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Delayed Presentation of Transfusion-Related Acute Lung Injury in the Emergency Department

Delayed Transfusion-Related Acute Lung Injury

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Abstract: Transfusion-related acute lung injury (TRALI) is a life-threatening complication of blood transfusion, characterized by acute hypoxemia and bilateral pulmonary infiltrates within 6–72 hours post-transfusion. Delayed TRALI, occurring 6–72 hours after transfusion, is underrecognized due to its temporal dissociation from the transfusion event, posing diagnostic challenges. We present the case of an 80-year-old woman with hypertension and atrial fibrillation who developed delayed TRALI 48 hours after receiving erythrocyte suspension for upper gastrointestinal bleeding. She presented with dyspnea, hypoxemia, and bilateral pulmonary edema, with no evidence of volume overload or infection. Management included non-invasive ventilation and diuresis, leading to rapid recovery. This case highlights the importance of considering delayed TRALI in elderly patients with new respiratory symptoms post-transfusion, even with non-plasma products. Early recognition and supportive care are critical, as delayed TRALI can progress to severe respiratory failure. Preventive strategies, such as using fresher blood units and male-donor plasma, may reduce risk. Clinicians must maintain a high index of suspicion for TRALI in high-risk populations to improve outcomes.

Keywords: Transfusion-related acute lung injury, transfusion-associated circulatory overload, Blood products, Transfusion

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INTRODUCTION

TRALI is a severe and potentially fatal complication of blood transfusion, characterized by acute hypoxemia and bilateral pulmonary infiltrates occurring within 6–72 hours post-transfusion (1). TRALI is categorized into two subtypes: immediate TRALI (onset ≤6 hours) and delayed TRALI (onset 6–72 hours). The latter is less frequently reported and often underdiagnosed due to its temporal dissociation from the transfusion event, making it a diagnostic challenge (2). The pathogenesis of TRALI is commonly explained by the "two-hit" model: the first hit involves patient-specific factors (e.g., inflammation, surgery, or critical illness) that prime neutrophils and endothelial cells, while the second hit arises from transfusion-derived biological response modifiers (e.g., anti-HLA antibodies, bioactive lipids) that trigger immune-mediated lung injury (3). Delayed TRALI is particularly concerning because its symptoms often overlap with other conditions, such as transfusion-associated circulatory overload (TACO), sepsis, or cardiac failure, leading to potential misdiagnosis and delayed treatment (4).

Despite significant advances in donor screening protocols, such as deferring multiparous female donors to reduce the risk of HLA antibodies, TRALI remains one of the leading causes of transfusion-related mortality, accounting for approximately 15% of reported fatalities (5). Elderly patients with comorbidities such as hypertension or atrial fibrillation are at heightened risk due to increased endothelial vulnerability, making them particularly susceptible to delayed TRALI (6). This case report presents an 80-year-old woman who developed delayed TRALI following erythrocyte transfusion for upper gastrointestinal bleeding, highlighting the importance of vigilance in high-risk populations and the need for early recognition and management.

CASE

An 80-year-old female patient with a medical history of hypertension and atrial fibrillation presented to the emergency department with complaints of dyspnea, fatigue, and generalized body pain. Two days prior, she had been hospitalized for upper gastrointestinal bleeding and received two units of erythrocyte suspension. Upon admission, she was tachypneic (respiratory rate: 27 breaths/min), agitated, and fatigued, with a Glasgow Coma Scale score of 14/15. Her vital signs included a blood pressure of 100/60 mmHg, oxygen saturation of 77% on room air, a heart rate of 101 beats/min, and a temperature of 37.3°C. Physical examination revealed accessory muscle use, diffuse crackles on auscultation, and short-sentence speech, consistent with mild to moderate respiratory distress. Electrocardiography showed atrial fibrillation without acute ischemic changes.

Laboratory results were unremarkable except for mild thrombocytopenia (platelet count: 100,000/μL). Hepatic and renal function tests were within normal limits. Transthoracic echocardiography performed by a cardiologist demonstrated a preserved left ventricular ejection fraction (55%) and chronic right atrial enlargement, with no evidence of systolic or diastolic dysfunction or significant valvular pathology. Chest radiography **(Figure 1)** and non-contrast thoracic computed tomography (CT) revealed new-onset bilateral pulmonary edema **(Figure 2).**

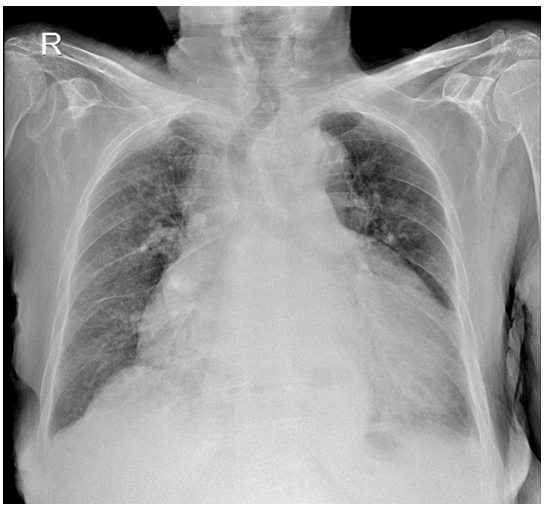

Figure 1. Chest radiography showed bilateral diffuse coarse reticular pattern

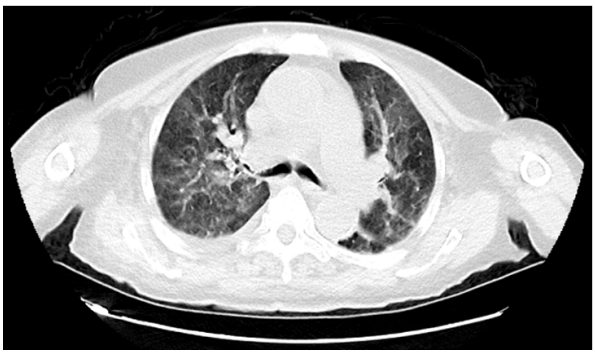

Figure 2. Non-contrast thoracic computed tomography demonstrated bilateral pulmonary edema

The patient required non-invasive ventilator support and was transferred to the intensive care unit. Diuresis with intravenous furosemide (40 mg/day) was initiated, leading to the gradual resolution of pulmonary edema. Respiratory support was weaned, and she was discharged on the fourth hospital day after complete symptom resolution.

DISCUSSION

This case exemplifies delayed TRALI, occurring 48 hours post-transfusion. The patient's advanced age, hypertension, and atrial fibrillation likely contributed to endothelial dysfunction, fulfilling the "first hit" in TRALI pathogenesis (7). The "second hit" may have involved transfusion-derived mediators, such as anti-HLA antibodies or bioactive lipids from stored erythrocytes. While HLA antibodies are classically implicated in TRALI, recent studies emphasize the role of bioactive lipids (e.g., lysophosphatidylcholines) in neutrophil priming, particularly in delayed cases (8). Notably, the patient received erythrocyte suspensions, which carry a lower TRALI risk than plasma-rich products (9). However, older blood units accumulate higher levels of pro-inflammatory lipids, potentially exacerbating lung injury (10).

Delayed TRALI diagnosis requires the exclusion of alternative etiologies. In this case, TACO was ruled out due to the absence of volume overload signs (e.g., elevated BNP, jugular venous distension) and rapid response to diuresis (11). Normal cardiac function on echocardiography further supported non-cardiogenic pulmonary edema. Thrombocytopenia, though mild, is a recognized feature of TRALI and may reflect platelet consumption in lung microvasculature (12). The absence of fever or leukocytosis helped exclude infectious causes.

This case underscores the importance of considering delayed TRALI in elderly patients with new respiratory symptoms following transfusion, even when plasma-rich products are not used. The delayed onset of symptoms can obscure the connection to the transfusion event, leading to diagnostic delays and potentially worse outcomes. Early recognition is critical, as delayed TRALI can rapidly progress to severe respiratory failure if not promptly managed (13).

Current TRALI management focuses on supportive care, including oxygen therapy and judicious fluid administration (14). Non-invasive ventilation, as used in this case, is preferred to avoid ventilator-induced lung injury (15). Diuresis remains controversial but may alleviate hydrostatic pressure in patients with concurrent volume overload (16). The patient's rapid recovery aligns with typical TRALI outcomes, where 80% of cases resolve within 96 hours with supportive measures (17).

This case highlights the need for heightened suspicion of delayed TRALI in elderly transfused patients, even when non-plasma products are administered. Implementing preventive strategies, such as using male-donor plasma and fresher blood units, could mitigate risk (18). Biomarkers like interleukin-8 (IL-8) or soluble CD40 ligand (sCD40L) may aid in early diagnosis but require further validation (19). Additionally, this case emphasizes the importance of multidisciplinary collaboration in managing TRALI, particularly in high-risk populations.

The delayed onset of symptoms, combined with the patient's complex medical history, underscores the need for clinicians to maintain a high index of suspicion for TRALI, even beyond the immediate post-transfusion period. Furthermore, this case highlights the potential role of bioactive lipids in delayed TRALI pathogenesis, suggesting that even

non-plasma products like erythrocyte suspensions can pose a risk, especially when older blood units are used. This has important implications for blood bank practices and transfusion protocols, particularly in elderly and critically ill patients.

CONCLUSION

Delayed TRALI is a rare but consequential complication of transfusion therapy, particularly in vulnerable populations such as the elderly. Clinicians must maintain a high index of suspicion in patients with new respiratory symptoms post-transfusion, even beyond the immediate 6-hour window. Multidisciplinary collaboration, adherence to preventive protocols, and ongoing research into pathogenetic mechanisms are essential to reduce TRALI-related morbidity and mortality. This case serves as a reminder of the importance of early recognition and prompt management of delayed TRALI, particularly in high-risk patients.

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