CASE REPORT

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Rhabdomyolysis and Acute Kidney Damage in a COVID-19 Patient

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ABSTRACT Coronavirus disease-19 (COVID-19) caused by the severe acute respiratory syndrome-coronavirus-2 virus is the greatest health-care problem today. Although the disease primarily involves the respiratory system, the involvement of many different systems can be seen in a broad clinical spectrum. Rhabdomyolysis is characterized by skeletal muscle destruction caused by an increase in cellular components such as creatine kinase, phosphorus, potassium and myoglobin as a result of cellular death. Rhabdomyolysis has been associated with viral infections, including other corona viruses such as influenza A and acute respiratory distress syndrome. Adult cases of rhabdomyolysis related to COVID-19 have been previously reported. The case presented here is a patient with rhabdomyolysis associated with COVID-19 who required hemodialysis in the intensive care unit because of acute kidney damage.

Keywords: Acute kidney injury; COVID-19; rhabdomyolysis

Rhabdomyolysis is a potentially life-threatening clinical syndrome resulting from the release of intracellular muscle proteins and enzymes into the blood circulation, which leads to musculoskeletal damage.[1]

Coronavirus disease-2019 (COVID-19) is generally associated with varying respiratory symptoms ranging from mild disease to severe acute respiratory distress syndrome (ARDS). The pathology is not limited to the respiratory tract only, but other organs may also be affected.[2]

The aim of this paper was to present the laboratory findings, clinical course, and treatment of a 44-year old male patient who developed rhabdomyolysis and acute renal failure during treatment for COVID-19 infection.

CASE REPORT

Patient consent was obtained. A 44-year old male with no known kidney disease or other chronic comorbidity presented at our Afyonkarahisar University of Health Sciences COVID-19 Emergency Department with the complaints of high temperature, cough and sore throat. The real-time polymerase chain reaction test applied to oropharyngeal and nasopharyngeal smear samples was reported as positive for the diagnosis of COVID-19. Outpatient treatment was started of hydroxychloroquine (initial dose 2x400 mg followed by 2x200 mg) as recommended in the COVID-19 guidelines prepared by the Turkish Ministry of Health.[3]

On the 5th day of treatment, the patient was hospitalised due to elevated temperature, increased com-

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plaints of shortness of breath, and the determination of a bilateral peripheral frosted glass appearance on thorax computed tomography (CT). Treatment was started of favipiravir at a loading dose of 2x1600 mg followed by 2x600 mg. On the 5th day of this treatment, the patient was transferred to the intensive care unit (ICU) due to a fall in oxygen saturation and tachypnea. On admittance to the ICU, blood pressure was measured as 120/70 mmHg, respiratory count was 26/min, heart rate was 93 bpm, temperature was 36.7 ˚C and arterial oxygen saturation was 91%. The laboratory test results were reported as creatinine: 0.8 mg/dL, aspartate aminotransferase (AST): 148 U/L, alanine aminotransferase (ALT): 84 U/L, lactate dehydrogenase (LDH): 692 U/L, creatine kinase (CK): 160 IU/L, C-reactive protein (CRP): 3.8 mg/dL, D-dimer: 0.75 g/mL, ferritin: 878 ng/mL, and procalcitonin 0.53 ng/mL.

On thorax CT, widespread dense areas of a frosted glass appearance were observed in the parenchyma of both lungs (Figure 1). As oxygen saturation was 88%, the patient was followed up with high-flow nasal oxygen (HFNO) and non-invasive mechanical ventilation, and was intubated when arterial oxygen saturation fell to 75.9%. An intravenous infusion of remifentanil 10.3 mcg/kg/min and dexmedetomidine 0.3 mcg/kg/hour was started for sedation. As there was an increase in D-dimer level to 68.9 µg/mL, bedside echocardiography was applied with an initial diagnosis of pulmonary embolism, and right ventricle 32 mm, systolic pulmonary artery pressure: 35-40 mmHg determined, compatible with pulmonary embolism. The treatment was continued with subcutaneous enoxaparin 2x0.6 mg and peroral acetyl salycylic acid 1x100 mg. High levels of CRP, ferritin and D-dimer were observed and as the clinical condition was consistent with cytokine storm, cytokine adsorption was performed on the 4th and 5th days in ICU. Following the cytokine adsorption treatment, the laboratory values of the patient were seen to recede (Table 1).

Hypoxemia recovered in the follow-up of blood gases and on the 10th day, the patient was weaned from the mechanical ventilator and followed up with HFNO. During the follow up, because of elevated CK and LDH, and hemoglobin positivity in the urine test, and as an initial diagnosis of rhabdomyolysis was made and ARDS was present, conservative fluid resuscitation was started. The urine output of the patient regressed to an oligo-anuric level (75-200 mL/day), and as acute kidney damage had developed, intermittent hemodialysis treatment was applied. Following 3 sessions of dialysis, the CK and creatinine levels recovered and the clinical findings of acute kidney damage improved (Table 1). The patient was transferred to the ward with nasal oxygen and later discharged with prescribed drugs.

DISCUSSION

Rhabdomyolysis is characterized by skeletal muscle destruction caused by an increase in cellular components such as CK, phosphorus, potassium and myoglobin as a result of cellular death.[4] Autoimmune myopathies, septicaemia, electrolyte abnormalities, alcohol abuse or infection are factors which can trigger rhabdomyolysis.[5] In the current case, there was no history of trauma, intense exercise, seizure, or connective tissue disorders.

It has also been reported that rhabdomyolyis developed in up to 10% of patients who previously had severe acute respiratory syndrome (SARS) and in 14% of those with Middle East respiratory syndrome.[6,7] In all of these cases, high-dose intravenous steroids and some neuromuscular blocking agents had been used, which could have caused rhabdomyolysis. These drugs that could cause rhabdomyolysis were not used in the current patient.

In a study of 1,099 COVID-19 patients in China, rhabdomyolysis was reported in only 0.2% and high CK levels in 13.7%.[8]

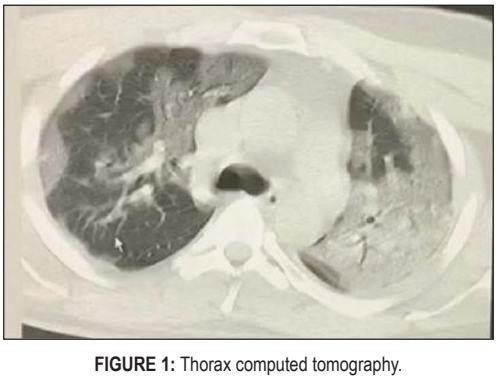

FIGURE 1: Thorax computed tomography.

TABLE 1: Laboratory findings of the patient.

Parametre	1st day	2nd day	3rdday	4thday*	5th day*	7th day	9th day	13th day**	15thday**	16thday**	17thday	18th day	20th day
Creatinine (0.5-1.2 mg/dL)	0.86	0.81	0.86	0.8	0.89	0.8	1.08	2.23	3.12	3.03	2.46	1.7	0.9
Ure (16.6-48.5 mg/dL)	34.6	46.6	55.5	55.6	64.5	71.8	80.7	123	142.6	126	117.5	88	18.4
AST (5-41 U/L)	148	104	65	157	121	107	116	112	107	76	76	57	18
ALT (5-41 U/L)	84	75	60	101	89	103	99	77	83	79	63	53	23
LDH (135-225 U/L)	692	839	1102	645	518	505	653	819	667	805	780	575	421
CK (0-190 IU/L)	160	159	427	650	878	1120	1558	3133	5144	5110	4497	1933	239
CRP (0-0.5 mg/dL)	3.8	7.4	17.7	20	11.3	8.6	5.3	4.1	3.3	3.1	3.1	1.4	0.1
D-dimer (0-0.5 µg/mL)	0.75	4.26	68.9	140.8	66.3	39.78	31.3	25.8	7.4	6.6	6.9	3.6	2.8
Procalcitonin (<0.05 ng/mL)	0.53	0.158	0.129	0.13	0.08	0.09	0.2	3.1	6.6	8.4	7.4	4.3	0.2
Ferritin (30-400 ng/mL)	878	965	1567	>2000	1989	1588	1322	1201	1196	1144	1034	906	774

*Cytokine adsorption treatment; **Hemodialysis treatment; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CK: Creatine kinase; LDH: Lactate dehydrogenase; CRP: C-reactive protein.

Chen et al. found no viral particles in muscle biopsies from SARS-CoV-1-related rhabdomyolysis cases, and suggested that the presence of high inflammatory markers was secondary to the cytokine storm rather than from direct viral invasion.[6]

A serum CK value 5-fold higher than normal is a classic laboratory finding for rhabdomyolysis diagnosis.[9] The plasma myoglobulin level is not as sensitive as CK because of the short half-life.[10]

Various mechanisms such as SARS-CoV-2, virus-mediated damage, cytokine storm, angiotensin-II pathway activation, complementary pathway irregularity, hypercoagulation, and microangiopathy may cause acute renal failure.[11] In the current patient, high D-dimer levels and cytokine storm were found to have contributed to acute renal failure.

When kidney damage develops secondary to rhabdomyolysis, it is recommended that dialysis treatment is applied according to emergency dialysis indications.[12] The decision for early dialysis was taken in the current case because of the development of oligo-anuria, and following 3 sessions of dialysis treatment, the kidney function tests and muscle-destructive enzymes returned to normal levels in a short time.

Before the COVID-19 pandemic, the development of rhabdomyolysis after the use of hydroxychloroquine and oseltamivir, which are used in COVID-19 treatment, had been reported.[13] In the current case, hydroxychloroquine and favipavir were used in the COVID-19 treatment. However, throughout the time of hydroxychloroquine use, the CK and serum creatinine levels were normal, indicating that rhabdomyolysis had not yet developed, and therefore, the development of rhabdomyolysis was not initially considered to be associated with the treatment.

In the follow-up of the patient, liver enzymes were seen to be high during treatment, and this was thought to be a side-effect of favipavir or related to rhabdomyolysis.

Aggressive fluid treatment is extremely important to increase renal perfusion and reduce the renal

damage formed by both vasoconstriction and myoglobulin. Furthermore, in critical COVID-19 patients, there is a need for conservative fluid resuscitation to prevent ARDS.

In the current case, after intubation because of ARDS, follow up with HFNO was applied after weaning off the mechanical ventilator, and conservative fluid treatment was started to avoid excessive fluid loading. As urine output was reduced and creatinine levels continued to be elevated, hemodialysis was applied at intervals. Following dialysis, the CK and creatinine levels regressed, urine output increased and the clinical table of acute renal failure recovered.

In the case described here, as there were none of the reasons for rhabdomyolysis which have been definitively proven to date, it was thought that there could be a relationship between rhabdomyolysis and COVID-19. There is a need for further studies to better understand the pathophysiological mechanisms between COVID-19 and rhabdomyolysis.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

All authors contributed equally while this study preparing.

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