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*Case report*

# Rhabdomyolysis and Acute Kidney Injury in a Patient with Severe Form of Covid-19 Pneumonia - A Case Report

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**Abstract**

**Introduction**. The ongoing pandemic with the novel Corona virus poses unprecented challenges for the medical professionals worldwide. Acute kidney injury is frequently seen in patients infected with corona virus and often associated with a poor patient outcome. Rhabdomyolysis has been recognized as one of the possible contributing mechanisms.

**Case.** A 68-year-old man was referred to the emergency department complaining of a dry cough, myalgia, general weakness with devastated energy feeling, chest pain and difficulties in breathing, symptoms he experienced in the past five days. He also noticed that his urine was dark and in reduced amount. Quick antigen test for SARS CoV2 was performed, and the patient found Covid-19 positive. He was admitted at the hospital ward in a covid-designated unit. Laboratory findings revealed elevation of the inflammatory markers and electrolyte disbalance**.** Metabolic degradation products were markedly increased, serum urea was 44mmol/L (RF=2.7-7.8 mmol/L) and serum creatinine 689umol/L (RF=45-109umol/L), when deterioration of the kidney function was diagnosed. Urgent intermittent hemodialysis treatment was initiated. Patient suffered from a severe form of covid-19 pneumonia and was continuously on high flow oxygen mask. Duration of the patient hospitalization was 30 days, and thereafter, he was transferred to the rehabilitation center for 28 days. Complete restoration of the physical motion and activity was accomplished, oxygen support was no longer needed, since he maintained blood oxygen saturation above 95%. Renal function has also been recovered with degradation products maintained within normal ranges.

**Conclusion.** Rhabdomyolysis in covid-19 patients should be always kept in mind. Sometimes it can be an initial clinical manifestation in covid-19 patients [15], but on the other hand it can be presented as a late complication sometimes caused by the therapy itself. Multidisciplinary and comprehensive approach in the diagnosis, treatment and follow up of the patients can only guarantee timely detection and wide range of therapeutical modality, leading to a better prognosis and outcome.

**Keywords**: Covid-19 infection, acute kidney injury, rhabdomyolysis, renal replacement therapy

## Introduction

The ongoing pandemic with the novel Corona virus poses unprecedented challenges for the medical professionals worldwide. According to World Health Organization statistics, so far more than 186 million cases, and more than 4 million deaths were registered as a result of infection with SARS CoV-2 [1]. Corona virus infection has a wide range of symptoms, and the clinical manifestation can vary from asymptomatic and mild cases to severe forms of disease with severe pneumonia, acute respiratory distress syndrome (ARDS), respiratory and multiorgan failure [2,3]. What was initially considered an isolated respiratory issue affecting the airways, lungs and its blood vessels, was shortly thereafter proven wrong. Numerous extrapulmonary manifestations had been seen, including neurological, gastrointestinal, endocrinologic, cardiovascular, dermatologic, renal and many others [2,3].

Acute kidney injury is frequently seen in patients infected with corona virus and often associated with a poor patient outcome. Studies were conducted to establish whether it was result of a direct effect of the virus (renal tropism and replication of the virus in kidney epithelial cells), or a consequence of numerous indirect factors such as the inflammatory process itself (cytokine mediated injury), nephrotoxin exposure, hemodynamic disorders and other factors [4,5]. Rhabdomyolysis has been recognized as one of the possible contributing mechanisms [6]. It is a condition characterized by muscle injury that leads to necrosis of the myocytes and release of intracellular contents into the circulation. Often seen

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causes are trauma/crush injury, infection (most common Influenza and other viral and bacterial), muscular strain, toxins/drugs, electrolyte disorders, inherited metabolic disorders and many others [8]. The classic presentation of this condition is a muscle pain, weakness, dark tea-colored urine (pigmenturia), and a marked elevation of serum creatine kinase (CK), five to ten times above the upper limit [7,8]. Myoglobin rises prior to CK levels and is removed through renal excretion in the first 24 hours, except when anuria occurs [8]. Electrolyte abnormalities usually include hyperkalemia, hypocalcemia, hyperuricemia, hyperphosphatemia and an anion gap acidosis [9]. In this report we present a case of a 68 year old man suffering from a severe form of covid-19 pneumonia, rhabdomyolysis and acute kidney injury, treated with renal replacement therapy until full recovery. A multidisciplinary approach in the treatment with well trained professionals from various specialties, (nephrology, pulmology, cardiology, endocrinology, transfusiology, infectology) warranted the best possible outcome for the patient's well-being.

**Case presentation**

A 68-year-old man was referred to the emergency department complaining of a dry cough, myalgia, general weakness with devastated energy feeling, chest pain and difficulties in breathing, symptoms he experienced in the past five days. He also noticed that his urine was dark and in reduced amount. No fever, high temperature or gastrointestinal symptoms were registered. His past medical history revealed Obesity, Diabetes type 2 on combined oral antidiabetics (Metformin) and insulin therapy; he also suffered from an acute myocardial infarction more than 3 years ago, for which a percutaneous coronary intervention, i.e. stent placement and a balloon angioplasty were performed. Beside antidiabetic drugs, his chronic therapy included antiplatelet therapy (Clopidogrel), diuretics (Furosemide and Spironolactone), ACE inhibitors (Lisinopril), nonselective B blocker (Carvedilol) and statin (Rosuvastatin) therapy. He has been taking this therapy for more than 3 years.

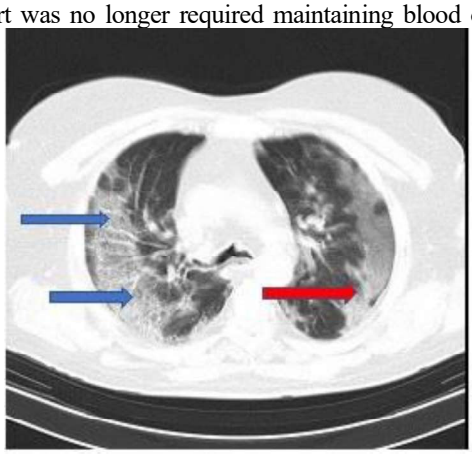
Quick antigen test for SARS CoV2 was performed, and the patient found Covid-19 positive. He was admitted at the hospital ward in a covid-designated unit. His nose swab PCR test was also positive for Sars CoV2.

The patient was dyspneic upon admission, with oxygen saturation 76% on ambient air, which raised up to 97% when he was put on oxygen support therapy with 12L/min flow face mask. Blood pressure was 80/40mmHg, heart pulse 95 beats per minute. Chest X-ray was performed and bilateral, diffuse zones of irregular consolidations with myopathic heart were revealed. Laboratory findings showed elevation of the inflammatory markers, C reactive protein 157mg/L (RF<6), white blood cells 12,6 per mcL of blood (RF=4,00-9,00) and ferritin >1500 ug/L (RF<500). Metabolic degradation products were markedly increased, serum urea was 44mmol/L (RF=2.7-7.8mmol/L) and serum creatinine 689umol/L (RF=45-109umol/L), when deterioration of the kidney function was diagnosed. Electrolyte disbalance showed hyperkalemia 6,73mmol/L (RF=3.8-5.5mmol/L), hyponatremia 129,63mmol/L (RF=137-145mmol/L) and hypocalcemia 1,76mmol/L (RF=2.1-2.6mmol/L). Creatinine kinase (CK) 1002U/L (RF=24-173) and lactate dehydrogenase (LDH) 559U/L (RF<248) were elevated, and a threefold increase of the hepatic enzymes was noted. Myoglobin tested dramatic increase of 1480.6 ng/ml (RF<75), normal range laboratory finding of cardiac troponin and electrocardiogram showed no sign of an acute cardiac event. Hemostatic investigation revealed increase of fibrin degradation products (D-dimer) up to 8000ngr/ml (RF=0-500).

Chest computer tomography (CT) scan was performed 5 days after the chest radiography was done, and small ground-glass opacites were seen in the perihilar and paracostal posterior parts of the left lung (Figure 1 and 2), but the right lung demonstrated huge ground-glass consolidation in the middle and inferior part (Figure 1 and 2).

Patient suffered from a severe form of covid-19 pneumonia and required oxygen delivery with high flow oxygen mask at the beginning of the treatment. In the following days, the oxygen requirements decreased, patient was switched to a regular face mask following a period of occasional supplemental oxygen of 2-5L/min on a nasal canule. He was treated with recommended doses of intra-venous corticosteroids, Azithromycin, Ceftriaxone, H2 blocker and hepatoprotective agents. Anticoagulant therapy with a low molecular weight heparin was administered, under the transfusion medicine specialist surveillance. The antiplatelet therapy was not interrupted. Urgent hemodialysis treatment was initiated at the first day of hospitalization. In total four hemodialysis treatments were performed. Diuresis was slowly restored after the third HD treatment. After an intensive fluid administration, the patient entered into the polyuric phase of acute kidney injury. Laboratory findings showed fast reduction in the urea, creatinine, myoglobin and CK values, while diuresis rose up to 5400ml per day. On day ten of hospitalization the femoral vascular catheter was removed and the patient was discontinued from hemodialysis treatment. Electrolytes were checked on a regular basis and substitutions were administered accordingly. Due to the treatment with corticosteroids, as well as the metformin effect prone to lactate acidosis, the glycemic control was disrupted and appropriate changes were made in the antidiabetic therapy. Namely, in consultation with the endocrinologist Metformin and mixed insulin were excluded from therapy, and rapid-acting and long-acting insulin combination was prescribed obtaining a better glycemic control. Duration of hospitalization was 30 days, and the patient was discharged and transferred to the rehabilitation center, where he stayed another 28 days. Complete restoration of

physical motion and activity was accomplished, oxygen support was no longer required maintaining blood oxygen saturation above 95%, and renal degradation pro-



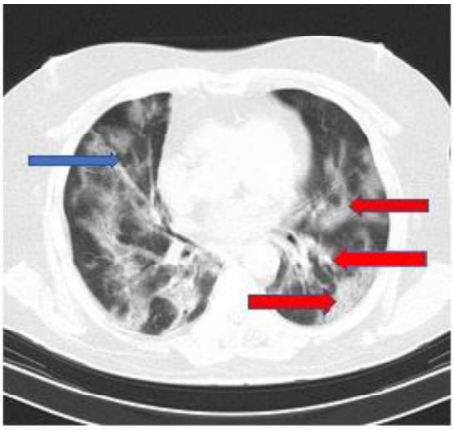


**Fig. 1 and 2.** Pulmonary CT scan: red arrows point at the small ground-glass opacities in the perihilar and para-costal posterior parts of the left lung and blue arrows at the huge ground-glass consolidation in the middle and inferior part of the right lung

ducts (urea and creatinine) balanced within normal ranges for a full recovery of renal function.

## Discussion

The novel corona virus and acute kidney injury were associated since the early beginning of the pandemy when the first cases of disease in Wuhan were confirmed [10]. The initial reports from Wuhan suggested that acute kidney injury occurs in small percentage of the infected patients ranging from 3% to 9%. [10,11]. Subsequent analysis showed that the percentage of incidence is much higher, and overrates 15%. [11]. In studies made in USA among hospitalized patients, the incidence of acute kidney injury was between 37% and 40% [12]. This makes the acute kidney injury a common complication among hospitalized patients with severe covid infection. It is a poor prognostic factor which increases the risk of death, especially of those requiring dialysis treatment [12]. The exact mechanism of acute kidney injury is not well understood, it can be a result of the direct effect of the virus, or a consequence of the systemic inflammatory response, accompanied with the nephrotoxin exposure and hemodynamic disorders [13]. Rhabdomyolysis is recognized as one of the factors to blame for development of acute kidney injury. In our case report all possible etiological factors for rhabdomyolysis were excluded, as he denied intense physical activity, alcohol abuse, nephrotoxic medication (statines were taken more than 3 years), he did not report fever, convulsions, crush injures, so the viral myositis remained the most probable cause of it. Pathogenesis of the skeletal muscle injury remained completely unexplained. Different scientific approaches tried to explain the mechanism of the viral muscle damage, one blaming the direct invasion of the muscle tissue, other one the effect of the released myotoxic cytokines [14].

What remains important in the end is that rhabdomyolysis is a serios life-threating condition, requiring an early recognition and urgent treatment. According to the study made in Bronx, rhabdomyolysis increases the incidentce of a new- onset renal replacement therapy. In-hospital mortality was much higher in patients with severe covid infection, when rhabdomyolysis occurred [6]. Out of 140 patients that were included in the same study 74(52,9%) were discharged and 66 (47,1%) died in hospital. Rhabdomyolysis in covid patients should be always kept in mind. Sometimes it can be initial and sole manifestation in covid patients [15], but on the other hand it can be presented as a late complication, based on the particular therapeutical approach, as described in several cases after treatment with lopinavir and meropenem (used for the viral and pulmonary infection) [16]. Since the outbreak of the pandemic, it has been apparent that the disease prognosis has been depended from the multiorgan involvement. Comorbidities, especially cardiovascular and diabetes (as described in our case report) are the most common risk factors for severity and mortality [2].

Multidisciplinary and comprehensive approach in the diagnosis, treatment and follow up of the patients can only guarantee timely detection and wide range of therapeutical modality, leading to a better prognosis and outcome.

## Conclusion

Novel corona virus was defined as a cause of various clinical manifestations, with wide spectrum of symptoms and severity forms. Acute kidney injury, as a result of rhabdomyolysis was described as bad prognostic factor for the patient outcome, very often underrated, and not recognized on time. Rhabdomyolysis in patients with covid-19 infection can occur at any time

of the patient illness, from the beginning till the recovery and thereafter. Prompt follow up of the patients by the multidisciplinary team is crucial for prevention, early recognition and urgent treatment of the multiorgan complication that can occur. Thus, the patient survival rate in this pandemic that took away many lives, could be markedly improved.

*Conflict of interest statement.* None declared.

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