

# World Journal of *Clinical Cases*

*World J Clin Cases* 2021 April 26; 9(12): 2696-2950



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**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Ji-Hong Lin; Production Department Director: Xiang Li; Editorial Office Director: Jin-Lai Wang.

**NAME OF JOURNAL**

*World Journal of Clinical Cases*

**ISSN**

ISSN 2307-8960 (online)

**LAUNCH DATE**

April 16, 2013

**FREQUENCY**

Thrice Monthly

**EDITORS-IN-CHIEF**

Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

**PUBLICATION DATE**

April 26, 2021

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<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

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# Timing of convalescent plasma therapy-tips from curing a 100-year-old COVID-19 patient using convalescent plasma treatment: A case report

Bo Liu, Kang-Kang Ren, Nian Wang, Xin-Ping Xu, Jue Wu

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**Author contributions:** Liu B collected the data for the case presentation and contributed to manuscript drafting; Wu J and Wang N contributed to supervision of the data collection, analysis of the data, and write-up of this manuscript; Ren KK and Xu XP contributed to the data analysis; All authors contributed to the critical review and final approval of the manuscript.

**Supported by** Medical Collaborative Science and Technology Innovation Research Project of Science and Technology Commission of Beijing, No. Z181100001918013; and Nanchang Science and Technology Bureau, No. 20203306.

**Informed consent statement:** Informed written consent was obtained from the patient for publication of this report.

**Conflict-of-interest statement:** The authors declare that they have no conflict of interest.

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## Abstract

### BACKGROUND

Convalescent plasma therapy is used for the treatment of critically ill patients for newly discovered infectious diseases, such as coronavirus disease 2019 (COVID-19) pneumonia, under the premise of lacking specific treatment drugs and corresponding vaccines. But the best timing application of plasma therapy and whether it is effective by antiviral and antibiotic treatment remain unclear.

### CASE SUMMARY

We describe a patient with COVID-19, a 100-year-old, high-risk, elderly male who had multiple underlying diseases such as stage 2 hypertension (very high-risk group) and infectious pneumonia accompanied by chronic obstructive pulmonary disease and emphysema. We mainly describe the diagnosis, clinical process, and treatment of the patient, including the processes of two plasma transfusion treatments.

### CONCLUSION

This provides a reference for choosing the best timing of convalescent plasma treatment and highlights the effectiveness of the clinical strategy of plasma

**CARE Checklist (2016) statement:**

The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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**Manuscript source:** Unsolicited manuscript

**Specialty type:** Medicine, research and experimental

**Country/Territory of origin:** China

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0  
Grade B (Very good): B  
Grade C (Good): C, C  
Grade D (Fair): 0  
Grade E (Poor): 0

**Received:** December 5, 2020

**Peer-review started:** December 5, 2020

**First decision:** January 7, 2021

**Revised:** January 18, 2021

**Accepted:** March 3, 2021

**Article in press:** March 3, 2021

**Published online:** April 26, 2021

**P-Reviewer:** Ciotti M, Frater JL

**S-Editor:** Fan JR

**L-Editor:** Filipodia

**P-Editor:** Wang LL



treatment in the recovery period of patients with COVID-19 pneumonia.

**Key Words:** COVID-19; Convalescent plasma therapy; Treatment; Elderly; Timing; Case report

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**Core Tip:** A 100-year-old coronavirus disease 2019 (COVID-19) patient with several underlying diseases including hypertension (stage 2 hypertension) accompanied by chronic obstructive pulmonary disease and emphysema was treated using convalescent plasma. Besides the effective maintenance of supportive treatment and no antiviral and antibiotic treatment, the convalescent plasma was infused into the patient in the early stage of the infection. This choice of time points (days 7 and 11 of hospitalization) provides a reference for choosing the best timing of convalescent plasma treatment and highlights the effectiveness of the clinical strategy of plasma treatment in the recovery period of patients with COVID-19 pneumonia.

**Citation:** Liu B, Ren KK, Wang N, Xu XP, Wu J. Timing of convalescent plasma therapy-tips from curing a 100-year-old COVID-19 patient using convalescent plasma treatment: A case report. *World J Clin Cases* 2021; 9(12): 2890-2898

**URL:** <https://www.wjgnet.com/2307-8960/full/v9/i12/2890.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v9.i12.2890>

## INTRODUCTION

The outbreak of coronavirus disease 2019 (COVID-19) pneumonia in Wuhan in 2019 has garnered intense attention. Most patients with this type of pneumonia have a good prognosis. A small percentage of patients fall critically ill, and critical illness and death occur mostly in the elderly. Therefore, elderly people are the high-risk group of COVID-19 pneumonia patients. Understanding the medical treatment of elderly patients with severe COVID-19 pneumonia can greatly reduce the mortality from novel coronavirus infection. According to a press release issued by the National Health Commission of the People's Republic of China on February 4, 2020, an analysis of current death cases found that most deaths (two-thirds) are in men and in senior citizens (> 80% are over 60 years old). Over 75% of patients who die from it have more than one underlying disease, mainly including cardiovascular and cerebrovascular diseases, diabetes, and cancer. Once infected with pneumonia, elderly people with underlying diseases are considered high-risk in clinical practice, and their mortality rate is very high<sup>[1]</sup>. Although numerous trials have reported the timing of convalescent plasma therapy<sup>[2,3]</sup>, to date, no trials have been conducted on extremely old persons or newly infected persons with multiple underlying diseases.

Here, we present a case of a 100-year-old (super elderly) patient with multiple underlying diseases (*i.e.* high-risk patient) who was cured of a novel coronavirus infection. We mainly describe the diagnosis, clinical process, and treatment of this case, including a description of two plasma transfusion treatments. The cure of this case provides a reference for formulating the treatment plans and the best timing of convalescent plasma treatment for elderly patients with various underlying diseases. This report was approved by Ethics Committee of Guanggu Branch of Hubei Maternal and Child Health Hospital.

## CASE PRESENTATION

### Chief complaints

The patient had a history of exposure and had repeated coughing and shortness of breath for 2 mo. He tested positive for the novel coronavirus using a nucleic acid test in Wuhan Community Health Center on February 22, 2020.

### **History of present illness**

The patient had repeated coughing and shortness of breath for 2 mo.

### **History of past illness**

The patient had a history of underlying diseases including hypertension for approximately 30 years, dementia, abdominal aortic aneurysm, cerebral infarction, and prostate hyperplasia.

### **Personal and family history**

The patient had lived in Wuhan, China for a long time, and had contact with COVID-19-confirmed patients (not confirmed at that time).

### **Physical examination**

Physical examination of the patient upon admission showed stable vital signs, with a body temperature of 36.6 °C, a pulse of 87 beats/min (regular), a respiratory rate of 18 breaths/min (regular), and blood pressure of 125/63 mmHg.

### **Laboratory examinations**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test results in patient at different time points (on hospitalization days 5, 9, 10, 12 and 13) are shown in [Table 1](#). The results of blood biochemistry (hepatic function, renal function, electrolytes, lipid, and glucose), blood cell analysis, and coagulation function are shown in [Table 1](#).

### **Imaging examinations**

On the second day after admission (February 25, 2020), a chest computed tomography (CT) scan revealed small amounts of abnormally dense shadows in both lungs, suggesting infectious pneumonia accompanied by chronic obstructive pulmonary disease and emphysema ([Figure 1](#)).

### **Further diagnostic work-up**

We sequenced the metatranscriptome of the anal swab from the patient on the Illumina NextSeq 500 PE150 platform, producing over 18 Million Pair-End reads ([Supplementary Table 1](#)). The sample contained approximately 3.21% human reads. For taxonomic classification, filtered reads were searched against the NCBI Ref-Seq database. This classified 99.24% of the filtered reads to the bacteria domain and 0.05% to the viral domain ([Supplementary Table 2 and Figure 2](#)). No SARS-CoV-2 reads were detected. This result was consistent with the clinical outcome that the patient had recovered completely from SARS-CoV-2 infection. In addition, the anal swab sample exhibited a high abundance of reads of the putative bacterial pathogens, 27.44% classified to *Escherichia coli*, 25.65% *Salmonella enterica*, and 8.55% *Klebsiella pneumoniae* ([Figure 2, Supplementary Figure 1 and Supplementary Table 3](#)).

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## **FINAL DIAGNOSIS**

The patient was confirmed with COVID-19 by positive SARS-CoV-2 oropharyngeal swab test and suggested infectious pneumonia accompanied by chronic obstructive pulmonary disease and emphysema, and a history of underlying diseases.

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## **TREATMENT**

The treatment plan adopted was supportive treatment with oxygen inhalation and frequent, low-volume nasal-feeding nutritional support with a daily maintenance of 1000 mL of Fresubin Diabetes (Enteral Nutritional Emulsion [Tpf-D]). Because lung changes due to COVID-19 pneumonia were mild and the patient was very old, no antiviral treatment was given at first. Intravenous supplementation with hypertonic sodium chloride was given to correct his hyponatremia, and intravenous infusion of human albumin was given to correct the hypoproteinemia. The antihypertensive drugs that the patient routinely took (telmisartan tablets and nifedipine sustained release tablets) kept stabilizing blood pressure.

On day 5 of hospitalization, the patient tested positive for SARS-CoV-2 nucleic acid.

**Table 1 Laboratory findings of patient infected with severe acute respiratory syndrome coronavirus 2 on admission to hospital**

| Hospital day                           | Reference range | Day 2        | Day 3        | Day 4        | Day 5        | Day 6        | Day 7       | Day 8       | Day 9       | Day 10         | Day 11      | Day 12      | Day 13      |
|--|-----------------|--------------|--------------|--------------|--------------|--------------|-------------|-------------|-------------|----------------|-------------|-------------|-------------|
|  |                 | Feb 25, 2020 | Feb 26, 2020 | Feb 27, 2020 | Feb 28, 2020 | Feb 29, 2020 | Mar 1, 2020 | Mar 2, 2020 | Mar 3, 2020 | Mar 4, 2020    | Mar 5, 2020 | Mar 6, 2020 | Mar 7, 2020 |
| Nucleic acid testing                   |                 |              |              |              | P            |              |             |             | P           | P              |             | N           | N           |
| Antibody                               |                 |              |              |              |              | IgG+         |             |             | IgG+        | Detection IgM+ | -           | IgM+        |             |
| IL6 in pg/mL                           | 0-10            | -            |              |              | 24.63↑       |              |             |             | 66.21↑      | 21.47↑         | -           |             |             |
| BNP in pg/mL                           | 0-100           |              | 78.8         |              | 135.4↑       |              |             |             |             |                |             | 242.1↑      |             |
| Albumin in g/L                         | 35-52           | 29.4         |              | 29.1         |              |              | 33.4        | 35          | 31.6        |                |             | 34.7        | 35.7        |
| Blood clean                            | 1-2.4           | 0.95↓        |              | 0.8↓         |              |              | 0.95        | 0.91        | 0.93        |                |             | 1.05        | 1.08        |
| Globulin, A/G/Glutamic pyruvic         | 0-55            | 49.3         |              | 34.2         |              |              | 17.4        | 20.7        | 16.4        |                |             | 13.7        | 17.3        |
| Transaminase, ALT in U/L, GGT in U/L   | 12-64           | 96↑          |              | 75↑          |              |              | 57          | 52          | 42          |                |             | 35          | 34          |
| TBA in μmol/L                          | 0-9.67          | 4            |              | 2.5          |              |              | 19.3        | 14.5        | 29.7        |                |             | 42.8        | 11.2        |
| CRE in μmol/L                          | 64-104          | 73.1         |              | 62↓          |              |              | 50.8↓       | 55.1↓       | 53.2↓       |                |             | 42.6↓       | 48.4        |
| UA in μmol/L                           | 210-420         | 293          |              | 346          |              |              | 246         | 256         | 241         |                |             | 118↓        | 116         |
| hs-cTn in pg/mL                        | 0-34.2          |              |              |              |              | 19           |             |             |             |                |             |             |             |
| MYO in ng/mL                           | 0-106           |              |              |              |              | 498.7↑       |             |             |             |                |             |             |             |
| CK-MB in ng/mL                         | 0-3.1           |              |              |              |              | 11.1 ↑       |             |             |             |                |             |             |             |
| D-Dimer in mg/L                        | 0-0.55          |              |              |              |              |              |             |             | 3.17        |                |             |             | 4.38        |
| LYM, %                                 | 20-50           |              |              |              |              |              | 12.1↓       |             | 14.9↓       |                |             | 12.8↓       | 14.4        |
| LYM, × 10 <sup>9</sup> /L              | 1.1-3.2         |              |              |              |              |              | 0.63↓       |             | 0.69↓       |                |             | 0.84↓       | 1.08        |
| RBC, × 10 <sup>12</sup> /L             | 4.3-5.8         |              |              |              |              |              | 3.29↓       |             | 3.35↓       |                |             | 3.27↓       | 3.22        |
| HGB in g/L                             | 130-175         |              |              |              |              |              | 100↓        |             | 100↓        |                |             | 97↓         | 95          |
| Red blood cell specific volume, HCT, % | 40-50           |              |              |              |              |              | 29.3↓       |             | 29.7↓       |                |             | 29.3↓       | 28.7        |
| hs-CRP in mg/L                         | 0-10            | 108.43↑      |              |              |              |              | 49.18↑      |             |             |                |             | 27.03       | 24.97       |
| tHb in g/L                             | 117-174         |              |              | 70↓          |              |              |             |             | 94↓         |                |             |             | 115         |

|                                   |         |       |      |     |
|-----------------------------------|---------|-------|------|-----|
| Carbon monoxide                   | 0.5-1.5 | 2.2↑  | 1.3  | 1.5 |
| COHb, % un-ionized<br>HHb, %      | 0--5    | -0.4  | 0.6  | 0.2 |
| Glucose in mmol/L                 | 3.6-5.2 | 10.9↑ | 6.2↑ | 8.1 |
| Base excess of blood in<br>mmol/L | -2-3    | -5.1↓ | 4.6↑ | 4.1 |
| Beeef in mmol/L                   | -2-3    | -5.6↓ | 5↑   | 4.7 |

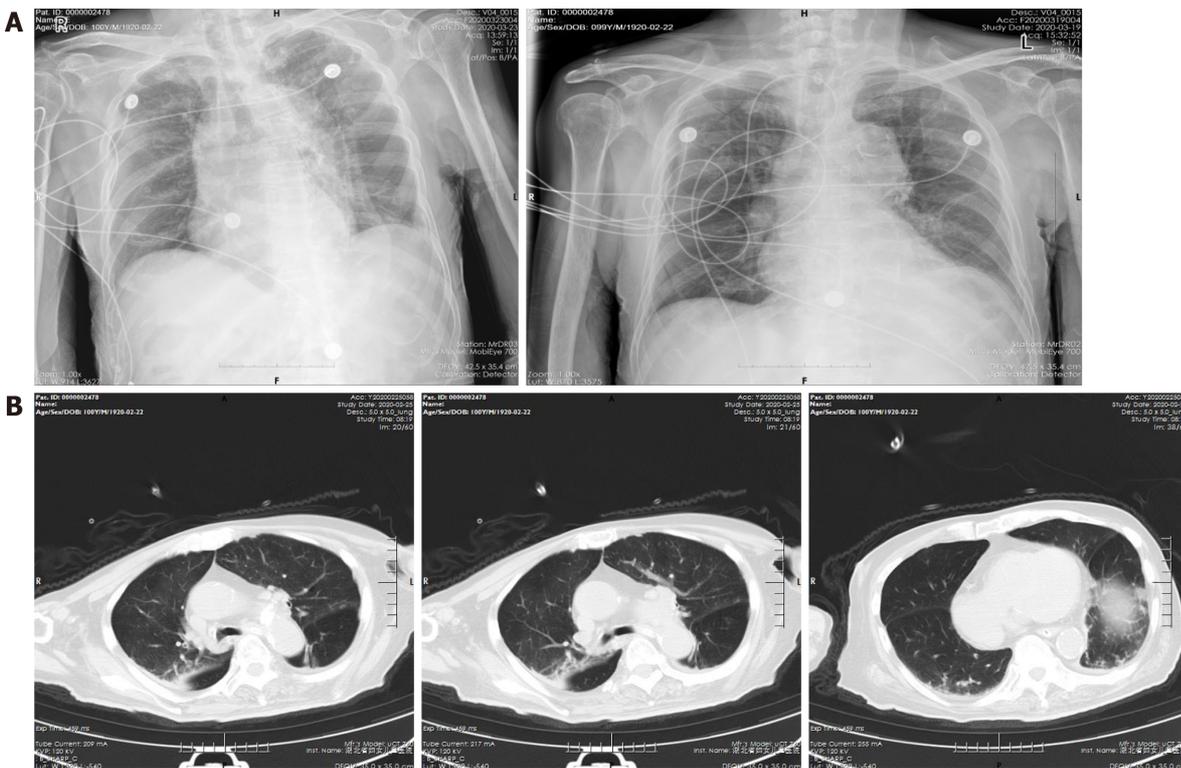
-: Negative; +: Positive; ALT: Alanine aminotransferase; Beeef: Base excess of the extracellular fluid; CK-MB: Creatine kinase isoenzyme-MB; COHb: Hemoglobin; CRE: Creatinine; GGT:  $\gamma$ -Glutamyl transferase; HCT: Hematocrit; HGB: Hemoglobin; HHb: Hemoglobin; hs-CRP: Hypersensitive C-reactive protein; hs-cTn: High-sensitivity cardiac troponin; Ig: Immunoglobulin; IL6: Interleukin-6; LYM: Lymphocyte absolute value; MYO: Myoglobin; N: Negative; P: Positive; RBC: Red cell count; TBA: Total bile acid; tHb: Total hemoglobin; UA: Uric acid.

The patient showed repeated coughing and shortness of breath. An urgent blood test showed hemoglobin at 100 g/L and absolute lymphocyte value at  $0.63 \times 10^9/L$ , suggesting that the patient had anemia and low immunity. CT showed infectious pneumonia with chronic obstructive pulmonary disease and emphysema. The above clinical indications together with a confirmed diagnosis of COVID-19 pneumonia and the patient's age qualified the patient for infusion of convalescent plasma for COVID-19 patients. On day 7 of hospitalization (March 1, 2020), plasma transfusion therapy using convalescent plasma of an infected patient was started. Intravenous infusion started at 21:45, and 200 mL plasma was infused at 01:30. Throughout the infusion process, the patient had no special discomfort and no adverse reactions to blood transfusion such as fever, chills, rash, or allergies. The patient's vital signs were stable, and the blood oxygen saturation was stabilized at above 95% under low flow oxygen inhalation. The patient continued to receive nutritional support treatment.

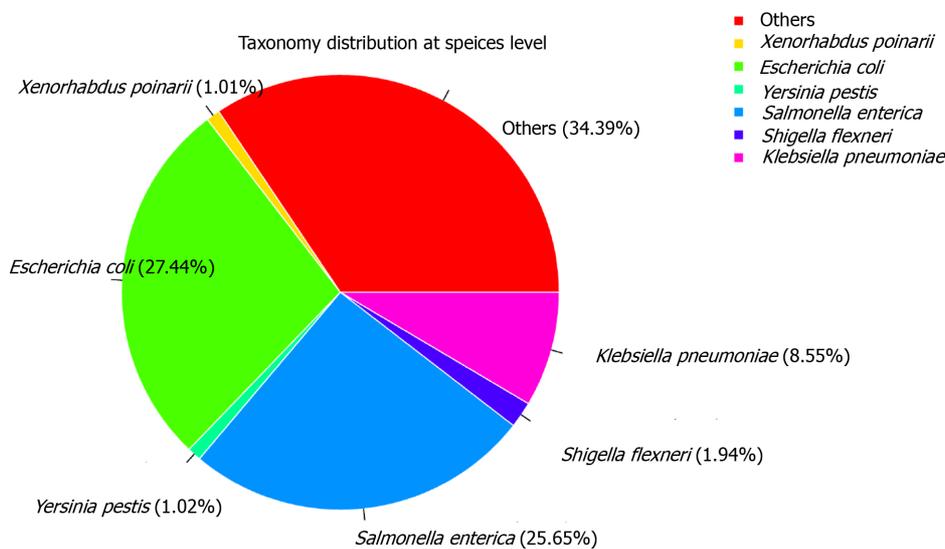
On day 11 of hospitalization (March 5, 2020), we conducted the second round of convalescent plasma treatment for SARS-CoV-2 infection using 200 mL plasma, which was infused first slowly and then quickly and ended at 20:40. There was no transfusion reaction during plasma infusion. The day after the blood transfusion, the blood routine test was conducted to evaluate the effects of plasma therapy. The laboratory test results showed that the red blood cell count and hemoglobin had improved and remained stable. This confirmed that the blood transfusion was effective. At the same time, the patient's B-type natriuretic peptide was higher than before, so hydrochlorothiazide tablet was added for diuretic supportive treatment.

## OUTCOME AND FOLLOW-UP

On day 11 (March 5, 2020) after admission, a throat swab was taken again, and the novel coronavirus nucleic acid test was negative. The SARS-CoV-2 antibody test



**Figure 1** Anterior-posterior chest radiograph and computed tomography chest scan on February 25, 2020 (day 2 of hospitalization). A: Anterior-posterior chest radiograph; B: Computed tomography chest scan. Small amounts of abnormally dense shadows in both lungs, suggesting infectious pneumonia; chronic bronchitis with pulmonary emphysema; old left upper lung lesion; bilateral pleural hypertrophy and calcification; aortic atherosclerosis; and small cyst of the left liver.



**Figure 2** Visualization of the taxonomy classification interactively. Filtered sequences from the anal swab sample were classified by Kraken 2 software and visualized by using Krona tools (<https://github.com/marbl/Krona>). The distribution of each organism at each taxonomy level can be see interactively. At the domain level, 99.24% of the sequence were classified as bacteria and only 0.05% were classified as viruses.

showed positive for the novel coronavirus immunoglobulin (Ig) G and IgM. On day 12 after admission, the results of physical examination, blood routine, and biochemical tests indicated that the vital signs were stable, the novel coronavirus nucleic acid test was again negative, and the patient's condition had improved. On day 13 after admission, a nasopharyngeal swab sample was collected, and the patient was subjected to metagenomic sequencing using next-generation sequencing. The SARS-CoV-2 reads were not detected in the sequencing results, which was consistent with the nucleic acid test results.

## DISCUSSION

Elderly people with underlying diseases, when they are infected with COVID-19 pneumonia, belong to the high-risk group in clinic practice, and their mortality rate is very high, especially patients over 60 years of age with hypertension, heart disease, diabetes, or cancer. In addition, the probability of becoming severely ill or critically ill is higher<sup>[4-7]</sup>. The treatment of severely ill and critically ill patients has put much pressure on Chinese medical teams at this time. When China's epidemic situation was at its peak, there were nearly 10000 severely ill and critically ill patients in Wuhan with critically ill patients accounting for approximately 5%. The material and manpower requirements were huge. Faced with this situation, we had to treat the patients scientifically and effectively, reduce the number of patients becoming critically ill, and ultimately reduce the mortality.

For the treatment of COVID-19 pneumonia, there are no particularly effective anti-disease drugs. In this case, treatment mainly includes strengthening nutritional therapy, applying oxygen therapy, such as oxygen masks, establishing early warnings for the functions of important organs, and administering intravenous immunoglobulin infusion or convalescent plasma infusion at early stages according to the disease condition. Convalescent plasma is a plasma product collected from patients who have been infected with the virus but have recovered after treatment, and its active ingredient is immunoglobulin. Convalescent plasma usually contains high-potency pathogen-specific antibodies. The collected plasma undergoes virus inactivation and is prepared after neutralizing antibody test and multiple pathogenic microorganism detection. It is used for the treatment of critically ill patients with infectious diseases. Compared with intravenous injection of human immunoglobulin, convalescent plasma contains more specific immunoglobulins for pathogenic microorganisms. Convalescent plasma from recovered patients contains more specific immunoglobulin than the ordinary human immunoglobulin for intravenous injection. For newly discovered infectious diseases, such as COVID-19 pneumonia, under the premise of lacking specific treatment drugs and corresponding vaccines, infusion of special plasma products collected from patients who have recovered from COVID-19 pneumonia can provide instant, massive, and passive immune support and eliminate pathogens. This greatly reduces the mortality of critically ill patients<sup>[8]</sup>. Convalescent plasma therapy has also been used in the past for the treatment of SARS, 2009 influenza A, avian influenza A, Ebola hemorrhagic fever, and other viral infections<sup>[9-11]</sup>. Therefore, convalescent plasma therapy has practical significance for the treatment of COVID-19 pneumonia in the absence of specific drugs and vaccines.

Recently, researchers at the Third People's Hospital of Shenzhen, China, treated five critically ill patients with convalescent plasma. All five of them had severe respiratory failure and were on a ventilator; two were accompanied by bacterial and/or fungal pneumonia; and one was under extracorporeal membrane lung oxygenation treatment. The four patients with no comorbid disease received plasma therapy on day 20 of hospitalization, and one patient with hypertension and mitral valve insufficiency received plasma therapy on day 10 of hospitalization. These patients showed improvement approximately 1 wk after infusion of plasma. At the same time, these patients were also receiving antiviral drugs, including lopinavir/ritonavir and interferon<sup>[12,13]</sup>. The study was not a randomized clinical study, and there was no control group that did not receive plasma therapy. The patients also received many other treatments, such as hormones and antibiotics. Therefore, it is difficult to determine the exact role of plasma therapy, the best timing for plasma therapy, and whether the earlier application of plasma therapy can lead to different clinical results. By contrast, the treatment plan for our patient at the early stage after the infection was detected was the effective maintenance of nutritional and supportive treatment and did not include antiviral and antibiotic treatment, while convalescent plasma was infused on day 7 after admission. Although the novel coronavirus nucleic acid test was still positive on the second day after infusion, the cycle threshold values were significantly higher than those on day 5 of hospitalization. There were no adverse reactions after blood transfusion, and the vital signs were relatively stable. On day 11 of hospitalization (the third day after the first blood transfusion), the patient received the second round of convalescent plasma therapy, and there was no transfusion reaction during the blood transfusion. The red blood cell count and hemoglobin both improved and remained stable. Afterward, the results of the novel coronavirus nucleic acid test were negative for two consecutive days.

According to the clinical classification<sup>[14]</sup>, although the clinical symptoms of this patient were moderate, clinical indications such as his high age and multiple high-risk factors, suggested a risk of critical illness. The treatment plan we adopted did not

include antiviral treatment but used nutritional and supportive treatment to alleviate the patient's symptoms, and we promptly carried out the treatment plan of convalescent plasma transfusion. The patient's immunity was significantly improved, and the patient became negative for the virus within 6 d and did not become severely ill.

Our experience treating this patient suggests that for the elderly and patients with underlying conditions, administering immune-enhancing treatment such as convalescent plasma transfusion while maintaining supportive treatment at the early phase after the beginning of symptoms can effectively reduce the number of patients who progress into critically illness. The success in plasma transfusion in this case also provides a reference for the selection of the optimal time point for plasma treatment. The successful treatment of this case also gave us increased confidence in curing elderly patients.

## CONCLUSION

Most patients with COVID-19 have a good prognosis, a small percentage of the patients are critically ill, and critical illness and death occur mostly in the elderly. The elderly is the high-risk group of COVID-19 pneumonia patients, so improving the medical treatment of elderly patients with severe COVID-19 pneumonia is of great significance. Our experience suggests that for patients with high-risk factors for COVID-19 pneumonia, such as old age and underlying diseases, improving the patients' immunity while maintaining supportive treatment in the early stages after they show symptoms can effectively reduce the number of patients who became critically ill. In addition, this patient was treated with convalescent plasma on days 7 and 11 of hospitalization and was successfully cured on day 12. This choice of time points provides a reference for choosing the best timing of convalescent plasma treatment and highlights the effectiveness of the clinical strategy of plasma treatment in the recovery period of patients with COVID-19 pneumonia. The results from this case report are encouraging, yet long-term data from more elderly COVID-19 patients with underlying diseases will be needed to draw definite conclusions and bring it into mainstream clinical practice.

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