Case Report

Rhabdomyolysis as a manifestation of a severe case of COVID-19: A case report✩,✩✩,✩★

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A R T I C L E   I N F O

Article history:
Received 25 June 2020
Revised 1 July 2020
Accepted 1 July 2020
Available online 7 July 2020

Keywords:
COVID-19
Myositis
Rhabdomyolysis

A B S T R A C T

Since the outbreak of the ongoing pandemic of the novel coronavirus disease (COVID-19) in Wuhan, China, from December 2019, we have learned that multiple organs can be affected with the potential for various complications. Although myalgia is a frequent symptom in COVID-19 patients, no imaging findings of rhabdomyolysis have been featured in the literature. We report a case of presumed rhabdomyolysis in a 38-year-old male with COVID-19 based on the clinical presentation, laboratory results and radiological findings. By discussing the diagnostic rationale and reviewing the relevant literature we hope to advance the existing understanding of this disease and its effects on the musculoskeletal system.

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Introduction

Since the emergence of the highly infectious coronavirus disease 2019 (COVID-19) and its subsequent declaration by the World Health Organization as a global public health emergency, there has been a concerted effort to simultaneously decipher the nature of the disease while conducting clinical trials for treatment and prevention (ie, vaccinations) [1].

Although the respiratory system is the main target of COVID-19 virus, renal, neurological, immune, and cutaneous systems have been reportedly affected [1–3]. Symptomatic patients usually present with fever, cough, fatigue, headache, and less commonly, gastrointestinal symptoms. Myalgia is a frequent symptom [1].

Rhabdomyolysis has been reported to be associated with COVID-19 [4–6], yet no concomitant CT findings were published. We present a case report of a clinically diagnosed

✩ Funding: The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

✩✩ Conflicts of Interest: None declared.

✩ The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

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https://doi.org/10.1016/j.radcr.2020.07.003

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Vital signs on admission were: T: 100°F, P: 122, BP: 141/81. Routine blood examination at admission showed: white blood cell (Low: 4.26) [Normal range: 4.5 to 11.0 × 10^9/L], red blood cell (Normal:4.63) [Normal range: 4.7-6.1 cells/ml], platelet (High: 154) [Normal range: 150-400 × 10^9/L], neutrophil percentage (High: 83) [Normal range: 40%-60%], and lymphocyte percentage (High:10.1) [Normal range: 20%-40%]. Most of the early biochemical examinations were within normal limits except for the following, that kept increasing during the hospital stay, reaching at a maximum of: C-reactive protein (High: 98.3) [Normal values < 10 mg/L], creatinine (High: 1.5) [Normal range: 0.84-1.21 mg/dL], PTT (High: 35.5) [Normal range: 25-35 seconds], fibrinogen (High: 572) [Normal range: 200-400 mg/dL], pro-calcitonin (High: 3.5) [Normal range ≤ 0.15 ng/mL], lactate dehydrogenase (High: 398) [Normal range: 140-280 U/L], alanine aminotransferase, (High: 58) [Normal range: 7-55 U/L], and aspartate aminotransferase (High: 61) [Normal range: 6-34 IU/L].

Conversely, calcium levels started dropping 1 day after admission (Low: 8.1) [Normal range: 8.6-10.3 mg/dL] and continued doing so over the following days.

From the 30th of March onward, the potassium levels started rising, reaching (High: 6.4) [Normal range: 3.6-5.2 mmol/L] on the 31st of March, along with glucose that reached (High: 255) [Normal range: 70-99 mg/dL] on the same day. As the insulin therapy failed, continuous veno-venous hemofiltration was initiated followed by intermittent hemodialysis.

On the 31st of March 2020 (10 days post admission), both troponin-I (High: 0.13) [Normal value <0.04 ng/mL] and creatinine kinase (High: 588) [Normal range: 22-198 U/L] were high. Creatinine kinase continued to rise, reaching its maximum at (High: 33,000) [normal value: 10-120 mcg/L] from the 7th of April till the 9th of April (17-19 days post admission), after which it gradually decreased to normal by April 28th (38 days post admission).

Forty-six days following the initial CT chest study, on the 7th of May, a second CT scan of the chest was performed showed scattered, evolving centrilobular ground glass opacities throughout the lungs as well as a new, partially loculated moderate to large right hydropneumothorax (empyema) with air-fluid level was seen with bilateral lower lobe consolidations. A thick-walled cavity within the right upper and middle lobes with an internal air-fluid level was proven to be due to a superimposed *E. faecalis* bacterial infection in the setting of prone positioning. Dilatation of the main pulmonary artery was in keeping with pulmonary hypertension (Fig. 2).

High attenuation foci approximately (174 HU) were noted, symmetrically infiltrating the bilateral deltoid, trapezius, supraspinatus, subscapularis, teres major, triceps, latissimus dorsi, serratus anterior and rhomboid major muscles on this non contrast CT scan (Figs. 3 and 4). Heparin therapy suggested the possibility of intramuscular hemorrhage, however, absence of muscle volume enlargement on the initial CT and subsequent loss of muscle mass (sarcopenia) was noted on follow-up studies. Based on marked elevation of creatinine kinase level, peaking around 33,000 in early April, [normal value: 10-120 (mcg/L)], the muscle changes were presumed to represent calcifications secondary to rhabdomyolysis.

During hospitalization, the patient became anemic (hemoglobin: 6.8) [Normal range: 13.5-17.5 g/dL] and was

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**Case report**

A 38-year-old male presented to the emergency department of Mount Sinai health system (New York City, NY) with chief complaints of fever, cough, shortness of breath and myalgia on March 22nd, 2020. Potential risk factors include a BMI of 29.9 and history of a daily vaping. There was no history of recent travel or known contact with COVID-19 positive individuals.

The patient underwent a CT angiogram to evaluate possible pulmonary embolism in the emergency department. There was no pulmonary embolism, however, bilateral numerous multifocal ground glass opacities were deemed compatible with multifocal viral pneumonia (Fig. 1). Based on CT findings, a SARS COV2 PCR nasopharyngeal swab test was conducted and confirmed that the patient was COVID-19 positive. He was placed on droplet precautions and contact isolation. Blood and sputum culture, urine/sputum legionella testing and mycoplasma IGM tests were performed, with negative results.

On admission, he was placed on subcutaneous Heparin (5000 units, every 12 hours) as his D-dimer was elevated (0.64) [Normal values <0.50], to be adjusted later during his hospital course due to multiple occurring events.

The patient decompensated, was intubated for acute hypoxemic respiratory failure and admitted to the intensive care unit over the course of 5 days since admission and was placed on Plaquenil (400 mg), supplemental oxygen, albuterol sulfate and tiotropium bromide and followed by Tocilizumab and Zithromax. His hospital course was complicated by multi organ failure including acute renal failure on the 28th of March (6 days post admission), sepsis on the 24th of April (34 days post admission), and toxic metabolic encephalopathy on the 29th of April (39 days post admission).

rhabdomyolysis in a young COVID 19 patient, with muscle changes on CT.

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**Fig. 1** – Patient’s first chest CT scan; on the day of admission. Axial CT scan in chest window showing bilateral scattered ground glass opacities (red arrows). (Color version available online.)

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transfused. A diagnosis of Hemophagocytic lymphohistiocytosis syndrome was made on the 8th of May.

Subsequent delirium was diagnosed as toxic metabolic encephalopathy in the setting of prolonged hospitalization and infections. Head CT was normal. CT chest scan was repeated on the 11th (Fig. 5), and 18th of May (Fig. 6), showing increasing, persistent bilateral posterior thoracic and shoulder muscular findings. To our knowledge, no other muscles exhibited similar changes. A magnetic resonance cholangiopancreatog-
As COVID-19 is known to incite an immune reaction in individuals, it remains unclear whether these changes are attributed to direct viral induced muscular damage or a secondary autoimmune reaction [4].

In our case, we reached the conclusion of rhabdomyolysis, secondary to COVID-19 based on the following 3 points:

1- The patient’s complaint of worsening muscular pain and weakness [4-6] with concomitant imaging findings of bilateral symmetrical shoulder and posterior thoracic muscle calcification that progressed in attenuation and extent on serial CT scans [8].

2- Progressive elevation of creatinine kinase, reaching (33, 000 mcg/L), the developing hypocalcemia, and the refractory hyperkalemia (out of proportion with the degree of renal function) were all in favor of rhabdomyolysis [7].

3- Significantly elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels [9].

Although myositis was considered, the presence of intramuscular calcification rather than low attenuation (muscle edema) and lab results favored of rhabdomyolysis [10].

With regards to radiological features in rhabdomyolysis, CT changes of rhabdomyolysis are reported more variable, as affected areas either appear hyperdense from calcification, or hypodense due to muscle edema [11,12]. The calcification seen within the muscles occurs either due to calcium sequestration, coinciding with reduced serum calcium (as in our case) and development of acute renal failure or as a result of administration of calcium to correct a hypocalcaemia [11]. There is feathery, streaky enhancement of affected muscles following intravenous contrast [12].

On MRI, acute and subacute rhabdomyolysis has been reported to exhibit iso to high signal intensity on T1weighted images and high signal intensity on T2 weighted images with contrast enhancement. T1 signal changes reflect the presence of methemoglobin, proteinaceous materials and fat, whereas T2 changes reflect accumulated water from myonecrosis. In chronic rhabdomyolysis, low signal intensity on T2 weighted images is attributed to the accumulated hemosiderin [11].

Two types of rhabdomyolysis have been described; type one is related to edema and the concomitant CT and MRI changes include homogenous density and signal intensity, on all sequences, respectively, in addition to the exhibition of a homogenous enhancement. While, type 2 is thought to result from myonecrosis, thus the related radiological changes are deemed heterogeneous in density, signal intensity and contrast enhancement [12,13].

A specific sign has been described on both CT and MRI images of rhabdomyolysis (stipple sign) which appears as an enhanced central dot or linear focus surrounded by an area of rim enhancement, which was found to be specific for type 2 rhabdomyolysis [12,13].

Although, MRI and nuclear medicine scan [technetium-99m medronate or pyrophosphate] [12] have the highest sensitivity for detecting rhabdomyolysis in acute setting, CT has kept its superiority in its ability of detecting calcification with fast scanning compared to the above modalities [8]. Ultrasound use has been encouraged as well, as it shows decreased echogenicity within the involved muscles [14]. Other advan-

Fig. 5 – Patient’s third chest CT scan; 50th day post admission. Plain CT Chest showing interval increase within the bilateral posterior thoracic and shoulder muscular density.

Fig. 6 – Patient’s fourth chest CT scan; 57th day post admission. Plain CT Chest showing progressive interval increase within the bilateral posterior thoracic and shoulder muscular density.

Discussion

Rhabdomyolysis is a life-threatening syndrome resulting from striated muscular breakdown, which may occur due to various factors, including metabolic, trauma, inflammatory, infectious, ischemic, and autoimmune conditions, as well as complications of drug therapy [7].

Viral infections, such as influenza A/B (most commonly), Epstein-Barr, herpes simplex, adenovirus, human immunodeficiency virus and cytomegalovirus have all been found to cause rhabdomyolysis. Patients usually present with myalgia, fatigue, and, in some cases, acute renal failure [4,6].

raphy examination was conducted on the 24th of June to further evaluate his elevated alkaline phosphatase, and while the examination was limited to the abdomen, limiting the field of view, the scout images did not exhibit any abnormalities within the visualized pelvic and proximal thigh muscles.

Three months post admission, with ongoing interdisciplinary rehabilitation therapy program; the patient is starting to recover with discharge arrangements being made.
tages of ultrasound include the low cost and lack of ionizing radiation.

Although muscle biopsy can be used to confirm the diagnosis, it has been discouraged (and was not performed in this case) due to the risk of multiple complications, including bleeding and prolonged recovery [11,15]. Some authors argue that it is unnecessary as the histopathological findings do not usually reveal the etiology [16].

Although our case is limited by the lack of histopathology results, and the confirmation of the main etiology (as it can be related to the SARS-CoV-2 virus or the provoked immune reaction), we have reached our diagnosis by combining the clinical history of muscular pain and weakness, elevated creatinine kinase levels and imaging findings [4,7,11].

Conclusion

COVID-19 infection has many manifestations that are not solely limited to the respiratory system. We present a case of a presumed rhabdomyolysis in a COVID-19 positive patient with a complicated clinical course, in hope to shed more light on this multifaceted disease and draw the attention of radiologists and other clinicians in the frontline to this entity that can take a devastating turn on patients’ prognosis.

Patient consent for publication

Not required.

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