Case Report

Acute Kidney Injury Secondary to Rhabdomyolysis and COVID-19: A Case Report and Literature Review

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1. Introduction

The novel coronavirus which emerged in late 2019, designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and responsible for COVID-19, has infected more than 85 million people worldwide and has grown into a global pandemic. The incubation period, disease severity, initial presentation, and laboratory findings are varied [1–4]. Multiorgan complications include respiratory failure, cardiac arrhythmias, cardiomyopathy, encephalopathy, thromboembolic events, and acute kidney injury (AKI) [5–7].

Kidney involvement in the setting of COVID-19 manifests as hematuria, proteinuria, and/or an AKI, which is associated with increased mortality and more severe infections [8, 9]. Estimates of the incidence of AKI range from 17% to 37% and between 5–15% require kidney replacement therapy [8, 10]. The etiology of kidney dysfunction remains unexplored and may be the result of direct viral infection, cytokine release, altered hemodynamics, or multifactorial, including rhabdomyolysis. Characterized as a clinical syndrome of muscle weakness, myalgia, tea-coloured urine, and muscle swelling, rhabdomyolysis is defined with a creatine kinase value greater than 1000 IU/L or higher than 5 times the upper limit of normal [11]. Rhabdomyolysis occurs due to trauma, drugs, electrolyte abnormalities, and also rarely, viral infections such as influenza A and B, coxsackievirus, Epstein–Barr, herpes simplex, parainfluenza, adenovirus, echovirus, HIV, cytomegalovirus, and most recently, COVID-19 [12, 13]. Thus, our aim in this case report is to present the symptoms, laboratory findings, and clinical course of a patient who presented with AKI secondary to rhabdomyolysis and COVID-19 and provide a literature review of the reported cases.

2. Case Report

A 62 year-old-African American male patient presented to the emergency department with a 3-day history of general feeling of malaise, poor appetite, decreased urine output, and blood in his urine. His comorbidities include hypertension, morbid obesity (BMI of 39.6), and suboptimally controlled type II diabetes. He was socially distancing alone at home and reported no known sick contacts. He denied taking any anticoagulation medication and had no symptoms of urinary urgency or dysuria. He also denied recent strenuous activity, alcohol ingestion, or taking any over-the-counter supplements. Home medications included aspirin 81 mg,
On presentation, he was febrile to 38.1°C with a heart rate of 103, respiratory rate of 20, blood pressure of 91/58 mmHg, and saturating well on room air. Physical examination yielded a patient with a large body habitus and mild respiratory distress. Pertinent initial laboratory findings revealed a sodium of 132 mmol/L, potassium 4.5 mmol/L, magnesium 2.0 mg/dL, phosphorus 8.9 mg/dL, corrected calcium 4.4 mg/dL, BUN 54 mg/dL, creatinine 4.90 mg/dL (baseline of 1.1 mg/dL), glucose 372 mg/dL, aspartate aminotransferase (AST) 1077 units/L (baseline of 16 units/L), alanine aminotransferase (ALT) of 158 units/L (baseline of 24 units/L), alkaline phosphatase 45 units/L, total bilirubin 0.4 mg/dL, glomerular filtration rate (GFR) 14 mL/min, and lactic acid of 2.1 mmol/L. Urine albumin-to-creatinine ratio was 30 mg/g. Creatinine kinase was 327, 629 units/L, and peaked on presentation. Creatine kinase is depicted in Figure 1, respectively.

On the third day and was red tinged. Urine output decreased to <100 mL of urine. Ultrasound of the abdomen showed hepatomegaly with fatty infiltration and no acute cholecystitis or cholelithiasis, as well as no hydronephrosis. The initial chest radiograph was significant for multifocal patchy air-space disease suggestive of atypical pneumonia or viral infection including COVID-19 (Figure 2).

Initial COVID-19 RNA PCR was negative. Respiratory viral panel for influenza and respiratory syncytial virus (RSV) was also negative. He was given a bolus of 2L lactated ringer (LR) and started on maintenance LR at 200 mL/hour as well as sevelamer 2400 mg three times a day. For the first 48 hours, he was anuric. He also received ceftriaxone and azithromycin for community-acquired pneumonia coverage, and heparin drip for suspected pulmonary embolism and was transferred to the intensive care unit (ICU).

In the ICU, he was started on a 10-day course of dexamethasone and weaned to a high-flow nasal cannula after 2 days. Remdesivir was never given due to kidney dysfunction. He was also intermittently treated with diuretics. By day 14 of his hospitalization, his daily urine output was 2.9 L and clear in color. He received an echocardiogram which showed an ejection fraction of 65–70% with no valvular or diastolic dysfunction. Ultrasound of the lower extremities was negative for deep vein thrombosis. As his respiratory status improved, he was weaned to 6L supplemental oxygen via a nasal cannula and was transferred out of the ICU. The patient gradually improved as he completed the 10-day course of dexamethasone, and at the time of discharge, 26 days after his presentation, his creatinine gradually decreased to 1.16 mg/dL and he was sent home, on room air.

3. Discussion

COVID-19-related kidney dysfunction occurs in a number of ways [14] and can manifest as (1) prerenal AKI from volume depletion or cardiorenal syndrome, (2) acute tubular injury in the setting of circulatory collapse, (3) thrombotic microangiopathy secondary to hypercoagulation, (4) collapsing glomerulopathy in APOL1 gene variants, and (5) myoglobin cast nephropathy due to rhabdomyolysis. Emerging literature has connected COVID-19 to the development of rhabdomyolysis and acute kidney injury, but only few cases have been reported (Table 1) and the physiology link remains unknown.

The proposed hypotheses include direct invasion of muscle tissue, release of toxic cytokines, namely, TNF-alpha, and destruction of muscle cell membranes by circulating toxins [25]. Approximately 5% of hospitalized COVID-19
Figure 1: Trend of creatinine kinase and creatinine.

Figure 2: Chest X-ray showing multifocal patchy airspace disease, COVID-19.

Figure 3: Chest X-ray on day 14 showing worsening bilateral infiltrates.
| Demographics | Clinical Presentation | Comorbidities | Pertinent labs | Clinical course and outcome |
|--------------|-----------------------|---------------|----------------|----------------------------|
| Taxbro et al. [15] | 38-year-old male | 1 week of fever, myalgia, nausea, emesis, dry cough, dyspnea, and abdominal pain | Type 2 diabetes, Gout | CRP: 145 mg/dL  Creatinine: 51 mmol/L  D-dimer: 0.19 mg/dL  No reported CK | Complete recovery after ICU admission requiring intubation  LOS: 23 days |
| Valente-Acosta et al. [16] | 71-year-old male | 1 week of dry coughing, mild dyspnoea and fever, and myalgia and arthralgia, predominantly in his legs | Benign prostatic hyperplasia | CRP: 2.9 mg/dL  Creatinine: 1.68 mg/dL  LDH: 541 U/L  D-dimer: 983 ng/mL  CK peak: 8,720 U/L  Creatinine 0.89 mg/dL  CK peak: 5,454 U/L | Complete recovery after ICU admission requiring intubation  LOS: 16 days |
| | 34-year-old male | Fever, cough, dyspnea, and weakness | Prediabetes | — | Died in hospital  LOS: not reported |
| | 71-year-old male | Fever, cough, and dyspnea | Hypertension, Schizophrenia, Seizures | Creatinine: 4.1 mg/dL  CK peak: 10,247 U/L  Creatinine: 2.25 mg/dL  CK peak: 2,628 U/L  Creatinine: 1.03 mg/dL  CK peak: 5,531 U/L  Creatinine: 3.8 mg/dL  CK peak: 4,330 U/L | Died in hospital  LOS: not reported |
| Singh et al. [17] | 88-year-old male | Confusion | Diabetes, Hypertension | — | Died in hospital  LOS: not reported |
| | 36-year-old male | Fever, cough, and dyspnea | None | — | Died in hospital  LOS: not reported |
| | 39-year-old male | Myalgias, fever, cough, and dyspnea | Hypertension | — | Died in hospital  LOS: not reported |
| Demographics   | Clinical Presentation                  | Comorbidities                                                                 | Pertinent labs                                                                 | Clinical course and outcome            |
|---------------|---------------------------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------|----------------------------------------|
| Husain et al. [18] | 38-year-old male                       | Sever, cough, dyspnea, and myalgia                                           | Not reported                                                                     | CRP: 98.3 mg/dL                        |
|               |                                       |                                                                                | Creatinine: 1.5 mg/dL                                                          | Complete recovery after ICU admission  |
|               |                                       |                                                                                | LDH: 398 U/L                                                                    | LOS: 3 months                          |
|               |                                       |                                                                                | CK peak: 33,000 U/L                                                            |                                        |
|               |                                       |                                                                                | CRP: 98.3 mg/dL                                                                 |                                        |
|               |                                       |                                                                                | Creatinine: 2.48 mg/dL                                                         |                                        |
|               |                                       |                                                                                | LDH: 2150 U/L                                                                   |                                        |
|               |                                       |                                                                                | CK peak: 464,000 U/L                                                           |                                        |
|               |                                       |                                                                                | Creatinine: 1.16 mg/dL                                                         |                                        |
|               |                                       |                                                                                | LDH: 459 U/L                                                                   | Died in hospital                       |
|               |                                       |                                                                                | D-dimer: 0.62 ng/mL                                                            | LOS: 21 days                           |
| Chedid et al. [19] | 51-year-old male                      | 2 days of diffuse myalgias, dry cough, and mild chills                      | Hypertension, Type 2 diabetes, OSA, CKD II                                      | CRP: 98.3 mg/dL                        |
|               |                                       |                                                                                | Creatinine: 3.8 mg/dL                                                          | Dialysis as outpatient                |
|               |                                       |                                                                                | LDH: 907 U/L                                                                   | LOS: not reported                      |
|               |                                       |                                                                                | D-dimer: 1.92 ng/mL                                                            |                                        |
|               |                                       |                                                                                | CK: 4,330 U/L                                                                  |                                        |
| Singh et al. [20]    | 67-year-old male                       | Fever and dyspnea                                                             | Hypertension                                                                     | Died in hospital                       |
|               |                                       |                                                                                | Creatinine: 2.0 mg/dL                                                          | LOS: 1 day                             |
|               |                                       |                                                                                | LDH: 805 U/L                                                                   |                                        |
|               |                                       |                                                                                | CK: 2.751 U/L                                                                  |                                        |
|               |                                       |                                                                                | CRP: 3.3 mg/dL                                                                 |                                        |
|               |                                       |                                                                                | Creatinine: 1.4 mg/dL                                                          |                                        |
|               |                                       |                                                                                | LDH: 854 U/L                                                                   |                                        |
|               |                                       |                                                                                | CK: 73,922 U/L                                                                 |                                        |
| Alejandro et al. [21] | 89-year-old male                   | Dyspnea, fever, cough, and malaise                                           | Hypertension, coronary artery disease, and heart failure with preserved          | Complete recovery                      |
|               |                                       |                                                                                | CK: 2.751 U/L                                                                  | LOS: 12 days                           |
|               |                                       |                                                                                | ejection fraction                                                              |                                        |
| Pellegrini et al. [22] | 34-year-old male               | 2 days of emesis, sore throat, nonproductive cough, and dyspnea              | Not reported                                                                     | Complete recovery                      |
|               |                                       |                                                                                |                                                                                | LOS: 8 days                            |
patients develop an AKI [26], and up to 40% of those are admitted to the ICU [27]. Studies have indicated that the development of stage II or III AKI incurs a poor prognosis with mortality rates as high as 70% in those requiring kidney replacement therapy [26, 28, 29]. In this case report, the patient developed stage III AKI secondary to his rhabdomyolysis which was the presenting symptom of COVID-19. Although he required kidney replacement therapy, he fortunately obtained complete recovery despite a prolonged hospital course and also requiring ICU level of care.

Rhabdomyolysis has been described as a late complication of COVID-19 [30], but in our case, it was the presenting clinical manifestation even before respiratory symptoms developed. Of the reported cases, the classic triad of weakness, myalgia, and tea-coloured urine was not seen in any patients and only 7 of 16 reported one symptom, most commonly myalgia. In this case report, the patient presented with tea-coloured urine, decreased urine output, and general malaise and weakness. Myalgia is a common complaint of viral infections, including influenza. Thus, in patients presenting with myalgia and respiratory symptoms or high suspicion of COVID-19, we recommend evaluating serum creatine kinase and serum creatinine and closely monitoring urine output. The development of rhabdomyolysis and AKI does not appear to have a predilection in patients with certain comorbidities or age. Additionally, it appears that peak creatinine kinase is not associated with in-hospital mortality. In this case, peak creatinine kinase was 327,629 units/L, the second highest of the reported cases, and the patient recovered completely. This contrasts with the cases reported by Singh et al. where peak creatinine kinase was less than <10,000 units/L and patients died during their hospitalization.

The favourable outcome of our patient may be linked to early identification and IV fluid therapy.

Regarding management of rhabdomyolysis, the mainstay continues to be correction of intravascular volume depletion and prevention of intratubular cast formation with fluid resuscitation. The initial recommended rate is 1 L/hour followed by 500 mL/hour thereafter with either isotonic saline or lactate ringers, although there is no strong evidence supporting either of these IV fluid formulations [31]. The goal of therapy is increased urine output; however, clinicians should be cognizant of volume overload in the setting of oliguria [32]. Additionally, electrolyte abnormalities such as hyperkalemia, hyperphosphatemia, and hypercalcemia or hypocalcaemia should be monitored closely and addressed quickly. Further evidence is needed on target therapies to prevent rhabdomyolysis-associated AKI [33].

A potential limitation to this report is that the patient was taking 20 mg simvastatin as a home medication, a
notable cause of myopathy and rhabdomyolysis. Statin-induced rhabdomyolysis is rare and occurs in <0.1% of cases [34]. Furthermore, in larger, follow-up studies, rhabdomyolysis-associated acute kidney failure only developed when statins were used in combination with ciclosporine, gemfibrozil, protease inhibitors, niacin, digoxin, and some antimicrobials [35], none of which this patient was taking at the time. Lastly, although myopathy can occur at any time during treatment with a statin, the onset of symptoms is usually within months of initiation of therapy. Approximately 2/3 of patients experience myopathy in the first six months of starting therapy [36], and the patient in this case report had been on statin therapy for eighteen months without changes in dose. Pioglitazone has been associated with rhabdomyolysis [37], although it appears to be at higher doses (75 mg/day) and rare. Risk factors for thiazolidinedione-induced rhabdomyolysis include concomitant therapy with fibrate, alcohol abuse, and asymptomatic mild creatinine phosphokinase elevation prior to initiating therapy. The patient in this report was on a lower dose of pioglitazone (30 mg/day) and had no further additional risk factors. Other causes of rhabdomyolysis were excluded with thyroid function tests and urine toxicology.

In summary, this is a unique presentation and complication of COVID-19 in a patient who initially tested negative for the virus. This case was unique in that the patient had a favourable prognosis and although being admitted to the ICU, recovered completely. Most described cases presented with respiratory symptoms or were diagnosed with COVID-19 and were subsequently found to have rhabdomyolysis and kidney dysfunction, unlike the case in this report. This case report also details the clinical presentation, hospital course, and treatment which adds to the existing literature on the phenomenon. It is imperative for clinicians to be aware of the potential for COVID-19 patients to develop rhabdomyolysis, initiate early treatment, and minimize the kidney dysfunction.

Consent

Written informed consent was obtained prior to the preparation of this manuscript.

Disclosure

The funder was not involved in the manuscript writing, editing, approval, or decision to publish.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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