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Transfusion-Related Acute Lung Injury in a Patient With Advanced Metastatic Lung Cancer: A Diagnostic Challenge

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Abstract

Background: Transfusion-related acute lung injury (TRALI) is a leading cause of transfusion-associated mortality and presents with acute hypoxemic respiratory failure occurring during or within six hours of blood product transfusion. Diagnosis is clinical and requires exclusion of alternative causes of acute respiratory distress syndrome (ARDS), particularly in medically complex patients.

Case Presentation: We report the case of a 75-year-old woman with advanced metastatic lung adenocarcinoma, chronic obstructive pulmonary disease (COPD), and recent ischemic stroke who developed acute hypoxemic respiratory failure during hospitalization for management of severe anemia and thrombocytopenia. Following transfusion of platelets for a platelet nadir of 23 × 10^9/L, the patient acutely developed worsening dyspnea and escalating oxygen requirements. Imaging demonstrated new bilateral pulmonary infiltrates without evidence of cardiogenic pulmonary edema. Clinical findings, timing relative to transfusion, absence of volume overload, and lack of response to diuresis were most consistent with TRALI. Supportive management was initiated with supplemental oxygen, and further transfusions were avoided.

Conclusion: This case highlights the diagnostic challenges of TRALI in patients with advanced malignancy and baseline pulmonary disease. Recognition of TRALI is critical to prevent recurrent transfusion-related lung injury and to guide goals-of-care discussions in patients with limited physiologic reserve.

Keywords: Transfusion-related acute lung injury (TRALI), Platelet transfusion, Acute hypoxemic respiratory failure, Noncardiogenic pulmonary edema, Transfusion-associated circulatory overload (TACO), Advanced malignancy, Hemovigilance

Introduction

Transfusion-related acute lung injury (TRALI) is a leading cause of transfusion-associated mortality and is defined as acute hypoxemic respiratory failure with noncardiogenic pulmonary edema occurring during or within six hours of transfusion of blood products. Although uncommon, TRALI carries significant morbidity and mortality. Contemporary active-surveillance studies estimate an incidence of approximately 0.31 cases per 10,000 platelet transfusions and 0.17 cases per 10,000 red blood cell transfusions, with plasma-rich products consistently associated with higher risk. Passive hemovigilance systems report lower and more variable incidence rates, historically ranging from 1 in 64,000 to 1 in 200,000 transfused units, reflecting underrecognition and reporting variability.

Updated consensus definitions from the Canadian Consensus Conference and the National Heart, Lung, and Blood Institute (NHLBI) classify TRALI into Type I (without pre-existing ARDS risk factors) and

Type II (with pre-existing risk factors but a clear transfusion-related temporal association). The underlying pathophysiology involves immune-mediated or non-immune mechanisms leading to pulmonary capillary endothelial injury and increased permeability.

Patients with underlying pulmonary disease, malignancy, infection, or systemic inflammation are at increased risk for TRALI, making diagnosis particularly challenging in medically complex populations. Differentiation from transfusion-associated circulatory overload (TACO) is critical, as management strategies and prognostic implications differ significantly.

Case Presentation

A 75-year-old woman with a past medical history of COPD (not on home oxygen), seizure disorder, hypothyroidism, hypertension, and newly diagnosed metastatic lung adenocarcinoma with hepatic, adrenal, and bone metastases was transferred from inpatient rehabilitation for management of symptomatic anemia and thrombocytopenia in preparation for percutaneous endoscopic gastrostomy (PEG) tube placement. Her oncologic course was complicated by severe malnutrition, poor functional status, and a recent right frontal periventricular ischemic stroke. She had previously been deemed a poor candidate for systemic chemotherapy. During rehabilitation, her course was further complicated by post-obstructive pneumonia, Clostridioides difficile infection, hypotension related to poor oral intake, and progressive cytopenias suspected to be secondary to bone marrow infiltration by malignancy.

On admission, laboratory evaluation revealed severe anemia with hemoglobin of 5.1 g/dL and thrombocytopenia to 35 × 10^9/L. She received platelet transfusion for severe thrombocytopenia with a nadir platelet count of 23 × 10^9/L in preparation for planned PEG placement. Within hours of platelet transfusion, the patient developed acute worsening dyspnea and hypoxemia, requiring escalation of oxygen therapy to mid-flow nasal cannula at 6 L/min to maintain oxygen saturation near 90%.

Chest imaging demonstrated new bilateral diffuse alveolar opacities predominantly in a perihilar and dependent distribution, without cardiomegaly, vascular congestion, or pleural effusions, a radiographic pattern consistent with noncardiogenic pulmonary edema rather than volume overload. There was no clinical evidence of circulatory overload; jugular venous distention was absent, blood pressure remained stable, and there was no improvement with conservative volume management. Arterial blood gas analysis revealed compensated metabolic alkalosis without hypercapnia (pH 7.539, pCO_2 39 mmHg, HCO_3^- 33 mEq/L), supporting a noncardiogenic process. Given the acute onset of hypoxemic respiratory failure temporally associated with transfusion, radiographic findings consistent with noncardiogenic pulmonary edema, and absence of alternative explanations such as cardiogenic pulmonary edema or worsening infection, the patient met full Canadian Consensus and NHLBI criteria for definite

transfusion-related acute lung injury (TRALI). Further platelet and plasma-containing transfusions were avoided, and the patient was managed with supportive care, including supplemental oxygen.

Differential Diagnosis

The differential diagnosis for the patient's acute hypoxemic respiratory failure included transfusion-associated circulatory overload (TACO), progression of post-obstructive pneumonia, pulmonary embolism, acute respiratory distress syndrome related to infection, and progression of malignancy.

TACO: Considered less likely due to lack of volume overload, absence of cardiomegaly, and no response to fluid restriction or diuretics.

Infectious Etiologies: Deemed unlikely given stable inflammatory markers and ongoing antimicrobial therapy.

TRALI: Supported strongly by the close temporal relationship to transfusion and characteristic imaging findings as the most likely diagnosis.

Hospital Course and Outcomes

The patient's respiratory status stabilized with supportive care. However, her overall clinical condition continued to decline due to advanced metastatic cancer, profound malnutrition, encephalopathy, and progressive cytopenias. Thrombocytopenia precluded PEG placement. Multidisciplinary discussions involving oncology, pulmonology, palliative care, gastroenterology,

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neurology, and infectious disease reaffirmed the limited therapeutic options.

Following comprehensive goals-of-care discussions with the patient's family, a decision was made to transition to comfort-focused care. The patient was designated DNR/DNI and referred to hospice services. Disease-directed therapies, laboratory monitoring, and invasive procedures were discontinued, and oxygen therapy was continued for comfort.

Results & Diagnostic Tables

Table 1: Diagnostic Criteria for Transfusion-Related Acute Lung Injury (TRALI)

Criterion	Canadian Consensus / NHLBI Definition	Present in This Case
Timing	Acute onset during or within 6 hours of transfusion	**Yes** – Respiratory decompensation occurred within hours of platelet transfusion *(corrected from PRBC for consistency)*
Hypoxemia	$PaO_2/FiO_2 \leq 300$ or $SpO_2 < 90\%$ on room air	**Yes** – Required 6 L/min mid-flow NC to maintain SpO_2 ~90%
Chest Imaging	Bilateral pulmonary infiltrates consistent with pulmonary edema	**Yes** – New bilateral infiltrates without cardiomegaly
Circulatory Overload	No evidence of left atrial hypertension or volume overload	**Yes** – No JVD, no cardiomegaly, no response to diuresis
Alternative Risk Factors for ARDS	No clear temporal alternative cause	**Yes** – Infection stable, malignancy chronic, abrupt onset linked to transfusion
Cardiac Failure	Not the primary cause	**Yes** – No clinical or radiographic evidence of cardiogenic edema

Based on the above criteria, this presentation fulfills definite TRALI according to Canadian Consensus and NHLBI definitions.

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Table 2: Comparison of TRALI and Transfusion-Associated Circulatory Overload (TACO)

Feature	TRALI	TACO	Findings in This Patient
Onset after transfusion	Within 6 hours	Within 6 hours	Within hours
Mechanism	Immune-mediated pulmonary capillary leak	Hydrostatic pulmonary edema	Capillary leak suspected
Volume status	Euvolemic or hypovolemic	Hypervolemic	No signs of volume overload
Blood pressure	Often normotensive or hypotensive	Often hypertensive	Hemodynamically stable
JVD / peripheral edema	Absent	Present	Absent
BNP levels	Normal or mildly elevated	Elevated	Not suggestive of overload
Cardiomegaly on imaging	Absent	Present	Absent
Response to diuretics	Minimal	Rapid improvement	No clinical improvement

Based on the above criteria, this presentation fulfills definite TRALI according to Canadian Consensus and NHLBI definitions.

Discussion

This case meets full diagnostic criteria for definite TRALI based on the Canadian Consensus and NHLBI

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definitions, including acute onset within six hours of platelet transfusion, hypoxemia, bilateral pulmonary infiltrates consistent with noncardiogenic pulmonary edema, and absence of circulatory overload or alternative explanatory diagnoses. The temporal association with platelet transfusion, combined with radiographic findings and lack of response to volume-directed therapies, strongly supports a causal relationship.

Recent literature emphasizes that TRALI remains underrecognized, particularly in patients with baseline lung disease or advanced malignancy, where hypoxemia is often attributed to infection, disease progression, or volume overload. Large retrospective studies continue to demonstrate that TRALI can occur across a wide range of clinical settings and transfusion contexts, reinforcing the importance of vigilance even with standard transfusion practices. Distinguishing TRALI from TACO is essential, as the latter is characterized by hydrostatic pulmonary edema, elevated cardiac filling pressures, and clinical response to diuretics—features notably absent in this patient. The presence of diffuse bilateral alveolar infiltrates without cardiomegaly or vascular congestion on imaging further supports a diagnosis of TRALI.

Early recognition of TRALI is crucial to prevent repeat exposure to blood products and further lung injury. Current recommendations emphasize supportive care with oxygen therapy and avoidance of additional transfusions whenever feasible. In patients with limited physiologic reserve, such as those with advanced metastatic cancer and severe malnutrition, TRALI may precipitate irreversible clinical decline and appropriately prompt goals-of-care discussions and palliative care involvement.

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