



# Complications of Coronavirus Disease-19 in a Hospitalized Patient: A Case Report

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## Abstract

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**BACKGROUND:** Coronavirus (CoV) disease (COVID)-19 infection is a major public health issue worldwide with no specific therapy or vaccine.

**CASE REPORT:** COVID-19-positive patient was hospitalized due to a dry irritating cough that has persisted for 3 days. The polymerase chain reaction test to severe acute respiratory syndrome-CoV-2 was positive. Computed tomography (CT) scan of the lungs showed massive bilateral consolidation. The patient was set to oxygen support (6 L/min). Two hours after referring the patient's condition worsened with shortness of breath, suffocation, wheezing, and decreased saturation (77%). The patient was given mechanical support with continuous positive airway pressure mask. Therapy included azithromycin 500 mg and ceftriaxone 2 g. On the 3<sup>rd</sup> day of hospitalization, there was a sharp deterioration of the condition and a decrease in saturation (40%). The patient was intubated and immediately placed on intermittent positive pressure ventilation. Azithromycin was now combined with meropenem 3 × 1 g. The next morning patient's condition further worsened with decrease in saturation and heart rate. The resuscitation was unsuccessful.

**CONCLUSION:** COVID-19 is primarily a respiratory infection, but the virus also affects other organs with poor outcome.

## Introduction

The coronavirus (CoV) disease (COVID)-19 infection is a major public health issue worldwide. By September 10, more than 27,700,000 cases were registered worldwide, of which there were over 899,000 deaths. Over 18,000,000 cases have been recovered [1]. In our country, until now, there are more than 15,000 cases, resulting in more than 600 deaths. Over 12,000 cases have been recovered [2].

It all started in December 2019, in Wuhan. No one expected a global pandemic to occur shortly thereafter. On December 31, the World Health Organization (WHO) was informed about a case of pneumonia of unclear etiology in Wuhan. Then, on January 7, 2020, Chinese authorities identified the cause as a new type of CoV, which was temporarily labeled as "2019-nCoV." CoVs are a large family of viruses that can cause a wide range of illnesses in humans, from the common cold to the severe illness. The new nCoV had not been identified in humans until February 11, 2020, and it was referred to as "COVID-19

virus" or CoV-2 of severe acute respiratory syndrome-CoV-2 (SARS-CoV-2). In a short time, there was a massive increase in the number of cases in China that was the reason for the declaration of a world pandemic on March 11 by the Director-General of the WHO [3].

In Republic of Macedonia, the first case of the new virus was identified on February 26. It was detected in a patient who returned from Italy which, at that time, was a hotspot of CoV in Europe. The patient was immediately hospitalized at the Clinic for Infectious Diseases and Febrile Conditions.

Those patients who are infected with COVID-19 show different symptomatology. However, the most common symptoms are fever and cough. The temperature can vary up to about 37°C in some patients. Other patients experience high fever, which can be over 40°C. The cough is usually dry, but can also be productive. In the same patient, the symptoms may change during the course of the disease. Other symptoms that may occur are joint and muscle pain, as well as shortness of breath. In some patients, the loss of sense of smell (anosmia) and the loss of sense of taste

(dysgeusia) are the most prominent findings. Although the majority of patients are complaining on the most common respiratory symptoms, a significant number of patients also experience gastrointestinal symptoms, such as loss of appetite, nausea, vomiting, and diarrhea. Dizziness and headache can be found in certain cases. There are also patients who are asymptomatic. Most often, however, patients present with a mild clinical course or a moderately severe clinical course. The cause is unknown, but in a certain proportion of patients, there is a severe clinical course that progresses into an acute respiratory distress syndrome. Finally, it is not uncommon situation when the COVID-19 patients experience the following conditions: Septic shock, blood clots, cytokine storm, or multiorgan failure [4], [5], [6].

The incubation period of COVID-19 lasts about 4–5 days. Symptoms are usually clinically manifested from 2 to 7 days after contact with the infected person. It is evident that SARS-CoV-2 is transmitted by direct contact, indirect contact with contaminated objects or surfaces, or close contact with infected people through mouth and nose secretions (saliva, respiratory secretions, or secretion droplets) that are released when an infected person coughs, sneezes, speaks, or sings. People may become infected by touching objects and surfaces with infected droplets on them and then touching their eyes, noses or mouths before cleaning their hands [7]. Therefore, the WHO recommends a social distance of 1 m [8]. On the contrary, the US Centers for Disease Control and Prevention has different opinions and they recommend a social distance of 2 m [9]. According to the recommendations of the WHO, protective masks and frequent hand washing should also be worn [8].

The standard detection of the disease is through polymerase chain reaction (PCR) testing [10]. The test is performed by taking a nasopharyngeal swab. The test results are usually ready in 4 h–2 days. Antibody testing is less commonly used. The reason is that antibodies do not always appear during the period when the patient is infectious. Serological tests are most useful after 3 weeks of the onset of symptoms in patients. Computed tomography (CT) thorax is usually used in COVID-19 patients, but it is not a standard diagnostic method [11].

There is still no specific drug or vaccine to treat the disease. Numerous clinical trials are underway. Antiviral drugs are the most commonly used which are ritonavir and chloroquine or its derivative hydroxychloroquine (HCQ) [12]. HCQ showed significant antiviral activity against COVID-19 within *in vitro* experiments and some small human studies [13], [14], [15], [16], [17], [18]. The bacterial macrolide azithromycin is also used for COVID-19 treatment [18], [19], [20], [21]. It is, therefore, recently analyzed in numerous studies. The mechanisms of action of azithromycin have not yet been studied in detail but it is thought to have great antiviral activity. Furthermore, according to some experiments, the macrolide azithromycin has a significant effect against the inflammatory response that occurs in the lungs [20], [22], [23].

## Case Report

Within the actual case report, we are presenting a case of COVID-19-positive patient and the clinical investigations and hospital care in that patient. A 62-year-old male patient has presented for examinations due to a dry irritating cough that has persisted for 3 days. The patient was diabetic and he has been treated with an oral antidiabetic therapy (repaglinide and metformin). Using the detailed medical history, we have obtained information that he has been subfebrile (body temperature of 37.5°C) during the previous day. Due to the current situation with the CoV pandemic, taking into consideration, the diagnostic suspicion that the same patient could be possible infected with SARS-CoV-2, he was referred to the City General Hospital 8<sup>th</sup> September, Skopje, as a country COVID-19 center.

The patient was checked up at the triage center of the City General Hospital 8<sup>th</sup> September. The measurement of the body temperature showed 37.1°C and after that the physical examination was performed. The blood pressure was 140/90 mmHg and electrocardiogram at rest revealed sinus rhythm, heart rate 90/min, as well as normal axis and ST segment without any changes in morphology and conductivity. Auscultation of the lungs showed pulmonary vesicular breathing with prolonged expiration and the breathing sounds were almost silent at the basal parts of the lungs, bilaterally. On auscultation, crackles were also detected at the basal pulmonary parts.

Oxygen saturation (SaO<sub>2</sub>) (that measures the percentage of hemoglobin binding sites in the bloodstream occupied by oxygen) was 94%. Laboratory tests and CT thorax have been performed. Laboratory analyses showed these findings: White blood cells (WBCs) 4 × 10<sup>9</sup>/L, hemoglobin 13.6 g/dL, hematocrit 40.2%, platelets (PLTs) 203 × 10<sup>9</sup>/L, percentage of lymphocytes 50%, C-reactive protein (CRP) 20 mg/L, aspartate aminotransferase (AST) 68 U/L, and alanine aminotransferase (ALT) 75 U/L. The PCR test for SARS-CoV-2 was positive.

Figure 1 demonstrates the CT scan of the lungs in our patient and it shows massive bilateral consolidation.

The patient was hospitalized and set to oxygen support with an oxygen mask (6 L/min). Two hours after hospitalization, the patient's condition worsened with manifestation of a shortness of breath, suffocation, and wheezing, while oxygen saturation dropped to 77%. The patient was put on a mechanical support with a continuous positive airway pressure (CPAP) mask. CPAP is a type of positive airway pressure ventilation. During this type of ventilation, a constant level of pressure that is higher than the atmospheric pressure is continuously applied to the upper airways. In addition, we have performed arterial blood analysis. Gas analyzes revealed the following results: pH



Figure 1: Computed tomography scan of the lungs showing massive bilateral consolidation in the case presented

7.50, PaCO<sub>2</sub> 30 mmHg, and PaO<sub>2</sub> 110 mmHg, clearly demonstrating respiratory alkalosis.

In this patient, we have started a therapy with azithromycin 500 mg and ceftriaxone 2 g. We have also ordinated fluids, Amp. Urbason 80 mg, Amp. Gastrosol 40 mg, and Amp. Fraxiparine 0.4 mL (sc). The patient was not taking any foods or drinks. Therefore, he has received parenteral nutrition through a central venous catheter (CVC) on the right vena jugularis interna because of the possibility of aspiration due to non-invasive ventilation. Parenteral nutrition solutions have high osmolality. Because of the high osmolality, it requires placement of a CVC. A CVC is a form of venous access that is usually applied in critically ill patients and patients who spend many days in hospital to administer medications and/or fluids. We usually apply these catheters in vena jugularis interna, vena subclavia, or vena femoralis.

On the next day, the condition of the patient was stable. He has been receiving the same therapy. The non-invasive mechanical ventilation was also used. The following vital parameters have been determined: Blood pressure 140/95 mmHg, heart rate 85/min, PaO<sub>2</sub> 95%, and diuresis 2300 mL.

On the 3<sup>rd</sup> day of the hospital care, despite the application of non-invasive ventilation, there was a sharp deterioration of the condition and a decrease of oxygen saturation to 40%. The patient was intubated and immediately put on mechanical ventilation with intermittent positive pressure ventilation (IPPV). IPPV is a type of mechanical ventilation using endotracheal or tracheostomy tube.

Control CT scan and control laboratory analyzes were performed. It has been observed that the consolidation was minimally resolved. The following laboratory results were obtained: WBC 8.8 × 10<sup>9</sup>/L, CRP 360 mg/L, hemoglobin 13.6 g/dL, PLT 80 × 10<sup>9</sup>/L, urea 20 mmol/L, creatinine 300 mmol/L, Na 140 mEq/L, and K 5.5 mmol/L. The patient had a diuresis of 600 mL. Dialysis has been taken into consideration but it was decided to wait and include diuretics in the

therapy. Antibiotic therapy was changed. Azithromycin was still applied, and ceftriaxone was changed with meropenem 3 × 1 g. The next day there was worsening of the condition, a further decrease in saturation, and a decrease in the heart rate. Approached resuscitation was unsuccessful and the patient died.

## Discussion

The COVID-19 pandemic is still increasing and every medical specialty is interested in the research aimed at effective diagnosis, treatment, and prevention of the disease and its clinical manifestations. The efforts of world leading medical centers are oriented toward detecting the best medical treatment of symptomatic COVID-19 disease as well as toward finding effective vaccine.

COVID-19 affects different people in different ways. Most infected people (about 80%) will develop mild-to-moderate illness and recover without hospitalization. In one out of five people, COVID-19 becomes serious condition and the affected people develop difficult breathing [24]. It is clearly shown that certain COVID-19 cases will develop severe viral pneumonia with respiratory failure, multiorgan and systemic dysfunctions in terms of sepsis and septic shock, and death [6], [25], [26]. However, the management of SARS-CoV-2 infection in those cases could be disadvantageous because of the abovementioned multiorgan response and failure.

The actual case report includes diagnostics and treatment of COVID-19-positive patient with severe clinical manifestation. Despite the combined antibiotic, corticosteroid, and supportive treatment, the condition of the patient has rapidly declined with minimally resolved consolidation. Since no vaccines or drugs for prevention and treatment have been approved so far, except remdesivir that has been authorized for use in several countries [19], [27], the team has used the combination of azithromycin with other antibiotics. It has been shown that azithromycin has significant immunomodulation and antiviral properties [19], [28], [29], [30], [31] and there are different aspects supporting its therapeutic effectiveness in SARS-CoV-2 infection.

In our case, what was the probable cause of death and how does COVID-19 act on the different organs?

### Lungs

If COVID-19 progresses into a more severe clinical picture, the first organs to be affected are the lungs. The entrance of the virus in the human body is mainly through the respiratory system. Fecal-oral transmission has been only speculated. After entering the nose, the virus multiplies in the cells of the mucosa and then reaches the lungs through the trachea. The most frequent, serious

manifestation of COVID-19 is found to be pneumonia, characterized by bilateral lower zone infiltrates displayed on radiographic chest imaging [6], [32].

The patient presented in this paper had pneumonia that was diagnosed by the CT scan of the thorax. The team has prescribed a combination of azithromycin with other antibiotics. The subsequent CT scan of the thorax showed minimally resolved consolidation, but there is still not enough evidence and knowledge whether this CT resolution was a result of the effects of azithromycin or not. It has yet to be confirmed in a large cohort of COVID-19 patients.

### Kidneys

Some of the patients infected with SARS-CoV-2 could have impaired renal function even though they have not had any kidney problems previously [6], [33]. It is suggested that the pathogenesis of kidney involvement in COVID-19 infection and acute tubular necrosis could be a result of sepsis, multiorgan failure, and shock [34]. Another hypothesis is that the kidney cells do not get enough oxygen due to a lung disorder. According to some studies, COVID-19 increases the hypercoagulability that results from the formation of blood clots able to occlude the renal blood vessels.

The similar thing happened in the patient currently presented. When his health condition has deteriorated, there was a significant decrease in diuresis and an increase in degradation products. The patient was also a diabetic, so it is not clear whether the renal impairment was a consequence of COVID-19 or diabetes.

### Liver

Mild and transient or severe liver damage can also occur in COVID-19 patients [6]. An increase in AST and ALT transaminases is a common finding in patients infected with SARS-CoV-2 [35]. According to most studies, however, liver damage is secondary and transient and it is not clear if the increase in AST and ALT is associated with COVID-19 or it is a result of the hepatotoxicity of the drugs used.

### Thrombocytopenia

Thrombocytopenia is also a common finding in patients with COVID-19. In the last laboratory result, the PLT in our patient were  $80 \times 10^9/L$ . The mechanism by which it occurs is not yet known, but there is some speculation according to several studies. According to some studies, the virus directly attacks the bone marrow, preventing the formation of PLT. Others' opinion is that PLT self-destruction is caused by the cytokine storm caused by the virus. Another possible cause is the PLT aggregation in the lungs and the formation of microthrombi.

## Conclusion

COVID-19 is primary a respiratory infection and SARS-CoV-2 enters the body through the respiratory system, but the virus also affects other organs and, therefore, the disease in certain cases has a poor outcome. No cure or vaccine has been found yet, although numerous studies are being done. Therefore, at the moment, it is the most important to follow the recommendations that include maintaining social distance, frequent hand washing, and personal hygiene as well as wearing personal protective equipment, both at the workplace and in community.

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