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CASE REPORT
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The success of non-ABO-identical convalescent plasma transfusion in coronavirus disease 2019 (COVID-19) related acute respiratory distress syndrome (CARDS): a case-report

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ABSTRACT:

Coronavirus disease 2019 (COVID-19) is pandemic with substantial fatality without specific treatment. Convalescent plasma is used to treat infectious diseases including severe acute respiratory syndrome coronavirus 1 and Middle East respiratory syndrome coronavirus infection, because of the effect of direct neutralizing and suppression of viremia, and immunomodulation effect. Although several anti-cytokine agents were suggested to improve outcomes of the patient, the unavailability of drugs will be a major problem for accessing. We reported the experience of convalescent plasma transfusion for COVID-19 related acute respiratory distress syndrome (CARDS), who refractory to standard treatment and clinically improvement after convalescent plasma transfusion, despite unidentical blood group.

Keywords: Convalescent plasma, Coronavirus disease 2019, Acute respiratory distress syndrome, Incompatible ABO-Blood Group, Thailand

INTRODUCTION

The most severe form of severe acute respiratory syndrome coronavirus 2 (SARCoV-2) infection is acute respiratory distress syndrome (ARDS), known as coronavirus disease 2019 (COVID-19) related ARDS (CARDS), which occurred in approximately 15% of cases and resulted in a high mortality rate [1]. Several measurements have been suggested for use in rescuing the most severe COVID-19 patients. [2]

The proposed mechanism of actions of convalescent plasma in infectious diseases were direct neutralizing and suppression of viremia, and immunomodulation effect. [3] Convalescent plasma transfusion was previously used in SARS-CoV-1 infection, Middle East respiratory syndrome coronavirus (MERS-CoV) infection, and Ebola viral infection, demonstrating a better clinical improvement and reduction of mortality [4]. Recently, the efficacy of ABO-compatible convalescent plasma transfusion of around 200-400 mL in patients with severe COVID-19 pneumonia with acute respiratory failure has been reported to improve gases exchange and possibly reduced mortality in selected cases [5]. However, plasma of the most compatible ABO-blood group is difficult to prepare, particularly due to the unavailability of plasma donors.

We report the success of convalescent plasma transfusion with the unidentical ABO-blood group for CARDS patients that is refractory to the current recommended medical treatment. This case report was registered and approved by the human research and ethics committee at Faculty of Medicine, Prince of Songkla University (EC number: REC.63-502-14-1).

CASE DESCRIPTION

A 45-year-old man, presented at a primary hospital with acute respiratory symptoms and hypoxemia. He had been well until about 5 days prior to arrival, when he developed acute respiratory symptoms with fever, coughing and minimal dyspnea on exertion. Subsequently, his nasopharyngeal swab for reverse transcription-polymerase chain reaction (RT-PCR) revealed detectable COVID-19.

His initial chest X-rays demonstrated bilateral diffuse inhomogeneous infiltration of both lungs. Therefore, COVID-19 related pneumonia was initially diagnosed and he was immediately given favipiravir, a combination of lopinavir and ritonavir, hydroxychloroquine, azithromycin and intravenous methyprednisolone. However, his respiratory condition did not improve and required high flow nasal cannula (HFNC) with fraction of inspired oxygen (FiO_2) 1.0 to maintain his oxygen saturation around 90-93%. However, his clinical condition did not significantly improve after treatment, and eventually required endotracheal intubation and mechanical ventilation. He was finally referred to our hospital.

On arrival, he was hypoxic with oxygen saturation of 90-94% and arterial partial pressure of O_2 and the fraction of inspired oxygen (PaO_2/FiO_2) ratio of 248 under controlled mechanical ventilator support with positive end-expiratory pressure (PEEP) of 12 cm H_2O and FiO_2 1.0. His chest x-rays are shown in Figure 1A. Therefore, CARDS was eventually diagnosed. He also had lymphopenia with an absolute lymphocyte count of 924.7 cell/mm^3. The inflammatory parameters revealed serum ferritin 1,022 ng/mL (30-400 ng/mL), interleukin-6 (IL)-6 2.8 pg/mL (0-7 pg/mL), C-reactive protein (CRP) 19.98 mg/L (< 5 mg/L) and D-Dimers 3.79 mcg/mL (<0.5 mcg/mL). All current medical treatment was continued with the addition of 12 mg of intravenous dexamethasone There was no immunomodulation agents including IL-6 inhibitor, and intravenous remdesivir available at that time. Nevertheless, we then considered convalescent plasma transfusion for this patient.

The 600 mL of convalescent plasma of COVID-19 was donated by our first patient, who recovered from pneumonia after almost 21 days. The donor was firstly checked for the quantitative circulating antibody level for COVID-19 before entering the plasmapheresis machine. The antibody level shown that immunoglobulin G (IgG) antibody against nucleocapsid was 4.862 AU/mL and IgG antibody against spike antigen was 6.89 AU/mL. The plasma donor was ABO-blood group "B" with Rh positive, but the current recipient was found to have ABO-blood group "O" with Rh positive. Therefore, unidentical blood group transfusion reaction could be seen.

After careful judgement, this patient was then transfused 200 mL of the convalescent plasma on the first day of admission, which was day 14th after onset of disease. He was subsequently transfused another 200 mL of the convalescent plasma on the next day, after no significant improvement of clinical status and gas exchanges. No transfusion reactions, neither hemolytic nor non-hemolytic, were detected after plasma transfusion was completed.

His clinical condition, including hemodynamic parameters, oxygenation and infiltration on chest X-rays, was gradually improving 48 hours after transfusion. The second and third nasopharyngeal swab test for COVID-19 was undetectable by RT-PCR, 24 hours apart. He was eventually extubated five days after admission.

His gas exchanges, and chest X-rays were subsequently improved within 5 days (Figure 1B) with the final PaO_2/FiO_2 of 461.90. Before discharge, absolute lymphocyte count was 2,390 cell/mm3, serum ferritin 919 ng/mL (30-400 ng/mL), IL-6 4.06 pg/mL (0-7 pg/mL), CRP 4.35 mg/L (<5 mg/L) and D-Dimers 1.23 mcg/mL (<0.5 mcg/mL). He was finally discharged home 9 days after admission.

KEY MESSAGES:

- Convalescent plasma is one of the several modalities to treat several viral infectious diseases, which main mechanisms are direct neutralizing and suppression of viremia and immunomodulation effect.
- From the proposed mechanism, the application of convalescent plasma should be effective during the first week of SARS-CoV-2 infection or during the viremic phase.
- Efficacy of convalescent plasma have been observed in several case reports and case series in a specific group of patients, the recent randomized control study did not support the outcomes of treatment.
- WHO recently recommended against the use of convalescent plasma to treat non-severe COVID-19, but they noted that convalescent plasma should be used in severe cases and suggested conducting the clinical study in this group of patients.

DISCUSSION

We illustrated the case report of unidentical ABO-blood group convalescent plasma transfusion to the patient with CARDS, which demonstrated good treatment outcomes. This treatment was given to the patient who was in critical condition despite aggressive pharmacological management including anti-viral agents, and corticosteroid. In addition, the convalescent plasma transfusion diminished inflammatory marker responses, improved lymphocyte counts and possibly enhanced viral clearance. We believed that the improvement of clinical condition of this patient could be a result of convalescent plasma rather than current medical treatment, because all medication did not significantly change from the primary hospital. A top up convalescent plasma was only changed modality, that was given after our admission and the effect of the convalescent plasma normally occurred within 48 hours after transfusion in other infectious disease.

Convalescent plasma transfusion has been introduced for some emerging viral infections, including SARS, MERS, H1N1 and Ebola, resulting in clinical improvement and survival benefit [4]. In COVID-19, reports from the latest case-series giving 400 mL of ABO-compatible plasma to the patients with severe COVID pneumonia showed improvement of clinical status and reduction of length of stay [5]. The proposed mechanism of convalescent plas-

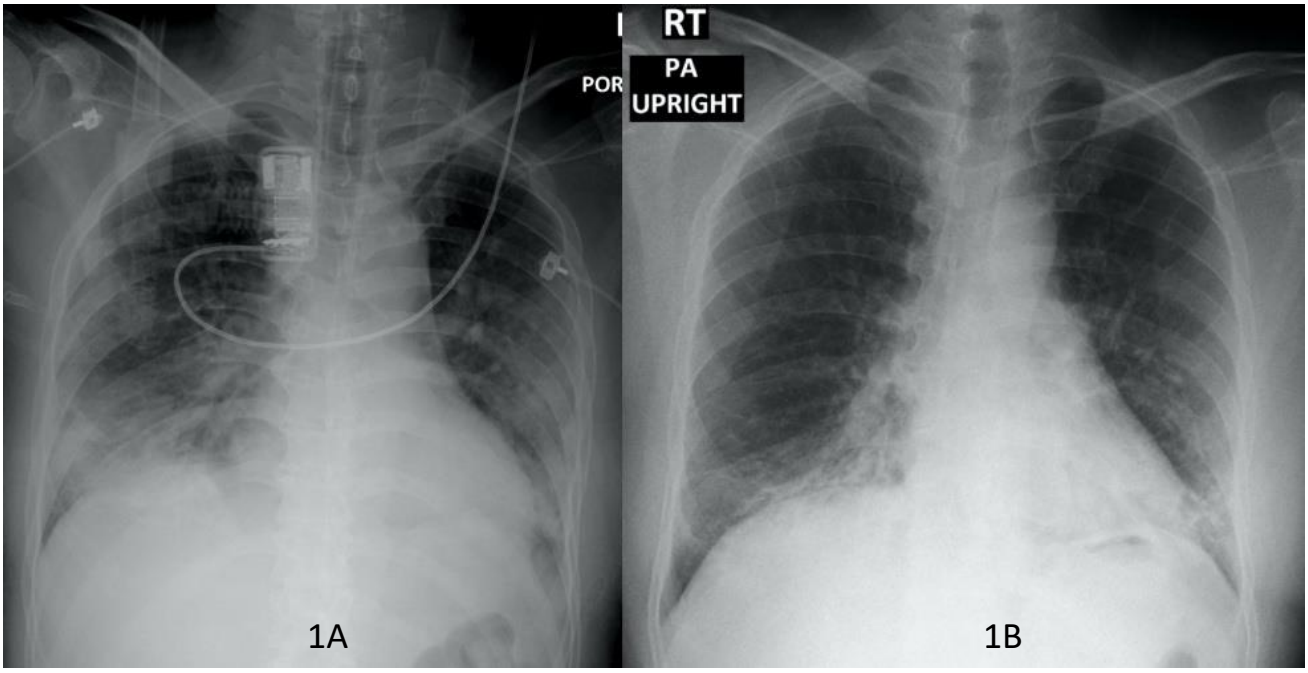

Figure 1. Chest x-rays(CXR): 1A CXR of the patient on admission (before convalescent plasma transfusion), 1B CXR of the patient on day 5th after convalescent plasma transfusion.

ma in emerging viral infection are anti-viral mechanism and immunomodulation effect [6]. Current reports on the application of convalescent plasma transfusion suggest use of the most ABO-compatible plasma to specific patients.

According to transfusion guidelines from several countries, most of them recommended use of plasma from the ABO-identical group or the most ABO-compatible group, unless it is necessary. Unfortunately, we did not have plasma from an ABO-identical donor for this patient at that time. From the transfusion immunology point of view, the recipient ABO-blood group "O", which expresses null antigen on their red cell surface, could practically receive the plasma components of either a ABO-group "A" or "B" donor without any immunologic reaction. However, monitoring of blood transfusion reactions, either hemolytic or non-hemolytic, must be performed if ABO-incompatible blood components are transfused.

In our case, we carefully decided to give the incompatible-ABO blood group convalescent plasma to rescue the deteriorated patient, who had received the optimal recommended medical therapy for almost a week. We weighed the risk and benefit of this measurement and closely monitored the transfusion reaction and clinical status of the patient. Finally, the patient improved without any complication and was eventually discharged 9 days after admission.

Although, the recent several randomized control studies of the effect of convalescent plasma in management of COVID-19 pneumonia evidenced that no beneficial particularly in non-severe patients, who majority required low flow nasal canula [7-10]. Nevertheless, the efficacy of convalescent plasma in the critically ill COVID-19 patients who required organ support remain inconclusive. In addition, the subgroup analysis of convalescent plasma in the patients with impairment of humoral antibody for SAR-CoV-2 may be beneficial [11].

WHO recently recommended against the use of convalescent plasma to treat non-severe COVID-19, but they noted that convalescent plasma should be used in the severe cases and suggested to conduct the clinical study in this group of patients [12]. Until the evidences come up, we believe that convalescent plasma could be specifically applied within the first week of symptoms or during the viremic phase, on top of the standard management, to the severe cases of COVID-19 pneumonia or to the patients with impairment of antibody responses to SAR-CoV-2.

CONCLUSION

We illustrated the CARDS patient, who refractory to the current standard medical treatment, dramatically responded to ABO-incompatible convalescent plasma transfusion without any transfusion reactions. We also asserted several pieces of current evidence that convalescent plasma transfusion in severe COVID-19 pneumonia is clinically useful, even in the less compatible ABO blood group. This is, however, is just only an anecdotal report, a larger study of convalescent plasma transfusion in the critically ill COVID-19 pneumonia is required before recommending this as standard treatment.

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AUTHORS' CONTRIBUTIONS

Chatchai Laopakorn: Conceptualization, Methodology, Investigation, Writing Original draft, Writing Review & Editing, Visualization, Project administration. Pimsai Kunakorn: Data curation, Writing Review & Editing. Petch Wacharasint: Software, Supervision, Data Curation

SUPPLEMENTARY MATERIALS

none

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