Observational Study

Medicine

OPEN

Convalescent plasma therapy for patients with severe COVID-19

A case series study

Jinbao Huang, MS[a], Heng Weng, BS[a], Changqing Lan, MS[b], Hongyan Li, BS[c,*]

Abstract

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

The clinical data of 3 imported patients with severe COVID-19 who underwent treatment with CP and who were quarantined and treated in a designated COVID-19 hospital from March 2020 to April 2020 were collected and analyzed.

The 3 patients, including a 57-year-old male, 65-year-old female, and 59-year-old female, were clinically classified as having severe COVID-19. The main underlying diseases included hypertension, diabetes, sequelae of cerebral infarction, and postoperative thyroid adenoma. The common symptoms included cough, fever, and shortness of breath. All patients received antiviral drugs and other supportive treatments. Additionally, CP treatment was administered. At 48 to 72 hours after the CP transfusion, all 3 of the patients exhibited an improvement and alleviation of symptoms, an elevated arterial oxygen saturation, and decreased C-reactive protein and interleukin-6 levels. The counts of the total lymphocytes and T lymphocytes (CD3+) and their subsets (CD4 + and CD8+) were also obviously increased. Repeated chest computed tomography also revealed obvious absorption of the lesions in the bilateral lungs. Only 1 patient had a mild allergic reaction during the CP infusion, but no severe adverse reactions were observed.

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

Abbreviations: SaO_2 = arterial oxygen saturation, CT = computed tomography, CP = convalescent plasma, COVID-19 = coronavirus disease 2019, CRP = C-reactive protein, IL-6 =interleukin-6, SARS-CoV-2 = severe acute respiratory syndrome-associated coronavirus-2.

Key words: convalescent plasma, COVID-19, SARS-CoV-2, x-ray computed tomography

1. Introduction

Coronavirus disease 2019 (COVID-19), which is induced by severe acute respiratory syndrome-associated coronavirus-2 (SARS-CoV-2), is a novel acute respiratory infectious disease that can lead to multiple-organ dysfunction in patients with severe disease.[1] The infection rate remains high in most countries. As of April 27, 2022, the COVID-19 pandemic has caused more than 511 million cases and over 6.22 million deaths worldwide (https://coronavirus.jhu.edu/map.html). However, there 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 demonstrated that CP therapy reduces mortality in patients with influenza.[3] Currently, several clinical studies have demonstrated that CP therapy can significantly improve the clinical symptoms and prognosis of severe and critically ill patients with COVID-19.[4–6] A randomized controlled trial in China further revealed that an early infusion of CP has a good therapeutic effect in patients with COVID-19 patients and that the therapeutic benefit is higher in patients with severe COVID-19 than in those with life-threatening COVID-19.[7,8] Nevertheless, there is also evidence against the benefit of CP.[9,10] This study retrospectively analyzed the clinical data of 3 patients with severe COVID-19 who underwent CP therapy and for whom CP therapy demonstrated good curative effects to further improve the understanding of the application value of this therapy in patients with severe COVID-19.

JH and HW contributed equally to this work.

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

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

[a] Department of Respiratory Medicine, People's Hospital Affiliated to Fujian University of Traditional Chinese Medicine, Fuzhou, China, [b] Department of Radiology, Fuzhou Pulmonary Hospital of Fujian, Educational Hospital of Fujian Medical University, Fuzhou, China, and [c] Department of Critical Care Medicine, People's Hospital Affiliated to Fujian University of Traditional Chinese Medicine, Fuzhou, China.

**Correspondence: Hongyan Li, BS, Critical Care Medicine, People's Hospital Affiliated to Fujian University of Traditional Chinese Medicine, No. 602 Middle 817 Road, Taijiang District, Fuzhou 350004, China (e-mail: 1353626039@qq.com).*

How to cite this article: Huang J, Weng H, Lan C, Li H. Convalescent plasma therapy for patients with severe COVID-19: A case series study. Medicine 2022;101:31(e29912).

Received: 8 January 2022 / Received in final form: 27 May 2022 / Accepted: 13 June 2022

http://dx.doi.org/10.1097/MD.0000000000029912

2. Materials and Methods

2.1. Patients

The clinical data, including epidemiological data, clinical manifestations, laboratory examination and imaging results, and treatment outcomes, were collected from 3 imported patients with severe COVID-19 who were quarantined 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 patients were positive for SARS-CoV-2 RNA by qualitative reverse transcription-polymerase chain reaction. 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.[11]

The disease severity in the COVID-19 patients was 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 a respiratory rate of ≥30 breaths/min in a resting state, an oxygen saturation of ≤93% in room air, an arterial partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) of ≤300, or significant lung lesion progression of >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 monitoring in the intensive care unit.[12] All patients in our study were clinically classified as having severe COVID-19 according to the above criteria.

During the period of hospitalization, respiratory tract specimens (throat swabs) of all 3 patients were continuously performed to monitor for viral shedding until the samples were negative for SARS-Cov-2 RNA for 2 consecutive days (at least 24 hours apart). This study was approved by the ethics committee of People's Hospital Affiliated to Fujian University of Traditional Chinese Medicine, and the patients provided informed consent for the publication of this paper.

2.2. Collection, storage, and use of CP

According to the Clinical Treatment Scheme of COVID-19 Convalescent Plasma,[13] CP was obtained from COVID-19 patients who had recently recovered and were discharged from the hospital. Before venous blood samples were collected, all donors underwent strict medical screening and evaluation, including meeting the quarantine and discharge standards according to the Diagnosis and Treatment Program for COVID-19,[10] at least 2 weeks after being 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, and syphilis were negative. Serum SARS-CoV-2 IgG antibody dilution titers of 3 donors were at least 1:80, and the total CP infusion dose of each patient was 200 to 400 mL (4–5 mL/kg). An early CP administration was defined as CP infusion initiated within 1 week after admission and 2 weeks following the onset of symptoms.[14–16] Adverse reactions to CP infusion were closely monitored during CP treatment, and the first efficacy assessment, including clinical symptoms, oxygenation function, inflammatory markers, lymphocyte counts, chest computed tomography (CT) manifestations, and more, was performed at 48 to 72 hours after transfusion.

3. Results

3.1. Plasma donors

Plasma was obtained from 3 COVID-19 patients who had recently recovered and were discharged from the COVID-19-designated hospital in Fuzhou. Among these donors, the anti-SARS-CoV-2 IgG titers were 1:160, 1:80, and 1:80. All of the recipients were treated with complete blood type ABO-compatible CP.

3.2. Clinical manifestations, treatment, and prognoses of plasma recipients

The main results are shown in Tables 1–3. During the study, 3 patients with severe COVID-19, 1 male and 2 females, were enrolled and underwent CP transfusion. This male patient was 57 years old, and the female patients were 65 and 59 years old. The main underlying diseases included hypertension, diabetes, cerebral infarction, and postoperative thyroid adenoma. The common symptoms included cough, fever, and shortness of breath. Blood laboratory examinations exhibited a decreased arterial oxygen saturation (SaO_2), increased C-reactive protein (CRP) and interleukin-6 (IL-6) levels, and decreased counts of

Table 1

Characteristics of the patients who underwent convalescent plasma therapy in the 3 cases.

Characteristics	Case 1	Case 2	Case 3
Importing nation	Brazil	America	France
Nationality	Chinese	Chinese	Chinese
Age (y)	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 adenoma
Symptom	Cough, expectoration, fever, breathlessness, headache	Cough, breathlessness, appetite, excessive fatigue	Cough, fever, breathlessness, dry throat
Chest CT feature	Multiple lesions	Multiple lesions	Multiple lesions
Complication	None	None	Hypovolemia, pulmonary bacterial infection
Blood type	Type B	Type A	Type B
SARS-CoV-2 IgG titer for infusion	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
Time from onset to CP infusion (d)	7	10	10
Time from admission to CP infusion (d)	2	2	7
Total CP volume (mL)	400	200	200
Adverse reactions related to CP infusion	None	Mild antianaphylactic reaction	None

BMI = body mass index, CP = convalescent plasma, CT = computed tomography; IgG = immunoglobulin G, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Table 2

Conventional treatment of the patients from the 3 cases after admission.

Conventional treatment	Case 1	Case 2	Case 3
Antiviral treatment	Abidol 0.2 g tid po. for 10 days Hydroxychloroquine 0.2 g bid po. for 7 days	Abidol 0.2 g tid po. for 10 days Lopinavir/ritonavir 0.5 g bid po. for 10 days IFN α-2b 16.7 TIU bid inh. for 6 days	Abidol 0.2 g tid po. for 10 days Lopinavir/ritonavir 0.5 g bid po. for 10 days IFN α-2b 16.7 TIU bid inh. for 5 days
Antibiotic therapy	None	None	Ceftriaxon 2.0 g qd i.v. for 10 days
Anti-inflammatory agent	Xuebijing 50 mL bid i.v. for 7 days Ulinastatin 100 TU tid i.v. for 7 days	Xuebijing 50 mL bid i.v. for 7 days Ulinastatin 100 TU tid i.v. for 7 days	Xuebijing 50 mL bid i.v. for 7 days Ulinastatin 100 TU tid i.v. for 7 days
Immunostimulant	Thymalfasin 1.6 mg qd s.t. for 15 days	Thymalfasin 1.6 mg qd s.t. for 11 days	Thymalfasin 1.6 mg qd s.t. for 30 days
Respiratory support	Ransnasal catheter oxygen therapy	Ransnasal catheter oxygen therapy	Ransnasal catheter oxygen therapy

bid = twice a day, IFN = interferon, inh. = inhalation, i.v. = intravenous injection, po. = per os, qd = once a day, s.t. = subcutaneous injection, tid = three times a day, TIU = thousand IU.

Table 3

Dynamics of the indicators during plasma therapy for the patients from the 3 cases.

Characteristics	Case 1	Case 2	Case 3
Pretreatment 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 lymphocytes (cells/μL; normal range: 1530–3700)	952	1331	755
48–72 h after CP treatment			
Symptom	Improvement	Improvement	Improvement
Lung lesion	Partially absorption	Partially absorption	Partially absorption
SaO_2 (%)	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 lymphocytes (cells/μL)	1298	1450	1239
9 days after CP treatment			
Lung lesion	Sustained absorption	Sustained absorption	Sustained absorption
SaO_2 (%)	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 lymphocytes (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 lymphocytes (cells/μL)	1878	3203	1074
Time from onset to a negative viral test result (d)	17	16	33
Duration of hospital stay (d)	17	13	33

CD3+ = T lymphocytes, 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.

the total lymphocytes (CD45+) and T lymphocytes (CD3+) and their subsets (CD4+, CD8+) (Fig. 1). Chest CT revealed multiple ground-glass opacities and consolidation and linear opacities in both lungs (Figs. 2A,B, 3A,B, and 4A,B). After admission, all the patients received transnasal catheter oxygen therapy and were administered antiviral treatment with arbidol, hydroxychloroquine, sulfatelopinavir/ritonavir, or recombinant human interferon α-2b, and 1 patient was treated with a combination of antibiotics. Other medicines, including immunostimulants (thymalfasin), anti-inflammatory agents (xuebijing injection and ulinastatin), and Chinese herbal medicines, were also administered.

On the basis of the conventional treatment after admission, the condition of these patients continued to worsen. Then, they all underwent additional CP therapy. All of the patients provided informed consent for the CP treatment before the transfusion was performed. The volume of the CP transfusion for the 3 patients was 400 mL (2 doses of 200 mL transfused 24 hours apart). At 48 to 72 hours after CP transfusion, all of the patients exhibited an improvement in and alleviation of symptoms, an elevated SaO_2, decreased CRP and IL-6 levels, and increased lymphocyte counts (Fig. 1). Repeated chest CT revealed obvious absorption of the lesions in the bilateral lungs (Figs. 2C,D, 3C,D, and 4C,D). On days 9 and 30 after the CP transfusion, the above-mentioned indicators continued to improve, and the conditions of the patients improved until they were discharged in stable condition. The latest outpatient follow-up was performed on May 7, 2020, when the patients remained well without signs of recurrence.

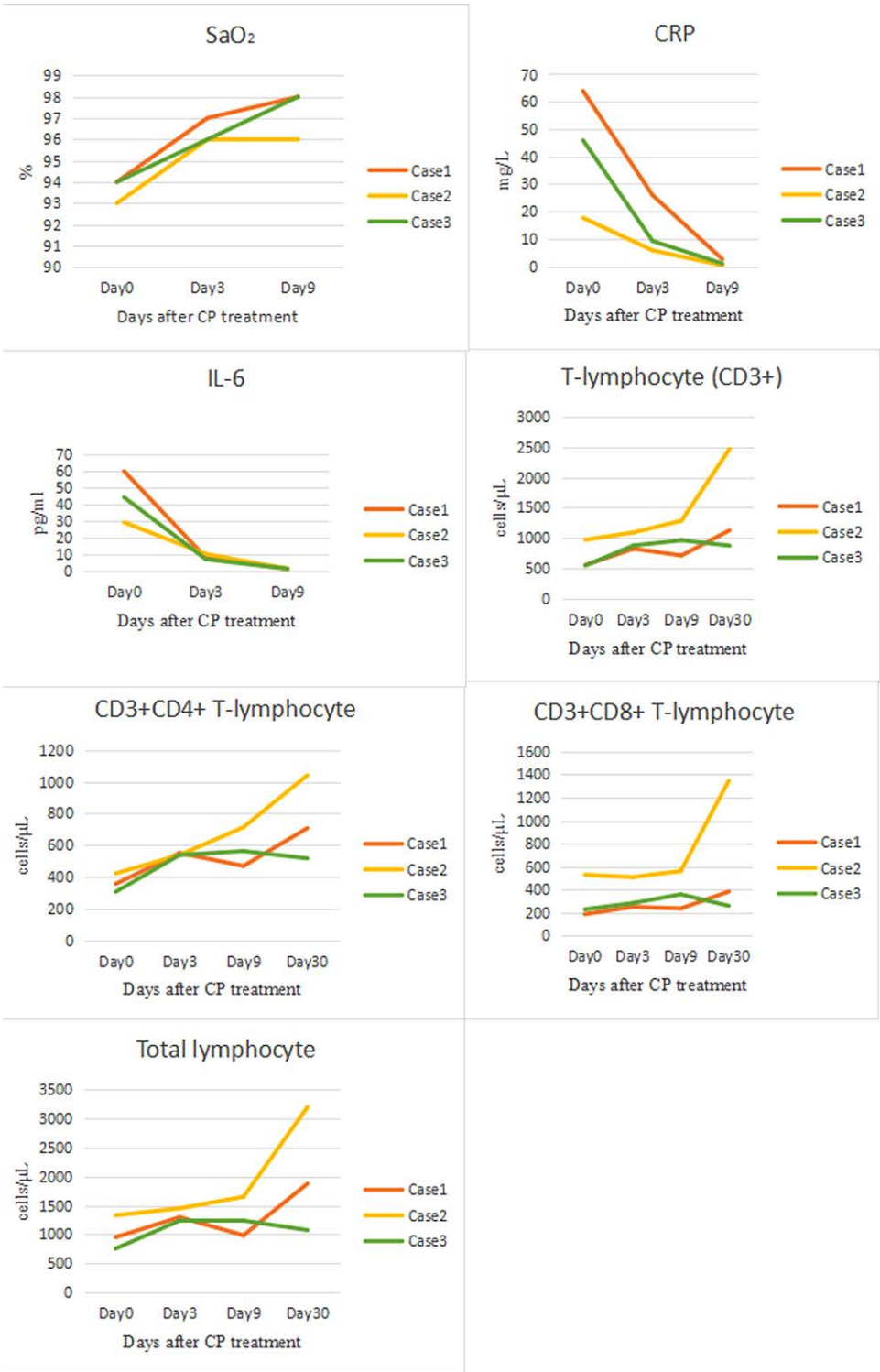

Figure 1. Dynamics of the laboratory indicators after plasma therapy. After plasma therapy, the arterial oxygen saturation increased, C-reactive protein and interleukin-6 levels decreased, and counts of the total lymphocytes and T lymphocytes (CD3+) and their subsets (CD4 + and CD8+) increased.

3.3. Adverse reactions related to CP transfusion

One patient (case 2) developed a red rash with pruritus around the infusion site of the right upper extremity 17 hours after the CP transfusion, and the rash extended to the whole body with pruritus 22 hours after transfusion. Considering the transfusion-related anaphylactic reaction, the patient underwent antianaphylactic treatment with 10% calcium gluconate infusion and oral ebastines. Then, the symptoms became gradually relieved, and the rash disappeared completely 5 days after the CP transfusion. No severe adverse reactions were observed in any of the patients.

4. Discussion

To date, COVID-19 is still rapidly spreading worldwide. Clinical data from China have demonstrated that the rate of

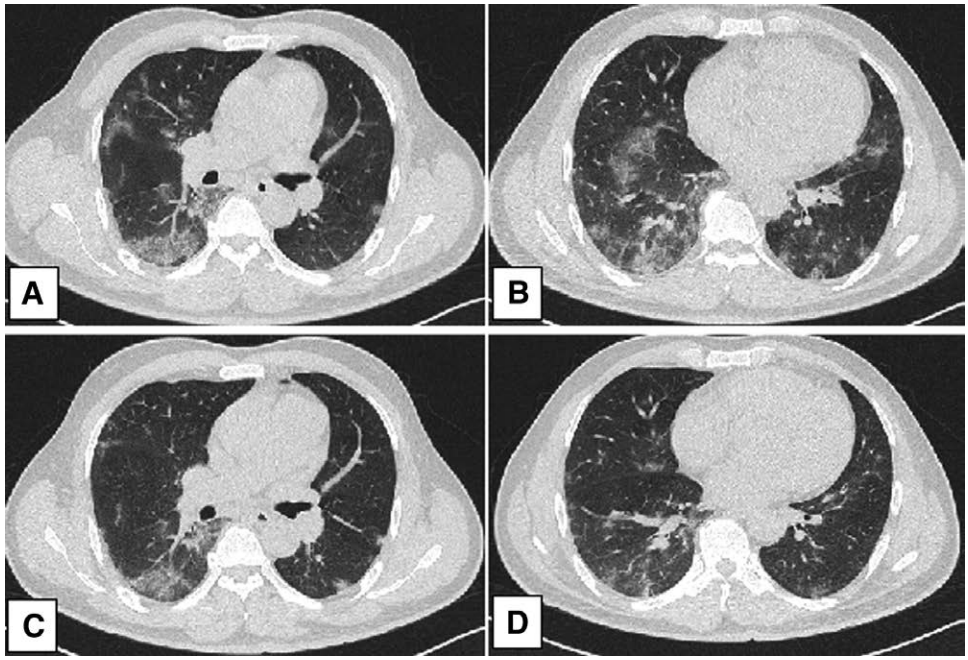

Figure 2. Case 1. On the second day of admission (6 days after onset), chest computed tomography demonstrated patchy and nodular ground-glass opacities and consolidation and linear opacities in the bilateral lungs, mainly in both lower lungs (A, B). The lung lesions were greatly absorbed at 70 h after the plasma treatment (C, D).

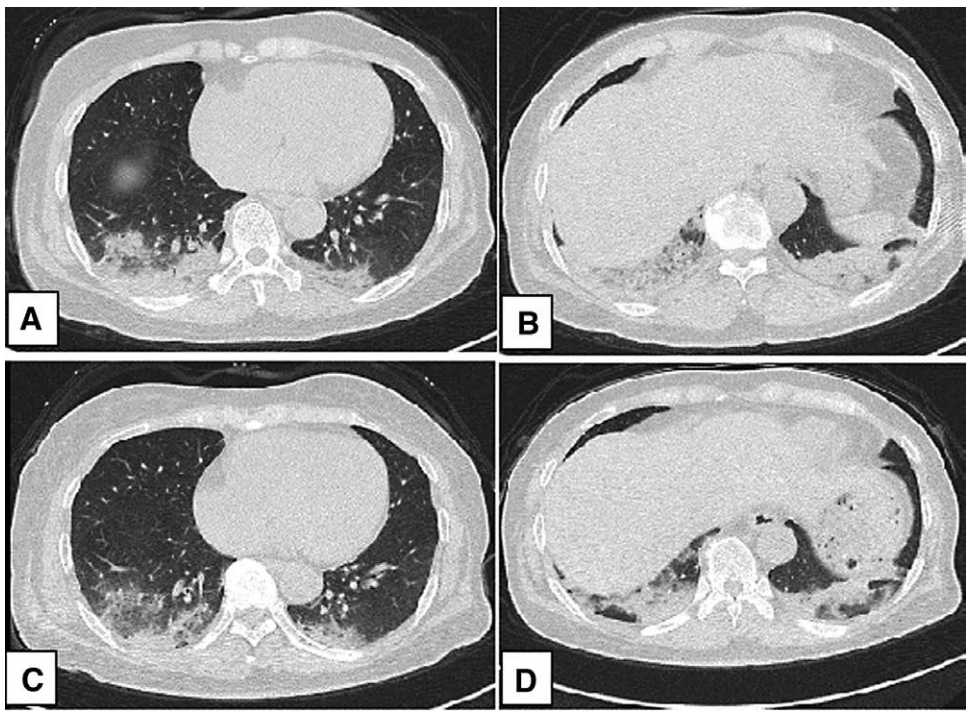

Figure 3. Case 2. On the second day of admission (9 days after onset), chest computed tomography demonstrated patchy consolidation and linear opacities in the bilateral lungs, mainly in both lower lungs (A, B). The lung lesions were greatly absorbed at 70 h after the plasma treatment (C, D).

severe COVID-19 was as high as 41.1% to 48.3% in the early stages of the pandemic.[17,18] Due to the rapid progression of disease and high mortality in patients with severe COVID-19, effective treatment strategies are urgently needed to control the disease. However, there are currently no antiviral drugs that have proven to be effective in treating infection from this novel virus.[19,20] A multicenter trial demonstrated that plasma therapy could accelerate the virus clearance rate and clinical recovery, shorten the length of hospital stay, and reduce the risk of death by 35% in patients with COVID-19.[7] Ibrahim et al reported that an early application of plasma therapy helped accelerate the clinical recovery and reduce the mortality rate in patients with COVID-19.[14] In a large retrospective case-control study, Xia et al also demonstrated that CP therapy improved the clinical symptoms, reduced the risk of intensive care unit admission, and reduced the mortality rate (the risk of mortality was

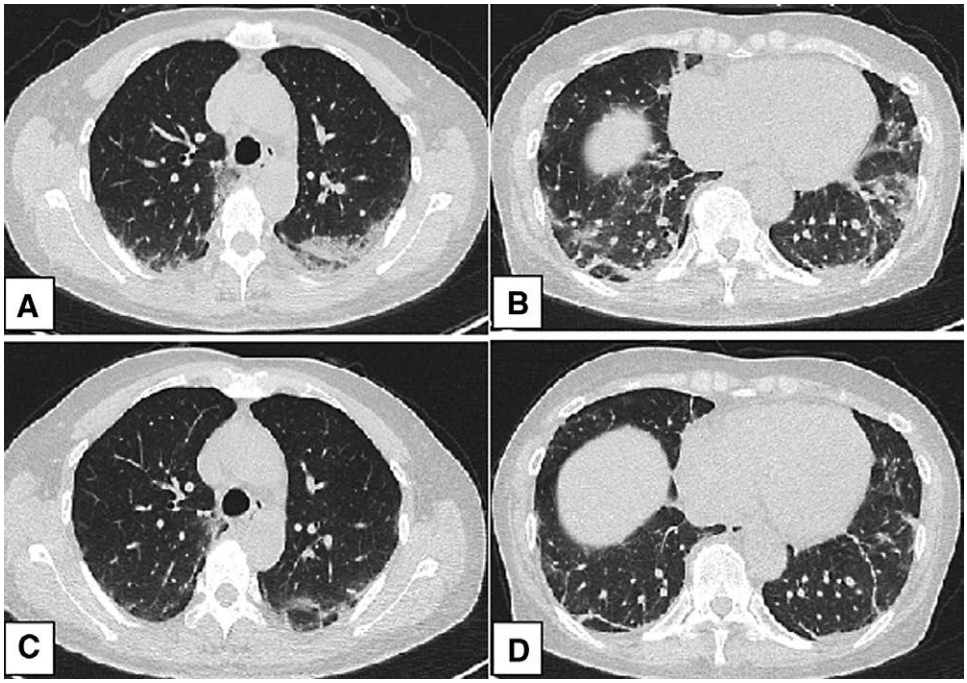

Figure 4. Case 3. On the seventh day of admission (9 days after onset), chest computed tomography demonstrated multiple patchy and nodular ground-glass opacities and consolidation and linear opacities in the bilateral lungs, mainly in the subpleural area (A, B). The lung lesions were greatly absorbed at 40 h after the plasma treatment (C, D).

reduced by 50%) in patients with COVID-19.[21] Previous studies have also demonstrated that an early application of plasma in patients with severe disease is more effective than a late application, while the overall benefit of CP in extremely critical patients, such as those with tracheal intubation or life-threatening conditions, was not significant.[7,14,21,22] The patients of the 3 cases in our study were severely elderly patients with underlying diseases, such as diabetes and high blood pressure, but without endotracheal intubation. After admission, the condition of these patients deteriorated rapidly, and there was a high risk of developing critical illness. Then, CP was administered based on conventional treatment. After the combined therapy was administered, the symptoms of the patients became rapidly alleviated and the lung lesions were significantly resolved, inflammatory indexes decreased, and oxygenation function and cellular immune function were improved in the patients. The remarkable improvement of these patients suggests that plasma therapy is an effective remedy for patients with severe COVID-19. Hegerova et al reported that patients who underwent CP within 1 week after admission had a markedly lower risk of death within 14 days (mortality was 0) than those who underwent CP later than 1 week after admission.[15] The timing of CP therapy in all of the patients in our study was within 1 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).[21] Significant improvement was achieved within 72 hours after treatment with CP in our research, suggesting that early CP therapy in patients with severe COVID-19 becomes even more effective.

Notably, although the 3 patients improved significantly after CP, one of them (case 3) remained positive for SARS-CoV-2 RNA for more than 1 month (33 days). At the beginning of the disease, the lymphocyte counts in the 3 patients all decreased and the number of lymphocytes gradually increased after CP, which is a result that is consistent with those of a previous report.[5] However, the lymphocyte counts in 1 patient (case 3) were still lower than the normal standards 30 days after CP, whereas those in the other 2 patients (case 1 and case 2) 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 exhibited that the titer of CP administered for case 1 was the highest (1:160) and the titer of CP administered for case 2 was positive for 1:80, whereas the titer of CP for case 3 was only weakly positive at 1:80. This suggests that this patient (case 3) received the lowest antibody level of CP in these 3 patients, which may have reduced the efficacy of the plasma therapy.[21]

Additionally, only 1 patient (case 2) had a mild anaphylactic reaction with erythema and pruritus in the early stages of the transfusion. No other serious adverse reactions were observed in the follow-up period. Generally, the plasma treatment in our study was safe and reliable, and this is consistent with other reports in the literature.[21,23]

Notably, there are some limitations to our research. First, this study included only 3 patients and was not a randomized controlled trial. Second, the patients were also administered other medications (including antiviral drugs, antibiotics, anti-inflammatory agents, immunostimulants, and Chinese herbal medicines) and treatments. Hence, this is a confounding factor. It is possible that these factors may play an important role in the recovery from, as well as in the synergy of, CP treatment. However, no effective antiviral drugs or other traditional therapies for controlling the novel virus were proven in our study. Combined CP therapy was initiated after the condition worsened after conventional treatment. Additionally, as mentioned previously, patients who underwent CP earlier have more-favorable clinical outcomes.[14] The CP remedy in our study was utilized in the early stages of the disease course. Moreover, the first evaluation of a curative effect was assessed in a short time after the CP transfusion (within 48 to 72 hours), and the findings, which demonstrated obvious improvement with clinical symptoms, radiological images, and laboratory tests, were encouraging. As a result, we believe that the marked efficiency should be mainly attributed to the additional treatment with CP.

In summary, the early application of CP therapy in patients with severe COVID-19 can rapidly improve the condition of the patient, and the therapy is generally effective and safe. This therapy can reduce the risk of COVID-19 progressing from severe

to critical, lower the mortality rate,[24] and help raise the rescue success rate in patients with severe disease. In the absence of effective anti-SARS-CoV-2 drugs, CP therapy is an alternative method for treating patients with severe COVID-19 using adjuvant therapy.[24]

Acknowledgments

We would like to thank the 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, and the patients for their willingness to participate in this study.

Author contributions

HL conceived the study and reviewed all drafts of the manuscript. JH drafted the manuscript. HW managed the data generation and data analysis and assisted in drafting the manuscript. CL helped to carry out the clinical data collection. JH and HW contributed equally to this study as senior authors. All authors read and approved the final manuscript.

References

[1] Qu J. 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;43:473–89.
[2] Bloch EM. Convalescent plasma to treat COVID-19. Blood. 2020;136:654–5.
[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;211:80–90.
[4] Shen C, Wang Z, Zhao F, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA. 2020;323:1582–9.
[5] Duan K, Liu B, Li C, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad Sci USA. 2020;117:9490–6.
[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;12:6536–42.
[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;324:460–70.
[8] Casadevall A, Joyner MJ, Pirofski LA. A randomized trial of convalescent plasma for COVID-19-potentially hopeful signals. JAMA. 2020;324:455–7.
[9] Simonovich VA, Burgos Pratx LD, Scibona P, et al. A randomized trial of convalescent plasma in Covid-19 severe pneumonia. N Engl J Med. 2021;384:619–29.
[10] Agarwal A, Mukherjee A, Kumar G, et al. Convalescent plasma in the management of moderate covid-19 in adults in India: open label phase II multicentre randomised controlled trial (PLACID Trial). BMJ. 2020;371:m3939.
[11] National health commission of the people′s Republic of China. Diagnosis and treatment of novel coronavirus pneumonia (Trial version 7) [D]. 2020. Available at: http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989/files/ce3e6945832a438eaae415350a8ce964.pdf. [Accessed date March 3, 2020].
[12] 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;43:414–20.
[13] National health commission of the people′s Republic of China. Clinical treatment protocol of convalescence plasma for COVID-19 patients (Trial version 2). [EB/ OL].[2020-03-04].http://www.nhc.gov.cn/yzygj/s7658/202003/61d608a7e8bf49fca418a6074c2bf5a2/files/a5e00234915344c6867a3e6bcfac11b7.pdf
[14] 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;9:913–26.
[15] Hegerova L, Gooley TA, Sweerus KA, et al. Use of convalescent plasma in hospitalized patients with COVID-19: case series. Blood. 2020;136:759–62.
[16] Rojas M, Rodríguez Y, Monsalve DM, et al. Convalescent plasma in Covid-19: possible mechanisms of action. Autoimmun Rev. 2020;19:102554.
[17] Chen L, Liu HG, Liu W, et al. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. Chin J Tuberc Respir Dis. 2020;43:203–8.
[18] Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol. 2020;77:683–90.
[19] World Health Organization. Coronavirus disease (COVID-19) pandemic. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019. [accessed June 9, 2020]
[20] Lu H. Drug treatment options for the 2019-new coronavirus (2019-nCoV). Biosci Trends. 2020;14:69–71.
[21] 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;136:755–9.
[22] Liu STH, Lin HM, Baine I, et al. Convalescent plasma treatment of severe COVID-19: a propensity score-matched control study. Nat Med. 2020;26:1708–13.
[23] Joyner MJ, Wright RS, Fairweather D, et al. Early safety indicators of COVID-19 convalescent plasma in 5000 patients. J Clin Invest. 2020;130:4791–7.
[24] 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.