



## Using Tocilizumab in Sars COV-2 Disease: Case Report

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### Abstract

Coronavirus 19 (COVID-19) may cause a cytokine release syndrome inducing the severity of the disease. Various immune modulating agents are suggested due to the lack of definitive treatment and vaccine. In this case report, we aimed to share the clinical course of a Covid 19 patient who was given tocilizumab (TCZ) for severe ARDS on the 5th day of hospitalization. Although, the patient was extubated 12 days after TCZ treatment with a rapid recovery, we believe that more cases are needed to determine the efficiency and timing of TCZ treatment.

### Case report

## INTRODUCTION

Covid-19 disease, which emerged in Wuhan, China in 2019, has turned into a pandemic with the number of cases worldwide increased to 3.062.000. According to the latest information in our country, 129,491 people were infected and 3520 cases died (the data of 5.5.2020). Generally the patients initially present with dyspnea, cough, tachypnea, fever, and gastrointestinal complaints, but about 5 % of them appear to progress to acute respiratory distress syndrome (ARDS), acute renal failure and multiorgan dysfunction (MODS). It has been determined that cytokine release syndrome plays an important role in the severity of the disease in COVID-19 pandemic. In severe cases, cytokines such as IL-6, interleukin-1B (IL-1B), induced protein (IP10) and monocyte chemoattractant protein-1 (MCP-1) increase highly when compared to mild cases<sup>1</sup>. Due to the lack of definitive treatment and appropriate vaccine yet in COVID-19 disease, the use of TCZ, corticosteroids and hydroxychlorocine as immunomodulatory therapies has been brought to the agenda in Covid-19 disease. In this case report we aimed to evaluate and share the clinic progress of a Covid-19 patient treated with Tocilizumab (TCZ) after obtaining his consent.

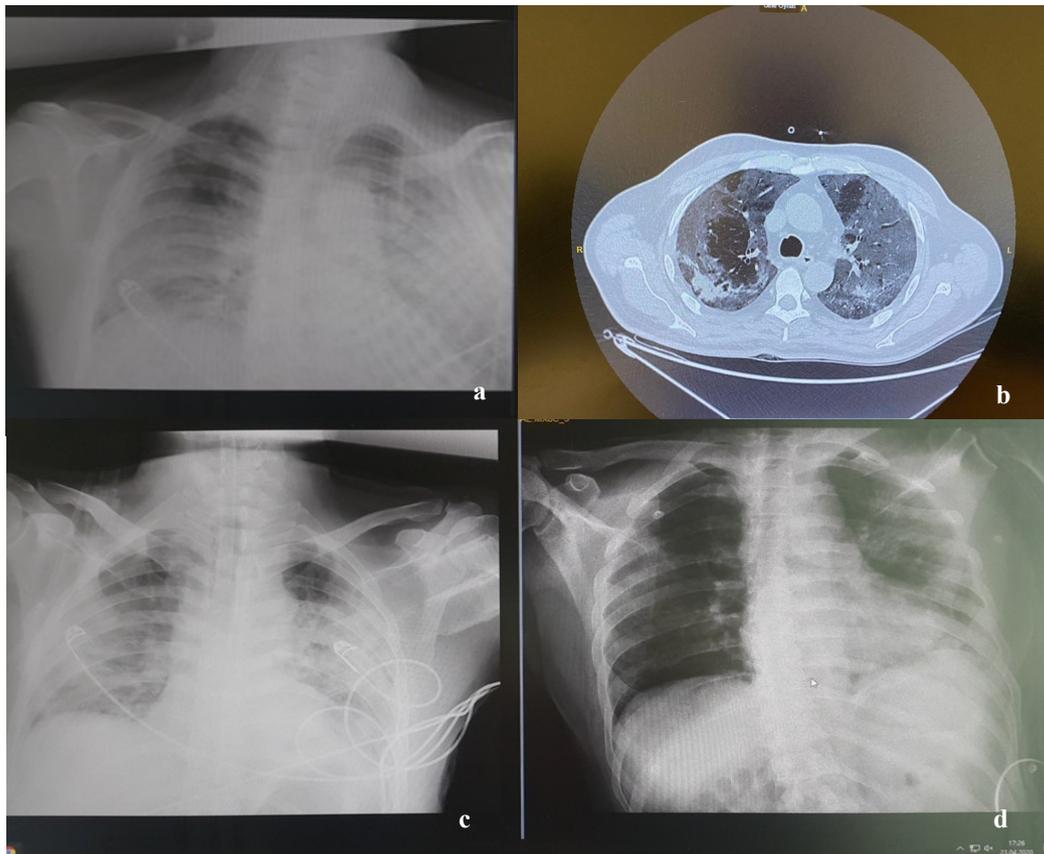
## CASE REPORT

Our case was admitted in the Infectious Diseases Clinic of Neurology-Orthopedics Hospital which was converted into Pandemic Hospital in Ankara City Hospital. He was a 55-year-old male patient with no comorbidity and he was diagnosed as positive with RT-PCR test with complaints of fever and cough. On 03.28.2020, the 3rd day of his admission, he was transferred to our intensive care unit due to the decrease in peripheral oxygen saturation (SpO<sub>2</sub>) despite the nasal oxygen supplement. Hydroxychloroquine, azithromycin, favipiravir and oseltamivir treatments were continued in our clinic.

In the thorax computed tomography (CT) obtained in ward, there were typical features of pandemic viral pneumonia in terms of diffuse patches with multilobar, multisegmenter involvement in both lungs, with diffuse patches, most of which were ground glass density, some of which progressed to consolidation (Figure 1). Considering the laboratory parameters of the case, the white blood cell count was  $8.95 \times 10^9 / L$ , the lymphocyte ratio was 7.3%, and the lymphocyte count was  $0.65 \times 10^9 / L$ . C-reactive protein value was 152 mg / dL, procalcitonin was 0.17 µg / L, ferritin value was 640 µg / L, and D-dimer value was 1.53 mg / L. Initially SpO<sub>2</sub> was around 90% during 6 L / min oxygen therapy with an

oral mask, but on the 3rd day of ICU, SpO<sub>2</sub> <85% and the patient was intubated due to deterioration of arterial blood gases. Since the PO<sub>2</sub> / FiO<sub>2</sub> ratio was 77, it was accepted as ARDS. Methylprednisolone 2x80 mg was added to the treatment since SpO<sub>2</sub> was around 88% despite FiO<sub>2</sub> 100% and PEEP 10 cmH<sub>2</sub>O

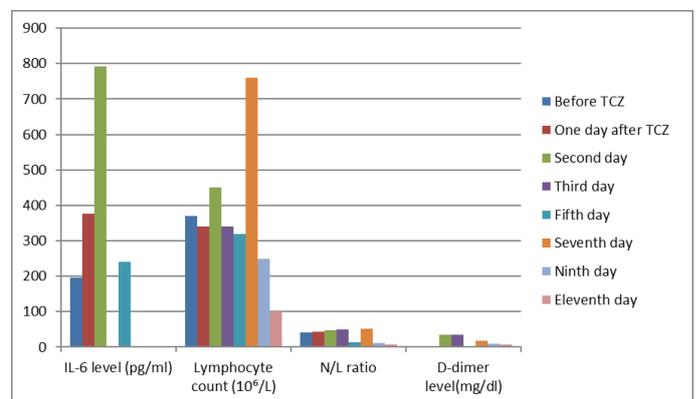
on SIMV PC mode. However, on the 5th day of hospitalization, a single dose of TCZ 600 mg ( 8 mg / kg) was given with an infusion of 100 ml of saline in 1-hour as the patient who had no improvement in mechanical ventilator parameters and showed progression on the PA AC radiograph.



**Figure 1:** PA AC and CT images of the patient during TCZ treatment, a,b; before TCZ treatment, c; one week after TCZ treatment, d; twelve days after TCZ treatment

There was a marked decrease in PA AC radiography after TCZ and a decrease in mechanical ventilator support (Figure 1). The PEEP value did not exceed 10 cmH<sub>2</sub>O throughout the treatment. In addition, the PEEP value decreased from 10 cmH<sub>2</sub>O to 7 cmH<sub>2</sub>O immediately after the TCZ treatment. The lymphocyte count was fluctuating and the lymphocyte count before TCZ treatment was 0.37x10<sup>9</sup> / L, although it was 0.76 x10<sup>9</sup> / L 1 week after TCZ treatment, there was no correlation between clinical improvement and lymphocyte count as it was seen as 0.101x10<sup>9</sup> / L in follow-up. In our case, D-dimer values decreased from 35.2 mg / L to 7.9 mg / L (normal value: <0.55 mg / L) during the clinical recovery period. In addition, there is a remarkable decrease in neutrophil / lymphocyte ratio (Figure-2).

Methylprednisolone treatment was given 2x80 mg/day for 5 days, then it was gradually decreased in 3 days and stopped in a total of 14 days. No side effects of methylprednisolone and TCZ were detected. The patient was extubated 12 days



**Figure 2:** Changes in IL-6, lymphocyte count, N / L (Neutrophil / lymphocyte) ratio and D-dimer level before and after the patient's Tocilizumab treatment

after TCZ treatment and oxygen therapy was continued with nasal high-flow oxygen. The COVID swab samples were tested as two times negative and the patient was transferred to ward again with nasal low flow oxygen on the 36th day of hospitalization.

## DISCUSSION

In studies conducted with COVID-19 patients, it was thought that IL-6 level may have a predictive value in predicting the severity of the disease <sup>1</sup>. In a retrospective study conducted in China, it has been suggested that severe COVID-19 patients with IL-6 levels above 20 pg / mL can be given TCZ <sup>2</sup>. In this study, TCZ treatment in 10 patients has been shown to reduce fever periods, improve radiological symptoms and restore lymphocyte count <sup>2</sup>. The TCZ dose applied in the study is 8 mg / kg (1 hour infusion in 100 mL of saline), and it is also recommended that it can be repeated after 12 hours <sup>2</sup>. In our case, the same dose was applied. No repeat dose was needed as the patient showed a gradual improvement. In another study, the criteria for administering TCZ are as follows: high viral load (at least 3 days after the onset of symptoms and / or symptoms), non-invasive or invasive mechanical ventilation need, increased inflammatory markers such as IL-6, CRP, ferritin, D-dimer <sup>3</sup>. However, in this study, it was stated that IL-6 value should be > 40 pg / ml for TCZ application <sup>3</sup>. The current clinical situation in our patient met the TCZ treatment indications and the IL-6 level was 196 pg / mL when TCZ treatment was started.

In a case report, a 64-year-old Chinese patient with no comorbidities developed severe dyspnea on the 7th day of his admission, and his CRP value decreased rapidly after the administration of two doses of TCZ therapy under the treatment of assisted mechanical ventilation <sup>4</sup>. He was managed to wean from the mechanical ventilation on the 14th day of hospitalization, and on control thorax CT shown significant regression <sup>4</sup>. In this patient, IL-6 level was determined to be 80 ng / L (normal value <6 ng / dL) when it was decided to start TCZ treatment <sup>4</sup>. In our case, after a single dose of TCZ treatment, the FiO<sub>2</sub> and PEEP values were significantly reduced, and the patient could be extubated.

In a study conducted in the early periods of pandemic in China, low doses (1-2 mg / kg / day) of corticosteroids, one of the immunomodulatory agents, were shown among the treatment regimens <sup>5</sup>. In various human studies, corticosteroids seem to be effective in reducing immunopathological damage, but there are concerns about the onset of the viral counterattack and side effects, including ARDS. For example, in a randomized controlled study, viral load was measured at regular intervals in non-intubated SARS-CoV patients and 2/3 of the infection in patients using corticosteroids compared to

placebo <sup>6</sup>. It was found that viral RNA concentration was higher after one week <sup>6</sup>.

It should also be kept in mind that WHO warns about lymphocytopenia and increase in proinflammatory responses due to glucocorticoid related stimulation of hypothalamic-pituitary-adrenal axis in viral diseases as Dengue <sup>7</sup>. Although our case has been shown to lead to a rapid recovery after TCZ treatment, we believe that more cases should be examined in order to determine the effectiveness and timing of TCZ treatment in Covid-19 patients.

### Conflict of interest

The authors declare that they have no conflict of interest.

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