Journal of Population Therapeutics & Clinical Pharmacology

Case report
DOI: 10.15586/jptcp.v27iSP1.691

Covid-19: A systemic disease treated with a wide-ranging approach: A case report

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Submitted: 28 April 2020. Accepted: 2 July 2020. Published: 3 July 2020.

ABSTRACT

At the end of December 2019, the Health Commission of the city of Wuhan, China, alerted the World Health Organization (WHO) to a pneumonia cluster in the city. The cause was identified as being a new virus, later named SARS-CoV-2. We can distinguish three clinical phases of the disease with a distinct pathogenesis, manifestations and prognosis. Here, we describe the case of a 45-year-old male, successfully treated for Coronavirus disease (COVID-19). The patient was feeling sick in early April 2020; he had a fever and pharyngodynia. When he came to our COVID hospital, his breathing was normal. The nasopharyngeal swab specimen turned out positive. High-resolution computed tomography (HRCT) showed mild interstitial pneumonia. The patient was admitted to our department and treated with hydroxychloroquine, ritonavir, darunavir, azithromycin and enoxaparin. On day seven of the disease, the patient's respiratory condition got worse as he was developing acute respiratory distress syndrome (ARDS). He was given tocilizumab and corticosteroids *and was immediately treated with n*on-invasive mechanical ventilation (NIMV). His condition improved, and in the ensuing days, the treatment gradually switched to a high-flow nasal cannula (HFNC); after 18 days, the patient's clinical condition was good.

The successful results we have been able to obtain are closely associated with avoidance of invasive ventilation that may lead to intensive care unit (ICU)-related superinfections. In our opinion, it is fundamental to understand that COVID-19 is a systemic disease that is a consequence of an overwhelming inflammatory response, which can cause severe medical conditions, even in young patients.

Keywords: *coronavirus disease, COVID-19, treatment, monoclonal antibodies, non-invasive mechanical ventilation*

INTRODUCTION

SARS-COV-2 causes respiratory tract infections that can range from asymptomatic diseases to interstitial pneumonia with respective pulmonary insufficiency.[1,3] We can distinguish three progressive phases of the disease: viral, respiratory and inflammatory.[4,5] The most common signs are fever, a dry cough, pharyngodynia and dyspnoea. When the virus causes pneumonia, scans show infiltrative interstitial lesions, while HRTC, in most cases, shows ground-glass opacities.[6]

This initially mild disease can progress to a severe condition; a fact that is more frequent in patients with risk factors such as hypertension, cardiovascular disease, diabetes, liver disease and/or various medical lung conditions.[3] The disease's incubation period ranges from 0 to 14 days, and the median is 5 days. The virus is either transmitted directly by microdroplets or indirectly by touching a contaminated object or surface. Air transmission is still uncertain but should be considered when procedures generate aerosol.[2] Treatments are still being studied. Since therapies have not yet been studied by means of controlled trials, they are still based on observational studies and/or expert opinion.[7–9] At present, in Italy, we use hydroxychloroquine, antivirals, corticosteroids and immunomodulators with different indications.[10,11]

Here, we present a case report of a severe COVID-19 patient who was treated successfully, with the aim of emphasising that COVID-19 is a systemic disease requiring a wide-ranging approach that includes antivirals, corticosteroids, low-weight molecular heparin, biological therapy and invasive or non-invasive ventilator support.[11,12]

CASE REPORT

Patient Information

On the 8th of April 2020, a 45-year-old man with a BMI of 24.4 kg/m^2 came to our Emergency Department. He reported having had fever and pharyngodynia for 4 days, both of which he had self-medicated with the following remedies: clarithromycin 500 mg modified release and oral prednisone. Due to his job as a nurse in an emergency department, the patient had an epidemiological COVID-19 risk factor. His clinical history included coeliac disease and a non-haemodynamically significant atherosclerotic plaque treated with acetylsalicylic acid. No diabetes, hypertension or immune deficiency diseases were reported.

Phase 1 (Days 4–6)

Clinical findings

The patient was admitted to the emergency department and isolated. At the initial medical examination, he presented with fever and pharyngodynia. The patient's breathing was regular, and his 6-min walking test was negative. Blood pressure, heart and respiratory rates were normal.

Diagnostic assessment

The nasopharyngeal swab specimen, tested for SARS-CoV-2 RNA by reverse-transcription polymerase chain reaction (RT-PCR), turned out to be positive. The patient's chest HRCT showed bilateral abnormalities, with peripheral distribution, consisting of ground-glass opacities with mild interlobular and intralobular septal thickening. The most affected areas were the medium and inferior lobes of the right lung and the basal inferior segment of the left lung. The laboratory values showed lymphopenia and monocytopenia.

Therapeutic intervention

The treatment included the following: hydroxychloroquine (400 mg twice daily; 200 mg twice daily from the second day onwards); ritonavir (100 mg once a day); darunavir (800 mg once a day); azithromycin (500 mg once a day) and enoxaparin (6,000 UI twice daily). Fever was resistant to paracetamol.

J Popul Ther Clin Pharmacol Vol 27(SP1):e26–e30; 3 July 2020.

Phases 2–3 (Days 7–12)

Clinical findings

On day seven of the disease, there was an episode of desaturation, and the patient *was treated with high-flow nasal cannula therapy (HFNC*). The day after, the patient's clinical condition got worse, with significant dyspnoea and rapidly decreasing oxygen saturation levels, as he developed ARDS with respiratory insufficiency.

Diagnostic assessment

Laboratory tests showed high interleukin 6 (32 pg/mL normal 0–16.4), thrombocytopenia (86 10^9/L), lymphopenia (0.55 10^9/L), neutropenia (0.73 10^9/L) and alanine aminotransferase (91 U/L range 7–55). Fibrinogen, C-reactive protein, Procalcitonin, QuantiFERON and HBV-reflex ferritin values remained normal.

Therapeutic intervention

The patient *was immediately treated with* NIMV. We used Puritan Bennet in order to perform cycles of alveolar recruitment, with maximum positive end-expiratory pressure values of 20–25 cm H_2O and PIP 35–40 cm H_2O for 5/10 min, three times a day. On day eight, the patient was given one shot of TOCILIZUMAB-2 vials subcutaneously (324 mg). At the same time, we started to administer dexamethasone (20 mg once a day for 5 days, then 10 mg once a day for the following 5 days).

FOLLOW-UP AND OUTCOME

After tocilizumab and corticosteroid treatment, the patient was finally without fever, and little by little, his respiratory condition got better. On day 12, he was given HFNC therapy, with alternating HFNC cycles and NIMV cycles. His respiratory status got better gradually. We also performed an ultrasound examination, which showed pattern B, areas of white lung as well as sub-pleural consolidations, predominantly in the right lung. The results of a serologic test, IgG and IgM were positive. On day 18 of the disease, the patient's clinical condition was good, and he performed respiratory exercises with a three-ball spirometer. He still requires cycles of HFNC, but he can walk by himself and might be discharged from hospital soon.

DISCUSSION

COVID-19 can be seen to have three progressive clinical phases with a distinct pathogenesis, manifestations and treatment.[1,7] The first viral phase is characterised by a mild clinical manifestation, which can simulate a flu-like viral infection. The second pulmonary phase is characterised by dyspnoea and hypoxia. The late phase is characterised by a cytokine storm, which can lead to respiratory insufficiency, disseminated intravascular coagulation (DIC), multiorgan failure and finally the death of the patient. One of the most helpful off-label treatments in the final phase is the use of monoclonal antibodies.[7,10,12]

Tocilizumab is a recombinant humanised monoclonal antibody that can directly bind the soluble IL-6 receptor and inhibit signal transduction. Tocilizumab is a drug used to treat patients suffering from rheumatoid arthritis, juvenile arthritis, giant-cell arthritis and, more recently, cytokine release syndromes associated with chimeric antigen receptor T-cell therapies. Literature about tocilizumab treatment for COVID-19 is lacking; several studies have confirmed the efficacy of such treatment,[12–16] but controlled trials are required in order to produce clinical evidence.

Pressure support ventilation (PSV) is a model of NIMV that allows respiratory function to be improved by increasing pressure in the patient's airway.[1,4] Indeed, high pressure can increase alveolar recruitment in the case of a serious inflammation which has compromised gas exchange in damaged lungs. This approach avoids orotracheal intubation and its related complications (sepsis, nosocomial pneumonia or the need

for a tracheotomy etc.). Obviously, this must be done with the cooperation and agreement of the patient.[17]

We would like to draw attention to what we have learned from the manifold experiences that we have been gathering. First of all, we think that the date of diagnosis (or, in other words, the point at which a patient is identified as having the disease) is a crucial factor in the fight against the disease because the earlier the treatment begins, the better the progression of the disease can be influenced and changed. Patients with similar flu-like symptoms should not self-medicate.[18, 19]

In a nutshell, the sooner we discover a COVID-19 infection, the better. Furthermore, we think it is necessary to avoid self-treatment because COVID-19 is a disease with different phases, each of which requires a different approach and different treatments that need to be administered in a precise order and with the utmost diligence.[20–23]

CONCLUSION

Based on the literature review and our experience, we believe it is fundamental to understand that COVID-19 is a systemic disease that is a consequence of an overwhelming inflammatory response (a cytokine storm), which can cause severe medical conditions, even in young patients. A delay in diagnosis and treatment can be fatal for the patient; tocilizumab is of vital importance in treating patients experiencing a cytokine storm.

The successful results we have been able to obtain in our treatment of COVID-19 patients are closely associated with the avoidance of invasive ventilation, a high-risk intervention that can lead to ICU-related superinfections.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

This study was not funded by anyone.

DATA AVAILABILITY STATEMENT

None

COMPLIANCE WITH ETHICAL STANDARDS

None

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