Transfusion related acute lung injury and necrotizing enterocolitis in a neonate

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Abstract
Transfusion related acute lung injury (TRALI) and transfusion associated NEC (TANEC) are potentially life-threatening complications of blood component transfusion. These are relatively under diagnosed entity in neonates with scant literature. We report a case of TRALI and TANEC in a relatively stable preterm newborn developing acute respiratory distress and abdominal distension within few hours of blood product transfusion.

Keywords: preterm, transfusion, necrotizing enterocolitis, respiratory distress.

Introduction
Adverse transfusion reactions in neonatal population are poorly understood and defined. RBC transfusion continue to be linked to the development of potentially fatal complications like acute lung injury and necrotizing enterocolitis in neonates. There are scant literatures about these entities despite high rate of blood transfusion in sick preterm newborns. Knowledge about these entities, and timely intervention helps to reduce mortality rate. We report a case of TRALI and TANEC in a preterm newborn within few hours of blood product transfusion in the absence of prior significant morbidity.

Case Report
A singleton, preterm male child born by lower segment cesarean section (LSCS) for fetal distress and meconium stained liquor with history of premature rupture of membrane at 32 weeks with a birth weight of 730gm was referred to our hospital on day 1 of life for respiratory distress. After admission to our hospital, the baby was put on nCPAP and blood investigations and chest x-ray were sent. 2D ECHO and chest x-ray were normal. In view of hypoglycemia, low platelet count, and altered aspirate in OG tube, baby was kept NPO, iv antibiotics and parenteral nutrition was started after sending blood culture. He was given 3 units of FFP for prolonged PT and aPTT and 1 unit of PRBC for low hemoglobin. Baby was started on OG tube feeding on day 6 of life and shifted to oxygen hood. Antibiotics were stopped on day 7 after blood culture and repeat sepsis screen became negative. Baby started maintaining well in room air, feeding gradually increased and TPN stopped. His brain ultrasound showed mild dilatation of lateral ventricle which was resolving on serial ultrasound. He was on full enteral feeding by day 19 of life. KMC and NNS...
was going on, breast milk fortifiers and multivitamins were stared. Baby was gaining weight, tolerating feeds and was maintaining well in room air. On day 32 of life for subnormal weight gain blood count was done, which showed hemoglobin of 8gm/dl and hematocrit of 23 for which he received packed red cell transfusion. Immediately after transfusion the baby developed respiratory distress with abdominal distension. Abdomen was tense, erythematous, and there was feeding residuals on gastric aspirate. X-ray chest and abdomen was done that showed patchy lung infiltrates and distended bowel loops. He was put on nCPAP. However, with increasing respiratory distress and inability to maintain oxygen saturation on nCPAP, the baby was mechanically ventilated. Blood gases showed mixed metabolic and respiratory acidosis with PH 6.8, Pco2 56.7, Hco3 9.2,BE (-)24.9 and hyponatremia with Na⁺ - 126meq/l. 2D Echo was done showing normal cardiac contractility. Sepsis screen was collected and iv antibiotic was started (meropenem and clindamycin). Successive x-ray showed worsening of radiographic picture. Over the next few hours he deteriorated very fast with severe metabolic acidosis and hypotension which was resistant to treatment. Despite all supportive and aggressive treatment, he died within few hours.

**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 physiologically similar to other forms of acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) but is temporally and mechanistically related to blood component transfusion.² The clinical manifestations begin within 6h of transfusion, and in most cases within 2h. It presents as acute onset hypoxemia, respiratory distress, bilateral infiltrate on chest radiograph without evidence of left atrial hypotension with or without hypotension. The pathophysiology is increased pulmonary capillary permeability leading to pulmonary edema. This is because of preformed leukocyte antibody in donor’s plasma which binds to neutrophils of the recipient, and other factors contributing to this are infection, birth asphyxia, cardio-pulmonary disease, or ventilator-induced lung injury for further injury.³

Transfusion associated NEC is a type of adverse reaction to a blood transfusion similar to TRALI.⁴ Several theories have been suggested for the occurrence of TANEC. Extreme anemia leading to impaired gut blood flow, exposure to biologically active mediators such as free hemoglobin, cytokines, or broken red cell fragments in the transfused blood triggering immunologic reaction in gut mucosa, ischemia/reperfusion injury, relative constellation of TANEC cases around 31 weeks of gestational age indicating a role of altered angiogenesis in the intestine, release of cytokines after leukocyte depletion of transfused blood, prolonged storage of blood leading to reduced deformability, increased adhesion and lower nitric oxide, adjuvant added to blood transfusion, transient loss of responsiveness of visceral vascular network to feed, and an immunological reaction causing polyagglutination are suspected theories.⁵
Our index case developed sudden onset respiratory distress and abdominal distension immediately after transfusion requiring intubation, and mechanical ventilation. Fluid overload and cardiac dysfunction was ruled out by clinical examination and 2D ECHO. Also, the sepsis screen was negative. The clinical and laboratory picture and radiographic signs were consistent with that of TRALI and TANEC. The management of TRALI consists of ventilatory and hemodynamic support. The hypotension may be fluid unresponsive requiring the use of inotropes. Diuretics are not useful and 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. The prognosis is usually good with rapid resolution (within 96h). A variable mortality of 6-10% has been reported in adults, but is likely to be higher in neonates due to the underlying risk factors and delay or lack of diagnosis. For TANEC the mortality tends to be higher compared to those who developed NEC not associated with transfusion.

Although it is not possible to completely prevent TRALI and TANEC, the frequency may be reduced by judicious use of blood products by use of restrictive hemoglobin threshold for transfusion, delayed cord clamping and obtaining fetal blood at delivery for all initial laboratory blood tests that reduces the degree of iatrogenic blood loss and subsequent need of blood transfusion, and increasing the awareness of these entities and high index of suspicion. Withholding feeds in the peritransfusion period reduces the incidence of TANEC in preterm infants, but more prospective randomized controlled trials are needed to validate this practice. In addition, any such events should be reported to the concerned blood bank, so that donor can be traced and investigated for anti HLA/antineutrophil antibodies and deferred for further transfusion.

References
Abbreviations
nCPAP: Nasal Continuous Positive Airway Pressure
OG: Oro Gastric
NPO: Nil Per Orally
IV: Intravenous
FFP: Fresh Frozen Plasma
PT: Prothrombin Time
aPTT: Activated Partial Thromboplastin Time
PRBC: Packed Red Blood Cell
TPN: Total Parenteral Nutrition
KMC: Kangaroo Mother Care
NNS: Non Nutritive Sucking
IV: Intravenous
HLA: Human Leucocyte Antigen