Radiographic manifestations of transfusion-related acute lung injury☆

Carolina Carcano a,⁎, Ndubuisi Okafor b, Felipe Martinez a, Jose Ramirez b, Jeffrey Kanne c, Jacobo Kirsch a

a Radiology Department, Cleveland Clinic Florida, Weston, FL 33331
b Pulmonary Department, Cleveland Clinic Florida, Weston, FL 33331
c Radiology Department, University of Wisconsin, Madison, WI 33331

1. Introduction

The transfusion-related acute lung injury (TRALI) is a potentially life-threatening complication of blood transfusion [1,2]. TRALI is reported as the leading cause of transfusion-related mortality in the United States [3], presumably related to the international agreement on its definition, which improved its recognition and increased the number of reported cases [4]. The National Heart, Lung, and Blood Institute working group and Canadian Consensus conference guidelines defined TRALI as a “new acute lung injury (ALI) that occurs during or within 6 hrs after a transfusion of blood products, with a clear temporal relationship, in patients with or without risk factors for ALI other than transfusion” [5,6]. For the diagnosis of this syndrome, the following criteria should be present: acute onset, normal pulmonary capillary wedge pressure or lack of clinical evidence of left atrial hypertension, bilateral opacities on chest radiograph, and hypoxia [6]. Still, the condition is thought to be clinically underdiagnosed given that the critically ill patients often have hypoxia due to pneumonia, sepsis, and major surgery [4].

We will review the clinical manifestations of TRALI as well as radiologic findings as the condition develops. An overview of the characteristics of transfusion-associated cardiac overload (TACO) will also be discussed given the importance of this alternative condition within the differential diagnosis of TRALI.

2. Incidence

The first noncardiogenic pulmonary edema termed “transfusion-related acute lung injury” was presented by Popovsky et al. in 1983 [7–9], although a case report linking symptoms of ALI, transfusion, and leukoagglutinins was described by Brittingham 25 years before that [7,10].

According to the records of the Food and Drug administration, 43% of the fatalities related to blood transfusion in 2011 were caused by TRALI [11]. The incidence ranges from 0.002% to 1.12% per product transfused and from 0.08% to 8% per patient transfused [9,12]. According to the US Department of Health, there is an estimated occurrence of TRALI in 1100 to 10,000 cases of the total of 14.6 million transfusions done per year in the United States [11]. However, during the past 7 years, since the standardized definition was developed by the consensus, there has been an overall decrease in the number of TRALI fatalities reported [7]. Hemovigilance studies showed that fresh-frozen plasma products from female donors, especially multiparous women, were involved in the majority of the cases of TRALI, as well as the blood products of a specific patient that had such a previous reported consequence [13,14].

3. Pathogenesis

The pathogenesis of TRALI has not been fully described, but it is known to occur with the transfusion of any cell-containing blood product, cryoprecipitates, intravenous immunoglobulins, and as little as 50 ml of plasma-rich blood product [13,15].

Two hypotheses have been formulated related to the lung injury related to the endothelial damage, capillary leak, and extravasation of neutrophils occur during TRALI [16,17]. The first hypothesis advocates
donor antibodies against human leukocyte antigens and human neutrophil antigens expressed in pulmonary capillaries of the recipient as the cause of pulmonary damage and capillary leak in TRALI; however, this association is not very strong [6]. A second hypothesis implicates a “two-hit” model. The patient has an inflammatory underlying condition, such as sepsis or recent surgery, that causes sequestration of neutrophils in the pulmonary compartment. The transfusion of blood products, which include antibodies or bioactive lipids that accumulated during blood storage, stimulates those neutrophils to release proteases [4,16,17].

4. Clinical manifestations

The clinical manifestations of TRALI are dyspnea, cyanosis, fever, tachycardia, hypoxia, hypotension, or less frequently hypertension [1]. These symptoms may present insidiously, as soon as 1 to 2 h in 90% of the cases, and can lead to the use of life-supporting techniques such as mechanical ventilation [6].

5. Radiographic manifestations

Chest radiograph is a routine exam for intensive care unit (ICU) patients. The radiographic features of TRALI are nonspecific. Habitually, the radiographic findings are worse than the physical exam findings [10].

An initial chest radiograph shows the combination of interstitial opacities and diffuse lung haziness, which obscures the pulmonary vasculature. Septal lines and pleural effusions occasionally develop. Findings simulate pulmonary edema; the degree of consolidation seen is related to the extent of alveolar epithelial injury and leakage of fluid with high protein content into the alveolar spaces [2,12].

The patchy opacities evolve into widespread bilateral alveolar and interstitial opacities over a short period of time [13]. These findings are usually indistinguishable from those of hydrostatic pulmonary edema [10,18]. The lung opacities usually clear within 96 h in 80% of patients diagnosed with TRALI, as represented in Case 1 (Fig. 1) [19].

Chest computed tomography (CT) evaluation can be helpful in further assessment of the findings depicted on chest radiograph. Parenchymal consolidation and air bronchograms, with or without ground-glass-appearing opacities, are seen in heterogeneous distribution. These findings can be seen in coexistence with normally aerated lung (as illustrated in Cases 2 and 3 [Figs. 2 and 3]) [12].

6. TRALI versus TACO

According to a Food and Drug Administration report, TACO is the second most common cause of transfusion-related fatalities (10% versus 65% associated to TRALI) [3].

Reviewing the patient’s medical history plays an important role in the differential diagnosis of TRALI and TACO. In patients without history of heart disease, with ALI risk factors, and negative or neutral fluid balance, dyspnea would make TRALI more likely than TACO. Conversely, the evidence of an S3 and elevated jugular venous pressure would favor TACO.

The profile of the patient at risk for TACO is 3 years or younger, or older than 60 years [20]. Echocardiography and B-type natriuretic peptide (BNP) measurements can aid the diagnosis [16]. Indeed, BNP was found to have significant predictive power independent of other
clinical signs in patients presenting symptoms suggestive of TACO. In the imaging study, identifying vascular congestion and pleural effusions favors TACO [8].

7. Management and prognosis

Management of TRALI is generally supportive, with most patients requiring supplementary oxygen. Diuretics, as used for cardiogenic pulmonary edema, may worsen the condition in a patient with transfusion-related edema. Corticosteroids have been used, but there are not adequate studies for or against the use of such therapy [13].

The mortality rate of TRALI has been reported to range from 6% to 10% up to 40% in cases that met all of the criteria of the Consensus Panel. Even though the mortality is still lower than that of ALI in general (32%), there is no apparent late occurrence of fibrosis or other structural damage to the lung parenchyma as a result of TRALI [12].

8. Conclusion

TRALI is the leading cause of transfusion-related mortality and occurs early after the beginning of a blood transfusion. With the chest radiograph being a frequently used tool in patients with acute respiratory distress in the ICU, the awareness of this entity by the radiologist is crucial as initial diagnosis depends on a high degree of suspicion.

References

Fig. 3. Case 3: frontal chest radiograph (A) shows multifocal air space opacities in the bilateral lungs with somewhat perihilar predominance. No significant enlargement of the cardiac silhouette. Axial images of the chest CT scan: lung windows (B and C) show confluent alveolar and ground-glass opacities in the bilateral lungs with perihilar predominance associated to smooth septal thickening. Please note absence of pleural effusions and normal-sized heart.