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# Successful extracorporeal membranous oxygenation for a patient with life-threatening transfusion-related acute lung injury

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**Abstract**
A case of transfusion-related acute lung injury (TRALI) that was successfully treated with extracorporeal membranous oxygenation (ECMO) is reported. A 58-year-old male patient underwent hepatectomy, and pulmonary edema occurred after the administration of fresh-frozen plasma and packed red cells. In the postoperative period, the impaired oxygenation progressively worsened, resulting in life-threatening hypoxemia, despite vigorous treatments. ECMO was therefore applied to the patient as a method of safe emergency support. Aggressive treatments under ECMO led to the successful improvement of the impaired oxygenation. TRALI is recognized as part of acute respiratory distress syndrome (ARDS). As a treatment for ARDS, ECMO does not cure the underlying disease of the lungs, however, with ECMO, TRALI, usually improves within 96 h with respiratory support. ECMO for TRALI-induced lethal hypoxemia is useful for providing time to allow the injured lung to recover. It is suggested that ECMO might be a useful option for the treatment of TRALI-induced, potentially lethal hypoxemia.

**Key words** Extracorporeal membranous oxygenation · Transfusion-related acute lung injury

## Introduction

Transfusion-related acute lung injury (TRALI) is characterized by acute severe hypoxemia with bilateral noncardiogenic pulmonary edema after the transfusion of a plasma-containing blood component [1]. Most cases of TRALI require oxygen supplementation and/or mechanical ventilation, and 6%-10% of TRALI cases are fatal [1]. In this report, a life-threatening case of TRALI that was successfully treated with extracorporeal membraneous oxygenation (ECMO) is described.

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## Case report

A 58-year-old man weighing 70 kg underwent extended right-lobe hepatic resection for the treatment of hepatocellular carcinoma with Child-Pugh class A. At preoperative examination, arterial blood gas analysis showed $Pa_{O_2}$ of 86.9 mmHg, $Pa_{CO_2}$ of 38.6 mmHg, and pH of 7.41 (room air). The preoperative spirogram revealed normal respiratory function. Results of a transthoracic echocardiogram and electrocardiogram showed normal function.

Perioperatively, tracheal intubation and intermittent positive-pressure ventilation were facilitated with vecuronium. Epidural anesthesia and general anesthesia were maintained with 1.5% lidocaine and nitrous oxide-oxygen-sevoflurane, respectively. Transfusion of fresh frozen plasma (FFP) and packed red cells (PRC) was initiated about 3 h after the beginning of the surgical procedure. The patient received 900 ml of FFP and 280 ml of PRC over a 2-h period. Prior to the completion of transfusion, all measurements of $Pa_{O_2}/F_{I_{O_2}}$ (P/F ratio) showed levels of more than 250 mmHg. $Pa_{O_2}$ gradually decreased and large amounts of clear, frothy fluid flowed out of the tracheal tube at 2 h after transfusion. Frequent suctioning of the tracheal tube was required for the removal of the plasma-like fluid. In order to maintain adequate arterial oxygenation under general anesthesia, the patient required pure oxygen inhalation and positive end-expiratory pressure (PEEP) at 10 $cmH_2O$. Blood gas analysis at 3 h after transfusion showed a pH of 7.20, $Pa_{O_2}$ of 87 mmHg, and $Pa_{CO_2}$ of 62 mmHg ($F_{I_{O_2}}$, 1.0; PEEP, 10 $cmH_2O$). Systolic blood pressure decreased to 70 mmHg with a central venous pressure of 11 mmHg, necessitating continuous intravenous administration of dopamine to maintain normal blood pressure. The patient received 500 mg of methylprednisolone to improve oxygenation. The operation was completed within 6 h. Postoperatively, the patient

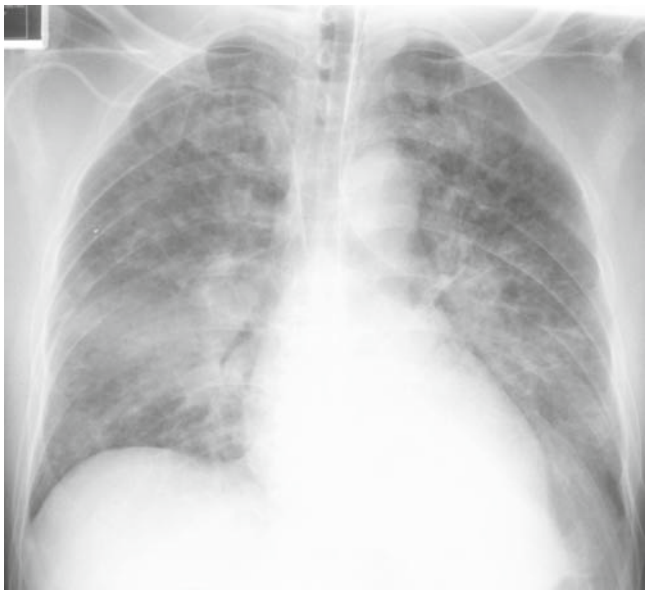

**Fig. 1.** Chest radiograph on intensive care unit (ICU) admission showed diffuse bilateral pulmonary infiltrates

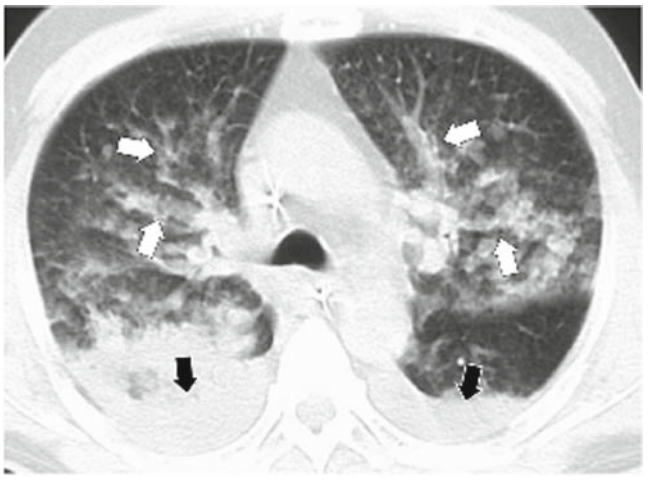

**Fig. 2.** Chest computed tomography (CT) scan on ICU admission showed bilateral gravitational atelectasis (*black arrows*) and peribronchial infiltrates (*white arrows*), but no pleural effusion

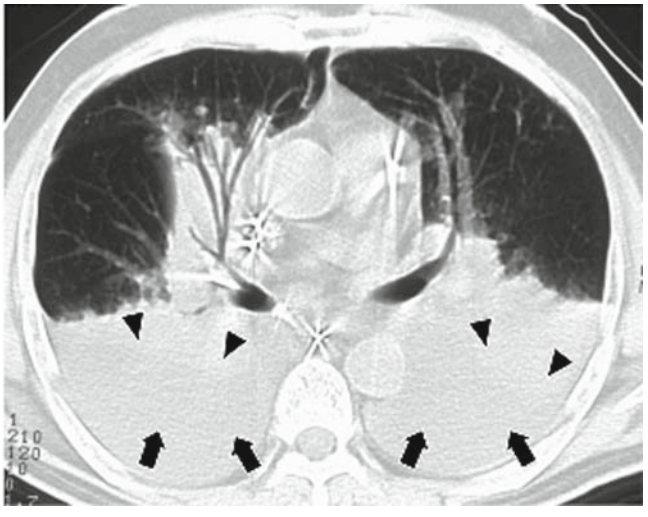

**Fig. 3.** Chest CT scan on the second day in the ICU showed bilateral compression atelectasis (*black arrowheads*) and pleural effusions (*black arrows*)

required mechanical ventilation because of impaired oxygenation.

On admission to the intensive care unit (ICU), chest radiography (Fig. 1) showed diffuse bilateral pulmonary infiltrates. Physical examination revealed that body temperature was 36.0°C, heart rate was 110 beats·min$^{-1}$, and blood pressure was 90/40 mmHg with the administration of 5 μg·kg$^{-1}$·min$^{-1}$ of dopamine. Arterial blood gas analysis on ICU admission was as follows: pH, 7.20; $Pa_{O_2}$, 110 mmHg; $Pa_{CO_2}$, 64 mmHg; base excess, –4.0 mEq·l$^{-1}$ ($F_{I_{O_2}}$,1.0; PEEP 10 cm$H_2O$). A transthoracic (external) echocardiogram showed normal left ventricular function with normal ejection fraction. Chest computed tomography (CT) scan showed bilateral gravitational atelectasis and peribronchial infiltrates but no pleural effusion (Fig. 2). Mechanical ventilation was performed with the patient in the prone position because of gravitational atelectasis, but the impaired oxygenation did not improve. On the second ICU day, the P/F ratio gradually decreased to 76 mmHg, and an exogenous surfactant protein was administered to the division of the bilateral main bronchus. At 3 h after the surfactant administration, the P/F ratio had decreased to a critical level of 52 mmHg. The patient therefore received venovenous ECMO, at 27 h after the final transfusion. Blood access was obtained via the right internal jugular vein as the inlet and the right femoral vein as the outlet. Blood flow, using a centrifugal pump, was maintained at a flow of 2–4 l·min$^{-1}$ to keep peripheral oxygen saturation ($Sp_{O_2}$) at 93% or more, and ventilator settings were reduced to rest settings which were approximately $F_{I_{O_2}}$ 0.6 or less, with peak inspiratory pressure of 25 cm$H_2O$ or less, and permitted hypercapnia ($Pa_{CO_2}$ > 45 mmHg). Chest CT scan was performed along with ECMO, and the findings of the chest CT (Fig. 3) revealed bilateral pleural effusion and bilateral compression atelectasis. Bilateral chest drainage tubes were inserted, and 1.5 l of fluid was discharged. In addition, bronchial secretion was aspirated using a bronchofiberscope under ECMO. On the third ICU day, the impaired oxygenation gradually improved, and the patient was weaned from ECMO on the fourth ICU day. Mechanical ventilation was discontinued and the tracheal tube was extubated on the eighth ICU day. On the ninth ICU day, the patient was discharged from the ICU. An investiga-

tion of the sera of the recipient, and the donor's FFP and PRC showed no granulocyte or HLA antibodies.

## Discussion

TRALI is a well-recognized complication of blood transfusion that is characterized by dyspnea, hypotension, and hypoxemia that usually develops during or within 6 h after transfusion [1]. A predominant clinical symptom of TRALI is impaired oxygenation caused by noncardiogenic pulmonary edema, which is induced by the increased permeability of the pulmonary vessels after the transfusion of a plasma-containing blood component [1]. In TRALI, two major causes of increased permeability have been proposed: leukocyte antibodies and biologically active substances such as mediators. Of these causes, biologically active mediators have never been identified in noncellular blood components, including cryoprecipitate and FFP [2].

The differential diagnosis of TRALI includes other causes of pulmonary edema, such as volume overload, congestive heart failure, and myocardial infarction. As evidence of myocardial infarction or congestive heart failure, segmental cardiac wall motion abnormalities or cardiac enlargement on echocardiogram can help rule out the diagnosis of TRALI [2]. The fulminant symptom is similar to acute respiratory distress syndrome (ARDS), but, unlike ARDS, most cases resolve within 96 h with oxygen inhalation and/or mechanical ventilation [1]. However, fatal impairment of oxygenation occurs in 6%-10% of TRALI cases, and the mortality is 6% [1].

In our patient, the cause of the increased pulmonary permeability was unclear, and the postoperative echocardiogram showed normal cardiac function. We clinically diagnosed this increased pulmonary permeability as TRALI. In spite of the treatment, including the administration of high-dose methylprednisolone and placement in the prone position, the P/F ratio decreased to 76 mmHg. We administered an exogenous surfactant protein, as this had been reported, by Spragg et al. [3], to improve the impaired oxygenation in ARDS patients during the initial 24 h. However, this agent failed to improve the P/F ratio, which decreased to 52 mmHg at 3 h after its administration. We eventually started ECMO to provide time to allow the injured lung to recover.

ECMO has been used in clinical practice for a number of years. It has been used successfully in the management of acute reversible pulmonary failure. Several reports have shown a higher survival rate in ARDS patients treated with extracorporeal support [4,5]. However, randomized controlled trials have failed to demonstrate that ECMO improves outcome in ARDS [6,7]. Therefore, the indication of ECMO for ARDS is controversial.

Nevertheless, we decided to apply ECMO to the patient until the impaired oxygenation was attenuated. The reasons were as follows. First, although severe hypoxemia per se is less likely to be a cause of death than unsolved septic shock and/or resultant multiple organ failure, long-term hypoxia might induce multiple organ failure. Early use of ECMO enables us to reduce the patient's $F_{I_{O_2}}$ and peak inspiratory pressure and can prevent ventilator-induced lung injury [4]. Second, ECMO makes it possible to perform bronchoscopic tracheal suction and chest CT scan, both of which are indispensable to improve the patient's lung condition. In conclusion, TRALI is transient and reversible, and resolves rapidly in most patients [1]. Lung support by ECMO until pulmonary permeability is reduced is one therapeutic option for the refractory and life-threatening hypoxemia induced by TRALI.

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