

Inflammatory cytokines depletion for severe COVID-19 infectious pneumonia: a case report

Bo Yang

Internal Medicine (Nephrology & Endocrinology), Naval Medical Center of PLA, Second Military Medical University <https://orcid.org/0000-0003-0680-1469>

Jing Yang

Internal Medicine (Nephrology & Endocrinology), Naval Medical Center of PLA, Second Military Medical University

Lan Zhou

Intensive care unit, Naval Medical Center of PLA, Second Military Medical University

Cheng Xue

Division of Nephrology, Changzheng Hospital, Second Military Medical University

Hongxian Li

Internal Medicine (Nephrology & Endocrinology), Naval Medical Center of PLA, Second Military Medical University

Weifeng Hu

Internal Medicine (Nephrology & Endocrinology), Naval Medical Center of PLA, Second Military Medical University

Nanmei Liu (✉ 13585996275@163.com)

Internal Medicine (Nephrology & Endocrinology), Naval Medical Center of PLA, Second Military Medical University

Case Report

Keywords: COVID-19, inflammatory cytokines depletion, Double filtration plasma pheresis, convalescent plasma, Tocilizumab, case report

DOI: <https://doi.org/10.21203/rs.3.rs-34626/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background

In the severe infected COVID-19 patients, besides the viral pneumonia, multi-organ/system injury could be observed. Recognizing and correcting the key and immediate dysfunctions may reduce the mortality.

Case presentation

Here, we report a male patient with severe SARS-CoV-2 infection from isolation Ward- Guanggu Branch of Hubei Province Maternity and Childcare Hospital, who is treated with combined inflammatory cytokines depletion therapy and convalescent plasma. The multi-modal therapy ultimately resulted in improvement of respiratory function and removal from mechanical ventilation. The case of ARDS with severe SARS-CoV-2 infection indicated the potential benefit of convalescent plasma and inflammatory cytokines depletion through combined measurements including double filtration plasma pheresis and Tocilizumab.

Conclusion

It is not safe to draw causal conclusions between cytokine depletion and clinical manifestations improvement with only one case, while this would be a potential research direction in facing the COVID-19 crisis.

Background

According to the latest World Health Organization (WHO) bulletin, the coronavirus disease 2019 (COVID-19) epidemic that began in December 2019 has caused more than 4,731,458 infections and 316,169 deaths worldwide. [1] The disease is caused by a type of novel coronavirus that was first discovered in Wuhan, China, and has since affected all provinces within the country, then spread globally. On January 30th, the WHO listed the situation as a public health emergency of international concern.1 COVID-19 was caused by SARS-CoV-2 infection, which is a novel member of coronavirus family. In the severe infected patients, besides the viral pneumonia, multi-organ/system injury could be observed. Since there is no specific antiviral for COVID-19, supportive care in ICU plays a crucial role in patient management. Recognizing and correcting the key and immediate dysfunctions may reduce the mortality.

we reported a previously healthy 66-year-old man infected with SARS-CoV-2. The disease progressed rapidly and the patient was transferred to ICU. ECMO was set up later on. With the time bought by ECMO and other supportive care, convalescent plasma and multiple cytokine depletion measurements including Double filtration plasma pheresis and Tocilizumab were performed. The patient responded to the treatments and ECMO was discontinued one week later.

Case Presentation

On March 14th, 2020, a 66-year-old previously healthy male patient were referred to the isolation ward in Guanggu Branch of Hubei Province Maternity and Childcare Hospital. He has had a high fever and non-productive cough for twenty days. On March 4th, 2020, he visited a local clinic for his symptoms. His oropharyngeal swab specimen was collected there and tested positive with SARS-CoV-2 RT-PCR assays, along with the chest CT showing ground-glass opacity in both lungs, which indicated viral pneumonia. Then he was admitted to the local hospital and be given supportive therapy and accumulated 600 mg methylprednisolone in ten days. However, the shortness of the breath deteriorated while the SPO₂ decreased to 85%-89% in the condition of non-invasive ventilation at the time of transferring. On examination, his temperature was 36.4° C, pulse 86/min, respiratory 21/min, and blood pressure 118/64 mmHg. Supportive care was then provided in the isolation ward and lab tests were performed also (table 1). On March 15th, the SPO₂ decreased further (80%-85%) with high-flow oxygen therapy (60L/min). Arterial blood gas analysis showed pH 7.41, PO₂ 72 mmHg and PCO₂ 55 mmHg. Intubation and mechanical ventilation were administrated. 10 cmH₂O positive end-expiratory pressure and 80% inspired oxygen were applied.

The next day, patient's symptom of dyspnea and chest tightness deteriorated and norepinephrine infusion is required for maintaining normal blood pressure. Veno-venous Extracorporeal Membrane Oxygenation (ECMO) was initiated and the inspired oxygen was down-regulated to 40%. After the procedure, SPO₂ increased to 98%-100% and BP 110/70mmHg. On March 19th, patient's serum IL-6 was tested and the result revealed a significantly high IL-6 level. 400 mg intravenous Tocilizumab was administrated, however, the IL-6 level increased even more the following day (Figure 1 A). 400 mg intravenous Tocilizumab was repeated. At the same time, the patient also received Continuous VenoVenous HemoDiaFiltration (CVVHDF) treatment daily from March 19th to March 22nd in order to decrease the IL-6 level quickly. However, the bedside chest X-ray still revealed severe pneumonia and the clinical manifestations did not improve (Figure 2). The inflammatory cytokines were still at high level. Continuous renal replacement therapy (CRRT) protocol was changed to Double filtration plasma pheresis (DFPP) with a plasma separator (plasmaflow-08w, Asahi Kasei) and a plasma fractionator (EC-20W, Asahi Kasei) three times from 23rd to 25th before it returned to CVVHDF in 26th. The estimated plasma volume was set as 3L, the substitution fluid was albumin solution, blood flow rate 100mL/min, plasma flow rate in separator 30mL/min, and waste flow rate 3.0mL/min. From 16th to 25th March, the patients received multiple blood transfusion (including 400mL convalescent plasma) to compensate the volume loss caused by ECMO and CRRT bypass. At 25th, March, due to the anticipation of prolonged mechanical ventilation, tracheotomy was performed. With the time bought by ECMO and CRRT, patient's homeostasis recovered, along with the recovering of chest imaging. At 27th, the ECMO discontinued according to the ECMO expert evaluation. The SPO₂ kept 100% in the condition of mechanical ventilation after the ECMO discontinuation. Since the hemodynamics and blood gas improved, all the intravenous catheters were removed at March 28th. Supportive care continued for several days then the patient was been transferred to non-ICU isolation ward. The typical inflammatory markers during this period of time were shown in

figure 1 while the D-dimer and platelet results should be interpreted with caution due to the anticoagulants use.

Discussion And Conclusions

In most of severe COVID-19 patients, acute respiratory distress syndrome (ARDS) is usually the most obvious manifestation and is the leading cause of mortality. [2] In case of failing maintain ideal SPO_2 with mechanical ventilation, ECMO is required. Only with the stabilized hemodynamics and SPO_2 , underlying disease progression could be tackled. Early and sufficient supportive care can buy time for inflammation clearance.

Emerging evidence suggests that cytokine storm syndrome exists in severe COVID-19 patients.[3] And it may contribute to the conversion from non-severe pneumonia to ARDS or even MODS. There are also research suggesting monitoring IL-6 to evaluate the cytokine storm syndrome in the severe cases. [4] In our case, we applied the suggestion and conducted investigational therapy of blocking IL-6. [5] In addition, multiple measurements including DFPP and Tocilizumab are also used to remove the cytokines from the plasma. Within the one-week intensive care the patient's condition improved significantly. Previous study has already revealed the potential benefit of using convalescent plasma in COVID-19. [6] The use of Tocilizumab in COVID-19 is been tested but no results reported so far. Although there is no solid evidence supporting the use of DFPP in COVID-19, the rationale for conducting DFPP is also the existence of cytokine storm and the high level of IL-6. Previous studies verified the effectiveness of DFPP in selectively removing pathogenic substances. [7–9]

In summary, it is not safe to draw causal conclusions between cytokine depletion and clinical manifestations improvement with only one case, while this would be a potential research direction in facing the COVID-19 crisis.

Abbreviation List

SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

COVID-19 = coronavirus disease 2019

ECMO = Extracorporeal Membrane Oxygenation

CVVHDF = Continuous Venovenous Hemodiafiltration

CRRT = Continuous renal replacement therapy

DFPP = Double filtration plasma pheresis

ARDS = Acute respiratory distress syndrome

Declarations

Funding: Top Medical Youth Training Project of PLA (19QNP017); Guanggu Branch of Hubei Province Maternity and Childcare Hospital Fund (2020-FYGG-088)

Acknowledgements

None.

Authors' contributions

All the authors read and approved the final manuscript. BY was the main contributor to drafting the manuscript. JY, LZ, WH, XZ and ML contributed to the data collection.

Availability of data and materials

All the data supporting our findings are contained within this article.

Ethics approval and consent to participate

The study was conducted in accordance with Declaration of Helsinki and ethically approved by the Ethics Committee of the Naval Medical Center of PLA, Second Military Medical University.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Disclosure

Any of the therapeutic measurement was followed by informed consent from the patient or proper surrogates.

References

1. Coronavirus disease 2019 (COVID-19) Situation Report – 120. 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200519-covid-19-sitrep-120.pdf?sfvrsn=515cabfb_2.
2. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med.* 2020. doi:10.1007/s00134-020-05991-x.
3. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet.* 2020;395:1033–4. doi:10.1016/S0140-

6736(20)30628-0.

4. Liu T, Zhang J, Yang Y, Ma H, Li Z, Zhang J, et al. The potential role of IL-6 in monitoring severe case of coronavirus disease 2019. medRxiv. 2020;:2020.03.01.20029769. doi:10.1101/2020.03.01.20029769.
5. Our Commitment to Providing Ongoing ACTEMRA Information During the COVID-19 Pandemic. 2020. <https://www.actemrainfo.com>.
6. Chen L, Xiong J, Bao L, Shi Y. Convalescent plasma as a potential therapy for COVID-19. Lancet Infect Dis. 2020;20:398–400. doi:10.1016/S1473-3099(20)30141-9.
7. Prouvot J, Aglaé C, Daniel L, Moranne O. A catastrophic antiphospholipid syndrome complicated with heparin-induced thrombocytopenia, successfully managed with double filtration plasmapheresis, steroids and a direct thrombin inhibitor. BMJ Case Rep. 2019;12. doi:10.1136/bcr-2019-231161.
8. Iwami D, Miura M, Chiba Y, Ota M, Matsumoto T, Hotta K, et al. Optimal Settings for Double Filtration Plasmapheresis With Targeted Removal Rate of Preexisting Antibody in Antibody-Incompatible Kidney Transplant. Transplant Proc. 2018;50:3478–82. doi:10.1016/j.transproceed.2018.05.023.
9. Tishko V V, Sokolov AA, Belskih AN, Ivanov AM, Meshkova ME, Skorinova TS. Impact of double filtration plasmapheresis on adhesion molecules levels in patients with stable coronary heart disease after coronary stenting. Atheroscler Suppl. 2017;30:92–8. doi:10.1016/j.atherosclerosis.2017.05.024.

Table

Table 1 lab tests results of the patient at referring

	results	reference range
WBC count	12.4	3.5-9.5 *10 ⁹ /L
lymphocyte	6.8	20-50 %
monocyte	3.9	3-10 %
eosinophil	0.1	0.4-8 %
basophil	0.0	< 1 %
neutrophil	89.2	40-75 %
RBC count	4.38	4.3-5.8 *10 ¹² /L
Hb	141	130-175 g/L
packed cell volum	40.1	40-50 %
mean corpuscular volume	91.7	82-100 fL
mean corpuscular hemoglobin concentration	32.1	27-34 pg
mean corpuscular hemoglobin	350	316-354 g/L
red blood cell volume distribution width	11.8	10.9-15.4 %
platelet count	141	125-350 *10 ⁹ /L
mean platelet volume	10.9	8-10 fL
serum total bilirubin	8.0	3.4-20.5 umol/L
Unconjugated bilirubin	4.9	0-14 umol/L
conjugated bilirubin	3.1	<8.6 umol/L
serum total protein	61.4	64-83 g/L
albumin	26.1	35-52 g/L
globulin	35.3	20-40 g/L
albumin/globulin	0.74	1-2.4
ALT	53.1	0-55 U/L
AST	36.1	5-34 U/L
ALP	93	40-150 U/L
gamma-glutamyl transferase	64	12-64 U/L
bile acid	3.5	<9.67 umol/L

lactate dehydrogenase	752	125-220 U/L
blood urea nitrogen	8.9	3.2-7.4 mmol/L
sodium	139	136-145 mmol/L
potassium	4.5	3.5-5.1 mmol/L
chlorine	111	98-108 mmol/L

Figures

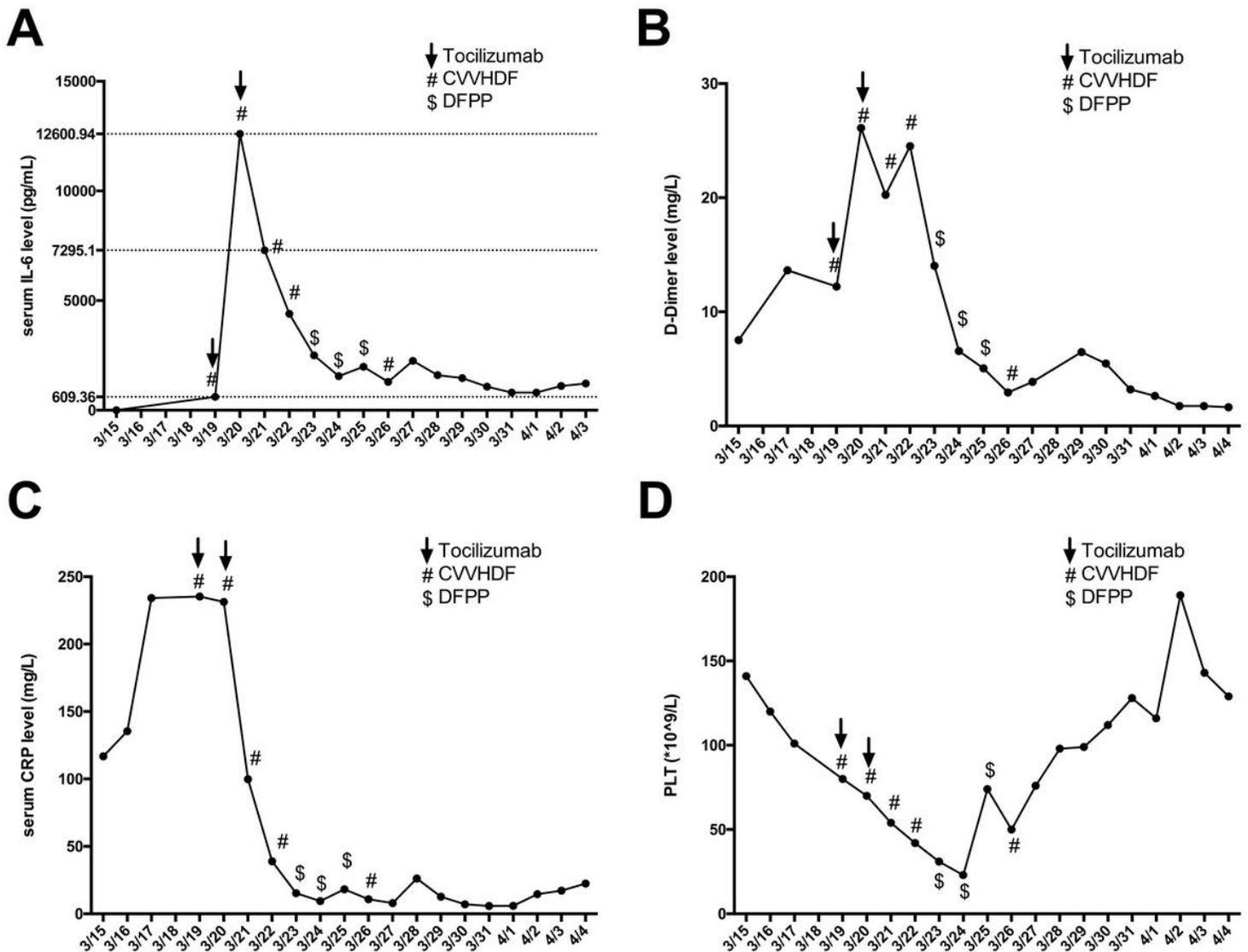


Figure 1

Typical inflammatory markers of the patient: A) Serum IL-6 level (The lab normal range is < 10pg/mL); B) D-Dimer (The lab normal range is < 0.55 mg/L); C) Serum C-reactive protein (The lab normal range is < 10 mg/L); D) Platelet level (the lab normal range is [125, 350] $\times 10^9/L$)

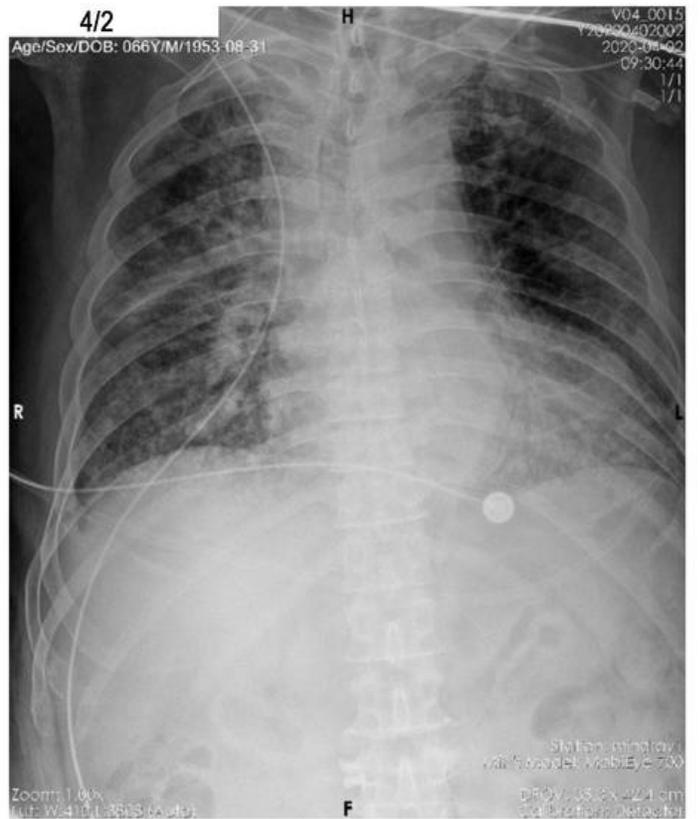


Figure 2

Chest X-ray images of the patient