Efficacy and safety of convalescent plasma therapy for severe COVID-19 patients：case series study and literature review

Jinbao Huang (huangnbao0@126.com)

The People's Hospital Affiliated to Fujian University of Traditional Chinese Medicine;

Changqing Lan

Fuzhou Pulmonary Hospital of Fujian, Educational Hospital of Fujian Medical University;

Research Article

Keywords: COVID-19, SARS-CoV-2, convalescent plasma, Tomography, X-ray computed

Posted Date: January 4th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1223109/v1

Abstract

Background

Coronavirus disease 2019 (COVID-19) is a new acute respiratory infectious disease which can lead to multiple organ dysfunction in severe patients. However, it is still a lack of effective antiviral drugs for COVID-19. Herein we investigated the efficacy and safety of convalescent plasma (CP) in the treatment of severe COVID-19, with an attempt to explore new therapeutic method.

Methods

Clinical data of three imported severe COVID-19 patients with CP treatment, who were under quarantine and treated in a designated COVID-19 hospital from March 2020 to April 2020, were collected and analyzed.

Results

The three patients were clinically classified as severe type, including one male and two females, aged 57, 59 and 65 years old, respectively. The main underling diseases included hypertension, diabetes, sequela of cerebral infarction and postoperative thyroid adenoma. The common symptoms included cough, fever and short of breath. All the patients received antiviral drugs and other supportive treatments. Additionally, CP treatment was also administrated for them. Forty-eight to seventy-two hours after CP transfusion, all the patients improved with alleviated symptoms, elevated arterial oxygen saturation, decreased C-reactive protein and interleukin-6 markers. And the total lymphocytes, T lymphocytes (CD3+) and their subsets (CD4+, CD8+) also obviously increased. Repeated chest CTs also showed obvious absorption of lesions in bilateral lung. Only one patient had mild allergic reaction during CP infusion, but no severe adverse reactions were found.

Conclusions

The early application of CP for severe COVID-19 patients can improve the condition rapidly, and the therapy is generally effective and safe.

1. Introduction

Coronavirus disease 2019 (COVID-19) induced by severe acute respiratory syndrome-associated coronavirus-2 (SARS-CoV-2))is a new acute respiratory infectious disease, which can lead to multiple organ dysfunction in severe patients.[1] Worryingly, the infection remains worsen in most countries and areas. As of January 2, 2022, COVID-19 epidemic has caused more than 289 million cases and over 5.44 million deaths worldwide (https://coronavirus.jhu.edu/map.html). However, it is still a lack of effective antiviral drugs for COVID-19.[1, 2] Convalescent plasma (CP) therapy has been used for treating influenza for more than a century. A meta-analysis of 32 studies showed that CP therapy could reduce mortality in influenza virus patients.[3] Currently, several clinical studies have shown that CP therapy can significantly improve the clinical symptoms and prognosis of severe and critically ill COVID-19 patients.[4–6] And a randomized controlled trial in China further revealed that early infusion of CP had a better therapeutic effect in COVID-19 patients, and more benefits could be obtained in severe patients than in life-threatening patients.[7–8] This study retrospectively analyzed the clinical data of three severe COVID-19 patients who received CP therapy and got well curative effect, so as to further improve the understanding of the application value of this therapy in severe COVID-19 patients.

2. Materials And Methods

Patients

Clinical data, including epidemiology, clinical manifestations, laboratory examinations, imaging results and treatment outcomes, were collected from three imported severe COVID-19 patients who were under quarantine and treated in a designated hospital in Fuzhou from March 2020 to April 2020. The last follow-up was completed on May 7, 2020. Respiratory tract specimens (throat swabs) of all enrolled cases were positive for SARS-CoV-2 RNA by reverse transcription-polymerase chain reaction (RT-PCR) qualitative detection. All patients met the diagnostic criteria according to the Diagnosis and Treatment Program for COVID-19 issued by the National Health and Family Planning Commission. [9]

The disease severity in COVID-19 patients were classified as follows : Mild COVID-19 was defined as mild clinical symptoms without pneumonia on chest imaging; Moderate COVID-19 was defined as clinical symptoms (e.g., fever and respiratory symptoms) with limited pneumonia on chest imaging; Severe COVID-19 was defined as any of the following: respiratory distress and respiratory rate ≥ 30 breaths per minute, or in resting state, oxygen saturation ≤ 93% on room air, or arterial partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) ≤ 300, or significant lung lesion progression ＞ 50% within 24 to 48 hours on chest imaging; Critically ill (Life-threatening) COVID-19 was defined as respiratory failure requiring mechanical ventilation, or shock, or other organ failure (apart from lung) requiring intensive care unit (ICU) monitoring. [10] All patients in our study were clinically classified as severe COVID-19 according to the above criteria.

During the period of hospitalization, respiratory tract specimens (throat swabs) of all patients were continuously monitored for viral shedding until the samples were negative for SARS-Cov-2 RNA for two consecutive days (at least 24 hours apart). This study was approved by the Ethics Committee of the People's Hospital Affiliated to Fujian University of Traditional Chinese Medicine, and the patients provided informed consents for paper publication.

2.2 Collection, storage and use of CP

According to the Clinical Treatment Scheme of COVID-19 Convalescent Plasma,[11] the CP was obtained from COVID-19 patients who had recently recovered and discharged from hospital. Before venous blood sample collection, all the donors had undergone strict medical screening and evaluation, including meeting the quarantine and discharge standards according to the Diagnosis and Treatment Program for COVID-19,[9] and at least 2 weeks after discharge. Respiratory specimens were negative for SARS-CoV-2 and other viral nucleic acids, and serum tests for hepatitis B virus, hepatitis C virus, human immunodeficiency virus (HIV) and syphilis were negative. Serum SARS-CoV-2 IgG antibody dilution titers of three donors were at least 1:80, and the total CP infusion dose of each patient was 200 to 400 ml (4 to 5 ml/kg) (Table 1). Early CP administration was defined as CP infusion was initiated within one week after admission and two weeks following symptom onset. [12-14] Adverse reactions of CP infusion were closely monitored during CP treatment, and the first efficacy assessment, including clinical symptoms, oxygenation function, inflammatory markers, lymphocyte counts, chest CT manifestations, etc. , was performed 48 to 72 hours after transfusion.

3. Results

3.1 Plasma donors (Table 1)

Plasma was obtained from three COVID-19 patients who had recently recovered and discharged from the COVID-19 designated hospital in Fuzhou. Among the these donors, the anti-SARS-CoV-2 IgG titer in one case (Case 1) was ≥1:160, and the antibody titers in the other two cases (Case 2 and Case 3) were ≥1:80. One patient (Case 2) with blood type A and negative for RhD received plasma from a donor with blood type A and positive for RhD, and the other two recipients were treated with complete blood type ABO and Rh-compatible CP.

3.2 Clinical manifestations, treatment and prognosis of plasma receptors (Tables 1, 2)

During the study, three severe COVID-19 patients with one male and two females were enrolled and received CP transfusion. These patients aged 57, 59 and 65 years old, respectively. The main underling diseases included hypertension, diabetes, cerebral infarction and postoperative thyroid adenoma. The common symptoms included cough, fever and short of breath. Blood laboratory examinations showed a decrease in arterial oxygen saturation (SaO_2), an increase in C-reactive protein (CRP) and interleukin-6 (IL-6), and a decrease in total lymphocytes (CD45+), T lymphocytes (CD3+) and their subsets (CD4+, CD8+) (Figure 1). Chest CT showed multiple patchy and nodular ground glass opacies, consolidation and linear opacities in both lungs (Figure 2A－2B, Figure 3A－3B, Figure 4A－4B). After admission, all the patients received transnasal catheter oxygen therapy, and were given antiviral treatment with abidol, hydroxychloroquine, sulfatelopinavir/ritonavir or recombinant human interferon α-2b spray, and one patient was treated with a combination of antibiotic. The other medicines including Immunostimulant (Thymalfasin), Anti-inflammatory agents (Xuebijing injection and ulinastatin) and Chinese herbal medicine were also administrated.

On the basis of conventional treatment after admission, the condition of these patients all continued to worsen. Then they all received additional CP therapy. All the patients provided informed consents for CP treatment before transfusion. The CP transfusion volume was 400 ml (two consecutive days, 200 ml per day), 200 ml and 200 ml, respectively. Fourty-eight to seventy-two hours after CP transfusion, all the patients improved with alleviated symptoms, elevated SaO_2, decreased CRP and IL-6, and increased lymphocyte counts (Figure 1). Repeated chest CTs also showed obvious absorption of lesions in bilateral lung ((Figure 2C－2D, Figure 3C－3D, Figure 4C－4D). On days 9 and 30 after

CP transfusion, the above indicators continued to improve, and the patients were getting better until they were discharged stably. The latest outpatient follow-up was done on May 7th, 2020 when the patients remained well without signs of recurrence.

3.3 Adverse reactions related to CP transfusion (Table 2)

One patient (Case 2) developed a red rash with pruritus around the infusion site of the right upper extremity at 17 hours after CP transfusion, and the rash extended to the whole body with pruritus at 22 hours after transfusion. Considering the CP transfusion related allergic reaction, the patient received antianathylactic treatment with 10% calcium gluconate infusion and oral ebastines. Then the symptoms were gradually relieved after treatment, and the rash completely disappeared 5 days after CP transfusion. No severe adverse reactions were found in all the patients.

4. Discussion

To date, the COVID-19 influenza is still rapidly spreading all over the world. Clinical data from China has shown that the severe COVID-19 rate can be as high as 41.1%~48.3% in early stage of epidemic.[15, 16] Due to the rapid progression with high mortality in severe COVID-19 patients, effective treatment is urgently needed to control the deterioration of the disease. However, there are no current proven antiviral drugs that could effectively treat the novel virus.[17, 18] A multicenter trial showed that plasma therapy could accelerate the rate of viral negative conversion and clinical recovery in COVID-19 patients, shorten the length of hospital stay, and reduce the death risk by 35%.[7] Ibrahim et al. reported that early application of plasma therapy was helpful to accelerate clinical recovery and reduce mortality.[12] In a large retrospective case-control study, Xia et al. also showed that CP therapy improved clinical symptoms, reduced ICU admission risk, and reduced mortality (the death risk reduced by 50%).[19] And previous studies have also shown that early application of plasma on severe patients was more effective, while the overall benefit of CP in the extremely critical patients such as tracheal intubation or life-threatening condition was not significant.[7, 12, 19, 20] The three cases in our study were severe elderly patients with basic diseases such as diabetes and high blood pressure, but without endotracheal intubation. After admission, the condition of these patients all progressed rapidly and there was a high risk of developing critical illness. Then CP was administrated to them based on the conventional treatment. After the combined therapy, the symptoms were alleviated rapidly, the lung lesions were significantly absorpted, the inflammatory indexes were decreased, and the oxygenation function and cellular immune function were improved. The remarkable improvement of these patients suggests that the plasma treatment is an effective remedy for severe COVID-19 patients. Hegerova et al. reported that patients who received CP within one week after admission significantly reduced the death risk within 14 days (mortality was 0).[13] The CP treatment time of all patients in our study was within one week after admission (within 10 days after onset), which was significantly earlier than the time reported by Xia et al. (the median time from onset to CP was 45 days).[19] The significant improvement was achieved within 72 hours of CP treatment in our research, suggesting that early active CP therapy in severe COVID-19 patients becomes even more effective.

Notably, although the three patients improved significantly after CP, one of them (Case 3) remained positive for SARS-Cov-2 RNA for more than one month (33 days). At the beginning of the disease, the lymphocytes counts in the three patients all decreased, and the number of lymphocytes gradually increased after CP, which was consistent with previous report.[5] However, the lymphocytes counts in one patient (Case 3) were still lower than the normal standards 30 days after CP whereas the other two patients (Case 1, Case 2) all returned to normal. The prolonged viral removal in Case 3 was considered to be associated with a prolonged period of immunodeficiency. Additionally, the donor plasma antibody titer results showed that the titer in Case 1 was the highest (≥ 1:160), and the titers in the other two patients (Case 2, Case 3) were ≥ 1: 80, but the antibody titer in Case 3 was only weakly positive at 1:80. This suggested that this patient (Case 3) received the lowest antibody level of CP in these three patients, which may reduce the plasma efficacy.[19]

Additionally, only one patient (Case 2) had mild allergic reaction with erythema and pruritus at the early period of transfusion, but no other serious adverse reactions were found in the follow-up. As previously described in our paper, the blood type of this patient (Case 2) was type A and negative RhD which was a rare Rh blood type. She later received CP with blood type A and positive RhD, suggesting that the allergic reactionin this patient might be related to the treatment with incomplete Rh-compatible plasma, but other serious adverse reactions such as acutehemolytic transfusion reaction and shock response were not found. Generally, plasma treatment in our reserch was safe and reliable, consistent with the literature reports.[19, 21]

Notably, there are some limitations in our research. In the first place, this study was only performed with 3 patients without solid controls (directly compared to patients with CP and without CP treatment). And in the second place, the patients were also given other medications (including antiviral drugs, antibiotic, anti-inflammatory agents, immunostimulant and Chinese herbal medicine)/treatment. Hence, this does serve as one of the confounding factors. It could be that these might played an important role in recovery as well in synergy with CP treatment. However, the fact is that there are no proved effective antiviral drugs or other traditional therapy in our study for controlling the

novel virus. And the combined CP therapy was initiated after the condition got worse with conventional treatment. Additionally, as mentioned previously, the patients who received CP earlier can have more favorable clinical outcomes.[12] And the CP remedy in our study was all utilized in early disease course. Moreover, the first curative effect evaluation was assessed in a short time after CP transfusion (within 48 to 72 hours), and the findings which showed obvious improvement with clinical symptoms, radiological images and laboratory tests were encouraging. As a result, we think the marked efficiency should be mainly attributed to additional CP treatment.

In summary, the early application of CP for severe COVID-19 patients can improve the condition rapidly, and the therapy is generally effective and safe. This therapy can reduce the COVID-19 progression risk from severe to critical, lower the mortality rate,[22] and is helpful to raise the rescue success rate of severe patients. Due to the absence of effective anti-SARS-Cov-2 drugs, CP therapy is an alternative adjuvant method to treat severe COVID-19 patients.[22]

Declarations

Acknowledgement

We would like to thank Fujian Provincial Medical Treatment Clinical Expert Group for COVID-19, the nurses and clinical staff who provided care for the patient in Fuzhou Pulmonary Hospital of Fujian, as well as the patient for her willingness to participate in this study.

Authors' Contributions

JH conceived of the study, drafted the manuscript, and reviewed all drafts of the manuscript. CL managed the data collection, data analysis, prepared figures and drafted the manuscript. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflicts of interest for this work.

Data availability statement

The data used to support the findings of this study are available from the corresponding author upon request.

References

1. Chinese Medical Association Respiratory Branch, Chinese Medical Doctor Association Respiratory Physician Branch. Expert advice for COVID-19 Prevention and Control. Chin J Tuberc Respir Dis 2020;43(6):473–89.
2. Bloch EM. Convalescent plasma to treat COVID-19. Blood 2020;136(6):654–655.
3. Mair-Jenkins J, Saavedra-Campos M, Baillie JK, et al. The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. J Infect Dis 2015;211(1):80–90.
4. Shen C, Wang Z, Zhao F, et al. Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma. JAMA 2020;323(16):1582–1589.
5. Duan K, Liu B, Li C, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad Sci U S A 2020;117(17):9490–6.
6. Zhang L, Pang R, Xue X, et al. Anti-SARS-CoV-2 virus antibody levels in convalescent plasma of six donors who have recovered from COVID-19. Aging (Albany NY) 2020;12(8):6536–42.
7. Li L, Zhang W, Hu Y, et al. Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients With Severe and Life-threatening COVID-19: A Randomized Clinical Trial. JAMA 2020;324(5):460–70.
8. Casadevall A, Joyner MJ, Pirofski LA. A Randomized Trial of Convalescent Plasma for COVID-19-Potentially Hopeful Signals. JAMA 2020;324(5):455–7.

9. National Health Commission of the People's Republic of China. Diagnosis and treatment of the novel coronavirus pneumonia (Trial version 7) [D]. Published 2020. Accessed March 3, 2020. http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989/files/ce3e6945832a438eaae415350a8ce964.pdf
10. Military forward expert group. Diagnosis and treatment program of novel coronavirus infection disease in Military medical team for assisting Hubei (Trial version 2). Chin J Tuberc Respir Dis 2020;43(5): 414–420.
11. Clinical treatment protocol of convalescence plasma for COVID-19 patients (Trial version 2). [EB / OL]. [20200304].http://www.nhc.gov.cn/yzygj/s7658/202003/61d608a7e8bf49fca418a6074c2bf5a2/files/a5e00234915344c6867a3e6bcfac11b7.pdf
12. Ibrahim D, Dulipsingh L, Zapatka L, et al. Factors Associated with Good Patient Outcomes Following Convalescent Plasma in COVID-19: A Prospective Phase II Clinical Trial. Infect Dis Ther 2020:1–14.
13. Hegerova L, Gooley TA, Sweerus KA, et al. Use of convalescent plasma in hospitalized patients with COVID-19: case series. Blood 2020;136(6):759–62.
14. Rojas M, Rodríguez Y, Monsalve DM, et al. Convalescent plasma in Covid-19: possible mechanisms of action. Autoimmun Rev 2020:102554.
15. Chen L, Liu H, Liu W, et al. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. Chin J Tuberc Respir Dis 2020;43(3): 203–8.
16. Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. JAMA Neurol 2020;77(6):683–90.
17. World Health Organization Coronavirus disease (COVID-19) pandemic. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019. Accessed 9 June 2020.
18. Lu H. Drug treatment options for the 2019-new coronavirus (2019-nCoV). Biosci Trends. 2020;14(1):69–71.
19. Xia X, Li K, Wu L, et al. Improved clinical symptoms and mortality among patients with severe or critical COVID-19 after convalescent plasma transfusion. Blood 2020;136(6):755–9.
20. Liu STH, Lin HM, Baine I, et al. Convalescent plasma treatment of severe COVID-19: a propensity score-matched control study. Nat Med 2020;26(11):1708–13.
21. Joyner M, Wright RS, Fairweather D, et al. Early Safety Indicators of COVID-19 Convalescent Plasma in 5,000 Patients. medRxiv [Preprint]. 2020:2020.05.12.20099879. Update in: J Clin Invest. 2020 Aug 10.
22. Wardhani SO, Fajar JK, Wulandari L, et al. Association between convalescent plasma and the risk of mortality among patients with COVID-19: a meta-analysis. F1000Res 2021;10:64.

Tables

Table 1 Characteristics of three patients with convalescent plasma therapy

Characteristics	Case 1	Case 2	Case 3
Importing nation	Brazil	America	France
Nationality	Chinese	Chinese	Chinese
Age (years)	57	65	59
Sex	Male	Female	Female
Body weight (kg)	82	50	58
BMI (kg/m^2)	27.7	22.2	20.3
Disease type	Severe	Severe	Severe
Underlying disease	Hypertension, Sequela of cerebral infarction	Hypertension, diabetes	Postoperative thyroid denoma
Symptom	Cough, expectoration, fever, breathlessness, headache	Cough, breathlessness, appetite, excessive fatigue	Cough, fever, breathlessness, dry thorat
Chest CT feature	Multiple lesions	Multiple lesions	Multiple lesions
Complication	None	None	Hypovolemia, pulmonary bacterial infection
Anti-viral treatment	Abidol, hydroxychloroquine sulfate	Abidol, lopinavir/ritonavir	Human interferonα-2b spray
Antibiotic therapy	None	None	Ceftriaxon
Anti-inflammatory agent	Xuebijing injection, ulinastatin	Xuebijing injection, ulinastatin	Xuebijing injection, ulinastatin
Immunostimulant	Thymalfasin	Thymalfasin	Thymalfasin
Respiratory support	Ransnasal catheter oxygen therapy	Ransnasal catheter oxygen therapy	Ransnasal catheter oxygen therapy
Blood type of CPR	Type B, positive for RhD	Type A, negative for RhD	Type B, positive for RhD
Blood type of CPD	Type B, positive for RhD	Type A, positive for RhD	Type B, positive for RhD
SARS-CoV-2 IgG titer of CPD	Positive at 1∶160, Negative at 1:320	Positive at 1∶80, Negative at 1:160	Weakly positive at 1∶80, Negative at 1:160
Timing from onset to CP infusion (d)	7	10	10
Timing from admission to CP infusion (d)	2	2	7
Total CP volume (ml)	400	200	200
Adverse reaction related CP infusion	None	Mild alergic reaction	None

BMI: Body mass index; CP: Convalescent plasma; CPR: Convalescent plasma recipient; CPD:Convalescent plasma donor

Table 2 Dynamics of indicators during plasma therapy

Characteristics	Case 1	Case 2	Case 3
Pre-treatment of CP			
SaO_2 (%)	94	94	93
CRP (mg/L, normal range 0-10)	63.9	17.6	45.9
IL-6 (pg/ml, normal range <7.0)	59.9	29.3	44.3
CD3+ (cells/μL, normal range 955-2860)	550	966	541
CD3+CD4+ (cells/μL, normal range 550-1440)	355	421	305
CD3+CD8+ (cells/μL, normal range 320-1250)	186	528	228
Total lymphocyte (cells/μL, normal range 1530-3700)	952	1331	755
48-72 hours after CP treatment			
Symptom	Improvement	Improvement	Improvement
Lung lesion	Partially absorption	Partially absorption	Partially absorption
SaO2 (%)	97	96	96
CRP (mg/L)	25.8	5.7	9.1
IL-6 (pg/ml)	8.1	10.3	7.2
CD3+ (cells/μL)	818	1087	872
CD3+CD4+ (cells/μL)	550	537	583
CD3+CD8+ (cells/μL)	250	508	282
Total lymphocyte (cells/μL)	1298	1450	1239
Nine days after CP treatment			
Lung lesion	Sustained absorption	Sustained bsorption	Sustained absorption
SaO2 (%)	98	96	98
CRP (mg/L)	2.5	0.62	0.92
IL-6 (pg/ml)	< 1.5	< 1.5	< 1.5
CD3+ (cells/μL)	707	1282	958
CD3+CD4+ (cells/μL)	468	713	562
CD3+CD8+ (cells/μL)	235	561	358
Total lymphocyte (cells/μL)	984	1651	1239
30 days after CP treatment			
CD3+ (cells/μL)	1122	2466	813
CD3+CD4+ (cells/μL)	707	1041	545
CD3+CD8+ (cells/μL)	382	1345	259
Total lymphocyte (cells/μL)	1878	3203	1074
Timing from onset to a negative viral test result (d)	17	16	33
Hospital stay (d)	17	13	33

CD3+: T-lymphocyte, CD3+CD4+: CD4+ T-lymphocyte subset, CD3+CD8+: CD8+ T-lymphocyte subset, CP: Convalescent plasma, CRP: C-reactive protein, IL-6: interleukin-6, SaO_2: arterial oxygen saturation.

Figures

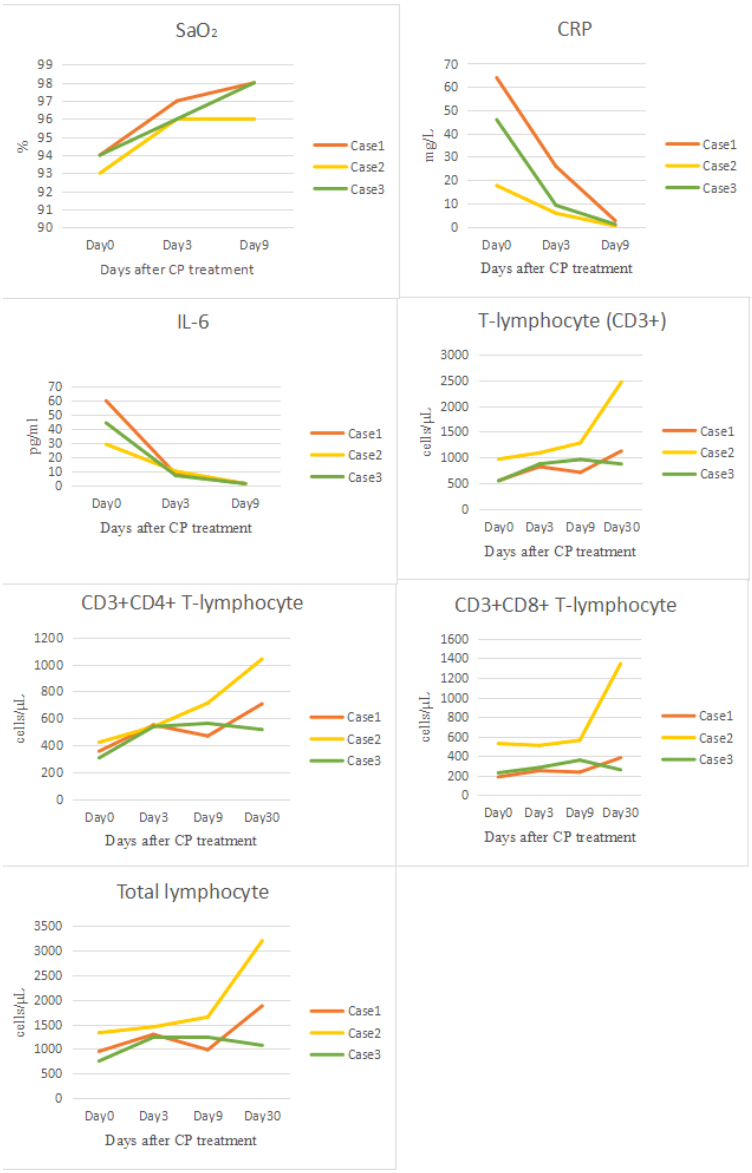

Figure 1

Dynamics of laboratory indicators after plasma therapy. Dynamics of laboratory indicators after plasma therapy. After plasma therapy, the results showed an increase in arterial oxygen saturation (SaO_2), a decrease in C-reactive protein (CRP) and interleukin-6 (IL-6), and an increase in total lymphocytes, T lymphocytes (CD3+) and their subsets (CD4+, CD8+).

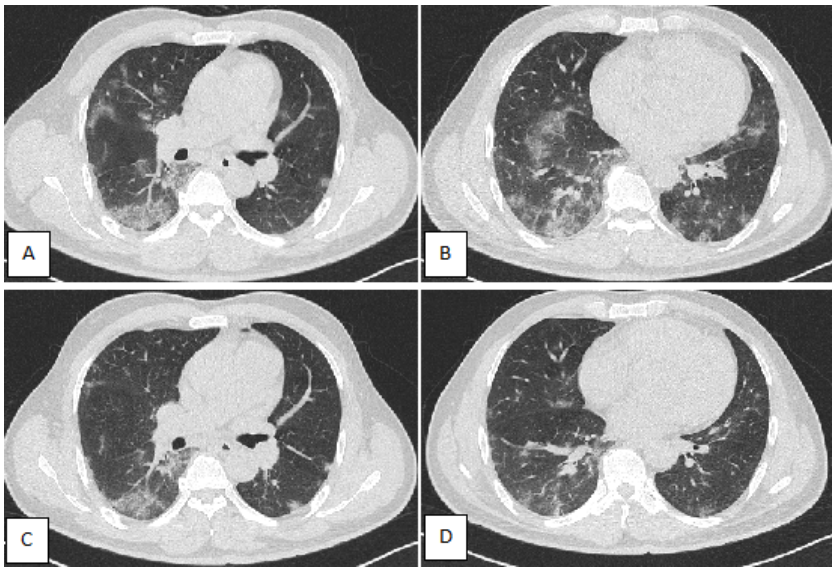

Figure 2

Case 1. On the second day of admission (the 7th day of onset), chest CT showed patchy and nodular ground glass opacies, consolidation and linear opacities in bilateral lung, mainly in both lower lungs (A, B). Seventy hours after plasma treatment, the lung lesions were significantly absorbed (C, D).

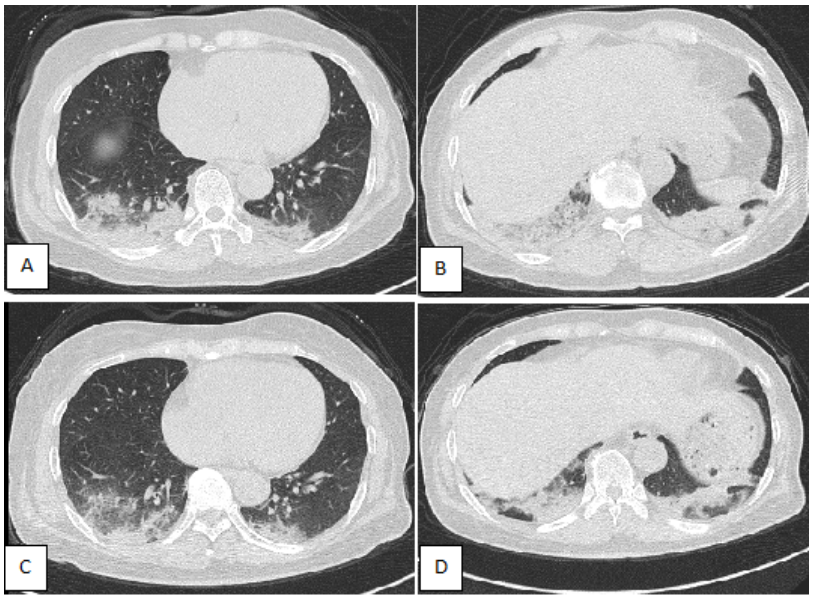

Figure 3

Case 2. On the second day of admission (the 10th day of onset), chest CT showed patchy consolidation and linear opacities in bilateral lung, mainly in both lower lungs (A, B). Seventy hours after plasma treatment, the lung lesions were significantly absorbed (C, D).

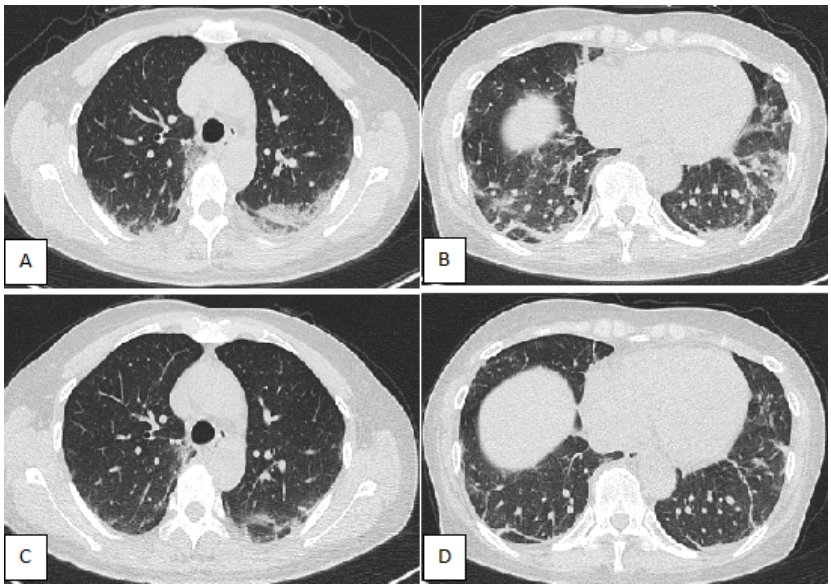

Figure 4

Case 3. On the 7th day of admission (the 10th day of onset), chest CT showed multiple patchy and nodular ground glass opacies, consolidation and linear opacities in bilateral lung, mainly in subpleural area (A, B). Fourty hours after plasma treatment, the lung lesions were significantly absorbed (C, D).