A case of self-limiting respiratory distress in a postpartum mother – transfusion related acute lung injury

Rajaratnam A¹* , Kularathne WKS¹

Abstract

A 37-year-old woman, treated for postpartum haemorrhage, developed sudden-onset acute respiratory distress characterised by tachypnoea, desaturation and widespread crepitations, on the first day postpartum. She had low partial pressure of oxygen to the fractional inspired oxygen concentration (PaO₂/FiO₂) ratio and bilateral patchy opacities in chest radiograph. Despite having a high oxygen requirement, her clinical and radiographic abnormalities spontaneously resolved in 30 hours, after a conservative treatment approach. This case report delves into the rare, yet serious entity of transfusion-related acute lung injury (TRALI) and underscores the importance of considering it among other potential causes of shortness of breath following blood transfusion in postpartum patients.

Keywords: transfusion related acute lung injury, postpartum dyspnoea, adverse blood transfusion reaction

Introduction

Transfusion-related acute lung injury (TRALI) is a relatively rare yet significant complication associated with blood transfusions, often culminating in severe acute adverse events and occasionally in fatalities. Defined by the Canadian Consensus Conference of 2004 as the development of acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) within 6 hours following a blood transfusion, TRALI has been recognised as early as 1957.(1, 2) Incidence rates vary widely, ranging from 0.1% to 15% among transfused patients, with higher prevalence observed within intensive care unit cohorts.(3, 4) Despite often being self-limiting within 72 hours, severe cases can be fatal, with mortality rates ranging from 5% to 25%, and even higher rates, up to 47%, reported within intensive care unit settings.(5, 6) The prognosis remains generally unfavourable due to the lack of effective therapeutic interventions.

This case report presents a noteworthy instance involving a young postpartum woman who experienced severe respiratory distress within the first day postpartum, ultimately resolving within 30 hours. After excluding alternative aetiologies, the episode was attributed to TRALI, stemming from a blood transfusion administered to address minor postpartum haemorrhage. By elucidating the clinical trajectory of TRALI, this case report and subsequent review offer valuable insights into its rare yet potentially grave implications in the postpartum period.

Case presentation

A 37-year-old woman, with gravidity-3, parity-2, having a history of chronic essential hypertension and mild intermittent asthma, both well-controlled with medications, presented in her third pregnancy.
She had previously delivered two children via vaginal delivery without complications. During this pregnancy, she was diagnosed with gestational diabetes at 28 weeks, which was effectively managed with dietary adjustments and Metformin. Her antenatal period was otherwise unremarkable. At 37 weeks and 3 days of gestation, she was admitted to the labour ward in early labour and received a slow infusion of oxytocin as a tocolytic. Due to slow progress, an emergency lower segment caesarean section was performed under spinal anaesthesia after ten hours of labour. Post-surgery, her recovery was uneventful.

Six hours after surgery, she received one pint of cross matched packed red blood cells due to a drop in haemoglobin levels by 1.5 g/dL from baseline, attributed to modest intraoperative and postpartum uterine bleeding. Approximately four hours into the transfusion, she reported sudden difficulty in breathing without associated symptoms such as fever, cough, or chest pain. She had been immobile since admission to the labour ward but denied painful asymmetric lower limb swelling. No significant family history or risk factors for thrombotic conditions were reported. Her COVID-19 vaccination status was up to date, and she had no known allergies. Physical examination revealed tachypnoea, increased work of breathing, and reduced chest movements with bilateral crackles and dullness on percussion at lung bases. There was no raised jugular venous pulsation or gallop rhythm. Cardiohaemodynamic parameters including pulse rate and blood pressure were within normal limits. Pulse oximetry showed an oxygen saturation of 85% on room air. Arterial blood gas analysis revealed respiratory alkalosis with a partial pressure of oxygen to the fractional inspired oxygen concentration (PaO2/FiO2) ratio of 158.0 with an FiO2 of 36%. The other biochemical parameters are summarised in Table 1. Chest radiography demonstrated bilateral lower zone consolidations (Figure 1, panel A). Bedside ultrasound ruled out effusions. Blood, urine, and high vaginal swab cultures yielded no growth. An urgent echocardiogram revealed normal systolic diastolic biventricular function, ruling out cardiomyopathies, left atrial abnormalities or massive pulmonary embolism. CT pulmonary angiogram and doppler ultrasound of deep veins of the legs ruled out pulmonary thromboembolic causes. A high-resolution CT of the chest was not performed. The diagnosis of TRALI was considered based on clinical presentation and exclusion of other causes.

A tentative diagnosis of TRALI was considered, due to the occurrence of symptoms within 6 hours of transfusion, on-air saturation less than 90%, on-air PiO2/FiO2 ratio below 300, presence of bilateral lung infiltrates on chest radiograph, and absence of left atrial anomalies on echocardiogram or any features of circulatory overload. Other postpartum-specific aetiologies such as venous thromboembolism, peripartum cardiomyopathy, amniotic fluid embolism, ARDS due to chorioamniotitis or placental abruption, tocolytic-induced pulmonary oedema and preeclampsia-related pulmonary oedema were unlikely. Acute asthma, respiratory tract infection, structural or functional heart disease, transfusion-related circulatory overload, post-transfusion anaphylaxis, and transfusion-related haemolysis too were unlikely. Gastric acid aspiration induced ARDS was also unlikely due to no suggestive history, though the occurrence of subclinical microaspirations cannot be ruled out completely.

Figure 1 - Serial chest radiographs showing resolution of bilateral radiographic changes. Panel A: 1 hour, Panel B: 14 hours, Panel C: 35 hours since symptom onset
## Table 1 - Summary of biochemical and arterial blood gas parameters

<table>
<thead>
<tr>
<th>Biochemical parameter</th>
<th>Patient’s value</th>
<th>Reference level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total white blood cell (x10⁹/L)</td>
<td>15</td>
<td>4 – 10</td>
</tr>
<tr>
<td>Absolute neutrophil count (x10⁹/L)</td>
<td>13.8</td>
<td>2 – 7</td>
</tr>
<tr>
<td>Haemoglobin level pretransfusion (g/dL)</td>
<td>8.8</td>
<td>11 – 13</td>
</tr>
<tr>
<td>Haemoglobin level posttransfusion (g/dL)</td>
<td>10.1</td>
<td>11 – 13</td>
</tr>
<tr>
<td>Platelet count (x10¹²/L)</td>
<td>184</td>
<td>150 – 450</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>8.8</td>
<td>&lt;6</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>15</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Alanine transaminase (U/L)</td>
<td>23.4</td>
<td>5-35</td>
</tr>
<tr>
<td>Aspartate transaminase (U/L)</td>
<td>20.1</td>
<td>13-31</td>
</tr>
<tr>
<td>Total bilirubin (umol/L)</td>
<td>3.6</td>
<td>3 – 21</td>
</tr>
<tr>
<td>Blood urea (mmol/L)</td>
<td>6.3</td>
<td>2 – 7</td>
</tr>
<tr>
<td>Serum creatinine (umol/L)</td>
<td>52.31</td>
<td>45-85</td>
</tr>
<tr>
<td>Serum sodium (mmol/L)</td>
<td>144</td>
<td>135 – 145</td>
</tr>
<tr>
<td>Serum potassium (mmol/L)</td>
<td>3.4</td>
<td>3.5 – 5.5</td>
</tr>
<tr>
<td>Troponin I (mg/L)</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Random blood sugar (mg/dL)</td>
<td>156</td>
<td>110 – 200</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.48</td>
<td>7.35 – 7.45</td>
</tr>
<tr>
<td>Arterial oxygen pressure (mmHg)</td>
<td>79</td>
<td>60 – 100</td>
</tr>
<tr>
<td>Arterial carbon dioxide pressure (mmHg)</td>
<td>28</td>
<td>40-45</td>
</tr>
<tr>
<td>Arterial bicarbonate (mmol/L)</td>
<td>20</td>
<td>22 - 26</td>
</tr>
</tbody>
</table>

The patient was managed with supplemental oxygen (15 L/min) via non-rebreather mask, nebulisation, and close monitoring in a high dependency unit, leading to resolution of symptoms within 30 hours. Follow-up chest radiographs showed improvement (figure 1, panel B and C).

### Discussion

Diagnosing TRALI relies on clinical and radiographic assessments. Symptoms typically manifest within 6 hours of transfusion, and characteristic radiographic findings include bilateral infiltrates, which may present as patchy, homogeneous, diffuse, or asymmetric patterns suggestive of alveolar or interstitial disease. In our case, the patient exhibited bilateral patchy pulmonary infiltrates on chest radiography. Hypoxaemia, often quantified by a PaO2/FiO2 ratio of less than 300 mmHg or oxygen saturation below 90% on room air, is a hallmark of TRALI.(1,7) Our patient demonstrated an oxygen saturation of 84% on air and a PaO2/FiO2 ratio of 158 mmHg, despite receiving an FiO2 of 35%. Although fever, cyanosis, and hypotension are common manifestations of TRALI, our patient did not exhibit these symptoms. Recent advancements in diagnostic criteria, such as those introduced in 2019, have refined TRALI classification into Type I and II based on the presence or absence of ARDS risk factors.(7)

Pathophysiological mechanisms underlying TRALI include immune and non-immune theories. The immune theory posits that antibodies targeting human leukocyte antigen (HLA) class 2 and human neutrophil antigen (HNA) class 3a in the donor blood
interact with corresponding antigens on the recipient's leukocytes. The non-immune "two-hit" model involves priming events and subsequent endothelial injury. (8, 9) Notably, the exact relationship between the administered dose of implicated blood products and the severity of TRALI remains elusive. Despite this uncertainty, evidence suggests that even trace amounts of plasma exposure may suffice to instigate the onset of TRALI. (10) Notably, the risk of TRALI varies across different blood components, with whole blood, platelets, fresh frozen plasma, packed red cells, granulocyte, cryoprecipitate, and human immunoglobulins exhibiting decreasing orders of risk.

Diagnosing TRALI in the postpartum period poses distinct challenges. Symptoms of TRALI often overlap with those of other common conditions encountered during this phase. Physiological manifestations such as tachypnoea and mild hypoxaemia are also expected after normal childbirth. Distinguishing TRALI from other critical postpartum conditions, such as amniotic fluid embolism, pulmonary embolism, and peripartum cardiomyopathy, proves intricate due to shared clinical features among these disorders. Additionally, postpartum women may present with dyspnoea attributed to various aetiologies, including anaemia, fatigue, or the physiological stress of labour itself. It is reported that among patients transfused for postpartum haemorrhage, those with a history of gestational hypertension and preeclampsia, particularly if they have not received antihypertensive therapy, exhibit a heightened risk of developing TRALI. (11) Our patient did not have such risk factors. Cohort studies state that the risk of TRALI in postpartum women is further exacerbated in those who receive three or more units of packed red cells. (12)

The lack of specific diagnostic markers for TRALI exacerbates the diagnostic challenge, contributing to its frequent under-recognition and underreporting within clinical settings. In light of the absence of definitive diagnostic tests for TRALI, clinicians must employ a comprehensive assessment approach. This involves meticulous consideration of the patient’s clinical presentation, radiological findings, and the systematic exclusion of alternative aetiologies.

To date, there are no established treatments for TRALI beyond supportive care. Essential steps in management should include immediately discontinuing transfusion, providing supplemental oxygen, administering intravenous fluids, conducting frequent monitoring of vital parameters, initiating empirical antibiotics, and notifying the blood bank to quarantine blood products from the same donor. (8) In severe cases, ventilation with a low-tidal volume strategy and extracorporeal membrane oxygenation (ECMO) may be necessary. (13, 14) However, we managed our patient with supplemental oxygen alone. While high-dose steroids were utilised, partly due to the assumption of an immunological cause, there is no direct evidence of their benefit. (15) A randomised controlled trial demonstrated improved 7-day survival in critically ill patients with TRALI following intravenous administration of high-dose ascorbic acid. (16) Neither steroids nor ascorbic acid was utilised in our patient.

Prevention strategies for TRALI entail several measures including avoiding the procurement of blood donations from multiparous women, who may have developed sensitisation from multiple fetoplacental blood transmissions, as well as from donors whose blood has previously resulted in TRALI. (17) Given that anti-HLA production increases over time, minimising the shelf time of blood products also contributes to TRALI prevention. Furthermore, it is advisable to refrain from using whole blood, as it poses a higher risk of TRALI compared to packed red cells. In developed countries, the implementation of strategies such as the introduction of male-only donors, male-dominated plasma, exclusion of all-exposure donors, and antibody screening has significantly reduced the morbidity associated with antibody-dependent TRALI. (8) However, the routine implementation of anti-leukocyte antibody screening faces challenges due to financial complexities. (18) Nevertheless, retrospective analyses have demonstrated that leukoreduction of blood components can substantially reduce the occurrence of TRALI cases by up to 83%. (19)

**Conclusion**

TRALI represents a severe yet under-recognised complication of blood transfusions, particularly in the postpartum period. Heightened awareness among clinicians is crucial for early recognition and management. Adequate supportive care plays a key role in improving outcomes for affected patients. TRALI can be prevented by avoiding blood donated by selected donors, avoidance of longer storage, and minimising products that can increase the risk. Addressing gaps in awareness and recognition is essential to minimise the morbidity and mortality associated with TRALI.
Declarations

Conflicts of interest
The authors declare that they have no conflicts of interest

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Author details
¹National Hospital Kandy, Sri Lanka

References


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