A case report of severe acute respiratory syndrome coronavirus-2 infected patient treated with infliximab

Mahdi Ghatrehsamani[1], Jafar Majidi[1], Ezat Shmsipoor Dehkordi[1], Akbar Soleymani Babadi[1], and Mohammad Mousavi[1]

[1]Shahrekord University of Medical Science

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Abstract

Extensive immune response associated inflammation is the major reason for the pathological outcome of COVID-19 infection. Infliximab is an anti tumor necrosis factor (anti-TNF) drug that is used to reduce inflammation through TNF-α inhibition. Inhibition of main inflammatory cytokine such as TNF-α may has a potential effect in COVID-19 treatment. Here, we report the clinical outcome associated with Infliximab treatment in a 65-year-old woman with confirmed COVID-19 infection. Infliximab therapy was started on day 9th, patient demonstrated clinical improvement and recovery from COVID-19. Our findings suggest that the association of TNF-α inhibition and clinical management together contributes to COVID-19 patient survival.

Abstract

Extensive immune response associated with inflammation is the primary reason for the pathological outcome of COVID-19 infection. Infliximab is an antitumor necrosis factor (anti-TNF) drug used to reduce inflammation through TNF-α inhibition. Inhibition of main inflammatory cytokine such as TNF-α may have a potential effect in COVID-19 treatment. Here, we report the clinical outcome of Infliximab treatment in a 65-year-old woman with confirmed COVID-19 infection. Infliximab therapy was started on day ninth; the patient demonstrated clinical improvement and recovery from COVID-19. Our findings\ suggest that the association of TNF-α inhibition and clinical management contributes to COVID-19 patient survival.

Introduction Novel Coronavirus 2019 (COVID-19), also known as Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was first reported in February 2019 in Wuhan, China[1]. Common symptoms of COVID-19 include fever, cough, fatigue, shortness of breath, myalgia, sputum production, headache, diarrhea, anorexia, ARDS, arrhythmia, acute kidney damage, varying degrees of liver damage, and septic shock[2,3]. Antibodies against tumor necrosis factor-alpha (TNF-α), such as infliximab, are increasingly being used to treat rheumatologic conditions such as rheumatoid arthritis, ankylosing spondylitis, and other diseases like inflammatory bowel disease and psoriasis[4]. Conversely, infliximab might also remit an aggravate immune response during COVID-19 infection, resulting in a potentially protective effect. The efficacy of infliximab in the COVID-19 treatment is unclear. In this study, we report a case of severe covid-19 who was treated with infliximab, leading to disease remission and discharge of a patient in good condition.

Case Description

A 65-year-old woman presented to the COVID-19 clinic of the hospital with complaints of fever, cough, myalgia, and dyspnea for five days. The patient underwent real-time PCR (RT-PCR) for SARS-CoV-

2 infection test and chest CT scan. The chest CT scan was normal (Figure 1a), but the PCR test for COVID-19 was positive. She was treated at home with naproxen 1000 mg per day and bed rest. Six days later, she returned to the hospital with a dry cough, tachypnea, and dyspnea. On admission, the patient's respiratory rate was 31breath/min, and SPO2 was 83%, which reached 93% with 5 liters of nasal oxygen. The patient's blood pressure was 100/70 mm Hg, and her temperature was 37.1C@. CT scan was performed again, and lung involvement was found multifocal, bilateral ground-glass pattern (GGO) in both lungs' lower and middle lobes (Figure 1b). The patient was treated with remdesivir 200mg in 0.9% Sodium Chloride 250ml IV infused over 60 minutes on the first day, then 100 mg daily on days 2-5, Enoxaparin 60mg every 12 hours subcutaneous, methylprednisolone 1 mg/kg/day infused in two divided doses in 0.9% Sodium Chloride 250ml, famotidine 40 mg PO every 12 hours, Diphenhydramine Hydrochloride 25 mg orally every 6 hours, paracetamol 500mg every 6 hours PO and Bromhexine orally 8mg three times a day. Despite the treatments, the patient's respiratory distress worsened with tachypnea and dry cough. The new CT showed significantly increased lung involvement associated with COVID-19 infection. There are widespread GGO's and crazy paving (figure 1c). Blood oxygen saturation percentage dropped to 76%. On day ninth, Remicade(Infliximab) was infused to the patient at a dose of 4 mg / Kg, after receiving negative results for PPD, Hbs Ag, HCV Ab, HIV Ab tests, and obtaining the consent form. Seventy-two hours after infusion, the general condition improved, shortness of breath disappeared and the SPO2 increased by 89 and 99% with reservation. One week after the infusion, there was no sign of respiratory distress, and the chest CT showed a significant reduction in lung involvement (Figure 1d). Cough and shortness of breath were stopped on the fifth day after infusion. The recovery process continued in the following days, and she was discharged one week after Remicade infusion. One month after receiving the drug, nearly the patient has returned to her pre-Covid infection condition, and chest CT scan showed mild GGOs pattern involvement (Figure 1e). The laboratory findings of the patient are listed in table1.

Discussion

COVID-19 disease might show different responses to different therapy because of differences in immune system function [5]. The previous study strongly supports a relationship between severe COVID-19 mortality and inflammation[6]. Studies show that 5-10% of Covid-19 patients develop cytokine storm, which can be fatal. Cytokine storm is observed in other conditions such as infections, autoimmune disorders, and hematological malignancies. When a cytokine storm occurs, the balance between pro-inflammatory and anti-inflammatory cytokines is disturbed, causing tissue damage[7]. Different cytokines are involved in different etiologies. Specific cytokines in covid-19 help differentiate between clinical intensities, mainly TNF-α, IL-1 β, IL-1Ra, IL-6, IL-7, IL-10, and IP-10[8]. TNF-α is a major pro-inflammatory cytokine responsible for inflammation consequences in COVID-19[9]. Thus, TNF-α contributes to the tissue inflammation of COVID-19.

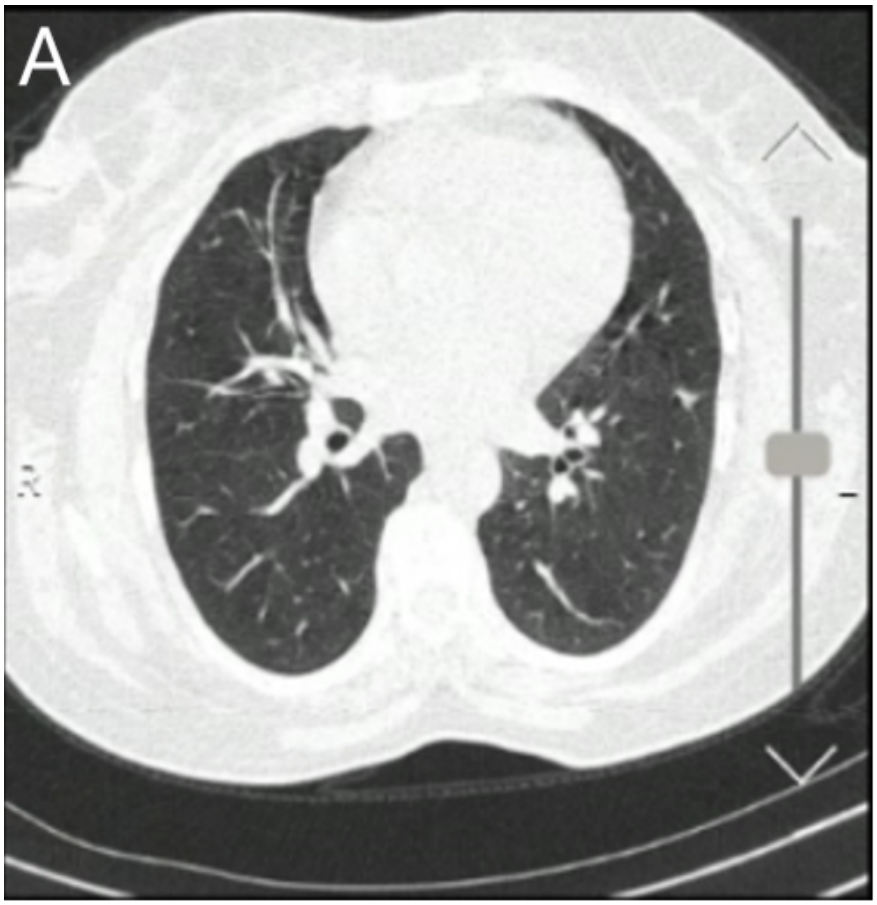
The reintroduction of oxygen may increase oxidative stress, which leads to the enhancement of inflammation[10]. Thus, treatment could be more effective before patients go on a ventilator. In the present case, our covid-19 patient did not respond to the immunosuppressive or antiviral drugs such as Methylprednisolone and Remdesiver. The patient was treated with infliximab before chose of the ventilator. A rapid disease remission and enhancement of SPO2 were found after administration of infliximab.

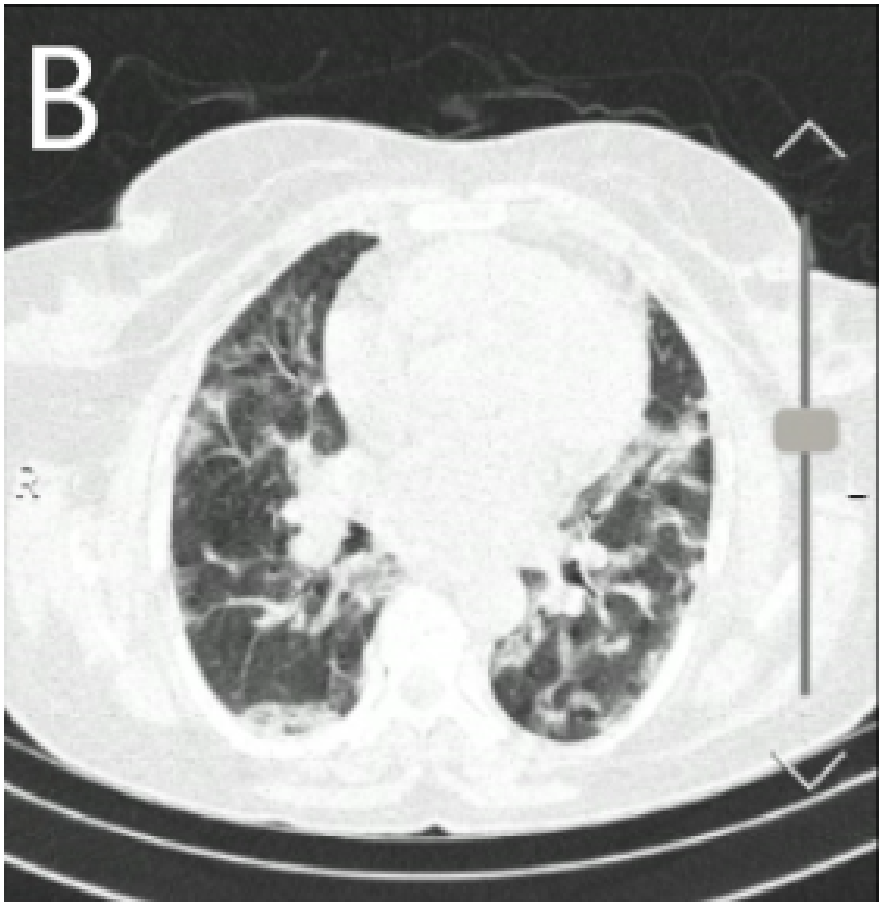
Conclusion

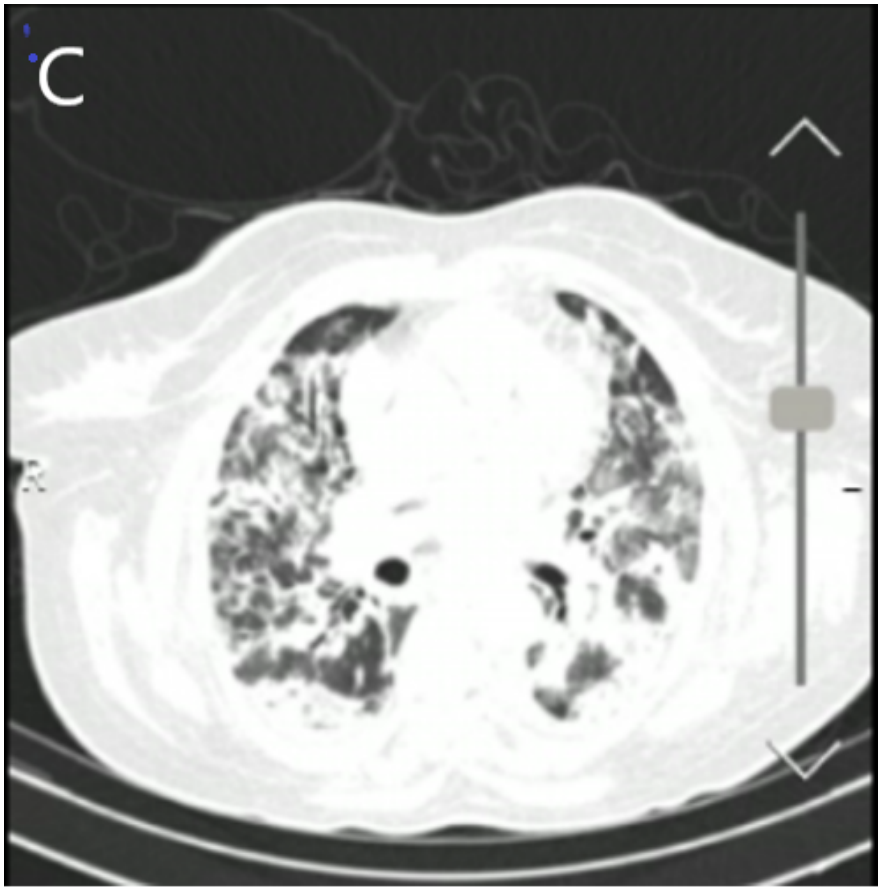
This report introduces the potentially beneficial effects of infliximab in the treatment of COVID-19 patients. Inhibition of TNF-α via infliximab may reduce the COVID-19 disease progression. The ventilator may increase complications in the COVID-19 patient, so TNF-α inhibition should occur before the ventilator's use. Large randomized study samples are necessary to investigate the efficacy of infliximab, and combinations with other immunomodulating drugs like Anakinra or chemokine inhibitors may reveal new treatment guidelines for COVID-19 patients.

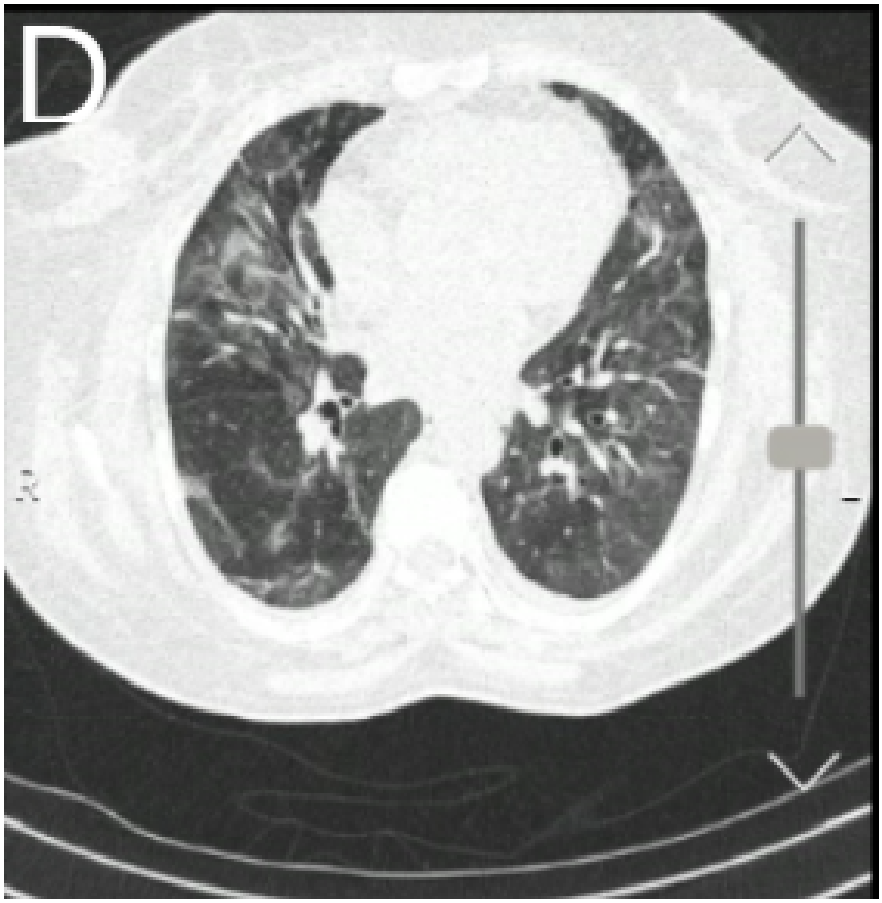
Conflict of interest

There is no competing of interest to declare.









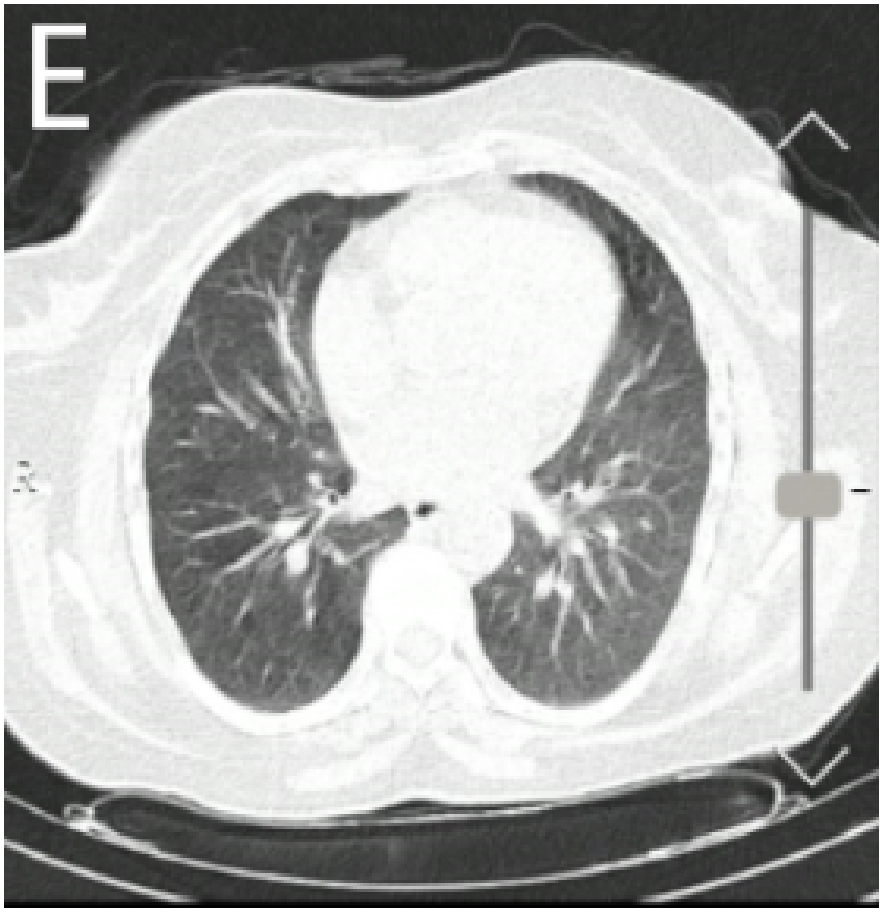


Figure 1. Chest CT scan result of patient.

Table

Table 1. The laboratory results during hospitalization:

Day 14th after infusion	Day 7th after infusion	Infliximab infusion day	Admission day
94	89	76	59
139.6	522	243	200
310	8560	673	113
437	464	526	341
Negative	Negative	2+	1+
97	98	358	119
12	13	18	11
0.8	0.8	0.9	0.9
48	-	48	17
44	40	42	42
30	27	24	24
163.4	-	23	-
7500 12.8 385000 33.1% 60%	11500 12.7 228000 15.3% 79.7%	8300 12.8 131000 9.7 85.2	4000 11.6 156000 19.2% 77.3%

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