

# Rhabdomyolysis in a hospitalized patient with COVID-19 – case report

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## ABSTRACT

**Introduction.** COVID-19 is a viral infection with a variable clinical spectrum, ranging from asymptomatic carrier state to severe pneumonia. It is associated with a variety of complications, including musculo-skeletal abnormalities. Whereas myalgia is a common clinical finding at these patients, only a few cases of COVID-19-associated rhabdomyolysis have been described in the literature.

**Case presentation.** We describe the case of a 42-year old male confirmed with SARS-CoV-2 infection who presented to the emergency department with an 11-day evolution of dyspnea, cough, fatigue, myalgia and hyperchromic urine. The physical examination revealed dyspnea and an oxygen saturation of 87% while breathing ambient air, being otherwise normal. Blood tests showed neutrophilia, increased inflammatory markers, COVID-19 associated coagulopathy and elevation of muscular enzymes creatine-kinase and myoglobin. The chest computer tomography was consistent with mixed pneumonia, distributed in all pulmonary segments and the case was interpreted as a severe form of SARS-CoV-2 infection, associated with acute respiratory failure and rhabdomyolysis. Upon treatment (Enoxaparin, Aspirin, Dexamethasone, Favipiravir, oxygen administered by face mask, fluid resuscitation), his condition considerably improved, along with the laboratory findings, and he was discharged, without developing acute kidney injury or other complications related to rhabdomyolysis during his admission.

**Conclusion.** COVID-19 patients can develop rhabdomyolysis, which can result in life-threatening complications.

**Keywords:** COVID-19, SARS-CoV-2, rhabdomyolysis, acute kidney injury, myalgia

## INTRODUCTION

Rhabdomyolysis is the dissolution of the skeletal muscle with the release of its toxic cellular components into the bloodstream (1). Symptoms include myalgia, myoglobinuria and fatigue, but they can also be absent. Establishing a diagnosis of rhabdomyolysis is based primarily on the appearance of myoglobin in the urine or by a marked elevation in serum creatine-kinase (CK) levels. Authors of several large case series of rhabdomyolysis agree that CK elevation 5 times the upper limit of normal is the

defining biochemical abnormality for this condition (2). Among the associated complications, the most significant are acute kidney injury and hyperkalemia (3).

The most common acquired causes are substance abuse (34%), medication (11%), trauma (9%) and less frequent causes including metabolic disturbances, viral infections (HIV, flu, herpes simplex), sepsis, prolonged immobilization, excessive heat or exercise. The main cause of rhabdomyolysis in children is viral myositis (4).

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COVID-19 is a viral disease, associated with a wide variety of complications, including skeletal muscle, neurological, joint and bone disorders. Whereas myalgia is frequent in patients with SARS-CoV-2 infection (range 11-50%) (4), only a few cases of COVID-19-related rhabdomyolysis have been reported (5-11).

We present a rare case of rhabdomyolysis in a patient diagnosed and hospitalized with SARS-CoV-2 infection.

**CASE PRESENTATION**

**Presenting concerns**

A 42-year old man with SARS-COV-2 infection (confirmed prior to his hospital presentation by positive SARS-CoV-2 PCR test from nasopharyngeal swab) presented to the emergency department with an 11-day evolution of dyspnea, cough, fatigue, myalgia (in the first 2 days) and hyperchromic urine (from the debut). His medical history was unremarkable.

At the initial evaluation, the patient reported persistent fatigue and cough and the resolution of muscle aches. He had taken paracetamol (750 mg), apixaban 2.5 mg/day and esomeprazole 20 mg/day. He denied recent trauma, use of drugs or exposure to toxins.

**Clinical findings**

The physical examination revealed a blood pressure of 118/86 mmHg and a pulse of 80 beats/min. His temperature was 36.3°C and his oxygen saturation was 87% while breathing ambient air. Otherwise, the physical examination was normal.

**Diagnostic focus and assessment**

Blood tests showed mild leukocytosis (10.4 x10<sup>9</sup>/l), neutrophilia (7.2 x10<sup>9</sup>/l), increased inflam-

matory markers (CRP 108 mg/l, Fbg 599 mg/dl), COVID-19 associated coagulopathy, marked elevation of muscle enzymes (CK at 13,006 U/l, myoglobin above 400 ng/ml), CK-MB 292 U/l), liver enzymes (TGP 131 U/l, TGO 284 U/l) and LDH (3,635 U/l). He did not have myoglobin in the urine at presentation or at the following urine tests.

His chest CT revealed mixed lesions distributed in all pulmonary segments represented by ground glass opacities and interlobular/septal thickening, along with a few small areas of consolidation.

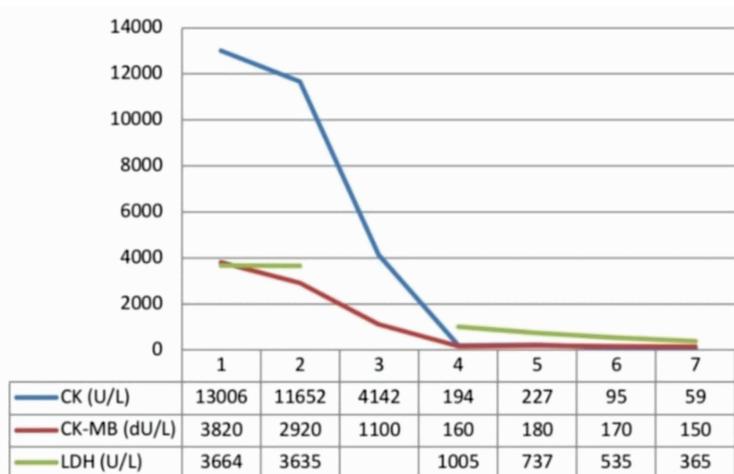
The case was interpreted as a severe form of SARS-CoV-2 infection, associated with acute respiratory failure on account of bilateral mixed pneumonia and rhabdomyolysis.

**Therapeutic focus and assessment**

The patient was admitted to the COVID-19 ward and started on Enoxaparin, Aspirin, Dexamethasone, Favipiravir and oxygen administered by non-rebreather mask. His condition considerably improved, along with the laboratory findings (inflammatory markers, muscular enzymes, hepatic tests, coagulation parameters etc.) (see Table 1) and he was discharged on the 11<sup>th</sup> day after admission, without developing acute kidney injury or other complications related to rhabdomyolysis during his admission.

**Follow-up and monitoring**

Upon discharge, the patient was recommended a pulmonary reevaluation at 3 months to assess the resolution of the pneumonic lesions/the persistent fibrotic lesions, along with a complete blood count, metabolic and coagulation panel at one month following his release, which were not carried out in our facility.



**FIGURE 1.** Trend of cytolitic enzymes

TABLE 1. Evolution of laboratory parameters

Parameter	On admission	2 <sup>nd</sup> day	3 <sup>rd</sup> day	5 <sup>th</sup> day	7 <sup>th</sup> day	9 <sup>th</sup> day	11 <sup>th</sup> day
WBC (count/mm <sup>3</sup> )	10,400	7,290	12,050	13,400	16,300	10,130	5,800
Lymphocytes (count/mm <sup>3</sup> )	1,400	1,470	1,310	1,800	3,000	2,080	2,900
CK (U/l)	13,006	11,652	4,142	194	227	95	59
CK-MB (U/l)	382	292	110	16	18	17	15
Myoglobin (ng/ml)	>400	354.2	333.4	290	169		142
LDH (U/l)	3,664	3,635		1,005	737	535	365
Creatinine (mg/dl)	0.8	0.7	0.8	0.7	0.8	0.7	0.9
Urea (mg/dl)	47	44	44	39	39	32	28
TGP (U/l)	132	131	120	138	239	286	325
TGO (U/l)	352	284	126	80	72	87	101
Direct bilirubin (mg/dl)	1.8	1.8		0.7	0.6	0.5	0.4
Indirect bilirubin (mg/dl)	2.3	2		1.2	1	1	1
CRP (mg/l)		109	44.2	18.9	8.34	3.81	
Potassium (mmol/l)	4	5.2	5.1	5.6	5.5	5.3	5.1
Sodium (mmol/l)	132	135	135	134	135	134	133
D-dimers (U/l)			334		3,888	321	1,227

## DISCUSSION

This case illustrates that rhabdomyolysis can be related to COVID-19, with a variety of possible mechanisms explored in the literature: direct viral invasion, release of myotoxic cytokines, drug-induced muscular lysis.

SARS-CoV-2 belongs to the coronavirus family of positive sense, single-stranded RNA viruses, which includes the highly pathogenic SARS-CoV-1, which causes severe acute respiratory syndrome (SARS), and MERS-CoV, which is responsible for Middle East respiratory syndrome (MERS) (12). Between the genetic sequences of SARS-CoV-2 and SARS-CoV-1 there is a high degree of resemblance. They both enter cells via the ACE2 receptor using the transmembrane protease, serine 2 (TMPRSS2) and are thought to have a very similar interaction with the host (13). Using muscle tissue collected postmortem from patients with SARS, several small studies have provided insight into the nature of muscle dysfunction as a result of SARS-CoV-1 infection (12, 14). Widespread muscle fiber atrophy was noted, with sporadic and focal muscle fiber necrosis and immune cell infiltration (14). Electron micrographs revealed myofibril disarray and Z disc streaming, which would disrupt force transmission as noted in other muscle diseases (14).

In the initial phase of the infection, SARS-CoV-2 is thought to mostly infect type II pneumocytes, which express ACE2 and TMPRSS2 (15). The compromised alveolar epithelium can sometimes facilitate the development of viremia (16), leaving cells from other tissues susceptible to direct viral infection. For human skeletal muscle tissue, a variety of cells express TMPRSS2, including endothelial cells,

smooth muscle cells, pericytes, muscle stem cells, macrophages, adaptive immune cells (B, T, or natural killer cells), and myonuclei (14).

Another proposed mechanism is the release of myotoxic cytokines. Many of the proinflammatory signaling molecules known to be elevated in patients with COVID-19 can also have a negative impact on the skeletal muscle. IFN- $\gamma$ , IL-1 $\beta$ , IL-6, IL-17, and TNF- $\alpha$  can directly induce muscle fiber proteolysis and decrease protein synthesis (17-21). IL-1 $\beta$  and TNF- $\alpha$  can shut off the proliferation and differentiation of satellite cells (which are progenitor cells), therefore interfering with muscle fiber growth, an important process in patients recovering from COVID-19 (18,22,23). IL-1 $\beta$  and IL-6 can induce muscle fibroblast activity and lead to fibrosis in the skeletal muscle (24,25).

To the best of our knowledge, there were 7 other cases of patients with COVID-19 and rhabdomyolysis/ myositis reported in the literature (6-11). Similarly to this case, five out of seven patients described in the literature, with COVID-19 and rhabdomyolysis, had their condition ameliorated upon treatment (which included fluid resuscitation in all cases), along with the improvement of inflammation parameters, coagulation markers and muscular enzymes (6,8-11). One of these further improved patients developed acute kidney injury as a complication, which was remitted after intravenous crystalloid therapy (8). Two patients became critical: one had deteriorating respiratory function and was transferred to the critical care unit (7) and the other one died due to worsening kidney function, resistant to treatment (intravenous fluids, diuretics, insulin, antibiotic etc.) (5).

## CONCLUSIONS

COVID-19 patients can develop rhabdomyolysis, which can result in life-threatening complications such as acute kidney injury, even in the absence of muscle weakness and/or myalgia. A better understanding of the mechanisms at play in rhabdomyolysis at these patients is required, in order for targeted therapy.

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All authors contributed equally to this paper.

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