CASE REPORT

A Case Report of Transfusion-related Acute Lung Injury (TRALI) Type II from A Heathy Male Donor

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ABSTRACT

Transfusion-related acute lung injury (TRALI) is an uncommon acute transfusion reaction, but it remains notable for its severe morbidity and mortality. TRALI has been categorised as Type I (without acute respiratory distress syndrome (ARDS) risk factors) and Type II (with ARDS risk factors or with mild pre-existing ARDS). Substantial evidences suggested that receiving blood products, especially from multiparous women, can be associated with TRALI due to presence of anti-white blood cell antibodies produced from sensitisation during pregnancy. Nevertheless, studies on the consequences of transfusion based on different types of TRALI are still uncommon. Thus, we report a case of TRALI Type II from an event of red blood cells transfusion from a young healthy male donor. In this case, not only multiple human leucocyte antigen (HLA) class I and II antibodies were detected in the donor, low levels of antibody towards the patient's antigen were also detected.

Keywords: Transfusion-related lung injury, TRALI Type II, Blood transfusion, Male donor

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INTRODUCTION

Transfusion-related acute lung injury (TRALI) is a clinical syndrome that has been recently classified as Type I (without acute respiratory distress syndrome (ARDS) risk factors) and Type II (with ARDS risk factors or with mild pre-existing ARDS) (1). Risk factors associated with TRALI and ARDS include sepsis, massive transfusion, surgery, non-cardiogenic shock, mechanical ventilation, and increased age (1,2). It is difficult to exactly establish the incidence of TRALI due to variations of clinical definition used. The reported incidences vary from 1 in 1,333-270,000 units of blood transfusion (2). Clinical manifestations of TRALI include acute respiratory distress, fever, hypotension, tachycardia, and chest radiographic finding of bilateral infiltration changes within 6-72 hours following blood transfusion (5).

The most common cause of TRALI is neutrophil-mediated pulmonary vascular injury. Kopko et al. (2018) emphasised that human neutrophil antigen (HNA) and human leucocyte antigen (HLA) class II antibodies are significant in the pathogenesis of TRALI, as compared to HLA class I antibodies (3). Previous studies have reported that white blood cell (WBC) antibodies are commonly found in multiparous women, which are induced from sensitisation during pregnancy (2,5). Notwithstanding the application of mitigation strategies, TRALI reactions are still evident. Over the years, different pathophysiological mechanisms for TRALI were proposed, which included 'antibody-mediated' and 'non-antibody-mediated' mechanisms, as well as the two-hit model and threshold model (2,5).

This paper describes an 80-years-old gentleman who was transfused with a unit of red blood cells (RBC), and subsequently passed away due to myocardial infarction secondary to TRALI.

CASE REPORT

An 80-years-old Malay gentleman with underlying gouty arthritis was admitted for infected left ankle tophaceous gout with maggot infestation. He underwent wound debridement with arthrotomy washout of left ankle under spinal anaesthesia. Intraoperatively, the patient's blood pressure (BP) ranged from 100-120/50-60 mmHg, heart rate ranged from 60-80 beats per minute (bpm), and electrocardiography (ECG) in cardiac monitor showed sinus rhythm, but noted ST depression at lead II, III, and aVF. However, the patient had no active complaint.

Post operation at the recovery bay, the patient's blood pressure ranged from 85-100/50-65 mmHg, heart rate

ranged from 80-90 bpm, with oxygen saturation of 99% under nasal prong oxygen. He developed an episode of hypoglycaemia as result of keep nil by mouth for 8 hours with less than 2 units of intravenous (IV) drip of normal saline given before the operation. The hypoglycaemic event was corrected with 50 mL bolus of IV Dextrose 50% (Dextrose stick test: 3.1 mmol/L to 8.2 mmol/L). Repeated ECG noted sinus rhythm with ST depression over leads V2-V6, which was similar to admission ECG. The patient was attended by the medical team and was given the impression of ECG changes corresponding to hypoperfusion/sepsis. The medical team suggested performing judicious fluid resuscitation and inotropes if hypotension persists. He was given a single unit of RBC transfusion by orthopaedic team, in view of a baseline haemoglobin level of 9.0 g/dL.

After one hour of ongoing RBC transfusion, the patient complained of sudden breathlessness and chest discomfort. He deteriorated rapidly with oxygen saturation falling to 74% under nasal prong oxygen, hypotension (BP: 85/45 mmHg), tachycardia (130 bpm), and tachypnoea (30 breath per minute), with crepitation up to bilateral upper zones of lungs on auscultation. Haemodynamic parameters gradually deteriorated to asystole. He received 4 boluses of IV adrenaline and chest compressions for 30 minutes. Upon return of spontaneous circulation, he developed ventricular tachycardia and required one cycle of cardioversion. In view of his unstable clinical condition, he remained intubated and supported with mechanical ventilation using a positive end expiratory pressure (PEEP) of 10 mmHg with multiple haemodynamic supporters (noradrenaline, dobutamine, vasopressin).

A panel of investigation was ordered immediately. An urgent chest radiograph was also done, which showed widespread confluent alveolar and interstitial opacities with perihilar predominance seen in bilateral lung fields (Figure 1A), as compared to previous normal chest radiograph (Figure 1B). This result was suggestive of acute fulminant inflammatory lung reactions, which caused diffused pulmonary oedema, whereby the causes may include infection, toxic fumes inhalation, and allergic reaction. Unfortunately, after a period of 48 hours in the intensive care unit, the patient's clinical condition further deteriorated (bradycardia 20-50 bpm) and had succumbed due to the above complication.

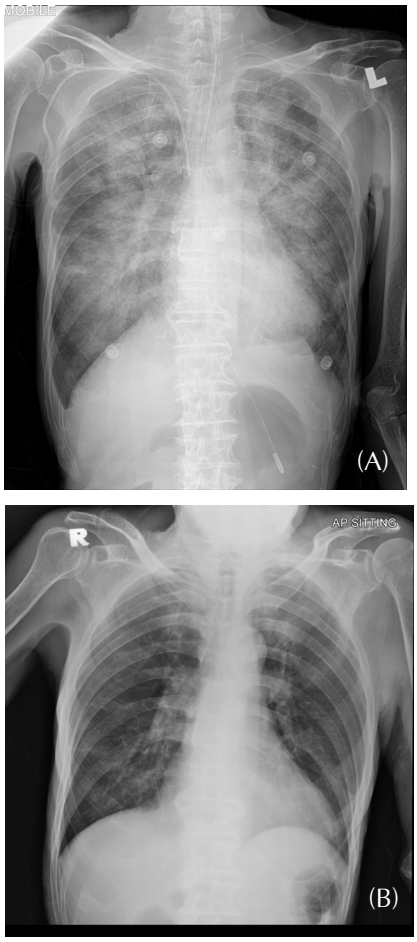

Figure 1: Figure 1: Chest radiographs of patient who presented with transfusion-related acute lung injury (TRALI). (A) Chest radiograph of patient after development of TRALI. Radiograph shows bilateral diffuse reticular opacities with upper lobe diversion in keeping with pulmonary oedema. (B) Chest radiograph of patient before development of TRALI. Radiograph shows fairly clear lung fields with no pleural effusion.

DISCUSSION

Redefinition of TRALI was recently proposed by an international expert panel in 2019 and the new terminology of TRALI Type I and TRALI Type II was introduced (1). This case has fulfilled the diagnostic criteria of TRALI Type II according to the new definition, whereby the patient developed symptoms of acute respiratory distress one hour after the commencement of blood transfusion, with evidence of reduced oxygen saturation and radiographic changes of bilateral lungs infiltration in keeping with pulmonary oedema. Other than being treated for infected left ankle tophaceous gout (ARDS risk factor of non-pulmonary sepsis), he had no signs of acute lung injury, pulmonary oedema, or circulatory overload prior to the event.

In our case, we detected 4% of HLA class I and 6% of HLA class II antibodies in the concerned blood donor. A low level of antibody towards the patient's antigen was also detected. HNA antibodies test was not performed as it is unavailable in the referral laboratory. The two-hit model theory and the detection of HLA class II antibodies most likely accounted for the development of TRALI in this patient. The 'first hit' involved the patient's predisposed risk factors. He is an elderly patient and in the condition of sepsis, who just underwent a surgical procedure. These factors contributed to the increased levels of cytokines and chemokines from upregulated lung endothelium, which promoted a pro-inflammatory environment causing neutrophil attraction

to the pulmonary vasculature (1,2). The 'second hit' involved the blood transfusion itself. Blood products containing HLA class I and class II antibodies can be attributed to the activation of neutrophils. This will lead to release of proteases, reactive oxidative species, and pro-inflammatory molecules through capillary leakage. Consequently, pulmonary endothelial injury and pulmonary oedema would occur (2).

It is well established that these WBC-antibodies are usually found in multiparous women due to sensitisation during pregnancy (2,5). Nonetheless, HLA antibodies can also be detected in 1% of the male population (5). We discovered that the concerned blood donor is an 18-years-old young healthy gentleman, who has no known medical illness and no history of blood transfusion, or prior hospital admission. This was his first blood donation. It is emphasised that HLA class II antibodies are significant in the pathogenesis of TRALI, which was reflected in our case, where 6% of HLA class II antibodies were detected in this blood donor. Therefore, the blood donor was counselled and deferred permanently to prevent TRALI in another recipient.

As yet, there is no definitive treatment for TRALI, and its diagnosis and management remain a challenge for clinicians (1,2). Hence, awareness of the updated pathogenesis, definition, risk factors, signs, and symptoms of TRALI will aid clinicians in preparing a meticulous approach for blood transfusion, particularly for patients who are at higher risk of developing TRALI, as well as to report TRALI cases to transfusion service providers (1,5). Meanwhile, transfusion services also play a vital role in investigating and managing concerned donors accordingly. Transfusion services should also partake an active role in preventing TRALI. Several mitigation strategies have been shown to reduce TRALI incidence: (i) male-only or antibody-negative donor recruitment; (ii) blood product management and restrictive transfusion; (iii) blood storage with platelet additive solution; (iv) washing RBCs; (v) pathogen reduction technology; and (vi) solvent/detergent plasma (2,4-5). In additionally, Silliman et al. (2014) proposed that pre-storage filtration of RBC may prevent TRALI by removing HLA and HNA antibodies, and decreasing lipid priming activity (4). In conclusion, interprofessional teamwork remains the best prevention method for TRALI.

CONCLUSION

In this report, a rare case of a young gentleman with anti-WBC antibodies and a patient's predisposing factors had precipitated the event of TRALI Type II after RBC transfusion. Other than diving into the diagnosis of TRALI and its type, it is utmost importance to report TRALI cases to the transfusion unit. These reports could lead to more research into the pathophysiology of TRALI and thus, more preventive measures can be undertaken.

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