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Case Report

A case of transfusion related acute lung injury in a thalassemic child

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Introduction

Transfusion-related acute lung injury (TRALI) is increasingly recognized as a major complication of blood product transfusions. TRALI has been reported in all age groups receiving blood products for ailments including hematology/oncology conditions, bone marrow and solid organ transplantation, autoimmune disorders, and congenital heart diseases. However incidence of TRALI in a case of thalassemia is not known.¹ We report a case of TRALI in 11-year-old girl with E β thalassemia.

Case report

An 11-year-old female child patient, a known case of E β thalassemia was admitted for blood transfusion. Patient was on regular blood transfusion at 6–8 weeks interval since 3 years of age and on adequate chelation therapy. Hemoglobin Electrophoresis revealed HbF-42.9%, HbE-53.80%, HbA-1.6% – double heterozygous for E β thalassemia. She had undergone splenectomy in 2012 and was on penicillin prophylaxis. On admission, her vitals were stable, pallor and hepatomegaly were present. Systemic examination was normal. Investigations revealed Hb-7.5 g/dl, TLC-11,600/mm³, P₁₀L₈₀M₀₂E₀₈, platelets-120 $\times$ 10³/mm³. Other biochemical parameters were within normal limits. Patient was transfused with triple washed leuco-depleted packed RBC's at rate of 10 ml/kg. She remained hemodynamically stable during transfusion. After 4 h of transfusion patient became dyspneic and her O₂ saturation fell to <90%. There were bilateral crackles on chest auscultation. There was no fever, rash, gallop rhythm or increase in hepatomegaly. Investigations revealed – Hb-8.6 g%, TLC-5800/mm³, platelets-160 $\times$ 10³/mm³, blood urea-24 mg/dl, S.creatinine-0.8 mg/dl, Na/K-138/4.3 mmol/l. Urine for hemoglobinuria was negative. On arterial blood gas- PaO₂/FiO₂ <200. Chest X-ray [Fig. 1] revealed bilateral diffuse fluffy infiltrates. She was put on intensive management with antibiotics, dexamethasone and

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Fig. 1 – Chest radiograph showing bilateral diffuse fluffy infiltrates, also note expanded ribs (bilateral), a feature of marrow hyperplasia.

respiratory support. However her urine output decreased approaching to anuria with rising azotemia (Urea-170 mg/dl and S. creatinine-4.7 mg/dl). Peritoneal dialysis was done for the same for next 48 h and patient showed a significant improvement in condition. Echocardiography was normal, ultrasonography of kidneys was normal and blood culture did not grow any organism. Patient responded to therapy and was discharged after 10th day of admission.

Discussion

Transfusion-related acute lung injury (TRALI) is a complication of blood transfusion and has been recently reported by the FDA as the most frequent cause of transfusion-associated fatality.² To better define the diagnosis of TRALI, a consensus panel was convened in April 2004 by the Canadian blood services and the International Society of Blood Transfusion's Committee on Biomedical Excellence for Safer Transfusion. It has named: (1) "TRALI", (2) "Possible TRALI", or "Not TRALI" based on clinical and radiographic criteria within 6 h of a completed blood transfusion (Table 1).

The risk of TRALI is reduced from 2.57 per 10,000 transfusion units in 2006 to 0.81 in 2009 due to reduced use of blood products.^{1,3} The most common setting of TRALI in children was induction chemotherapy for acute lymphoblastic leukemia (ALL). In published series of TRALI, plasma-containing blood components are most commonly implicated with maximum risk in whole blood-derived platelet concentrates (WB-PLTs), followed by FFP, PRBCs, whole blood, aphaeresis platelet concentrates (A-PLTs) granulocytes, cryoprecipitate and intravenous immunoglobulin (IVIG).⁴

The pathogenesis of TRALI has usually been explained by the transfusion of a blood product that contains anti-human leukocyte antigen (anti-HLA) or anti-human neutrophil antigen (anti-HNA) antibodies that recognize cognate antigen in the transfusion recipient. Allo-recognition by such antibodies

Table 1 – Canadian Consensus Conference Panel TRALI definitions.

Term	Definition
TRALI	<ul style="list-style-type: none"> • Acute lung injury (defined below) occurring within 6 h of completion of transfusion of blood component • No pre-existing acute lung injury • No other temporally associated risk factors for acute lung injury
Possible TRALI	<ul style="list-style-type: none"> • Acute lung injury occurring within 6 h of completion of transfusion of blood components. • No pre-existing acute lung injury. One of more temporally associate risk factors for acute lung injury.
Acute Lung Injury [ALI]	<ul style="list-style-type: none"> • New onset • Hypoxemia SpO₂ <90% or PaO₂/FiO₂ <300 mm Hg on room air, or other clinical evidence of hypoxemia • Bilateral infiltrates on frontal chest X-ray

leads to neutrophil-dependent ALI, characterized by robust neutrophilic inflammation of the lung and disruption of the lung alveolar-capillary permeability barrier. Cognate antibodies may not be detected in all clinically diagnosed cases of TRALI. Biologically active lipids have been implicated in the pathogenesis by breakdown products of cell membrane phospholipids. Not all recipients transfused with a blood product containing a matched anti-HLA or anti-HNA antibody develop evidence of TRALI. Thus, it is likely that factors other than transfusion of any of these antibodies are capable of initiating TRALI, and that co-factors, related either to the transfused product or to the recipient, are important in the pathogenesis of antibody-mediated TRALI. These observations have led to a multiple event hypothesis of TRALI pathogenesis, which states that a transfusion recipient must have an underlying medical condition, which may leads to a susceptibility to TRALI via immune printing that is then triggered by the transfusion of alloantibody or other bioreactive substances.⁵

Although TRALI develops within 6 h of transfusion, most occurrences take place during transfusion or within the first 1 or 2 h after it. Clinical findings of TRALI consist of the rapid onset of tachypnea, cyanosis, dyspnea, and in few cases fever (1 °C or higher).⁶ Auscultation of the lungs reveals diffuse crackles and decreased breath sounds, especially in dependent areas.^{4,7} Physiologic findings include acute hypoxemia, with PaO₂/FiO₂ less than 300 mm Hg, and decreased pulmonary compliance despite normal cardiac function. Radiographic examination reveals diffuse, fluffy infiltrates consistent with pulmonary edema. In short, the clinical diagnosis of TRALI is identical to that of acute lung injury (ALI).⁷ The pulmonary edema can be confirmed to be non-cardiogenic by measuring the protein concentration of the pulmonary edema fluid or by performing trans-oesophageal echocardiography. A pulmonary edema fluid to serum protein ratio of >0.75 is highly suggestive of a noncardiogenic edema, whereas ratio <0.65 is consistent with hydrostatic edema. Decrease in the white blood cell count, neutrophils, complement, lymphocytes and monocytes is due to

sequestration in the pulmonary vascular bed, with count recovery occurring after an appropriate bone marrow response.⁸

TRALI may be distinguished from TACO (Transfusion associated circulatory overload) and cardiogenic pulmonary edema by a normal central venous pressure (CVP) and normal pulmonary capillary wedge pressure (PCWP) and a clinical response to diuretics. Allergic and anaphylactic transfusion reactions are marked by laryngeal edema or bronchospasm with wheezing and a normal CXR. Transfusion transmitted bacteremia may present with fever, hypotension, and culminate in severe sepsis with associated acute lung injury which may be difficult to distinguish from TRALI. The presence of positive blood cultures is a useful delineating finding.⁹ We had ruled out these aetiologies in our case. The mortality rate from TRALI ranges from 5 to 25%. However, the data regarding TRALI are limited, and the attendant morbidity and mortality may be under appreciated because of lack of recognition and under reporting.¹⁰

Treatment of TRALI is supportive. Mild forms of TRALI may respond to supplemental oxygen therapy. Severe forms may require mechanical ventilation and ICU support. As with ARDS, there is no role for diuretics or corticosteroids. The majority of patients recover within 72–96 h, to their baseline pulmonary function without apparent sequelae. However, some patients are slower to recover and may remain hypoxic with persistent pulmonary infiltrates up to seven days.¹¹ To minimize the risk of TRALI in patients who are chronically transfused and allo-immunized, it might be helpful to use filtered red blood cells, which would reduce the amount of antigenic donor leukocytes.¹² Indeed, leuko-reduction has been shown to decrease the incidence of transfusion reactions, including TRALI. Red cell washing does not effectively remove leukocytes and is not recommended to prevent TRALI.^{4,12}

In the United Kingdom, reports from the whole country are monitored through a centralized institution called Serious Hazards of Transfusion (SHOT). The SHOT project is a system for collecting voluntary, anonymous and independent notifications of adverse transfusion events, with an educational aim of building, through annual reports, an evidence base to support decisions, guidelines, clinical training and improvements in transfusion practices. There is no centralized haemovigilance system in the USA and the only obligation is to inform the FDA of transfusion-related deaths. These haemovigilance systems in the UK, France and USA identified TRALI to be the most frequent cause of transfusion-associated death, even if cases of ABO mistransfusion are included.¹³ The TRALI is a serious complication of blood transfusion, even in patients on regular transfusion like thalassemia, and need to be kept in mind.¹⁴

Conclusion

TRALI in pediatric patients is under-recognized and under-reported. The diagnosis of TRALI may be done early, if

echocardiography or the pulmonary edema fluid protein/plasma protein ratio may suggest to a non-cardiogenic etiology. TRALI should be considered in the differential diagnosis of patients who develop sudden respiratory distress suggesting acute lung injury (ALI) during or within 6 h of a blood product transfusion. Until research provides effective preventive strategies, pediatricians who transfuse plasma-containing products to children can help reduce morbidity and mortality from TRALI through heightened awareness of the syndrome and reporting of all cases to the blood bank.

Conflicts of interest

All authors have none to declare.

REFERENCES

1. Toy P, Gajic O, Bacchetti P, et al. Transfusion-related acute lung injury: incidence and risk factors. *Blood*. 2012;119(7):1757–1767.
2. Holness L, Knippen MA, Simmons L, Lachenbruch PA. Fatalities caused by TRALI. *Transfus Med Rev*. 2004;18:184–188.
3. Wallis JP, Lubenko A, Wells AW, Chapman CE. Single hospital experience of TRALI. *Transfusion*. 2003;43:1053–1059.
4. Silliman CC, Boshkov LK, Mehdizadehkashi Z, et al. Transfusion-related acute lung injury: epidemiology and a prospective analysis of etiologic factors. *Blood*. 2003;101:454–462.
5. Sayah DM, Looney MR, Toy P. Transfusion reactions: newer concepts on the pathophysiology, incidence, treatment, and prevention of transfusion-related acute lung injury. *Crit Care Clin*. 2012 Jul;28(3):363–372.
6. Sachs UJ. Pathophysiology of TRALI: current concepts. *Intensive Care Med*. 2007 Jun;33(suppl 1):S3–S11.
7. Kopko PM. Review: transfusion-related acute lung injury: pathophysiology, laboratory investigation, and donor management. *Immunohematology*. 2004;20:103–111.
8. Looney MR, Gropper MA, Matthay MA. Transfusion-related acute lung injury: a review. *Chest*. 2004;126:249–258.
9. Kopko PM, Marshall CS, MacKenzie MR, Holland PV, Popovsky MA. Transfusion-related acute lung injury: report of a clinical look-back investigation. *JAMA*. 2002;287:1968–1971.
10. Wallis JP. Transfusion-related acute lung injury (TRALI)—under-diagnosed and under-reported. *Br J Anaesth*. 2003;90:573–576.
11. Church GD, Price C, Sanchez R, Looney MR. Transfusion-related acute lung injury in the paediatric patient: two case reports and a review of the literature. *Transfus Med*. 2006;16(5):343–348.
12. Sanchez R, Toy P. Transfusion related acute lung injury: a pediatric perspective. *Pediatr Blood Cancer*. 2005;45:248–255.
13. Prinoth O. System for monitoring transfusion risk. *Blood Transfus*. 2008 Apr;6(2):86–92.
14. Koussi A, Trachana M, Pliaki P, Gombakis N, Athanassiou-Metaxa M. Transfusion related acute lung injury syndrome (TRALI) in a patient with thalassaemia. *Pediatr Blood Cancer*. 2006;46:829–830.