Acute respiratory distress syndrome in a neonate due to possible transfusion-related acute lung injury

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Abstract:
Transfusion-related acute lung injury (TRALI) is a potentially life-threatening complication of blood component transfusion. It is a relatively under-diagnosed entity in neonates with scant literature. We report a case of TRALI in a preterm neonate developing acute respiratory distress within 6 h of blood product transfusion in the absence of pre-existing lung disease. Prompt ventilator and supportive management were instituted. The baby showed clinical and radiological improvement within 12 h; however, he succumbed to death due to acute massive pulmonary hemorrhage 36 h later. Possibility of TRALI should be kept if there is sudden deterioration of lung function after blood transfusion.

Keywords: Blood product, complication, newborn, pulmonary, transfusion

Introduction
Transfusion-related acute lung injury (TRALI) is a rare but acute life-threatening complication of blood component transfusion. It is a relatively under-diagnosed entity in neonates with scant literature despite high rates of blood transfusions in sick neonates. Early diagnosis and timely management of the entity reduces the mortality rate. We report a case of possible TRALI in a preterm neonate who developed acute respiratory distress within 6 h of blood product transfusion in absence of significant lung disease.

Case Report
A singleton, preterm male child born at 31 weeks to a primigravida mother with a birth weight of 1135 g was referred to our hospital on day 6 of life. The baby had received surfactant for respiratory distress syndrome on day 1 of life. Subsequently, he developed culture-positive bacterial sepsis and Stage III B necrotizing enterocolitis (NEC) (intestinal perforation) for which resection anastomosis was done on day 4 of life. After admission to our hospital, the baby was managed with appropriate antibiotics, parenteral nutrition, and other supportive care in consultation with pediatric surgery. Feeds were started on day 12 post-operatively and gradually built up. The baby was tolerating feeds well, sepsis screen with blood cultures turned negative, and there was no evidence of fungal sepsis as well. There were no metabolic derangements as well. Serial two-dimensional (2D) Echo’s and roentgens of chest were normal [Figure 1]. The baby was otherwise recovering, but as the hematocrit was <18%, a packed cell transfusion was planned on day 23 of life. Twelve milliliters of packed red blood cells (10 ml/kg) was transfused slowly. Within 6 h of transfusion, the baby developed tachypnea, sub-costal, and intercostal retractions with nasal flaring and increase in Silverman score. There were no signs of fluid overload. The baby was put on continuous positive airway pressure (CPAP). However, with increasing...
respiratory distress and inability to maintain oxygen saturations on CPAP, the baby was mechanically ventilated. Due to this sudden deterioration, possibility of collapse of lung, pneumothorax, pulmonary hemorrhage, and reopening of patent ductus arteriosus was kept. X-ray showed complete white out of bilateral lung fields [Figure 2]. Blood gas analysis revealed severe metabolic acidosis and hypoxemia (pH-6.8, PaO$_2$-42 mm Hg PaO$_2$/FiO$_2$ < 100). However, the baby remained hemodynamically stable without any inotropic support. Aggressive management with high ventilator settings, 100% FiO$_2$, and supportive treatment was done. Repeat sepsis screen, kidney function tests, and echocardiography performed were normal. The sample of patient’s blood and transfused blood was cross-matched again for ABO and Rh incompatibility to rule out transfusion reaction. Direct Coombs test on both samples was negative. The baby showed signs of recovery within 12 h in the form of decrease in ventilator settings and X-ray clearance [Figure 3]. Supportive treatment was continued and the baby was stable on minimum ventilator settings for next 24 h. However, the baby succumbed to acute massive pulmonary hemorrhage after 36 h of intubation. The event was immediately reported to the blood bank. The blood was of a male donor; however, he could not be traced and anti-human leukocyte antigen (HLA) and antineutrophil antibody test on donor plasma could not be performed. However, no reaction was reported to any other blood components of this donor.

**Discussion**

Transfusion-related acute lung injury (TRALI) is a rare but acute life-threatening complication of blood component transfusion and is currently one of the leading causes of mortality following transfusion of blood products.[1] TRALI is defined as a new ALI that occurs within 6 h of transfusion without preexisting lung disease.[2] It presents as acute onset hypoxemia (PaO$_2$/FiO$_2$ = 300 or SpO$_2$ <90% on room air), bilateral infiltrates on chest radiograph without evidence of left atrial hypertension, and no other risk factors. Although the exact etiology and pathophysiology of TRALI is uncertain, there is increased pulmonary capillary permeability leading to pulmonary edema. The proposed mechanisms for this are that either there is a preformed leukocyte antibody in donor’s plasma which binds to neutrophils of the recipient or a multi-hit mechanism in which the lung is primed by certain factors such as infection, birth asphyxia, cardiopulmonary disease, or ventilator-induced lung injury for further injury.[3]

No laboratory test is confirmatory for the diagnosis of TRALI. Tests can be performed to confirm the presence of HLA and/or neutrophil antibodies in the donor plasma. However, the absence of such antibodies does not exclude the diagnosis.
Our index case developed sudden onset respiratory distress within 6 h of packed cell transfusion. The baby was recovering from his primary illness and there was no evidence of concurrent cause for ALI. Fluid overload and cardiac dysfunction were ruled out by clinical examination and 2D-Echo. The baby’s condition improved within 12 h with clearing of haziness in X-ray chest ruling out the possibility of pneumonia. However, underlying risk factors such as prematurity, sepsis, and NEC could have been predisposing factors in this case.

The management of TRALI is essentially supportive and consists of ventilator and hemodynamic support, prevention of volume overload and identification, and treatment of complications. The hypotension may be fluid unresponsive requiring the use of inotropes. Diuretics are not useful and are contraindicated in patients who present with hypotension. Definite role of other modalities of treatment such as corticosteroids, prostaglandin E1, and surfactant has not been established. Resolution is usually rapid (within 96 h) and prognosis is good with mortality rate of 6%–10% in adults.

Literature search revealed very few case reports of TRALI in neonates. Considering the high frequency of blood product transfusions in sick neonates, the possibility of TRALI should always be kept if there is sudden deterioration in the lung function post-transfusion after excluding other causes. Mortality in adults ranges from 6% to 10%. The prognosis and outcome may be poorer in neonates as compared to adults due to the underlying risk factors and delay or lack of diagnosis. As in our case, whether massive pulmonary hemorrhage was a consequence of TRALI or an unrelated event remains to be demystified. An early diagnosis and prompt treatment may help improve the prognosis. Although it is not possible to completely prevent TRALI, the frequency may be reduced by judicious use of blood products, increasing the awareness of this entity and high index of suspicion. In addition, any such event should be reported to the concerned blood bank. The donor should be traced and deferred for further transfusions or investigated for anti-HLA/antineutrophil antibodies. Direct donation from mother to infant carries a high risk and should be discouraged.

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Conflicts of interest
There are no conflicts of interest.

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