



## Case report

# Successful recovery from COVID-19 pneumonia after receiving baricitinib, tocilizumab, and remdesivir. A case report: Review of treatments and clinical role of computed tomography analysis



Pietro Sodani<sup>a,b,\*</sup>, Luciano Mucci<sup>a</sup>, Rita Girolimetti<sup>a</sup>, Silvia Tedesco<sup>a</sup>, Francesca Monaco<sup>a</sup>, Daniele Campanozzi<sup>a</sup>, Marino Brunori<sup>a</sup>, Stefania Maltoni<sup>a</sup>, Samuele Bedetta<sup>a</sup>, Anna M. Di Carlo<sup>a</sup>, Piero Candoli<sup>c</sup>, Mauro Mancini<sup>d</sup>, Alberto Rebonato<sup>f</sup>, Francesca D'Adamo<sup>g</sup>, Maria Capalbo<sup>e</sup>, Gabriele Frausini<sup>a</sup>

<sup>a</sup> Internal Medicine Center, Marche Nord Hospital, Pesaro, Fano, Italy

<sup>b</sup> Charité Hospital, Berlin, Germany

<sup>c</sup> Pneumology Department, Marche Nord Hospital, Pesaro, Fano, Italy

<sup>d</sup> Pharmacy Department, Marche Nord Hospital, Pesaro, Fano, Italy

<sup>e</sup> General Direction, Marche Nord Hospital, Italy

<sup>f</sup> Radiology Department, Marche Nord Hospital, Pesaro, Fano, Italy

<sup>g</sup> Hematology and Stem Cell Transplant Center, Marche Nord Hospital, Pesaro, Italy

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## ABSTRACT

The novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a pandemic, threatening global public health. In the current paper, we describe our successful treatment of one COVID-19 pneumonia patient case with high mortality risk factors. Our experience underlines the importance of the use of a multidisciplinary therapeutic approach in order to achieve a favorable clinical outcome. Further, enhancing the capability of the COVID-19 diagnosis with the use of the chest imaging modalities is discussed.

## 1. Introduction

Since late December 2019, there has been an outbreak of a novel enveloped RNA betacoronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This virus causes coronavirus disease 2019 (COVID-19), whose spread has become an ongoing pandemic. The novel coronavirus SARS-CoV-2 is the seventh member of the Coronaviridae family known to infect humans [1]. The estimated mortality rate of COVID-19 so far is lower than that of SARS or Middle East respiratory syndrome COVID19 [2]. However, the ongoing COVID-19 pandemic is a significant health threat worldwide [3]. The clinical symptoms of COVID-19 pneumonia are the same as the common upper respiratory tract infection, but the chest CT has a certain specificity [4, 5]. Unfortunately, there are no vaccines or medicines approved for the novel coronavirus infection [6], but more than 80 clinical trials have been launched to test coronavirus treatments, including some drug repurposing or repositioning for COVID-19 [7].

## 2. Case description

A 50-year-old man was admitted to our hospital with ongoing fever, chills, cough, fatigue, and shortness of breath for more than 20 days. In 2018, he had a history of Follicular non-Hodgkin lymphoma previously treated with chemotherapy. At the time of the last hospitalization he was in hematological remission. The initial physical examination revealed a BT of 39,4 °C, blood pressure of 93/53 mm Hg, pulse of 87 bpm, respiratory rate of 20 breath/min, and SPO2 of 96% room air. The laboratory results reflected WBC  $1,66 \times 10^3$  lymphopenia ( $0,35 \times 10^3$ ), aspartate aminotransferase 38 U/L, alanine aminotransferase 22 U/L, (in the normal range), C-reactive protein 9,37 mg/dl (range 0,00-0,49 mg/dl), and lactate dehydrogenase 350 U/L (range 0–247U/L). Blood gas analysis showed PH:7510; PCO2:30,0 mmHg; PO2:109,0 mmHg. High-resolution computed tomography (HRCT) scan showed an alveolar interstitial thickness defined by ground-glass opacities with bilateral perihelia and peripheral distribution in combination with thickened

\* Corresponding author. Internal Medicine Center, Marche Nord Hospital, Pesaro, Fano, Italy  
E-mail address: [p.sodani@libero.it](mailto:p.sodani@libero.it) (P. Sodani).

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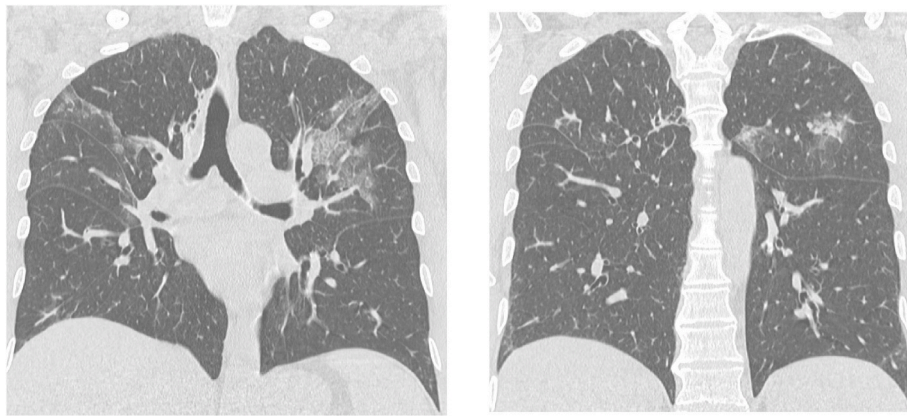
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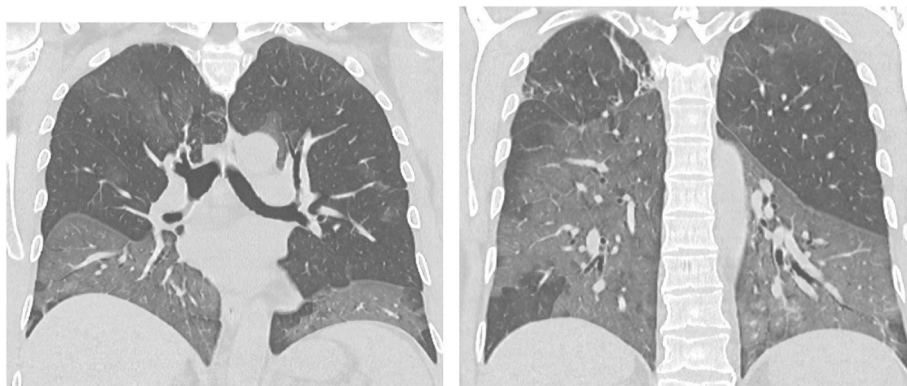
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**Fig. 1.** Ground-glass opacities with bilateral perihilar and peripheral distribution in combination with thickened interlobular and intralobular lines.

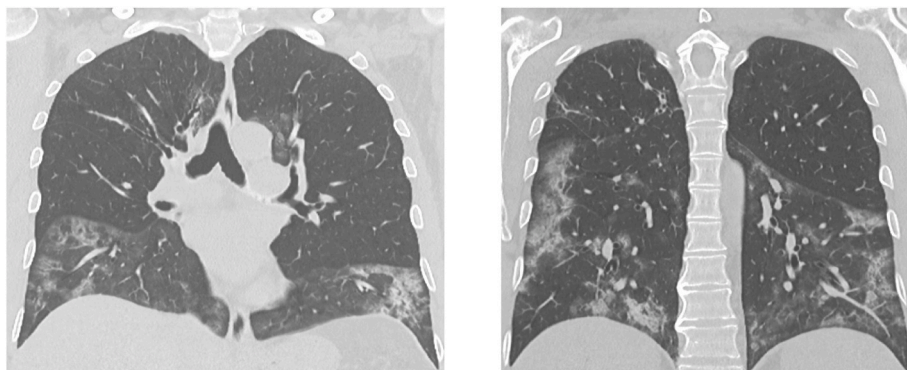


**Fig. 2.** Ground-glass pattern with a widespread bilateral posterior predominance.

interlobular and intralobular lines resembling an interstitial infection (Fig. 1). The nucleic acid test of nasopharyngeal swabs was negative on two occasions. A diagnosis of severe COVID-19 pneumonia and moderate acute respiratory distress syndrome (ARDS) was made by bronchoscopy and by concurrent bronchoalveolar lavage (BALF), and the patient was placed in isolation. He was tested negative for influenza A/B virus, respiratory syncytial virus (RSV), *Mycoplasma pneumoniae*, *Cryptococcus haemolyticus* antigen, *Aspergillus* antigen, Epstein-Barr virus capsid antigen IgM, and Epstein-Barr virus. On the other hand, the BALF sample tested positive for SARS-CoV-2 ribonucleic acid. This suggests that the lung is possibly the main target of the SARS-CoV-19 virus [8]. He was immediately admitted to the isolation ward. Initial management consisted of hydroxychloroquine, azithromycin, and large spectrum

antibiotics for SARS-CoV19 pneumonia and possible concomitant bacterial infection. In order to reduce viral infectivity, viral replication, and the aberrant host inflammatory response, baricitinib tablets 4 mg/day was started. Baricitinib is an inhibitor of Janus Kinase JAK 1 and JAK 2 and therefore it might help in managing the inflammation [9]. However, his cough, dyspnea, fatigue, and fever did not improve. When the patient's respiratory symptoms worsened in the setting of persistently elevated inflammatory markers, (interleukin 6 (IL)6 was 191 pg/mL) treatment with steroids 1mg/kg and the anti-interleukin (IL) 6 receptor blocker tocilizumab, with 8 mg/kg body weight intravenously was started.

After tocilizumab administration, the IL-6 level decreased gradually, (from 196 pg/ml to 73 pg/mL) with gradual improvement of the



**Fig. 3.** Reduction of ground-glass pattern, appearance of parenchymal consolidation with inferior lobar prevalence and perilobular and peribronchovascular distribution.

respiratory symptoms and lung function, and his fever disappeared. HRCT after 4 days from tocilizumab infusion showed an increase of ground-glass pattern with a widespread bilateral posterior predominance (involving 80% inferior lobes).

The alterations described are highly suggestive for interstitial pneumonia which is highly concerning for changes secondary to viral pneumonia (Fig. 2). The patient's clinical condition worsened, with dyspnea and SPO<sub>2</sub> to 91% under ambient air. Given the radiographic findings and laboratory results (IL6 was increased to 580 pg/mL and Ferritin was 3.160,0 ng/m), the idea of persistent or active 2019-nCoV RNA viral replication was considered. Clinicians pursued use of an investigational antiviral therapy. A request for the use of remdesivir was submitted. Remdesivir arrived and a 200 mg IV loading dose was administered to the patient. This was followed by orders for remdesivir 100 mg IV maintenance dose every 24 hours for the next 9 days. Supportive measures, in addition to hydroxychloroquine and steroids, were maintained.

During the following 24 hours, the patient's clinical conditions improved, including dry cough and shortness of breath, and his SPO<sub>2</sub> improved to 92%–100% under ambient air. HRCT (Fig. 3) confirmed the improvement: reduction of ground-glass pattern, appearance of parenchymal consolidation with inferior lobar prevalence and peribronchovascular distribution. The patient continues to be in stable condition on room air, his walking test is absolute negative, and he is progressing toward discharge.

### 3. Discussion

Several host factors regulate the replication of coronaviruses and they simultaneously induce dramatic changes in the host cellular structure and function. T cell exhaustion is a state of T cell dysfunction that arises during many chronic infections and cancer. It is defined by poor effector function, sustained expression of inhibitory receptors, and a transcriptional state distinct from that of functional effector or memory T cells [10]. Persistent stimulation by the virus may induce T cell exhaustion, leading to loss of cytokine production and reduced function [11,12]. The number of total T cells and CD4<sup>+</sup> and CD8<sup>+</sup> T cells were dramatically reduced in COVID-19 patients, especially in patients requiring Intensive Care. This case report describes that the positive rate of bronchoalveolar lavage for detection of new coronavirus nucleic acid was high, and BALF analysis for suspected or confirmed new coronavirus pneumonia patients with negative detection of nucleic acid in pharynx swabs but showing residual lung lesions was helpful for early diagnosis, treatment, and prognosis. We speculate that the virus migrates from the upper respiratory tract to the lower respiratory tract as the infection progresses, which may explain the negative test results of nasopharyngeal swabs. The application of potent antiviral treatments to prevent the progression to T cell exhaustion in susceptible patients may thus be critical to their recovery. We have read with great interest the successful application of Remdesivir to cure a COVID-19 patient, and clinical trials indicate that this drug may have significant potential as an antiviral [13, 14,15]. There are some limitations to this report that must be considered. Our context comes from a single patient treated with remdesivir in the course of the disease. This patient also received hydroxychloroquine, large spectrum antibiotic, Janus kinase inhibitor, anti-JAK, and Tocilizumab. It is possible that these medications may have impacted his clinical course. He is also a 50-year-old patient with few comorbidities and his most significant risk factor for mortality is a history of Follicular non-Hodgkin lymphoma previously treated with chemotherapy in 2018, with additional recurrent pneumonia infection.

### 4. Conclusions

This case report described an effective supportive medication scheme to treat SARS-COV-2 infected patients and emphasized the necessity of detection of the viral genome using BALF samples. Our observation confirms that the radiologist plays a crucial role in the rapid identification and early diagnosis of new cases, which can be of great benefit not only to the patient but also to the larger public health surveillance and response system. The unconventional aspect of this case is that the analysis of the patient's upper respiratory tract specimen was repeatedly SARS-COV-2 negative while that of BALF sample was positive for SARS-COV-2 virus. Our report strongly suggests that Tocilizumab can block the downstream signal transduction by binding mL-6R and sIL-6R, and it plays a role in the treatment of cytokine storm caused by COVID-19. Previous literature has shown significantly reduced lung viral load and improved clinical signs of disease following remdesivir administration [16] and highlights that early initiation of remdesivir may be effective in treating SARS-CoV-2.

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