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Treatment with convalescent plasma for COVID-19 patients in Wuhan, China

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Abstract

The discovery of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the outbreak of coronavirus disease 2019 (COVID-19) are causing public health emergency. A handful of literatures have summarized its clinical and radiologic features, whereas therapies for COVID-19 are rather limited. In order to evaluate the efficacy of convalescent plasma therapy in COVID-19 patients, we did this timely descriptive study. 6 laboratory confirmed COVID-19 patients were enrolled and received the transfusion of ABO-compatible convalescent plasma. The efficacy of this intervention was determined by the alleviation of symptoms, changes in radiologic abnormalities and laboratory tests. No obvious adverse effect observed during the treatment. Transfusion of convalescent plasma led to a resolution of ground glass opacities (GGOs) and consolidation in patient #1, #2, #3, #4 and #6. In patient #1 and #5 who presented with SARS-CoV-2 in throat

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swab, convalescent plasma therapy elicited an elimination of virus. Serologic analysis indicated an immediate increase in anti-SARS-CoV-2 antibody titers in patient #2 and #3, but not in patient #1. This study indicates that convalescent plasma therapy is effective and specific for COVID-19. This intervention has a special significance for eliminating SARS-CoV-2 and is believed to be a promising state-of-art therapy during COVID-19 pandemic crisis.

Keywords: SARS-CoV-2; COVID-19; convalescent plasma therapy

Running title: Convalescent plasma therapy for COVID-19

1. Introduction

The global outbreak of a novel human coronavirus, newly named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the international committee on taxonomy of viruses, has attracted increasing attentions and public emergency [1,2]. This virus was initially detected in Wuhan, China, in December 2019. A cluster of pneumonia patients manifesting as fever, cough, and dyspnea with unknown etiology emerged at that time [3-5]. The virus was presumed to be zoonotic because preliminary investigation demonstrated that the first generation patients in Wuhan geographically linked to Huanan seafood whole sale market where live animals were sold. While patients outside of Wuhan usually had traveled to the city, or had contact with city residents [6]. These epidemiologic findings strongly suggest that SARS-CoV-2 transmits from human-to-human, and causes the disease now named coronavirus disease 2019 (COVID-19) [7]. By the end of March, 2020, COVID-19 has spread up to 199 countries and causing more than 27000 deaths [8].

SARS-CoV-2 belongs to the β-coronavirus family. Its genome is a single-stranded RNA composed of about 30 kb nucleotides, which encodes four

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major structural proteins: spike protein (S), membrane protein (M), envelope protein (E), and nucleocapsid protein (N). Among these proteins, the S protein is of special interest because this club-shaped glycoprotein spikes give the virus a crown-like appearance [9]. Translational studies have demonstrated that the interaction between the receptor binding motif of S protein and the angiotensin-converting enzyme 2 (ACE2) mediates the recognition and entry of SARS-CoV-2 into the host cells, and ACE2 is defined as a putative receptor for SARS-CoV-2 [10,11]. The homogeneity in the receptor binding domain between SARS-CoV-2 and SARS-CoV underlies their overlapping pathogenicity and biological properties. Indeed, the clinical manifestations and radiologic features of COVID-19 and those of SARS are quite similar [12,13]. For example, both diseases are highly infectious, and the incubation period ranges from several days to two weeks. Common symptoms at the onset of disease include fever, cough, myalgia and shortness of breath. Laboratory test may indicate white blood cell count below normal range, lymphopenia, hypoxaemia, deranged liver and renal function [3,5]. The typical radiologic abnormalities include multifocal ground glass opacities (GGOs) and subsegmental areas of consolidation [14-16].

At the moment, therapeutic strategy for COVID-19 is largely supportive [17]. Several off-label anti-viral and anti-HIV agents seem to be clinical beneficial, but their efficacy is far from satisfactory [18]. To this end, there are urgent needs to develop COVID-19-specific treatment to alleviate the symptoms and reduce the mortality. Previous experience with SARS suggested that convalescent plasma exhibit a neutralizing antibody response directed against the viral S protein. This antibody blocks SARS-CoV-ACE2 entry and can be detected even 24 months after infection [19]. A retrospective study by Soo and colleagues compared the clinical outcome of convalescent plasma therapy verses high-dose steroids pulse therapy in SARS patients with deteriorated disease. They found that patients in the

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plasma group had a shorter hospital stay and lower mortality than the comparator group, and no immediate adverse effect noted after plasma infusion [20]. A systemic meta-analysis involving 1703 influenza pneumonia patients who received influenza-convalescent human blood products, showed reduced virus load and pooled absolute reduction of 21% in mortality [21]. Since the number of COVID-19 cases and disease-related death is increasing at an incredible speed, an urgent question that needs to be addressed promptly is whether it is also effective to use convalescent plasma therapy in the COVID-19 setting. One going clinical trial is recruiting patient for anti-SARS-CoV-2 convalescent plasma therapy in Shanghai, China, but no relevant data has been announced yet (NCT04292340). The outcomes of this trial are definitely essential for formulating the principles of therapeutic strategy.

In this study, we provided preliminary data showing the efficacy of convalescent plasma therapy in COVID-19 patients. We found this intervention was effective in improving patient's symptoms and ameliorating radiologic abnormalities. More timely multi-center randomized clinical trials are warranted to determine the safety and efficacy of convalescent plasma therapy for COVID-19.

2. Methods

2.1 Patients and ethics

During the outbreak of SARS-CoV-2 infection in Wuhan, the number of COVID-19 patients far exceeded the capacity of local hospital. Therefore, the government built two designated hospital in Wuhan, one of which was named Huoshenshan. We did this study in 6 COVID-19 patients admitted to Wuhan Huoshenshan Hospital from February 11th to March 12th, 2020. All the patients

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were laboratory confirmed COVID-19 cases by using throat swab SARS-CoV-2 real-time PCR. Upon admission, all the COVID-19 patients have been empirically treated with anti-viral drug arbidol, which is also recommended by the New Coronavirus Pneumonia Diagnosis and Treatment Program (6thedition) published by the National Health Commission of China[1]. Our inclusion criteria were: (1) laboratory confirmed cases; (2) patients with abnormalities in chest CT (Case #5 was an exception); (3) patients with deteriorated symptoms after standard treatment; (4) patients with persistent positive result of throat swab; (5) critically ill patients. Exclusion criteria were: (1) patients allergic to plasma contents; (2) patients positive for HBV, HCV and HIV; (3) patients with uncontrolled bacterial mixed infection; (4) patients with malignant tumors; (5) patients who developed multiple organ dysfunction syndrome. Eligible patients' baseline characteristics were listed in Table 1. This study was reviewed and approved by the Medical Ethical Committee of Wuhan Huoshenshan Hospital. Written informed consent was obtained from each participant.

2.2 Donors and convalescent plasma transfusion

Convalescent plasma was collected from patients who had recovered from COVID-19. Recovery was defined as an afebrile status for at least 3 days, alleviation of respiratory symptoms, negative for SARS-CoV-2 nucleic acid for consecutive two RT-PCR tests, and at least 3 weeks following disease onset. The donors need to be seronegative for anti-HBV, HCV and HIV, and seropositive for

[1]Available at http://www.nhc.gov.cn/yzygj/s7653p/202002/8334a8326dd94d329df351d7da8aefc2.shtml

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anti-SARS-CoV-2. As a routine check with plasma donation, the convalescent plasma was also confirmed free of residual SARS-CoV-2 by real time PCR.

Eligible patients received the transfusion of ABO-compatible convalescent plasma as soon as the plasma was available to the institution. In accordance with the New Coronavirus Pneumonia Convalescent Plasma Therapy Guidance of China (2nd edition)[2], patients received at least one cycle of ABO-compatible convalescent plasma transfusion (200ml for each cycle). Each transfusion was administered over a 30-minute period.

2.3 Throat swabs analysis

Throat swabs were taken and immediately put into transport tube. All the tested samples were processed under airborne precaution. The SARS-CoV-2 nucleic acid was detected by reverse transcription and real-time PCR assays using commercial detection kit (Changsha Sansure Biotech). Two independent primers that match the open reading frame1ab (ORF1ab) and the nucleocapsid protein (N) fragments were used. RNase P was used as equal loading control. Reverse transcription and real-time PCR were performed according to the manufacturer's recommendations. Each transcript provided a cycle threshold value (Ct value), which is the number of cycles required for the fluorescent signal. A Ct value less than 40 was defined as a positive result, and a Ct value exceeds 40 was defined as a negative test.

[2]Available at http://www.nhc.gov.cn/yzygj/s7658/202003/61d608a7e8bf49fca418a6074c2bf5a2.shtml

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2.4 Serum anti-SARS-CoV-2 IgM and IgG array

Serum anti-SARS-CoV-2 IgM and IgG were measured by chemiluminescence using commercially available kits (Shenzhen YHLO Biotech). Briefly, blood sample was centrifugated at room temperature and the supernatant was removed and incubated with the SARS-CoV-2 antigen-coated magnetic beads. The antigen-antibody complex captured by the beads slurry was gently precipitated by a magnetic separation rack. The beads were then incubated with acridinium ester-labeled mouse anti-human IgM or IgG antibody and reacted with hydrogen peroxide in excitation buffer. Relative luminescence intensity was recorded in an iFlash-3000 chemiluminescence system.

2.5 Safety and therapeutic outcome evaluation

Adverse events and serious adverse events associated with convalescent plasma transfusion were assessed by the treating clinician. During transfusion, patients were under continuous supervision, with vital signs checked every 15 minutes and at 4 hours after the end of the intervention.

The primary outcome was the improvement in symptoms and chest CT in the following days after indicated intervention. Blood and swab samples were obtained to measure serum anti-SARS-CoV-2 IgM and IgG titers and throat SARS-CoV-2 nucleic acid, respectively.

3. Results

A total number of 6 patients were assessed during the study period. This study was initially designed in the middle of February, however, the ABO-compatible convalescent plasma was not available until the beginning of March. We actually recruited the first participant on March 5th and the last participant on March 18th,

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respectively. The other issue needed to be addressed was that Wuhan Huoshenshan Hospital did not receive COVID-19 patients directly from the community, instead, our patients were transferred from other non-designated hospital. Therefore, our patients had been treated elsewhere and were at a relatively late course of the disease when admitted to the institution. Most patients manifested as fever, shortness of breath and non-productive cough at the onset of the disease. Other common clinical manifestations included fatigue and myalgia (Table 1). As the patients have been treated previously, blood cell count, coagulation test and biochemical analysis upon admission was mostly normal. In terms of inflammation indicators, patient #3 had a slight increase in C-reactive protein (6.73mg/L) and procalcitonin (0.17μg/L). No adverse reactions were observed in the six patients during plasma transfusion and in the following three days.

3.1 COVID-19 patient with persistent SARS-CoV-2 detection

A 69-year-old man complained recurrent fever (Tmax 39^{o}C), shortness of breath and myalgia since February7th. He admitted to a local hospital and chest CT showed diffused GGOs in bilateral lungs. He was treated with levofloxacin for 3 days and his temperature became normal on February 10th. The patient was tested for SARS-CoV-2 and the throat swab result was positive. He was sent to our institution on February25th. At admission, his vital signs were stable and his saturation was 96% on ambient air. Chest CT examination on February 29th indicated patchy areas of GGOs in the right lung (Figure 1). The serum anti-SARS-CoV-2 antibody titers on March 3rd were 104 and 180 for IgM and IgG, respectively. While throat swab test on February 29th, March 3rd and March 8th led to a persistently positive result. He received ABO-compatible convalescent plasma therapy on March 10th, but throat test on March 12th was still positive for

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SARS-CoV-2. Repeated transfusion of convalescent plasma was given on March 13th and March 16th, respectively. Chest CT on March 14th indicated that the GGOs were resolved (Figure 1). Unfortunately, throat swab test on March 18th still led a positive result. However, the result turned to negative in the following two consecutive tests. Moreover, serum anti-SARS-CoV-2 antibody titers on March 11th and March 14th were comparable to those before plasma therapy. After carefully evaluation, the patient was considered as cured and was ready to discharge from hospital.

3.2 COVID-19 patient with consolidation

A 75-year-old woman had fatigue and shortness of breath on February 2nd. She did not have fever and myalgia. She was positive for SARS-CoV-2 throat test and admitted to our hospital on February 12th. At admission, her saturation was 75% and she received oxygen therapy through nasal catheter. Chest CT scan on February 22nd showed multiple subpleural consolidation in bilateral lungs (Figure 2). Her throat swab was negative for SARS-CoV-2, but she still felt respiratory distress and need oxygen supplement. On March 5th, repeated chest CT examination suggested a partial resolution of the consolidation in the left down lobe, whereas the majority of lesions in the right lung were not resolved (Figure 2). Therefore, the convalescent plasma was given on March 5th. Before the treatment, serum anti-SARS-CoV-2 antibodies titers for IgM and IgG were 47 and 106, respectively. The patient reported that she felt an alleviation of respiratory distress after the treatment and the second cycle of convalescent plasma was given on March 9th. Re-evaluation of serum anti-SARS-CoV-2 antibodies on March 11th suggested a two-fold increase in IgM and IgG titers. Although chest CT on March 11th did not indicated a radiologic improvement, the patient did not require oxygen therapy and the saturation was 99% on ambient air. In order to track the dynamic

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changes of consolidation, repeated chest CT scan was done on March 18th. Figure 2 showed representative images illustrating the evolution of consolidation. After two cycles of convalescent plasma intervention, the density of consolidation was gradually reduced and turned into scattered GGOs with subpleural line. Three independent throat swab tests were all negative for SARS-CoV-2. The patient was considered as cured and was under further clinical monitoring.

3.3 COVID-19 patient with extensive lung lesions

A 56-year-old man admitted to our hospital on February 12th. He had fever (Tmax 37.8°C) and non-productive cough since February 2nd. At admission, he complained shortness of breath and his saturation was 95% on 5L/min oxygen inhalation. Laboratory tests indicated normal blood count values and coagulation test. The patient had a slight increase in C-reactive protein (6.73mg/L) and procalcitonin (0.17μg/L). Chest CT on February 21st showed consolidation in the right upper lobe and multiple GGOs in bilateral lungs. Reticular opacities with vacuole inside and fibrosis streak were evident in the right down lobe (Figure 3). Throat swab tests on February 23rd and February29th were negative. Repeated chest CT was done on March 5th and it indicated a partial resolution of the consolidation and GGOs. Serological examination showed the anti-SARS-CoV-2 IgM and IgG titers were 273 and 72, respectively. However, the patient still had respiratory distress, and the arterial blood gas analysis indicated a ratio of the partial pressure of oxygen (PO2) to the fraction of inspired oxygen (FiO2) of 180 (>300 under normal condition). The patient received transfusion of convalescent plasma on March 5th, and he reported an improvement of his symptom. The second and third cycle of intervention was given on March 6th and March 9th, respectively. As expected, serum IgM and IgG titers increased after plasma transfusion. Repeated chest CT examination on March 11th and March 15th

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showed a complete resolution of the consolidation and gradually resolution of GGOs around the reticular vacuole. Of noted, a septal line appeared in left down lobe (Figure 3). Arterial blood gas analysis on March 15th indicated a PO2/FiO2 ratio of 330. The patient was cured and has discharged from hospital.

3.4 COVID-19 patient with Sjögren syndrome

A 63-year-old woman with ten years history of Sjögren syndrome had fever (Tmax 39°C), cough, shortness of breath and decreased exercise tolerance on January 31st. She was treated with levofloxacin, but her disease deteriorated. The patient was positive for SARS-CoV-2 throat swab test and admitted to our hospital on February 11th. Chest CT examination indicated peripheral and central distribution of multiple GGOs with partial consolidation and fibrosis streak. Air bronchogram sign could be seen inside consolidation (Figure 4). The patient received arbidol and oxygen treatment, whereas glucocorticoid was not used to avoid virus dissemination. The treatment led to a remission of the patient's symptoms, and the result of throat swab tests on February 24th, February 25th and March 1st was negative. Chest CT on March 5th showed the resolution of solidified lesions, and the residual lesions presented as GGOs with partial consolidation (Figure 4). This radiologic presentation would be attributed to either SARS-CoV-2 infection or Sjögren syndrome-associated interstitial lung disease. To exclude the possibility of SARS-CoV-2 infection, we treated the patient with convalescent plasma transfusion on March 10th, and repeated chest CT was done on March 14th. The density of GGOs tended to reduce, while the distribution pattern was not changed (Figure 4). Serological examination showed that the patient was positive for anti-SARS-CoV-2 IgM and IgG and the patient had a negative throat swab result on March 11th. The patient was discharged from our hospital on March 16th and received treatment for Sjögren syndrome.

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3.5 Post-discharge SARS-CoV-2-positive COVID-19 patient

A 28-year-old woman experienced fatigue and myalgia on February 10th. Her throat swab was positive for SARS-CoV-2 but her chest CT was otherwise normal. Before discharge from a local hospital, two consecutive throat swab tests were negative. She was asymptomatic and sent to our hospital for further clinical evaluation on March 5th. At admission, serologic anti-SARS-CoV-2 antibody test was positive. The first throat swab test in our institution was negative, whereas it turned positive on the following days. Chest CT examination on March 8th did not showed lung lesions (Figure 5). This asymptomatic patient without radiologic abnormalities was recognized as a post-discharge SARS-CoV-2-positive COVID-19 patient, and could be a potential source of infection. Thus, convalescent plasma therapy was used on March 13th. Several consecutive SARS-CoV-2 throat swab tests after the intervention were negative. The patient was discharged from hospital on March 19th.

3.6 COVID-19 patient with GGOs

A 57-year-old man had fever, cough, shortness of breath and myalgia since January 29th. He was tested for throat swab SARS-CoV-2, and the result was positive. He was sent to our hospital on March 12th. Laboratory blood test indicated titers of anti-SARS-CoV-2 IgM and IgG were 16 and 217, respectively. Chest CT examination on March 14th showed GGOs without clear boundary in the peripheral region and down lobe of bilateral lungs (Figure 6). Although repeated throat swab test after admission was negative, the patient complained that he still had respiratory distress. The convalescent plasma was given on March 18th, and the patient reported a markedly relief of symptom. Figure 6 showed the radiologic changes 3 days after indicated intervention, in which GGOs were generally

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resolved after convalescent plasma transfusion. The patient was discharged from hospital on March 22nd.

4. Discussion

This descriptive study highlights convalescent plasma therapy as an effective and specific treatment for COVID-19. According to the experience of SARS and severe influenza, convalescent plasma is recommended to use as early as possible because the production of endogenous IgM and IgG antibodies peaks at two weeks and four weeks after infection, respectively [20,21]. However, patients admitted to Wuhan Huoshenshan Hospital have already been treated elsewhere and the duration from the onset of disease to admission usually exceeds four weeks. Fortunately, convalescent plasma therapy is still functional in the 6 patients, and all patients did not admit to ICU during treatment. To the best of our knowledge, this is a timely study evaluating the efficacy of convalescent plasma therapy in COVID-19 patients with distinct radiologic, laboratory and clinical features.

In compliance with the New Coronavirus Pneumonia Diagnosis and Treatment Program (6th edition), the principle of discharge was based on a relief of symptoms, obvious absorption of abnormalities in chest CT, abatement of fever, and viral clearance with throat swab for two consecutive tests. In our study, we found detectable SARS-CoV-2 in patient #5 who has already discharged from a local hospital. This is in agreement with a previous report that the virus RNA persists for a median of 20 days in survivors.[3] Strikingly, patient #5 represents a group of post-discharge asymptomatic “walking COVID-19” cases that might serve as a possible source to propagate the outbreak [22]. Indeed, a recent autopsy study of COVID-19 patient’s lung indicates the presence of SARS-CoV-2 particles in bronchial mucosal epithelial and type II alveolar epithelial cells [23].

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This has important implications for reconsidering the period of patient isolation, the principle of discharge, and warrants highly efficient that can eliminate SARS-CoV-2. Yeh and colleagues tested the efficacy of convalescent plasma therapy in three SARS patients, and they found viral load dropped from 495×10^3, 76×10^3 or 650×10^3 copies/mL to zero or 1 copy/mL one day after transfusion. Anti-SARS-CoV IgM and IgG also increased in a time-dependent manner following transfusion [24]. This treatment is also effective for influenza A (H5N1) infection, in which convalescent plasma therapy led to a 12-fold decrease in blood virus load during the first 8 hours after transfusion, and the virus was undetectable within 32 hours [25]. These findings recommend a specific and effective strategy to eliminate residual virus. In agreement with this hypothesis, we found a clearance of SARS-CoV-2 in throat swab test in patient #5 who received the transfusion of convalescent plasma. Of special interest, patient #1, who has persistent positive result for throat swab test, is free of SARS-CoV-2 after the same intervention. It is not surprising to notice that his serum anti-SARS-CoV-2 antibody titers after three cycles of convalescent plasma therapy are not increased, probably because residual virus consumes the protective anti-SARS-CoV-2 IgM and IgG, and the antibody titer starts to increase after virus clearance (Figure 1 and Supplementary Figure S1). These findings strongly indicate that convalescent plasma transfusion is a specific and effective therapy for COVID-19.

Another important finding in our study is the dynamic change of radiologic abnormalities. We found a rapid and dramatic radiologic improvement in patient #6, who manifested as extensive pure GGOs. This effect could be recaptured in patient #2 and patient #3, while the absorption of consolidation takes a relatively longer time. Intriguingly, our initial chest CT evaluation of patient #3 showed the patient's lung was in bad condition and respiratory distress did not relieve after standard supportive treatment. Although he was negative for throat swab test and

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the anti-SARS-CoV-2 IgM and IgG were detectable, it is reasonable to believe a clearance of virus in the upper respiratory tract, while SARS-CoV-2 may still exist in the lower respiratory tract and lung. Bronchoalveolar lavage fluid SARS-CoV-2 test would be informative, but bronchoscopy examination was not applicable in case of air-borne droplets transmission. We treated patient #3 with the transfusion of convalescent plasma. As a consequence, the patient had a significant improvement of his symptom, as well as a gradually resolution of consolidation.

Our study is different from previous SARS and influenza cases because convalescent plasma was used in a relatively late course of disease. We found it is still clinically beneficial in all the 6 cases. The mechanism of action in this setting was not fully understood. We speculated that the anti-SARS-CoV-2 IgM and IgG directly neutralizes the virus, and the anti-inflammatory contents may prevent cytokine storms. For the latter hypothesis, there is great debate of using corticosteroids. Evidence in SARS suggests that corticosteroids do not reduce mortality, but rather delayed viral clearance [26]. Therefore, corticosteroids should not be routinely given, like what we have done in patient #4 with Sjögren syndrome.

This study is limited by the small sample size. However, by including representative patients with distinct radiologic, laboratory and clinical features, we believe our study population is representative of COVID-19 patients in Wuhan. Since more and more patients have recovered from the infection of SARS-CoV-2, voluntary donation of convalescent plasma would be definitely encouraged and appreciated. Taken together, COVID-19 is becoming a global health threat, reliable treatment is crucial for reducing mortality and preventing disease outbreak. SARS-CoV-2-specific therapies, including convalescent plasma from

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recovery patient, would be highly effective weapons to win the war against COVID-19.

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Conflict of interests

We declare no competing interests.

Author contributions

MY, XX, and TL conceived and designed the study. MY, DF, YR, and DW took care of the patient and contributed to the acquisition of data. XX contributed to the development of methodology. MY, XX, and TL contributed to analysis and interpretation of data. FW, FZ, and TL contributed to study supervision. MY and TL wrote this paper.

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Figures

Figure 1. **A diagram summarizes the treatment and major laboratory findings of patient #1.** This patient had persistent positive result for throat test. Transfusion of convalescent plasma was given on March 10th, 13th and 16th, respectively. Representative chest CT images on February 29th and March 14th suggest the absorption of patchy scattered GGOs in the right lung (indicated by white arrows). Repeated throat swab test indicate a clearance of residual SARS-CoV-2.

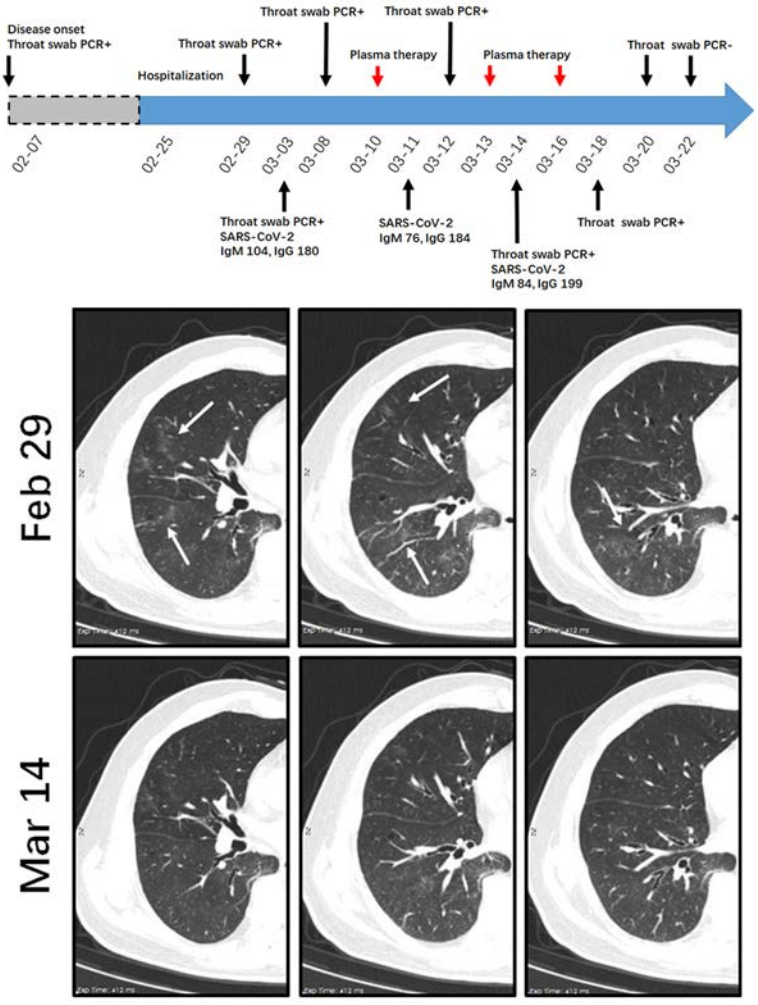

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Figure 2. **A diagram summarizes the treatment and major laboratory findings of patient #2.** The patient manifested as consolidation involving multiple subsegmental lobes. The patient received convalescent plasma on March 5th and 9th. The dynamic evolution of consolidation was presented by chest CT on February 22nd, March 5th, March 11th and March 18th, respectively.

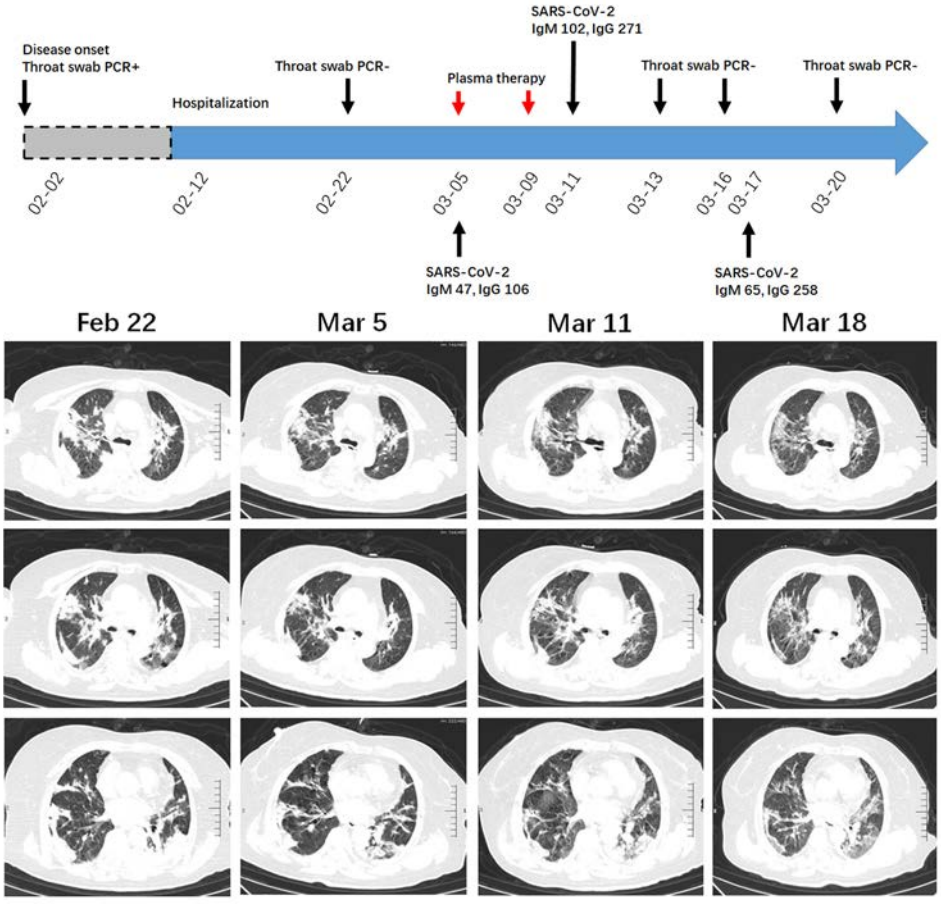

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Figure 3. **A diagram summarizes the treatment and major laboratory findings of patient #3.** Chest CT on February 21st showed consolidation, multiple GGOs, reticular opacities with fibrosis streak. The patient received three cycles of convalescent plasma therapy and this intervention led to an alleviation of symptom, as well as a gradually radiologic improvement. A septal line appeared in left down lobe after indicated treatment.

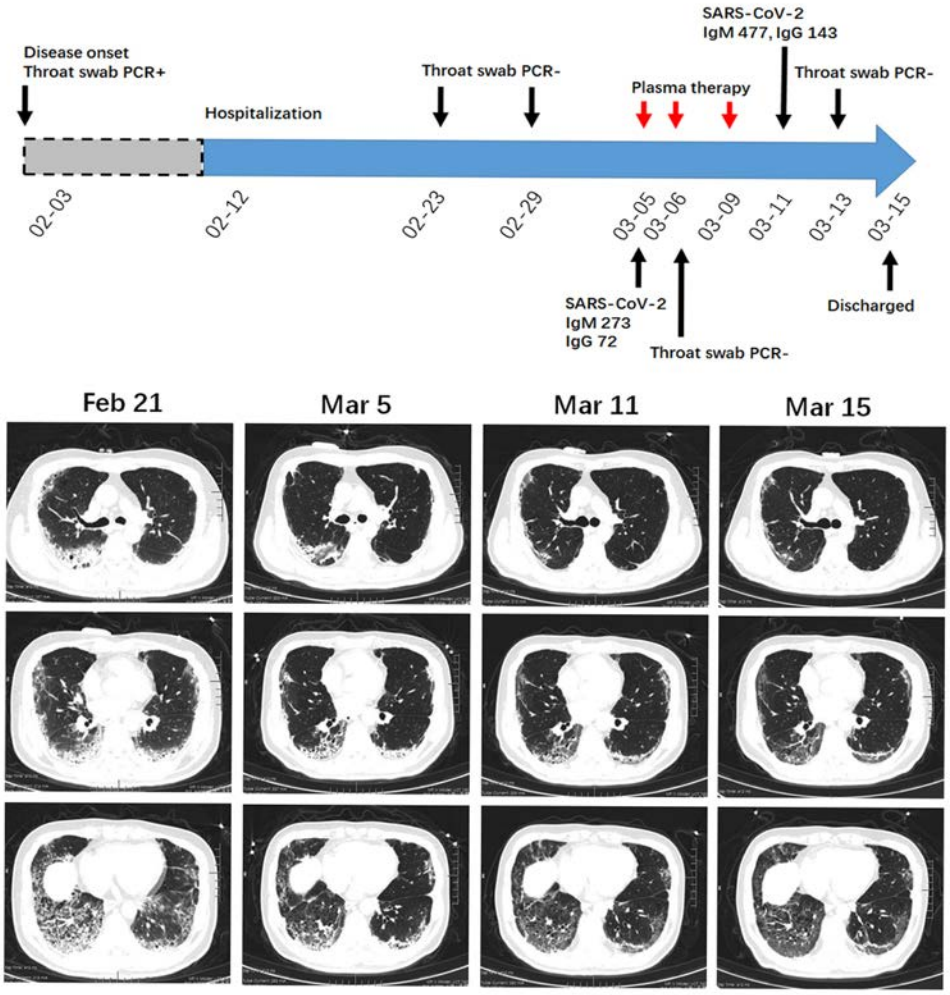

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Figure 4. **A diagram summarizes the treatment and major laboratory findings of patient #4.** The 63-year-old female patient concurrent with Sjögren syndrome had multiple GGOs with partial consolidation and fibrosis streak at admission. After indicated treatment, she presented as GGOs with partial consolidation. Transfusion of convalescent plasma was done on March 10th, and repeated chest CT showed a slight decrease in the density of GGOs.

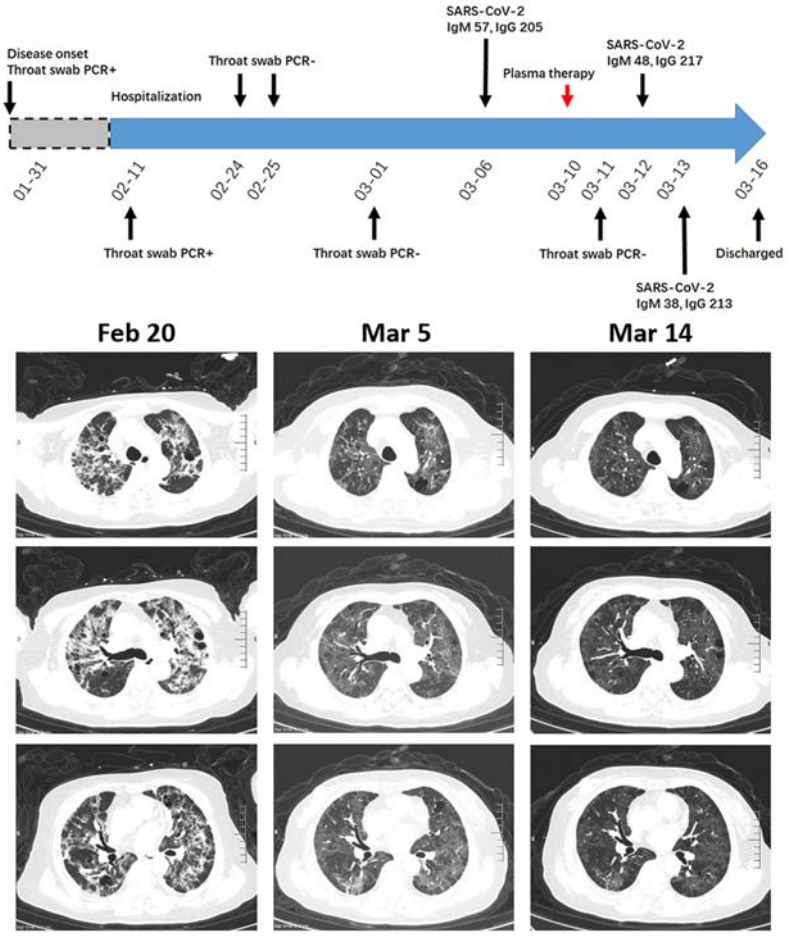

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Figure 5. **A diagram summarizes the treatment and major laboratory findings of patient #5.** The patient was defined as post-discharge SARS-CoV-2-positive COVID-19, and treated with convalescent plasma on March 13th. Consecutive SARS-CoV-2 throat swab tests indicated an elimination of residual SARS-CoV-2.

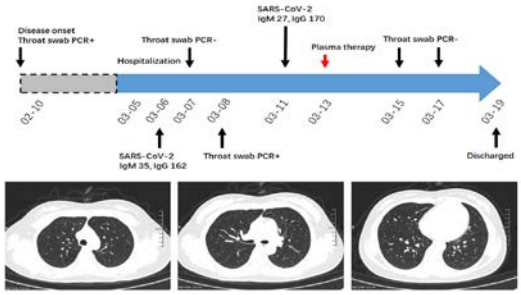

Figure 6. **A diagram summarizes the treatment and major laboratory findings of patient #6.** The radiologic feature of this patient is extensive GGOs. The convalescent plasma was given on March 18th, and repeated chest CT showed a remarkable resolution of GGOs after the intervention.

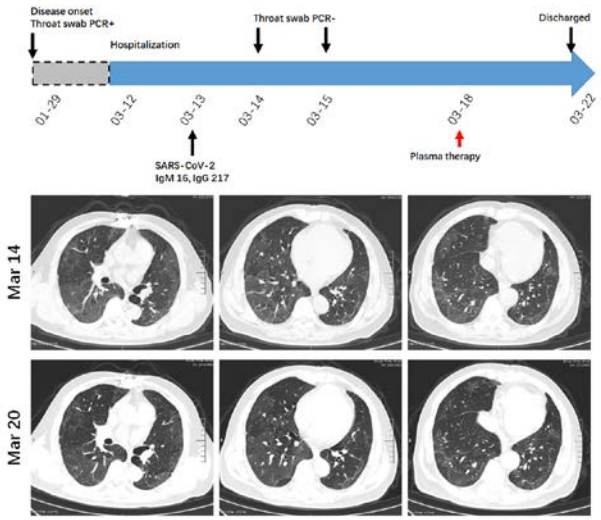

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Table 1. Characteristics of the 6 participants.

	Patient #1	**Patient #2**	**Patient #3**	**Patient #4**	**Patient #5**	**Patient #6**
Sex	Male	Female	Male	Female	Female	Male
Age	69	75	56	63	28	57
Comorbidity	No	No	Bronchitis	Sjögren syndrome	No	No
Fever	Tmax 39^{o}C	No	Tmax 37.8^{o}C	Tmax 39^{o}C	No	Tmax 37.5 ^{o}C
Cough	No	No	Yes	Yes	No	Yes
Fatigue	No	Yes	No	Yes	No	No
Myalgia	Yes	No	No	No	No	Yes
Dyspnea	Yes	Yes	No	Yes	No	Yes
Diarrhea	No	No	No	No	No	No
Date of disease onset	Feb 7	Feb 2	Feb 2	Jan 31	Feb 10	Jan 19
Date of admission	Feb 25	Feb 12	Feb 12	Feb 11	Mar 5	Mar 12
Low white blood	No	No	No	No	No	No

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cell count						
Lymphopenia	No	No	No	No	No	No
Requirement on oxygen supplement	No	Yes	Yes	Yes	No	Yes
Radiologic presentation	Patchy areas of GGOs	Multiple consolidation	Multiple GGOs, reticular opacities and fibrosis streak	Multiple GGOs with consolidation and fibrosis streak	Mostly normal	Extensive bilateral GGOs
Date of convalescent plasma therapy	Mar 10,13, 16	Mar 5,9	Mar 5,6,9	Mar 10	Mar 13	Mar 18
Cycle of convalescent plasma therapy	3	2	3	1	1	1
Symptom improvement	Yes	Yes	Yes	Yes	Not applicable	Yes
Radiologic improvement	Yes	Yes	Yes	Yes	Not applicable	Yes

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