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Neonatal transfusion-related acute lung injury a rare complication of exchange transfusion - A case report

Ranjana Singh[1], Atul Kumar Saroj[2]

[1]Senior Resident, Department of Paediatrics, M. L. N. Medical College, Prayagraj, [2]Senior Resident, Department of Orthopedic Surgery, King George Medical University, Lucknow, Uttar Pradesh, India

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ABSTRACT

Transfusion-related acute lung injury (TRALI), a life-threatening condition, remains an under reported complication, especially among neonates postexchange transfusion for unconjugated hyperbilirubinemia. Appropriate recognition and prompt treatment change the prognosis for good. The present case emphasizes that TRALI must be kept as a differential diagnosis in previously well neonates presenting with sudden onset hypoxia within or during 6 h of transfusion with evidence of bilateral infiltrates on a frontal chest radiograph, and no evidence of circulatory overload, left atrial hypertension, or pre-existing respiratory distress before transfusion. We report the rare occurrence of TRALI and its successful management with supportive hemodynamic management and corrective ventilator strategies.

Key words: Neonatal transfusion-related acute lung injury; Exchange transfusion; Unconjugated hyperbilirubinemia

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INTRODUCTION

Transfusion-related lung injury is a condition that should be considered whenever a patient develops hypoxemic respiratory insufficiency during or shortly after the transfusion of any blood product. Transfusion-related acute lung injury (TRALI) is clinically diagnosed based on criteria established by the NHLBI's working group as well as the Canadian Consensus Conference (CCC). The presence of new acute-onset respiratory distress syndrome occurring during or within 6 h of blood product administration, as documented by hypoxemia and abnormal chest imaging, is required by these criteria. Furthermore, there should be no evidence of circulatory overload, left atrial hypertension, or any pre-existing ALI or ARDS before transfusion. The subject of neonatal transfusion-related lung injuries has been very rarely reported so far. The diagnosis and early identification of the symptoms become challenging since they are similar to those of other neonatal diseases requiring ventilator support. According to studies conducted by Rashid et al.[1] and Malik et al.[2], the incidence of TRALI reported among neonates was 12.6% and 13.7%.

We present the case of a term neonate who developed acute-onset severe respiratory distress with massive pulmonary hemorrhage and signs of impaired perfusion and oxygenation, as well as severe metabolic acidosis, within 6 h of receiving an exchange transfusion and improved dramatically after proper management.

Address for Correspondence:
Dr. Ranjana Singh, Senior Resident, Department of Paediatrics, M. L. N. Medical College, Prayagraj, Uttar Pradesh, India.
Mobile: +91-7355499260. **E-mail**: ranjanasinghsaroj3@gmail.com

CASE REPORT

A 32-year-old woman with the blood groups gravid-3, para-2, abortion-1, live-2, and B negative delivered a 2500-g female baby via lower segment cesarean section at 37 weeks of gestation. The mother had one abortion when she was 4 months pregnant, and this was her third delivery, during which the baby developed hyperbilirubinemia. The mother received prenatal care, and her course during pregnancy was uneventful. The baby was born outside in a private hospital, cried soon after birth, and appeared to be in good health, so she was discharged from that hospital. On day 3 of life, parents noticed that the baby had a yellowish tinge, poor feeding, and excessively loud crying, so it went outside.

On examination, the baby had increased tone in all four limbs, a shrill cry, was irritable, had icterus involving the palms and soles, and was hemodynamically stable with no evidence of cardiopulmonary compromise. The baby was kept on phototherapy, injection phenobarbitone was given i.v. without posturing, relevant investigations were sent, and blood for an exchange transfusion was being arranged in the meantime. The baby's blood group came out to be B positive; the reticulocyte count was 5.6%; the direct Coombs test was positive. A sepsis screen was sent to rule out any associated infection, and it was negative. A provisional diagnosis of term appropriate for gestation with neonatal hyperbilirubinemia with Rh-incompatibility with acute bilirubin encephalopathy (bilirubin-induced neurologic dysfunction score 6) was made. The required procedure of an exchange transfusion was started within a few hours of the hospital stay and was completed aseptically within 2 h with intensive vital monitoring and intermittent blood gas monitoring. Calcium gluconate and sodium bicarbonate were injected during the procedure. Furthermore, an episode of hyperglycemia was noted, for which injection insulin was given. The baby was hemodynamically stable throughout the procedure and was maintaining saturation. 3 h post-exchange transfusion, the baby developed acute-onset respiratory distress with pulmonary hemorrhage and severe chest retractions, so he was immediately intubated. In addition, the baby became mottled simultaneously; with prolonged capillary refill time, blood pressures were nonrecordable, and pulses were very feeble, so vasopressors were started after the saline bolus. On auscultation, the chest had bilateral new-onset coughs (Figure 1).

Arterial blood gas was suggestive of severe mixed acidosis (pH=6.8, pCO_2=76.8 mmHg, HCO_3=11.7%, pO_2=59.3 mmHg, SPO_2=72.9%, lactate=10.0 mmol/L), and the radiograph showed bilateral infiltrates with the preserved cardiac silhouette. As TRALI was suspected, the baby was immediately kept on pressure-regulated volume control mode of ventilation with Vt=5 mL/kg, Ti=0.35, positive end-expiratory pressure (PEEP)=6, FiO_2=100%, and RR=50 m. Echocardiogram results were suggestive of normal ventricular contractility. The sepsis screen and biochemistry reports done within a half hour of onset were within normal limits. There was also an episode of fever documented. Anti-human leukocyte antigen (HLA) and anti-granulocyte antibodies could not be done due to some technical issues. Initially, the baby was not maintaining saturation (SPO_2 between 62% and 78%), but gradually within a few hours, the baby was able to maintain saturation (SPO_2 between 93% and 98%), with the resolution of hypoxemia and hypercarbia in blood gas (pH=7.2, pCO_2=34.5 mmHg, HCO_3=15.3, pO_2=221 mmHg, SPO_2=98.6%, lactate=5.5 mmol/L). Perfusion improved noticeably, as did the disappearance of mottling and pink frothy secretions (Figure 2). Hypotension was also resolved.

Finally, vasopressors were tapered off within a span of 17 h, ventilator settings were tapered within 3 days, and

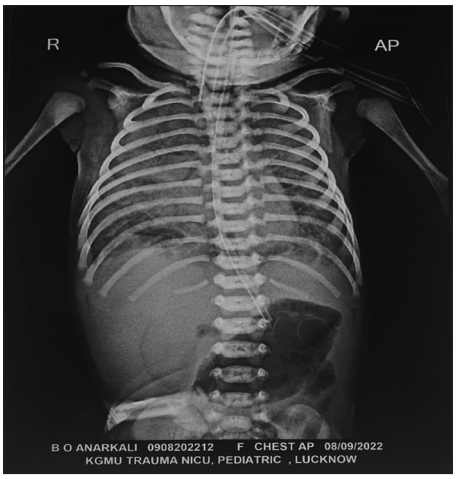

Figure 1: Chest radiograph showing bilateral white-out lungs few hours after exchange transfusion

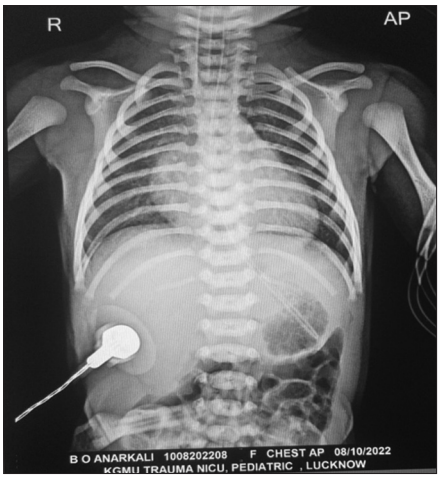

Figure 2: Radiograph of the next day showing the clearing of lung fields with dramatic clinical improvement

the baby was weaned off from invasive to noninvasive modes of ventilation. The baby was successfully extubated to oxygen by the hood on the 4th day and weaned off to room air on the 5th day.

DISCUSSION

There are only a handful of case reports talking about neonates who underwent exchange transfusions and developed TRALI. Sivakaanthan et al.[3] reported on a case of TRALI occurring in a 40-day-old neonate post-packed red blood cells transfusion in view of anemia (polycythemia vera 20%). They emphasized the importance of diagnosing this condition in neonates as well and suggested instituting timely interventions to improve the prognosis. TRALI, a post-exchange transfusion procedure, was developed in two neonates, according to Rzayev et al.[4] They emphasized the importance of diagnosing TRALI in neonates, which is often overlooked. Maria et al.[5] reported a neonate who developed respiratory distress posttransfusion of packed red blood cells and died at 36 h of age due to a massive pulmonary hemorrhage, emphasizing the importance of prompt recognition of symptoms for better management.

In a study conducted around 1983, TRALI was associated with passive transfusion of anti-leukocyte antibodies and clinical microvascular pulmonary injury, and the incidence, as estimated was around 0.02% per unit and 0.16% per patient transfused. Factors posing a major risk for TRALI, according to Jin et al.[6], include the transfusion of plasma-rich components, which are apheresis platelets, stored cellular products, fresh frozen plasma, the donor being a female, especially a multiparous female, and finally, the presence of anti-leukocyte antigens or anti-neutrophil antigen antibodies.

When blood is stored, bioactive lipids (lysophosphatidylcholine) and cytokines accumulate, which has been linked to the development of TRALI in isolated perfused rat models. These agents are potent neutrophil priming agents in the lung epithelium, leading to an inflammatory reaction along with stored leukocyte antibodies in donor blood targeting recipient white blood cells.

There exists a "two hit" hypothesis, as pointed out by Silliman et al.[7], which states that the patient's neutrophils are primed for activation beforehand due to an underlying condition; the "second hit" refers to the activation of these neutrophils by substances in the transfused product that are antibodies to HLA, etc.

Popovsky et al.[8] suggested that TRALI was associated with passive transfusion of anti-leukocyte antibodies and clinical pulmonary microvasculature injury, and the incidence, as estimated was around 0.02% per unit and 0.16% per patient transfused.

TRALI, like acute respiratory distress syndrome, is characterized by the acute onset of respiratory distress shortly after transfusion, usually within 1–6 h, according to Kleinman et al.[9] Our patient had a classic presentation, which was recognized timely since all symptoms occurred within 6 h of an exchange transfusion, so our attention was drawn toward it. From acute deterioration of conditions involving fatal distress, pulmonary hemorrhage, mottling, and circulatory collapse to rapid reversal of symptoms in a neonate who almost seemed to die, awareness regarding this condition among this population is important. With appropriate management, shock improved within a span of 17 h, severe respiratory distress also resolved, and the neonate was weaned off the ventilator within 3 days.

CONCLUSION

TRALI, a rare but potentially fatal complication, should be suspected in neonates who have sudden deterioration of lung function that is temporally related to transfusion and should be managed intensively with proper ventilation strategies such as controlled oxygenation, low tidal volume, high PEEP, careful fluid administration, prone positioning, ionotropic support if required, sedation, and drug administration such as surfactant if not responding to suction.

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Authors' Contributions:
RS- Concept and design of the study, clinical work, prepared first draft of manuscript; **AS**- Assisted in clinical work, interpreted the results, coordination and revision of the manuscript.

Work attributed to:
King George Medical University, Lucknow, Uttar Pradesh, India.

Orcid ID:
Dr. Ranjana Singh - https://orcid.org/0009-0008-6459-9477
Dr. Atul Kumar Saroj- https://orcid.org/0000-0002-4401-9788

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