

Transfusion Related Acute Lung Injury in a Child with Leukemia

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Transfusion-related acute lung injury is a rare form of acute respiratory distress syndrome of possible immune etiology that develops immediately after a blood product transfusion. Clinicians need to be aware of this condition as prompt recognition and supportive management can prevent unwanted morbidity and mortality.

Key words: Blood transfusion, Transfusion related acute lung injury, Respiratory distress.

Transfusion-related acute lung injury (TRALI) is a form of acute respiratory distress syndrome (ARDS) wherein an acute lung injury (ALI) occurs within 6 hours of blood transfusion in a patient with no preexisting ALI prior to transfusion and has no temporal relationship to other causes of ALI [1]. It occurs at a frequency of 1 in 5000 units of blood products transfused and can occur with any blood component [2]. It has been reported more commonly in pediatric patients receiving blood transfusions for chronic anemia [3]. Pediatric patients undergoing treatment for acute leukemia receive frequent blood product transfusions and are likely to be at recurrent risk of TRALI; however, literature for the same is sparse in pediatric hematological malignancies.

CASE REPORT

A 14-year old girl with B-precursor acute lymphoblastic leukemia (ALL) in complete remission was receiving consolidation chemotherapy. She initially received one bag of platelet rich plasma followed by one bag of group specific and cross-matched packed red blood cell transfusion. Prior to the transfusions, she was asymptomatic and her complete blood count was hemoglobin 7.6 g/dL, white blood cell count 2870/dL, absolute neutrophil count 410/dL and platelets 87000/dL. The platelet transfusion was planned two days prior to the PRBC transfusion due to low platelet counts; the patient, however, missed her appointment for platelet transfusion and received platelet transfusion inadvertently along with PRBC even though her platelet counts had improved by then. Just after completion of the PRBC transfusion, she developed acute respiratory distress and circulatory shock manifesting as tachypnea, tachycardia, hypoxia in room air and hypotension. Arterial blood gas analysis revealed PaO₂/FiO₂ of 125 mm Hg. She required resuscitation with intravenous normal saline fluid boluses and dopamine

infusion. Intravenous hydrocortisone and intramuscular adrenaline was administered for a possible diagnosis of anaphylaxis. She responded to initial resuscitative measures with stabilization of blood pressure in 2 hours and partial improvement in respiratory distress. She also developed fever 1 hour after onset of symptoms, and a diagnosis of septic shock was also considered. She was empirically started on intravenous antibiotic combination of ceftazidime-sulbactam and amikacin. The patient did not have clinical features of congestive cardiac failure. Chest radiograph performed an hour after onset of symptoms showed bilateral diffuse fluffy infiltrates with no cardiomegaly; chest high resolution computed tomography (HRCT) scan done 12 hours later showed diffuse symmetrical ground glass opacities in both lungs consistent with diffuse alveolar damage. Since the patient had recently received high dose steroids as part of consolidation chemotherapy for ALL, and the respiratory distress was out of proportion to the chest signs on auscultation as also the radiologists' opinion of a possible *Pneumocystis carinii* pneumonia (PCP) prompted the empiric initiation of intravenous trimethoprim and sulfamethoxazole and oral prednisolone. The respiratory distress and chest radiograph findings normalized within 48 hours. Dopamine along with oxygen was tapered and stopped after 3 days. The antibiotics were stopped after 3 days as the patient had become afebrile and the blood cultures were sterile. The patient was discharged in a stable condition on 4th day of admission. There was no clinical or laboratory evidence of miss-match transfusion or transfusion associated acute hemolysis. She has no residual sequelae, tolerated further blood product transfusions with no adverse event, and is currently receiving maintenance chemotherapy. In retrospect, a diagnosis of TRALI was considered as the most likely etiology for ARDS in our patient, as it was temporally

associated with blood transfusion and other possible causes of ARDS in the patient were excluded. However, we did not have any donor samples to analyze for antibodies against recipient human leucocyte antigen (HLA) or human neutrophil antigen (HNA). The donors (both males) were advised not to voluntarily donate blood in future. However, they declined to provide further samples for testing.

DISCUSSION

TRALI is an important cause of transfusion-related mortality [1] and appears to be a great mimicker of a variety of conditions. The differential diagnosis of sudden onset respiratory distress in such a setting includes infections, pulmonary embolism, pneumothorax, congestive cardiac failure, fluid overload, leucostasis, pulmonary hemorrhage, and anaphylactic reactions. TRALI is a diagnosis of exclusion and based on clinical criteria. The diagnosis of anaphylaxis, septic shock and PCP pneumonia was considered initially in our patient and the possibility of TRALI in our patient was only considered after 48 hours of onset of symptoms. There are few case reports of TRALI in patients undergoing treatment for hematological malignancies including stem cell transplantation [4-7]. There have been two case reports of TRALI in the Indian literature in a patient with aplastic anemia and road traffic accident, respectively [8, 9]. Both these patients required intubation and mechanical ventilation unlike our case.

Immune (performed antibodies) and non-immune mechanisms (products in stored blood) have been suggested as causative factors for TRALI, although both these mechanisms are not mutually exclusive [1]. Laboratory demonstration of donor-recipient antibody-antigen incompatibility in TRALI patients has been shown in various studies to range from 25%-73% [6]. Interestingly, control donors with no history of TRALI with their blood have also demonstrated anti-HLA or anti-HNA antibodies, suggesting that susceptible host factors are also needed for this entity [6]. No donor sample may be available after a transfusion to identify the HLA and HNA antibodies, as was in our case and in such a situation the diagnosis of TRALI is based only on clinical and radiological findings. Recent evidence suggests that a 'two-hit' process might be responsible for TRALI implicating a non-immune pathogenesis [2]. Infections or other inflammatory triggers accounts for the first hit wherein there is chemokine release, upregulation of adhesion molecules and endothelial cell activation leading to neutrophil sequestration in the lungs. The first hit occurs in the host prior to the transfusion. In the second hit, there

is amplification of the above primed pathway by the products in the transfused blood. Management of TRALI is supportive with major emphasis on respiratory care [8]. Complete recovery from TRALI, both clinically and radiologically without any permanent sequelae is expected to occur in 3 to 4 days unlike other causes of ARDS. Currently there are no mechanisms to prevent TRALI as no laboratory test can identify patients who are likely to get TRALI [2]. Respiratory distress after transfusion can be due to other causes like transfusion associated circulatory overload, dyspnea and allergy [10]. However, the temporal association of this symptom complex after blood transfusion with supportive radiological findings and clinical course suggest a diagnosis of TRALI.

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