TRALI Syndrome Complicated by Retroperitoneal Bleeding

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ABSTRACT

Transfusion-related acute lung injury (TRALI) is an underdiagnosed and under-reported syndrome which by itself is the third leading cause of transfusion-related mortality. The incidence of TRALI is reported to be 1 in 2000 to 5000 transfusions. When combined with uncontrollable bleeding, survival is unachievable. We report the case of a 25-year-old man, who underwent open heart surgery as an infant to correct his congenital heart disease in association with right pulmonary artery atresia. He presented with hemoptysis secondary to aspergilloma and required a pneumonectomy of the nonfunctional right lung. During pneumolysis, significant bleeding occurred from the superior vena cava. The patient required a blood transfusion and was placed on cardiopulmonary bypass to control the bleeding. Simultaneous occurrence of severe pulmonary edema and retroperitoneal bleeding were noted. Approximately 8 L of frothy edema fluid were drained from the only functional left lung starting ~15 minutes after the transfusion and lasting for several hours until the end of the case. It most likely represented TRALI syndrome. Increasing abdominal girth and poor volume return to the pump were consistent with and pathognomonic for retroperitoneal bleeding. Though primary surgical bleeding in the chest was controlled successfully and a pneumonectomy performed without further difficulty, we were unable to separate the patient from cardiopulmonary bypass due to the inability to oxygenate. As a result, we could not reverse the anti-coagulation which potentially exacerbated the retroperitoneal bleeding. After multiple unsuccessful attempts the patient succumbed. This ill-fated case demonstrates the quandary of obtaining vascular access for emergency cardiopulmonary bypass while in the right thoracotomy position. It may be beneficial to have both the femoral artery and vein cannulated before positioning a patient in a lateral decubitus position. In addition, early direct access to the right atrium may obviate a need for femoral venous cannulation. Also, adult extracorporeal membrane oxygenation may be indicated if faced with such a severe pulmonary edema without ongoing hemorrhage.

KEYWORDS: Transfusion, lung injury, pulmonary atresia, retroperitoneal hematoma

Transfusion-related acute lung injury (TRALI) is one of the most common causes of transfusion-associated major morbidity and death. TRALI has been identified as a significant adverse event of transfusion, and the reported mortality rates vary from 5 to 25%.^{1–3}

First described in 1951,⁴ noncardiogenic lung edema related to transfusion has been widely reported using various names. In 1983, Popovsky et al⁵ were credited with the term “transfusion-related acute lung injury.” TRALI has been reported from all types of blood

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components including whole blood, red cells, aphaeresis platelets, whole blood platelets, fresh frozen plasma, cryoprecipitate, granulocytes, stem cell products, and even IV immunoglobulin preparations.⁶⁻⁸ TRALI is underdiagnosed and underreported as many clinicians are not familiar with the syndrome. This is equally true for severe cases of TRALI where transfusion may not be considered as a possible cause and may be regarded as acute respiratory distress syndrome (ARDS) but also for mild case where mechanical ventilation is not required. The exact mechanism of TRALI is still not fully understood. At present we know that the common denominator is the end of the pathway which presents with increased pulmonary capillary permeability, and results in movement of plasma into the alveolar space causing pulmonary edema.

TRALI is a complication of blood transfusion and has been recently reported by the FDA as the most frequent cause of transfusion-associated fatality.⁹ The reported incidence of TRALI varies from 1 in 5000 to 1 in 13,000 transfusions in the United States.¹⁰ We present a case where TRALI was complicated further by uncontrollable intraoperative hemorrhage. Survival in this situation appears to be unachievable.

CASE REPORT

A 25-year-old man, who underwent open heart surgery as an infant to correct his congenital heart disease in association with right pulmonary artery atresia, presented with hemoptysis secondary to aspergilloma and required a pneumonectomy of the nonfunctional right lung. During pneumolysis, significant bleeding occurred from the superior vena cava. The patient required a blood transfusion for the considerable amount of bleeding we had encountered. Peripheral cannulation for cardiopulmonary bypass was initiated to gain control of the patient's hemodynamics. As the patient was placed in the left lateral decubitus position for the intended procedure, the ability to gain access to the femoral vessels for peripheral cannulation was made more daunting. After a few attempts, both the femoral vein and artery were accessed for cardiopulmonary bypass. Shortly thereafter, a simultaneous occurrence of severe pulmonary edema and retroperitoneal bleeding were noted. Approximately 8 L of frothy edema fluid were drained from the only functional left lung starting ~15 minutes after the transfusion and lasting for several hours until the end of the case. It most likely represented TRALI syndrome. Increasing abdominal girth and poor volume return to the pump were consistent with and pathognomonic for retroperitoneal bleeding. This most likely was secondary to the attempts that were made to gain access to the femoral vasculature. Though primary surgical bleeding in the chest was controlled successfully and a pneumonectomy was performed without further diffi-

culty, we were unable to separate the patient from cardiopulmonary bypass due to the inability to oxygenate. At the same time, we could not reverse the heparin to control the retroperitoneal bleeding. After multiple unsuccessful attempts, the patient succumbed.

DISCUSSION

TRALI is an underdiagnosed and underreported syndrome. It is a form of ARDS that occurs after transfusion caused by antibodies in plasma of a single donor unit reacting with leukocyte antigens in the recipient. The incidence of TRALI is reported to be 1 in 2000 to 5000 transfusions. It is characterized by the sudden onset of marked noncardiogenic pulmonary edema, and possibly with systemic hypotension. This phenomenon occurs within a few hours of transfusion. A chest radiograph typical of ARDS and copious frothy yellow or pink fluid in the trachea also can be seen.

TRALI is an underrecognized entity due to the ambiguity in terms of its definition. There are no laboratory markers to confirm the diagnosis. In essence, the diagnosis of TRALI is made by the patient presenting with above-stated symptoms shortly after a blood transfusion. To fully realize this diagnosis, one must exclude other confounding factors such as previous acute lung injury and/or congestive heart failure. The pathophysiology remains unclear. There is some preliminary suggestion that the reaction is secondary to antibodies in donor plasma against antigens present on the recipient's leukocytes. These may be antibodies to epitopes of the human leukocyte antigen system or to other leukocyte antigen. Experimental evidence from an animal model also suggests that complement may also be a vital component.

There remains no true means of prevention. At this point, if a patient is presumed to have TRALI, they are being identified and possibly restricted from donating blood. There are multiple registries that are compiling information about all blood transfusion reactions, of which TRALI is an entity that is identified. Management of patients with this diagnosis is similar to the treatment of ARDS. Essentially, it is to provide support in the form of adequate oxygenation and ventilation. Mechanical ventilation is often used to abate any transient respiratory collapse.

This patient's unfortunate circumstance of surgical bleeding was exacerbated by what we feel was TRALI syndrome from the intraoperative transfusion that he received. Furthermore, the fact that he underwent a pneumonectomy further worsened the situation. In essence, the patient's remaining lung could not ventilate to sustain life since he now was experiencing severe pulmonary edema. In retrospect, these circumstances could be avoided in two ways. First, as always, avoiding surgical bleeding is the optimal means of preventing such unwanted outcomes. However,

surgical bleeding can occur, despite the use of meticulous technique. The second method to avoid the above scenario is to prevent the possible formation of TRALI. Broad preventive measures of TRALI are still unknown. It may be impractical to prevent all cases of TRALI. Nevertheless, there are certain methods that can be taken to at least prevent TRALI to a large extent. Specific measures that could include adhering to evidence-based triggers for transfusion and minimizing blood loss due to sampling. Another preventive method is to permanently defer all implicated donors from donation of blood.¹¹

This patient demonstrates the dilemma of obtaining vascular access for emergency cardiopulmonary bypass while in the right thoracotomy position. It may be beneficial to have both the femoral artery and vein cannulated before positioning a patient in a lateral decubitus position. In addition, early direct access to the right atrium may obviate a need for femoral venous cannulation. Also, adult extracorporeal membrane oxygenation may be indicated if faced with such a severe pulmonary edema without ongoing hemorrhage.

REFERENCES

1. Renaudier PC, Vo Mai MP, Azanowsky JM, et al. Epidemiology of transfusion-related acute lung injury in Gifit, the French haemovigilance database. A study of the French haemovigilance network. *Transfusion* 2004;44: 23–27
2. Graul A, Heiden M, Gräf K, Keller-Stanislawski B. Hämovigilanz in Deutschland – Berichte an das Paul-Ehrlich-Institut über Verdachtsfälle von Transfusionsreaktionen im Beobachtungszeitraum Januar 1995 bis Dezember 2002. *Transfus Med Hemother* 2003;30:232–238
3. Joergensen J, Taaning E. DART – a volunteer system of haemovigilance in Denmark. *Transfusion Alternatives*. *Transfus Med* 2003;5:260–264
4. Barnard RD. Indiscriminate transfusion: a critique of case reports illustrating hypersensitivity reactions. *N Y State J Med* 1951;51(20):2399–2402
5. Popovsky MA, Moore SB. Diagnostic and pathogenetic considerations in transfusion-related acute lung injury. *Transfusion* 1985;25(6):573–577
6. Toy P, Popovsky MA, Abraham E, et al; National Heart, Lung and Blood Institute Working Group on TRALI. Transfusion-related acute lung injury: definition and review. *Crit Care Med* 2005;33(4):721–726
7. Silliman CC, Paterson AJ, Dickey WO, et al. The association of biologically active lipids with the development of transfusion-related acute lung injury: a retrospective study. *Transfusion* 1997;37(7):719–726
8. Wallis JP, Lubenko A, Wells AW, Chapman CE. Single hospital experience of TRALI. *Transfusion* 2003;43(8):1053–1059
9. Holness L, Knippen MA, Simmons L, Lachenbruch PA. Fatalities caused by TRALI. *Transfus Med Rev* 2004;18(3): 184–188
10. Silliman CC, Ambruso DR, Boshkov LK. Transfusion-related acute lung injury. *Blood* 2005;105(6):2266–2273
11. Mair DC, Hirschler N, Eastlund T. Blood donor and component management strategies to prevent transfusion-related acute lung injury (TRALI). *Crit Care Med* 2006;34 (5, Suppl):S137–S143