Rhabdomyolysis as a late complication of COVID-19 [2] infection.

Rhabdomyolysis is a life-threatening disorder that typically manifests with myalgias, fatigue, and pigmenturia. Severe cases tend to also present with abdominal pain, nausea, and vomiting. Common complications of Rhabdomyolysis include Acute Kidney Injury (AKI) and electrolyte abnormalities. Rhabdomyolysis is characterized by muscle injury that leads to leakage of myoglobin into vascular circulation [3]. Viral infections, especially influenza virus infection, are occasionally known to lead to rhabdomyolysis [4]. In this case report, we report a young male in his thirties without comorbidities presents early in his COVID-19 infection with severe Rhabdomyolysis.

## Case Presentation

A 34-year-old male with no significant past medical history was brought in by EMS for multiple episodes of vomiting for the past five days. The patient stated he had multiple episodes of vomiting white/green liquid that was associated with epigastric abdominal pain, which he described as sharp, intermittent, non-radiating and 5 out of 10 in severity. He also endorsed sore throat, non-productive cough, mild dyspnea, subjective fever, headache, and chills over the past two days. Recently, he had tested positive for COVID-19 at an outside facility after being exposed to his landlord, who was confirmed as COVID-19

positive. He denied any recent travel, chest pain, and dizziness. Vital signs on admission were significant for tachycardia up to 123 bpm, tachypnea to 24 rpm, adequate pulse oxygenation on room air, normotension, and afebrile. Physical exam revealed tenderness to palpation of the epigastrium; lungs were clear to auscultation bilaterally, normal mentation with no focal deficits. Initial abnormal laboratory findings showed a white blood cell count of 3.76 k/mm<sup>3</sup> (normal is 4.50 – 11.00 k/mm<sup>3</sup>), absolute lymphocytes of 0.74 k/mm<sup>3</sup> (normal 1.50 – 4.00 k/mm<sup>3</sup>), sodium of 135 mmol/L (normal 136 – 145 mmol/L), creatinine of 1.4 mg/dL (normal 0.7 – 1.3 mg/dL), ALT of 127 U/L (normal 7 – 40 U/L), AST of 261 U/L (normal 13–40 U/L), alkaline phosphatase of 37 U/L (normal 46 – 116 U/L), lipase of 59 U/L (normal 12–53 U/L), creatine kinase of 16,516 U/L (normal 46 – 171 U/L), ferritin 591.2 ng/mL (normal 10.5 – 307.3 ng/mL), c-reactive protein 3.3 mg/dL (normal 0.0 – 0.9 mg/dL), lactate dehydrogenase 854 U/L (normal 120–246 U/L). Chest x-ray was performed at admission and revealed airspace opacities at the mid and lower left lung field consistent with atypical pneumonia (Figure 1). Initially, the patient received aggressive IV fluid hydration with bolus of three liters of sodium chloride 0.9% and was continued with 200 cc/hr of sodium chloride 0.9% as maintenance fluids. Obtained blood cultures had no growth of organisms on final report. The patient was kept NPO, given anti-emetic medication (Zofran and Reglan), Morphine for pain, Plaquenil, Azithromycin, Ceftriaxone, Flagyl, N-acetylcysteine (150 mg/kg intravenously) and Tylenol. An abdominal ultrasound was only significant for fatty infiltration of the liver. On day 3 of admission, CK trended up to a peak of 73,922 U/L, lipase trended up to a peak of 252 U/L, AST trended up to a peak of 1,140 U/L, Cr trended to 1.1 mg/dL, and patient was febrile to T<sub>max</sub> of 103.6 F (Figure 2). The admission lasted a total of 8 days with gradual resolution of symptoms on day 3 and improvement in lab findings after days 3 and 4. Lipase peaked on day 4 with a level of 252 U/L, while CK peaked on day 3 with a level of 73,922 U/L. AST and ALT also peaked on day 3 with levels of 1,140 U/L and 426 U/L, respectively. Cr was able to trend to 1.0 mg/dL by day 3 of admission, confirming resolution of the patient's AKI. The patient was eventually discharged once medically stable and sent home with instructions for self-isolation and primary care follow up.

## Discussion

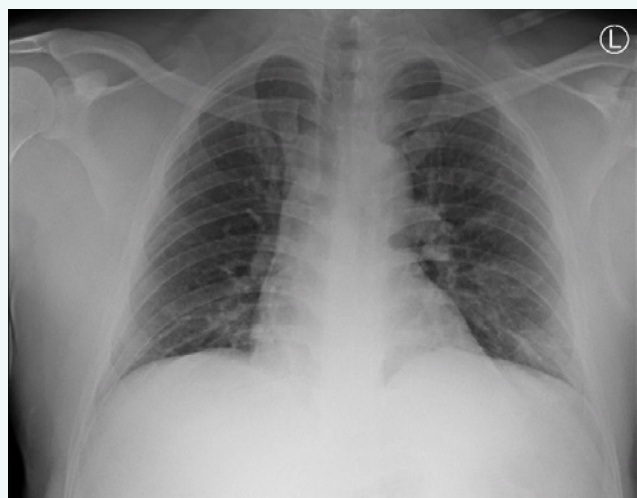
It has been found that patients with SARS (Severe Acute Respiratory Syndrome) and concurrent Rhabdomyolysis have a high incidence of bacterial infection, Acute Kidney Injury (AKI), and mortality [5]. One study showed that during hospitalization AKI was documented in 3.2% of COVID-19 patients [6], though AKI prevalence has also been reported as low as 0.5% [7]. While the occurrence of AKI is low in SARS patients, when it does occur

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**Figure 1** Chest X-ray findings of the COVID-19 infected patient admitted with Rhabdomyolysis and acute kidney injury showing airspace opacities at the mid and lower left lung field consistent with atypical pneumonia.

it is associated with a mortality rate as high as 77% [5]. It is also demonstrated that AKI was exceedingly higher in patients with elevated baseline serum creatinine (SCr) than patients with normal baseline SCr. Baseline SCr is elevated in 15.5% of patients on admission with a peak SCr of  $94 \pm 102 \mu\text{mol/L}$  during hospitalization [6]. Proteinuria is present in 44.0% patients, and relatively fewer patients also demonstrated hematuria, 26.9%. These patients also developed a more severe AKI with in-hospital mortality of 30.9% compared to a death rate of 9.2% in patients with normal baseline creatinine [6]. When 95 adult COVID-19 CK levels were tested, 12 had levels 200–400 U/L, 9 had levels 400–600 U/L, and 7 had levels > 600 U/L [8].

SARS-CoV renal involvement mechanisms are divided into three possible aspects encompassing cytokine storm, organ crosstalk, and systemic effects [9]. A study proved that SARS-CoV-1-associated Rhabdomyolysis was secondary to cytokine storm rather than direct viral invasion. This was deduced based on the presence of high inflammatory markers, with a lack of viral particles seen on muscle biopsies [10]. Cytokine storms are known to cause Acute Respiratory Distress Syndrome (ARDS) in patients with SARS-CoV-2 infection, further supporting this mechanism of damage to the kidney [4]. This seems to further suggest that the mechanism of COVID-19-induced Rhabdomyolysis is from an excessive immune response and cytokine storms [11]. These three mechanisms are also implicated in Rhabdomyolysis-induced influenza A infection, though the favored reasoning is suggested to be due to direct viral invasion of myocytes [4].

Renal abnormalities were analyzed by light microscopy, ultrastructural observation and immunostaining in 26 autopsies of patients with COVID-19. Of the patients, 9 (34.6%) showed clinical signs of renal damage, which included elevated serum creatinine with or without new-onset proteinuria [12]. In receptors of SARS-CoV-2, Angiotensin-converting enzyme 2 (ACE2) was found to be upregulated and immunostaining with SARS-CoV nucleoprotein

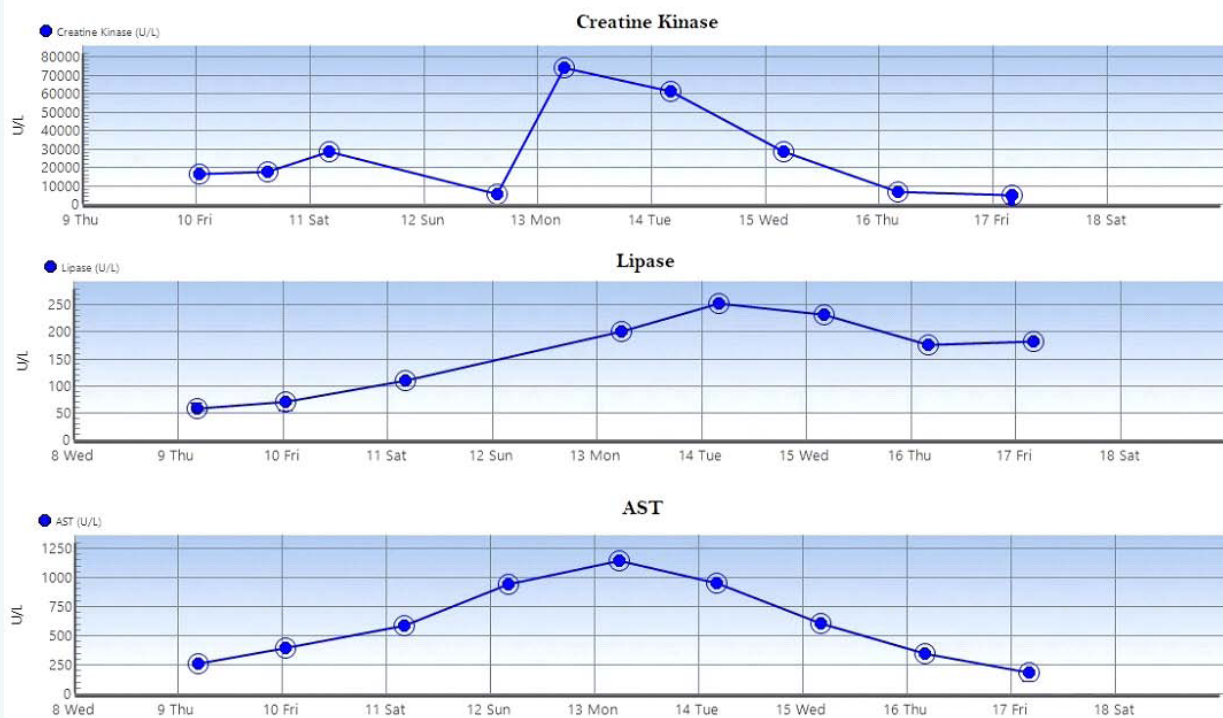
antibody was positive in tubules showing a direct virulence of SARS-CoV-2. Other factors contributing to the AKI seen in these patients included systemic hypoxia, abnormal coagulation, and possible drug or hyperventilation-relevant Rhabdomyolysis. This study also showed that a direct viral effect on the muscle may be partially responsible [12].

Prior to the emergence of the COVID-19 strain, few SARS cases were shown to be complicated with Rhabdomyolysis [10,13]. Of those cases approximately 10% of patients had complications of acute renal failure [10]. Chan et al. showed that elevated CK and Rhabdomyolysis can be the sole initial presentation of patients with COVID-19 [2] in a report of two cases of SARS-CoV-2 induced Rhabdomyolysis. The initial presentation consisted solely of weakness and elevated CK [2]. Suwanwongse et al. similarly presented a case of an elderly male who presented with initial Rhabdomyolysis and later was diagnosed with COVID-19 [11]. Their patient developed mild acute kidney injury with a maximum CK of 13,581 U/L and was effectively treated with Intravenous fluids [11]. Min et al. showed COVID-19-associated Rhabdomyolysis in a 60-year-old male in Wuhan, China for whom a maximum CK of 17,434 U/L was reported, but unlike Suwanwongse et al., the patient was without any subsequent acute kidney injury [2]. Gefen et al. reported a pediatric patient that suffered from acute kidney injury who was discharged 12 days after admission. Though SCr levels were normal, the patient's CK levels were reduced to 6,526 U/L, from 427,656 U/L upon initial presentation. Treatment consisted of isotonic intravenous fluids containing sodium bicarbonate in order to maintain a urine output of 100–200 mL/h and urine pH > 7.0 [14].

Rhabdomyolysis is often associated with increased levels of Aminotransferases. Elevated AST levels were detected in 95 percent of Rhabdomyolysis cases and elevated ALT in 73 percent [15]. This phenomenon is consistent with muscle release of AST and ALT. AST rather than ALT is often found in large quantities in skeletal muscle. This leads to serum AST levels coinciding with CK levels. As was seen in this patient, AST concentrations fell in parallel with CK concentrations (Figure 2).

## Conclusion

The management of Rhabdomyolysis in COVID-19 patients is challenging. Aggressive fluid administration is recommended to prevent AKI, but may cause a further decrease in respiratory function, leading to further hypoxia in patients with acute respiratory distress syndrome (ARDS) if a fluid overload occurs [2,11]. Small boluses of intravenous fluid administration with close clinical observation has been recommended to reduce this risk. Continuous monitoring of oxygen saturation in addition to serial blood work for SCr and CPK may also help to manage your patient. If the patient's creatinine rises, repeat small boluses of fluid should be given [11]. In this case we present a unique scenario where a patient presented solely with features of Rhabdomyolysis. Given the high risk of ARDS in patients with COVID-19 infection, aggressive fluid resuscitation should be approached with extreme caution. This patient was treated with aggressive IV fluids while being constantly monitored for worsening respiratory symptoms. Our goal in presenting



**Figure 2** Creatinine Kinase, Lipase and AST levels in a 34-year-old COVID-19 infected male admitted with Rhabdomyolysis and acute kidney injury from admission to discharge.

this case report is to demonstrate successful management of Rhabdomyolysis in the context of a rare clinical presentation of COVID-19 and raise awareness to these clinical features and complications.

## References

1. McMichael, Temet M., et al. "Epidemiology of Covid-19 in a Long-Term Care Facility in King County, Washington: NEJM." *New England Journal of Medicine*, 10 Apr. 2020, [www.nejm.org/doi/full/10.1056/NEJMoa2005412?query=featured\\_coronavirus](http://www.nejm.org/doi/full/10.1056/NEJMoa2005412?query=featured_coronavirus).
2. Jin, M., & Tong, Q. (2020). Rhabdomyolysis as potential late complication associated with COVID-19. *Emerg Infect Dis*, 26(7), 10-3201. <https://doi.org/10.3201/eid2607.200445>
3. Ayala E, Kagawa FT, Wehner JH, Tam J, Upadhyay D. Rhabdomyolysis Associated With 2009 Influenza A(H1N1). *JAMA*. 2009;302(17):1863–1864. doi:10.1001/jama.2009.1582
4. Fadila, M. F., & Wool, K. J. (2015). Rhabdomyolysis secondary to influenza a infection: a case report and review of the literature. *North American journal of medical sciences*, 7(3), 122.
5. Tsai HB, Huang JW, Chen KY et al. Acute renal failure and renal replacement therapy in SARS patients. Presented at the *Annual Committee on American Society of Nephrology*, San Diego, November 12–17, 2003
6. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, Li J, Yao Y, Ge S, Xu G. Kidney impairment is associated with in-hospital death of COVID-19 patients. *MedRxiv*. 2020 Jan 1.
7. Guan, W. J., Ni, Z. Y., Hu, Y., Liang, W. H., Ou, C. Q., He, J. X., ... & Du, B. (2020). Clinical characteristics of coronavirus disease 2019 in China. *New England journal of medicine*, 382(18), 1708-1720.
8. Zhang, G., Zhang, J., Wang, B., Zhu, X., Wang, Q., & Qiu, S. (2020). Analysis of clinical characteristics and laboratory findings of 95 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a retrospective analysis. *Respiratory research*, 21(1), 1-10.
9. Ronco, C., & Reis, T. (2020). Kidney involvement in COVID-19 and rationale for extracorporeal therapies. *Nature Reviews Nephrology*, 1-3.
10. Chen LL, Hsu CW, Tian YC, Fang JT (2005) Rhabdomyolysis associated with acute renal failure in patients with severe acute respiratory syndrome. *Int J Clin Pract* 59:1162–1166
11. Suwanwongse, K., & Shabarek, N. (2020). Rhabdomyolysis as a presentation of 2019 novel coronavirus disease. *Cureus*, 12(4).
12. Su H, Yang M, Wan C, Yi LX, Tang F, Zhu HY, Yi F, Yang HC, Fogo AB, Nie X, Zhang C. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. *Kidney international*. 2020 Apr 9.
13. Wang, J. L., Wang, J. T., Yu, C. J., Chen, Y. C., Hsueh, P. R., Hsiao, C. H., ... & Yang, P. C. (2003). Rhabdomyolysis associated with probable SARS. *The American journal of medicine*, 115(5), 421-422.
14. Gefen AM, Palumbo N, Nathan SK, Singer PS, Castellanos-Reyes LJ, Sethna CB. Pediatric COVID-19-associated rhabdomyolysis: a case report. *Pediatric Nephrology* (Berlin, Germany). 2020 May 23:1.
15. Weibrecht, K., Dayno, M., Darling, C., & Bird, S. B. (2010). Liver aminotransferases are elevated with rhabdomyolysis in the absence of significant liver injury. *Journal of Medical Toxicology*, 6(3), 294-300.