Transfusion-Related Acute Lung Injury Resulting From Designated Blood Transfusion Between Mother and Child

A Report of Two Cases

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Abstract

Transfusion-related acute lung injury (TRALI) is an underdiagnosed serious complication of blood transfusion characterized by the rapid onset of respiratory distress, hypoxia, and noncardiogenic pulmonary edema during or soon after blood transfusion. The presence of anti-HLA and/or antigranulocyte antibodies in the plasma of donors is implicated in the pathogenesis of TRALI. We report 2 cases of TRALI that were caused by designated blood transfusion between mothers and their daughters; one in a 4-month-old girl who received designated packed RBCs donated by her mother and the second in a 78-year-old mother who received blood from her daughter. In both cases, examination of mother’s serum revealed panel-reactive cytotoxic HLA antibodies. It is most likely that the mothers were sensitized from earlier pregnancy and produced HLA antibodies against the daughters’ paternally derived HLA antigens. Designated blood transfusion between multiparous mothers and children might add an additional transfusion-related risk owing to the higher likelihood of the HLA antibody-antigen specificity between mother and child.

Transfusion-related acute lung injury (TRALI) is an underdiagnosed and underreported complication of the transfusion of plasma containing blood products.¹ It accounts for 13% of cases of transfusion-associated deaths and is the third leading cause of transfusion-related death.² TRALI is characterized by the rapid onset of respiratory distress, pulmonary edema, hypoxia, and hypotension developing during or immediately after transfusion. The clinical manifestations often are indistinguishable from those of adult respiratory distress syndrome (ARDS), but the prognosis is much better if treated properly.³

The pathogenesis of TRALI has implied that passively transferred HLA or granulocyte antibodies from donor blood react with the recipient’s WBCs, which causes leukoagglutination in the pulmonary microcirculation with complement activation, resulting in pulmonary edema.⁴,⁵ The efforts to identify high-risk populations, both recipients and donors, for this complication have not been very successful. It has been shown that multiparous women have a higher incidence of HLA antibodies in their serum.⁶ Theoretically, there should be a higher incidence of TRALI associated with designated blood transfusions from multiparous mothers to their children, since the HLA antibody in the mother’s serum might be specifically against the paternally derived HLA antigen in the child. However, such a case has not been reported, possibly because of the failure to recognize this transfusion-related complication. We describe 2 cases of TRALI that resulted from designated blood transfusions between mothers and daughters.

Case 1

A 4-month old girl underwent repair of atrial and ventricular septal defects. One unit of designated packed
RBCs from an unrelated donor was used as pump prime during the uneventful surgery. As the patient came off the pump, 1 unit of designated fresh frozen plasma and half a unit of single donor platelets donated by the father were transfused. Eight hours later, half a unit of RBCs was transfused, which had been donated by the mother to improve the low hemoglobin concentration (8.2 g/dL [82 g/L]). Two hours after completion of the transfusion, respiratory distress, hypoxia, hypotension, decreased urine output, and fever (temperature, 102°F [38.9°C]) developed. The chest radiograph revealed a bilateral infiltrate, which progressed into an ARDS-like clinical picture. The cardiogenic cause of pulmonary edema was ruled out by cardiac catheterization and echocardiogram. The patient was treated with mechanical ventilation support, oxygen therapy, and diuretics. Her condition improved in 2 days, and the chest radiographic findings returned to normal in a week. The laboratory workup was negative for hemolytic transfusion reaction. Blood culture results from the patient were negative. The serum from the mother had panel-reactive cytotoxic HLA antibodies that reacted with 6 of 20 panel cells tested, suggesting specificity. The other designated donor’s plasma was negative for HLA antibody.

**Case 2**

A 78-year-old woman underwent right hip replacement. Relevant medical history included hypertension and coronary artery disease. Her preoperative hemoglobin level was 10.6 g/dL (106 g/L). The day following the surgery, the patient was given 1 unit of packed RBCs donated by her daughter to treat a low hemoglobin concentration (9.3 g/dL [93 g/L]). After infusion of 100 mL of packed RBCs, severe respiratory distress developed and the oxygen saturation dropped to 70% while the patient was breathing room air. The transfusion was discontinued. The workup for hemolytic transfusion reaction was negative. The chest radiograph revealed pulmonary edema, and the patient required intubation and mechanical ventilation. The pulmonary artery catheter wedge pressure was consistent with noncardiogenic pulmonary edema. A diagnosis of TRALI was made. Twenty-four hours after supportive treatment was initiated, the pulmonary edema was cleared. Serum samples from the patient and donor were tested and showed the presence of anti-HLA antibodies (classes I and II) and absence of granulocyte antibodies. A lymphocyte crossmatch was not performed.

**Discussion**

TRALI is often a diagnosis of exclusion. The incidence of TRALI, fatal or nonfatal, is on the increase, possibly owing to better recognition of the events. The severity of symptoms can range from mild to severe, and the treatment requires oxygen support and mechanical ventilation. If treated properly, most patients with TRALI recover within 96 hours.

The blood products that have been reported to cause TRALI include whole blood, RBCs, granulocytes, platelet concentrates, fresh frozen plasma, cryoprecipitate, and immunoglobulins. Pathophysiologically, TRALI has been associated with the presence of granulocyte antibodies, HLA antibodies (classes I and II), and biologically active lipids (neutrophil priming agents) in donor plasma. Preexisting conditions such as major surgery, sepsis, and trauma also might have a role. It has been shown that multiparous women have a higher incidence of HLA antibodies in their serum, and a randomized, controlled trial concluded that plasma from multiparous blood donors might impair pulmonary function in patients in the intensive care unit.

In the present cases, the characteristic clinical manifestations, exclusion of the other causes for ARDS, rapid improvement with treatment, and the demonstration of HLA-specific antibodies in the patient’s and/or donor’s blood strongly supported the diagnosis of TRALI. These cases also demonstrated the role of HLA antibodies in the pathogenesis of TRALI in the setting of a designated blood transfusion between mother and child. In case 1, the mother had never received transfusion of blood products and had undergone 1 previous termination of pregnancy. As such, pregnancy was the only alloimmune stimulus for the HLA antibody production in that mother, and the panel-reactive HLA antibodies most likely were targeted against the paternally derived HLA antigens of the infant. In case 2, the HLA antibodies in the patient (the mother) would have had specificity against the donor’s (the daughter) WBCs, which likely was the cause of TRALI, even though the donor also had HLA antibodies (classes I and II).

Considering the important role of HLA antibodies in the development of TRALI, screening blood donors for HLA antibodies or exclusion of multiparous female donors are options to prevent TRALI, but this will eliminate approximately one third of the female donor pool. In view of the shared specificity of antigens unique in a parent and child, the likelihood of TRALI resulting from transfusion between a multiparous mother and her child must be higher than the reported incidence of TRALI resulting from transfusion from an unrelated donor. Based on the observations in case 1, we recommend that clinicians avoid designated blood transfusion from a mother to her child within 1 year after a pregnancy. This 1-year deferral might or might not prevent all possible cases of TRALI, since HLA antibodies are known to persist for a long time. The second case illustrated that designated transfusion from children to their mother also might increase the risk for TRALI.
This is the first report, to our knowledge, of TRALI resulting from designated blood transfusion between mother and child. The HLA antibodies in the mother’s plasma most likely were responsible for the development of TRALI in these cases. Donor deferral of multiparous women as designated donors to their children or an HLA antibody screen of the mother’s blood before transfusion to the child is recommended.

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