Transfusion-related acute lung injury in a COVID-19–positive convalescent plasma recipient: a case report

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Abstract
We present a case of transfusion-related acute lung injury as a complication of convalescent plasma transfusion in a patient who presented with COVID-19–related severe acute respiratory syndrome. Despite treatment with tocilizumab, remdesivir, and intravenous steroids, worsening dyspnea prompted adjunctive treatment with convalescent plasma. Two hours after completion of the plasma transfusion, the patient developed hypoxia-induced cardiac arrest secondary to transfusion-related acute lung injury. This case sheds light on life-threatening transfusion reactions and emphasizes the need to investigate post-transfusion monitoring protocols as well as the possible role of surveillance equipment.

Keywords
Transfusion-related acute lung injury, COVID-19, convalescent plasma, transfusion reaction, case report, severe acute respiratory syndrome

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Introduction
Transfusion-related acute lung injury (TRALI) is a frequently misdiagnosed, fatal adverse event associated with blood product transfusion. A unique form of acute respiratory distress syndrome (ARDS) that occurs within 6 hours of
transfusion, TRALI is caused by antibodies in the plasma of a single donor unit reacting with leukocyte antigens in the recipient.\textsuperscript{1,3,4} Amid the COVID-19 pandemic, convalescent plasma obtained from patients who have recovered from COVID-19 remains a viable treatment modality.\textsuperscript{5,6} Few adverse events secondary to convalescent plasma have been reported in the biomedical literature.\textsuperscript{7} We herein present a case of TRALI that occurred 2 hours after convalescent plasma transfusion. This case serves as a reminder for clinicians to be cautious when considering convalescent plasma treatment, and it emphasizes the role of continuous pulse oximetry and close video monitoring of plasma recipients.

Case presentation

A previously healthy 59-year-old man presented to our hospital with shortness of breath, coughing, and subjective fever. He was admitted with suspected COVID-19 pneumonia. The patient had no reported significant medical or family history. On examination, he was noted to be in respiratory distress with diffuse rhonchi bilaterally. Assessment of his vital signs showed an oxygen saturation of 81% on room air, which improved to 96% with application of a non-rebreather mask (NRBM); blood pressure of 131/88 mmHg; pulse of 87 beats/minute; and respiratory rate of 26 breaths/minute. The results of initial laboratory tests, including a complete blood count, measurement of electrolytes, and kidney and liver function tests, were unremarkable; however, the concentrations of inflammatory markers including D-dimers (388 ng/mL), ferritin (664.8 ng/mL), and C-reactive protein (49.30 mg/L) were elevated. COVID-19 infection was confirmed with a positive SARS coronavirus 2 (SARS-CoV-2) polymerase chain reaction swab. Although supplemental oxygen with an NRBM briefly resolved his symptoms, worsening hypoxic respiratory failure prompted the transition to a combination of a high-flow nasal cannula with an NRBM as well as administration of remdesivir and intravenous steroids. Rising serial inflammatory markers led to the addition of tocilizumab on day 5. On day 8, the patient developed frequent desaturations, and the critical care specialists recommended conscious proning with avoidance of positive-pressure ventilation because pneumomediastinum was seen as an incidental finding on serial chest X-rays.

On day 12, the patient was scheduled for transfusion of adjunctive convalescent plasma because of a slow decline in his oxygen saturation. Blood typing and screening showed that his ABO blood type was O, Rhesus factor (Rh) was positive, and antibody screening was negative. He received a transfusion of 2 units of adjunctive convalescent plasma (214 mL and 209 mL for the first and second unit, respectively). The donor blood was from a male patient (ABO type O, Rh positive, and negative for anti-HLA antibodies) who had received blood products in the distant past. The patient’s vital signs were recorded 1 hour prior to each transfusion, every 15 minutes during the transfusions, and 1 hour after each transfusion according to our hospital transfusion protocol. The patient was also monitored by telemetry and continuous pulse oximetry. He completed the convalescent plasma transfusion and remained hemodynamically stable during transfusion with no change in values compared with those prior to transfusion (blood pressure of 109/76 mmHg, pulse of 90 beats/minute, respiratory rate of 21 breaths/minute, and oxygen saturation of 89%). Two hours after completion of transfusion, a code blue was called and an advanced cardiovascular life support protocol was initiated; return of spontaneous circulation was achieved within 10 minutes. The patient was intubated and
transferred to the intensive care unit for further care.

Post-cardiac arrest laboratory testing showed the following results: lactate, >10 mmol/L; aspartate transaminase, 712 U/L; alanine transaminase, 1176 U/L; total bilirubin, 0.7 mg/dL; serum bicarbonate, 9 mmol/L; serum blood urea nitrogen, 54 mg/dL; serum creatinine, 1.57 mg/dL; serum troponin, 0.06 ng/mL; and serum B-type natriuretic peptide, 84 pg/mL. Point-of-care ultrasound showed no signs of pericardial effusion, no reduced ejection fraction, and adequate inferior vena cava collapse with respiration with absence of B-lines on lung ultrasound. A frontal chest X-ray obtained post-intubation showed diffuse bilateral infiltrates that were markedly worse than those on the prior chest X-ray obtained in the morning (Figures 1 and 2), demonstrating a clear temporal relationship with the convalescent plasma transfusion and alluding to TRALI. Unfortunately, the patient went into cardiac arrest twice during the next 8 hours and could not be resuscitated. The case was reported to the hospital transfusion medicine department as per protocol for further investigation with the blood bank and the donor. The reporting of this case conformed to the CARE guidelines.8

Discussion

COVID-19-related SARS has brought to the forefront treatment challenges and the emergent need for pilot projects during the pandemic. Along with novel antiviral agents (e.g., remdesivir), anti-inflammatory medications (e.g., corticosteroids), and interleukin 6 inhibitors (e.g., tocilizumab), transfusion of convalescent

![Figure 1. Frontal chest radiograph on the morning of admission day 12. The radiograph showed patchy bilateral airspace disease, no pneumothorax, stable pneumomediastinum, and no cardiomegaly. These findings were consistent with COVID-19 infection.](image-url)
plasma from patients who have successfully recovered from COVID-19 is considered a viable therapeutic option. Experience from prior outbreaks with other coronaviruses, such as SARS-CoV-1, shows that such convalescent sera contain neutralizing antibodies to the relevant virus. This has led to the transfusion of thousands of patients with convalescent plasma within the last several months.

TRALI is defined as new acute lung injury/ARDS occurring during or within 6 hours after blood product administration. In 2019, a modified classification scheme was advocated based on new observations related to transfusion reactions. Depending upon the concomitant risk factors for ARDS, TRALI is subclassified into type I and type II. Type I TRALI occurs in the absence of other known risk factors for ARDS, whereas type II TRALI is characterized by acute deterioration of the respiratory status after transfusion despite pre-existing mild ARDS. The patient in the present case had COVID-19–related SARS with minimal infiltrates for 12 days. He developed acute worsening of hypoxic respiratory failure within 2 hours of transfusion and exhibited radiographic evidence suggesting a diagnosis of type II TRALI (Figures 1 and 2).

The role of continuous pulse oximetry and closer monitoring during the initial hours post-transfusion can be life-saving in such patients. Further research is required to determine the precise protocol.
that can be used universally. Although no major adverse events have been reported thus far in the literature on COVID-19 treatment with convalescent plasma, the highest risk of mortality following plasma transfusion is likely due to pulmonary complications of transfusion reactions. This case highlights the need for a standardized protocol surrounding administration of convalescent plasma. The possibility of life-threatening transfusion-related adverse events must be taken into consideration before initiating convalescent plasma transfusion.

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Informed consent
Verbal informed consent was obtained from the patient’s family for his anonymized information to be published in this article.

Declaration of conflicting interest
The authors declare that there is no conflict of interest.

Ethics approval
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