ARCHIVES OF HELLENIC MEDICINE: ISSN 11-05-3992

SHORT COMMUNICATION
ΒΡΑΧΕΙΑ ΔΗΜΟΣΙΕΥΣΗ

ARCHIVES OF HELLENIC MEDICINE 2025, 42(5):707–709
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2025, 42(5):707–709

Acute lung injury associated with blood transfusion

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Οξεία πνευμονική βλάβη που σχετίζεται με μετάγγιση αίματος

Περίληψη στο τέλος του άρθρου

Key words: Acute respiratory distress syndrome, Blood transfusion, TRALI, Treatment

Acute lung injury related with blood transfusion (TRALI) is a scarcely reported severe potentially fatal condition often misdiagnosed or underdiagnosed, manifested by sudden hypoxia and non-cardiogenic pulmonary edema within six hours after the transfusion.[1–8] The incidence of TRALI is 1:130,000 blood products transfused; whereas the mortality rate may be up to 25% among general patients, and up to 40% in those critically ill.[3–5] The management of TRALI includes mechanical ventilation, oxygen supplementation, corticosteroids, thromboembolism prophylaxis, and also inhaled nitric oxide (iNO).[1–8] TRALI type I includes diverse biological response modifiers (proteins, lipids, proinflammatory substances, and extracellular vesicles) found in aged red blood cells or platelets, whereas TRALI type II is associated with anti-leukocyte antibodies, more specifically the human leukocyte antigens I and II or neutrophil antigen antibodies.[2,5,6,8] Anti-leukocyte antibodies activate neutrophils that damage the pulmonary endothelium, causing vascular leakage in the alveoli; or the non-antibody mediated mechanism of the patient's underlying illness activates pulmonary endothelium and primes neutrophils.[5,8] The next phase occurs when blood components with antibodies or biological response modifiers are transfused and activate primed and bound neutrophils, producing TRALI.[5,8] Experimental TRALI in rats showed increased levels of inflammatory cytokines and high-mobility group box 1 (HMGB1)/receptor-interacting protein kinase 3 (RIP3); therefore, these inflammatory mediators could be diagnostic markers for early stages of TRALI.[5,8] In this setting, short comments on more recent case studies of the topic are presented.[1–4,7]

A 50-year-old woman with blood type B (III) Rh+ submitted to hysterectomy due to fibromyomas, had a transfusion of 676 mL erythrocyte mass to control anemia on the eve of surgery, and post-operatively presented signs of respiratory distress, severe hypoxemia, besides radiological findings of TRALI.[1] She presented dyspnea, palpitations, fatigue, and associated reduction in SpO_2 to 61%; pulmonary embolism was a differential diagnosis, but the D-dimer's level was normal; chest images showed bilateral infiltrates of pulmonary edema consistent with TRALI.[1] Promptly managed by oxygen supplementation, corticosteroids, and thromboembolism prophylaxis with enoxaparin, her hospital discharge occurred on day 6 after admission.[1] The authors emphasized the inclusion of TRALI among the differential diagnostic hypothesis of patients presenting with respiratory distress following blood transfusions.[1] A six-year-old girl with the antecedent of juvenile idiopathic arthritis and macrophage activation syndrome developed TRALI after the transfusion of whole blood filtered and irradiated platelets to treat severe thrombocytopenia.[2] She presented dyspnea, hypoxemia, and bilateral pulmonary edema about one hour post-transfusion; and was promptly intubated and placed on mechanical ventilation for 40 hours.[2] The clinical, laboratory, and pulmonary findings were consistent with the diagnosis of TRALI; the blood immunology tests revealed neither anti-human neutrophil antigen nor anti-leukocyte antigen class I or

Submitted 31.5.2024
Accepted 6.7.2024

class II antibodies in the donor's or the patient's plasma.[2] The authors stressed the exceeding rarity of a child with juvenile idiopathic arthritis and macrophage activation syndrome who had TRALI type II after the platelet transfusion.[2] A 52-year-old diabetic man was reported with head and neck necrotizing fasciitis caused by *Staphylococcus aureus* and *Serratia marcescens* for over a month.[3] The leukocyte count was 14.36×10^9/L with 73.9% neutrophils, and the erythrocyte count was 3.03×10^{12}/L, with hemoglobin of 8.4 g/L. Between day 2 and 6 of admission, he received four packed red blood cell units to control anemia and 2,400 mL of frozen plasma; on day 7 he suddenly presented respiratory distress and hypoxemia after 100 mL of plasma, not improved by the facemask oxygen at 60 L/min, besides dexamethasone.[3] As the chest images revealed bilateral pulmonary infiltrates, the patient was intubated, mechanically ventilated, and transferred to the intensive care unit due to worsened status.[3] The specific antibodies HLA-DRB1*07:01 and HLA-DQB1*02:02 were further detected in the donor plasma, and were considered responsible for the development of TRALI.[3] The authors highlighted the needed more proactive measures for managing TRALI cases in China, which would minimize both the occurrence and the associated mortality rates.[3] A 71-year-old hypertensive diabetic man who had total aortic arch replacement was transfused with four units of packed red blood cells and five units of fresh frozen plasma.[4] Half an hour after the last transfusion hypoxemia occurred (PaO_2/FiO_2 ratio at 171 and positive end-expiratory pressure of 5 cmH_2O).[4] After the transfusions had been discontinued and the alveolar recruitment maneuver plus lung-protective ventilation with the PCV:PEEP 8 cmH_2O performed, the surgery ended.[4] With the complete cardiological evaluation, the patient's condition was diagnosed as acute respiratory distress syndrome associated with the development of TRALI type I.[4] Further deterioration occurred with a mean pulmonary artery pressure over 20 mmHg and a PaO_2/FiO_2 ratio of 103; a new alveolar recruitment maneuver had no success, while iNO at 20 ppm to 40 ppm decreased the mean pulmonary artery pressure to under 20 mmHg.[4] The authors highlighted the use of iNO for better respiratory management of TRALI after additional evaluation in the perioperative phase, or in patients undergoing intensive care.[4] A 14-year-old teenager with hereditary spherocytosis presented with episodes of dizziness and palpitations due to severe anemia (hemoglobin 7.0 g/dL and hematocrit 23%) and received a transfusion of 300 mL of packed red blood cells.[7] Two hours later she developed fever, tachypnea, cyanosis, hypotension, and hypoxemia; chest radiographs showed bilateral consolidations in the central regions of the lungs, and computed tomography (CT) revealed bilateral ground-glass opacities, interlobular septal thickening and bilateral pleural effusions, compatible with TRALI.[7] On day 12 of admission, she had good clinical and radiological improvement. The authors emphasized the development of irregular opacities that can evolve into bilateral interstitial and alveolar infiltrates indistinguishable from pulmonary edema; however, a recent transfusion of blood products should suggest the diagnosis of TRALI.[7]

In conclusion, the present comments aim to emphasize the inclusion of TRALI among the main differential hypotheses of acute respiratory distress developing within six hours after blood transfusion, and earliest diagnosis that favors prompt management.

ΠΕΡΙΛΗΨΗ

Οξεία πνευμονική βλάβη που σχετίζεται με μετάγγιση αίματος

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Η οξεία πνευμονική βλάβη που σχετίζεται με τη μετάγγιση αίματος (TRALI) είναι μια σπάνια αλλά δυνητικά θανατηφόρα κατάσταση, η οποία συχνά διαγιγνώσκεται εσφαλμένα ή υποδιαγιγνώσκεται και εκδηλώνεται με αιφνίδια εμφάνιση υποξίας και μη καρδιογενές πνευμονικό οίδημα εντός 6 ωρών μετά τη μετάγγιση. Τα αντισώματα κατά των λευκοκυττάρων ενεργοποιούν τα πολυμορφοπύρηνα, οδηγώντας σε βλάβη στο πνευμονικό ενδοθήλιο και προκαλώντας αγγειακή διαρροή στις κυψελίδες ή ο μηχανισμός της υποκείμενης νόσου του ασθενούς ενεργοποιεί το ενδοθήλιο του πνεύμονα και διεγείρει τα πολυμορφοπύρηνα. Η κατάσταση εμφανίζεται όταν συστατικά του αίματος, όπως αντισώματα ή τροποποιητές βιολογικής απόκρισης, μεταγγίζονται και ενεργοποιούν τα πολυμορφοπύρηνα. Η αντιμετώπιση του TRALI περιλαμβάνει μηχανικό αερισμό, χορήγηση οξυγόνου, ενδοφλέβια χορήγηση κορτικοστεροειδών, προφύλαξη από θρομβοεμβολή και επίσης εισπνοή μονοξειδίου του αζώτου.

Λέξεις ευρετηρίου: Θεραπεία, Μετάγγιση αίματος, Σύνδρομο οξείας αναπνευστικής δυσχέρειας, TRALI

References

1. BIELINSKYI M, HALANDZHII MA, DASHCHENKO Y, CHAPLYNSKA N. Acute lung injury associated with blood transfusion in a hysterectomy patient: A case report. *Galician Med J* 2024, 31:e-GMJ2024-A08
2. GAGRO A, TOMIČIĆ M, ŠKARIĆ I, DAWIDOWSKY B. Case report: Suspected transfusion-related acute lung injury type II in a child with refractory systemic juvenile idiopathic arthritis complicated by macrophage activation syndrome. *Front Pediatr* 2024, 11:1237111
3. HUANG M, WANG X, WANG L, CHEN G. Transfusion-related acute lung injury (TRALI) caused by antibodies to HLA-DRB1*07:01 and HLA-DQB1*02:02: A case report. *Clin Case Rep* 2023, 11:e8284
4. KOMETANI S, MISAWA R, KAWAI M, SEKI H, TABATA M. A case report of inhaled nitric oxide for transfusion-related acute lung injury. *Cureus* 2023, 15:e41552
5. LIU S, LIN R, ZHANG X, LV Y, ZHU J, CHEN G ET AL. The alarmin effect of HMGB1/RIP3 on transfusion-related acute lung injury via TLR4/NF-κB or MAPK pathway. *Shock* 2023, 60:400–409
6. LIU Y, WANG R, SONG C, DING S, ZUO Y, YI K ET AL. Crosstalk between neutrophil extracellular traps and immune regulation: Insights into pathobiology and therapeutic implications of transfusion-related acute lung injury. *Front Immunol* 2023, 14:1324021
7. MARCHIORI E, HOCHHEGGER B, ZANETTI G. Transfusion-related acute lung injury: An uncommon cause of pulmonary edema. *J Bras Pneumol* 2023, 49:e20230175
8. YOS E, PATRICK-EISENBERG A, CAMPBELL J. To transfuse or not to transfuse: A case of unresectable renal cell carcinoma-induced warm autoimmune hemolytic anemia. *Cureus* 2023, 15:e48345

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