

Diagnostic challenges in distinguishing TRALI from COVID-19 ARDS

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ABSTRACT

Severe acute respiratory syndrome caused by the SARS-CoV-2 virus (COVID-19) presents with a wide spectrum of clinical manifestations, ranging from asymptomatic infection to acute respiratory distress syndrome (ARDS) and multiorgan failure. Transfusion-related acute lung injury (TRALI) is a serious complication of blood transfusion and is associated with significant morbidity and mortality. A 46-year-old male patient with known chronic kidney disease presented to the emergency department with dyspnea and cough. The patient oxygen saturation was 78%. Laboratory findings revealed elevated white blood cell count, C-reactive protein, and D-dimer levels, along with lymphopenia; hemoglobin level was 7.3 g/dl. Chest computed tomography demonstrated diffuse bilateral ground-glass opacities with focal areas of consolidation. The patient was monitored in the intensive care unit with nasal oxygen therapy. Following blood transfusion for anemia, respiratory status deteriorated at the sixth hour post-transfusion, necessitating endotracheal intubation and initiation of mechanical ventilation. The deterioration in the patient's respiratory status requiring mechanical ventilation was attributed to several differential diagnoses, including ARDS secondary to COVID-19 or other microorganisms, TRALI, and transfusion-associated circulatory overload (TACO). Bedside chest radiography demonstrated bilateral diffuse pulmonary opacities. Transthoracic echocardiography showed no evidence of left atrial hypertension (LAH), thereby excluding TACO. Accordingly, in our patient, who had risk factors for ARDS but a stable respiratory status for 36 hours before transfusion, the diagnosis of Type II TRALI was considered. The patient was successfully extubated on day 9. Repeated SARS-CoV-2 PCR tests and rapid antibody tests were negative, and blood and urine cultures showed no growth. The patient was discharged to the ward on day 20. TRALI may develop even in the presence of risk factors for ARDS. For the differential diagnosis of TRALI, TACO, and ARDS, a comprehensive evaluation using clinical findings, laboratory parameters, and objective criteria such as echocardiography is recommended.

Keywords: ARDS, COVID-19, TACO, TRALI

INTRODUCTION

On December 31, 2019, an outbreak characterized by severe respiratory illness emerged in Wuhan, China. The virus responsible for this outbreak was identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes Coronavirus Disease 2019 (COVID-19).¹⁻⁴ The outbreak rapidly spread worldwide, resulting in millions of cases and thousands of deaths.

COVID-19 ARDS is diagnosed when someone with confirmed COVID-19 infection meets the Berlin 2012 ARDS diagnostic. ARDS develops in 42% of patients presenting with COVID-19 pneumonia, and 61-81% of those requiring

intensive care. COVID-19 ARDS causes the typical ARDS pathological changes of diffuse alveolar damage in the lung.⁵ Hypoxemic respiratory failure in ARDS generally results from intrapulmonary ventilation-perfusion mismatch or shunt and usually requires mechanical ventilation (MV). It was reported that 69% of patients admitted to the intensive care unit required mechanical ventilation. The mortality rates for ICU patients and those receiving mechanical ventilation were 28.3% and 43%, respectively. As the onset time of COVID-19-related ARDS was 8-12 days, it suggested that the 1-week onset limit defined by ARDS Berlin criteria did not apply to COVID-19-related ARDS.⁶⁻⁸

Transfusion-related acute lung injury (TRALI) is a serious complication of blood transfusion and is among the leading causes of transfusion-related morbidity and mortality in most developed countries. In 2019, an international expert consensus modified and redefined the original TRALI definition established in 2004, and proposed new terminology.⁹ TRALI is defined by the development of acute hypoxemia accompanied by bilateral pulmonary edema occurring during blood product transfusion or within six hours following transfusion.¹⁰ Epidemiological data suggest that the incidence of TRALI is approximately one case per 130,000 transfused blood products; however, this estimate may differ according to the diagnostic criteria applied and the sensitivity of surveillance and reporting systems.^{10,11} The pathogenesis of TRALI is complex and multifactorial. According to the widely accepted two-hit model, an initial inflammatory or pre-existing pulmonary condition primes the pulmonary vasculature, followed by a second hit-typically donor-derived antibodies or bioactive lipids in transfused blood products- leading to neutrophil activation, endothelial injury, and pulmonary edema.¹²

In this case report, we evaluated the deterioration in respiratory status that developed after blood transfusion in a 46-year-old patient hospitalized with suspected COVID-19 pneumonia according to the TRALI diagnostic criteria newly defined in 2019. The aim of this report is to highlight the possible association between COVID-19-related inflammatory status and TRALI, to discuss the diagnostic challenges in differentiating TRALI from other causes of acute respiratory deterioration, and to increase awareness of this rare but serious transfusion complication in the post-COVID-19 era.

CASE

A 46-year-old male smoker with known chronic kidney disease not requiring dialysis presented to the emergency department with dyspnea and cough. On admission, he was tachycardic, hypertensive, and tachypneic, with bilateral basal crackles on lung auscultation. He was afebrile, and oxygen saturation (SpO₂) was 78% on room air.

Non-contrast chest computed tomography revealed diffuse bilateral ground-glass opacities involving both upper and lower lobes, with focal areas of consolidation (Figure 1). Given the presentation during the COVID-19 pandemic, findings were considered consistent with COVID-19 pneumonia. Laboratory evaluation demonstrated elevated white blood cell count, C-reactive protein, and D-dimer levels, along with lymphopenia. Hemoglobin was 7.3 g/dl, creatinine 2.38 mg/dl, pH 7.21, and pCO₂ 37.3 mmHg. Supplementary investigations obtained during the hospital course are summarized in Table.



Figure 1. Chest computed tomography at emergency department admission

The patient was admitted to the intensive care unit. During the intensive care unit stay, the patient’s vital signs were as follows: body temperature 36.2°C, blood pressure 176/101 mmHg, heart rate 115 beats/min, respiratory rate 28 breaths/min, and oxygen saturation 95% with nasal oxygen supplementation, decreasing to 88% on room air. Empirical treatment with favipiravir and azithromycin was initiated for suspected COVID-19, along with piperacillin-tazobactam and levofloxacin for possible bacterial infection. SARS-CoV-2 PCR testing was negative. Prior to transfusion, blood samples were collected for peripheral blood smear analysis and assessment of vitamin B12 and folate levels. Due to anemia, the patient received 2 units of packed red blood cells (PRBCs). The peripheral smear demonstrated hypochromic microcytic anemia. Serum vitamin B12 and folate levels were within

Table. Values of selected laboratory parameters

| | Normal | Day 1 | Day 2 | Day 3 | Day 5 | Day 7 | Day 9 | Day 12 | Day 18 |
|---------------------------------------|-----------|-------|-------|-------|-------|-------|-------|--------|--------|
| WBC count 10 ³ /mCL | 4-10 | 28.73 | 8.35 | 29.52 | 8.49 | 13.89 | 7.23 | 9.92 | 3.24 |
| Lymphocyte count 10 ³ /mCL | 0.8-3.2 | 0.94 | 0.74 | 0.8 | 0.23 | 0.29 | 0.26 | 0.36 | 0.67 |
| Hemoglobin g/dl | 13-16 | 7.3 | 7.2 | 10.8 | 8.3 | 8.4 | 7.7 | 8.5 | 7.9 |
| Hematocrit (%) | 37-47 | 27.5 | 25.8 | 35.5 | 28.1 | 28.7 | 22.6 | 28.1 | 26.3 |
| CRP mg/L | 0-5 | 40.3 | 62.3 | 55.9 | 67.7 | 30.8 | 32.6 | 35.5 | 69.7 |
| ESR mm/h | 0-15 | 29 | 19 | 17 | 29 | 12 | 42 | 49 | 22 |
| D-dimer mcg/L | 0-500 | 1730 | 720 | 2050 | 1630 | 1290 | 1090 | 1000 | 840 |
| Fibrinogen (mg/dl) | 2000-4000 | 4000 | | 4720 | 4060 | 3650 | 3970 | 4190 | 3770 |
| LDH (U/L) | 140-280 | 278 | | 391 | 300 | 290 | 235 | 263 | |
| Creatinine (mg/dl) | 0.6-1.3 | 2.38 | 2.52 | 2.34 | 2.83 | 2.73 | 2.05 | 2.39 | 1.65 |
| Ferritin mcg/L | 15-400 | 51 | 61 | 67 | 97 | 89 | 86 | 171 | 254 |
| Procalcitonin mcg/L | 0-0.5 | 0.35 | 12.68 | 10.39 | 46.20 | 19.65 | 6.4 | 1.14 | 0.25 |

WBC: White blood cell, CRP: C-reactive protein, LDH: Lactate dehydrogenase, ESR: Erythrocyte sedimentation rate

normal ranges. Despite the presence of acute inflammation, the low ferritin level was attributed to iron deficiency anemia and anemia of chronic disease. On day 2, hemoglobin remained low (7.2 g/dl), with normal bilirubin levels and negative direct and indirect Coombs tests; therefore, hemolytic anemia was excluded, and 3 additional units of PRBCs were transfused. The patient had a stable respiratory status for at least 36 hours prior to transfusion. Prior to blood transfusion, the patient had an oxygen saturation of 97-100% with nasal oxygen supplementation and 91-93% on room air, with a respiratory rate of 18-23 breaths/min. Six hours after transfusion, the patient developed tachypnea (38 breaths/min), tachycardia (134 beats/min), hypertension (174/112 mmHg), and hemoptysis, without fever. Oxygen saturation decreased to 50%, and the patient was subsequently intubated and placed on mechanical ventilation. The ventilator was set to pressure-regulated volume control (PRVC) ventilation mode with an FiO₂ of 70%, a respiratory rate of 12 breaths/min, a tidal volume of 490 ml, and a PEEP of 10 cmH₂O.

With a PaO₂/FiO₂ ratio of 221, the clinical picture was consistent with mild acute respiratory distress syndrome (ARDS). The deterioration in the patient's respiratory status requiring mechanical ventilation was attributed to several differential diagnoses, including ARDS secondary to COVID-19 or other microorganisms, secondary bacterial infection, TRALI, and transfusion-associated circulatory overload (TACO). Treatment targeting other potential microorganisms was expanded with the addition of trimethoprim-sulfamethoxazole, piperacillin-tazobactam was discontinued, and meropenem was initiated. Central venous pressure was 8 mmHg, and bedside chest radiography demonstrated bilateral diffuse pulmonary opacities (Figure 2). Transthoracic echocardiography showed no evidence of left atrial hypertension (LAH), thereby excluding TACO. Based on the presence of ARDS risk factors without established ARDS and respiratory deterioration within 6 hours of transfusion, the patient was diagnosed with TRALI Type II.



Figure 2. Post-transfusion chest X-ray

On day 3, vancomycin was added to the treatment regimen due to an elevated white blood cell count of $29.5 \times 10^3/\mu\text{L}$ and a procalcitonin level of 10.33 ng/ml. The patient was successfully extubated on day 9. Repeated SARS-CoV-2 PCR tests and rapid antibody tests were negative, and blood and urine cultures showed no growth. The patient was discharged to the ward on day 20.

DISCUSSION

The most common symptoms of COVID-19 include fever, dry cough, dyspnea, fatigue, and myalgia.¹³ COVID-19-related ARDS develops in approximately 17% of patients as a result of alveolar damage, typically occurring 8-14 days after symptom onset.⁶ Laboratory findings associated with COVID-19 include elevated white blood cell count, AST, ALT, high-sensitivity C-reactive protein (hs-CRP), and D-dimer levels, as well as lymphopenia and hypoalbuminemia.^{14,15} Characteristic chest computed tomography findings consist of ground-glass opacities, often accompanied by areas of consolidation.¹⁶ In the present case, the patient's clinical presentation, laboratory results, and radiological findings were consistent with COVID-19. Furthermore, ARDS developed approximately two weeks after symptom onset, which is in accordance with the typical disease course reported in the literature.

TRALI was redefined in 2019 and reclassified into TRALI Type I and TRALI Type II, with the term "possible TRALI" being eliminated. TRALI Type I is defined as an acute onset condition in patients without risk factors for ARDS, characterized by hypoxemia (SpO₂<90% on room air or a PaO₂/FiO₂ [P/F] ratio<300), bilateral pulmonary edema demonstrated by ultrasound, radiography, or computed tomography, absence of LAH, and symptom onset during or within 6 hours of transfusion. TRALI Type II includes the criteria of Type I and additionally applies to patients with risk factors for ARDS who do not meet ARDS diagnostic criteria or who have mild ARDS (P/F ratio 200-300), but whose respiratory status deteriorates following transfusion, with a stable respiratory status during the 12 hours preceding transfusion.⁹

For the differential diagnosis of TACO, it is recommended that pulmonary edema and LAH be objectively assessed using echocardiography and pulmonary imaging, rather than relying solely on indirect clinical signs such as hypertension or tachycardia.⁶ In some cases, measuring brain natriuretic peptide (BNP) levels at the onset of pulmonary symptoms may be helpful, with BNP levels <300 pg/ml suggesting exclusion of TACO. Additionally, a pretransfusion-to-posttransfusion BNP ratio >1.5 has been reported to further rule out TACO.⁹ In our case, BNP levels were not measured because there was no known history of cardiac disease and volume overload was assessed by echocardiography.

In our patient, who was initially managed for pneumonia, risk factors for ARDS were present, but respiratory status remained stable for at least 36 hours prior to transfusion. Respiratory deterioration occurred within 6 hours after transfusion, and post-transfusion chest radiography demonstrated bilateral pulmonary opacities. LAH was not detected on echocardiography, thereby excluding TACO. Accordingly, the patient was diagnosed with TRALI Type II. Accordingly, the patient was diagnosed with TRALI Type II.

The mainstay of treatment for TRALI is supportive care. If a blood transfusion is ongoing, it should be immediately discontinued. While a conservative approach with supplemental oxygen is sufficient in mild cases, mechanical

ventilation and intensive care support are required in more severe cases. The use of corticosteroids and diuretics is not recommended.¹⁷ In some patients, recovery may take longer than one week.¹⁸

CONCLUSION

TRALI may develop even in the presence of ARDS risk factors, such as pneumonia, making the diagnosis challenging. For the differential diagnosis of TRALI, TACO, and ARDS, a comprehensive clinical assessment supported by laboratory findings and objective tools such as echocardiography is recommended. The occurrence of any transfusion-related complication should be reported to the respective blood transfusion services. We believe that as clinicians publish their cases, differential diagnoses related to this condition will be better established and overall awareness will increase.

ETHICAL DECLARATIONS

Informed Consent

Written informed consent was obtained from the patient(s) included in this report. Signed consent forms are retained by the authors and are available upon request.

Peer Review Process

This report underwent external peer review.

Conflict of Interest

The authors declare no conflicts of interest.

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Author Contributions

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REFERENCES

- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506. doi:10.1016/S0140-6736(20)30183-5
- Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*. 2020;395(10224):565-574. doi:10.1016/S0140-6736(20)30251-8
- Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020;382(8):727-733. doi:10.1056/NEJMoa2001017
- Zengin EN. Research trends and global productivity on mechanical ventilation with the impact of COVID-19: a bibliometric analysis in the period 1980-2021. *JHSM*. 2022;5(4):1051-1061. doi:10.32322/jhsm.1122437
- Gibson PG, Qin L, Puah SH. COVID-19 acute respiratory distress syndrome (ARDS): clinical features and differences from typical pre-COVID-19 ARDS. *Med J Aust*. 2020;213(2):54-56.e1. doi:10.5694/mja2.50674
- Li X, Ma X. Acute respiratory failure in COVID-19: is it "typical" ARDS? *Crit Care*. 2020;24(1):198. doi:10.1186/s13054-020-02911-9
- Chang R, Elhousseiny KM, Yeh YC, Sun WZ. COVID-19 ICU and mechanical ventilation patient characteristics and outcomes-a systematic review and meta-analysis. *PLoS One*. 2021;16(2):e0246318. doi:10.1371/journal.pone.0246318
- Zengin EN. Research trends and global productivity on mechanical ventilation with the impact of COVID-19: a bibliometric analysis in the period 1980-2021. *JHSM*. 2022;5(4):1051-1061. doi:10.32322/jhsm.1122437
- Vlaar APJ, Toy P, Fung M, et al. A consensus redefinition of transfusion-related acute lung injury. *Transfusion*. 2019;59(7):2465-2476. doi:10.1111/trf.15311
- Sivakaanthan A, Swain F, Pahn G, et al. Transfusion-related acute lung injury (TRALI): a retrospective review of reported cases in Queensland, Australia over 20 years. *Blood Transfus*. 2022;20(6):454-464. doi:10.2450/2022.0020-22
- White SK, Schmidt RL, Walker BS, Metcalf RA. The epidemiology of transfusion-related acute lung injury: a scoping review and analysis. *Transfusion*. 2023;63(1):104-116. doi:10.1111/trf.17185
- Silliman CC, Voelkel NF, Allard JD, et al. Plasma and lipids from stored packed red blood cells cause acute lung injury in an animal model. *J Clin Invest*. 1998;101(7):1458-1467. doi:10.1172/JCI1841
- Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507-513. doi:10.1016/S0140-6736(20)30211-7
- Chen G, Wu D, Guo W, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. *J Clin Invest*. 2020;130(5):2620-2629. doi:10.1172/JCI137244
- Levi M, Thachil J, Iba T, Levy JH. Coagulation abnormalities and thrombosis in patients with COVID-19. *Lancet Haematol*. 2020;7(6):e438-e440. doi:10.1016/S2352-3026(20)30145-9
- Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: a multicenter study. *AJR Am J Roentgenol*. 2020;214(5):1072-1077. doi:10.2214/AJR.20.22976
- Goldberg AD, Kor DJ. State of the art management of transfusion-related acute lung injury (TRALI). *Curr Pharm Des*. 2012;18(22):3273-3284. doi:10.2174/1381612811209023273
- Moore S. B. Transfusion-related acute lung injury (TRALI): clinical presentation, treatment, and prognosis. *Crit Care Med*. 2006;34(5):S114-S117. doi:10.1097/01.CCM.0000214312.20718.3E