CASE REPORT

Transfusion-related acute lung injury management in a pediatric intensive care unit

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Abstract
Transfusion-related acute lung injury (TRALI) constitutes a life threatening complication of blood transfusion. In severe TRALI cases supportive care with mechanical ventilation in intensive care unit is needed. We present two severe TRALI cases caused by leukocyte depleted, ABO compatible, packed red blood cell transfusions, coming from multiparous women donors. In the first case diagnosis was based on clinical findings and established by the identification of leukocyte antibodies in donor's unit and recipient's serum and she deal with invasive mechanical ventilation. In the second case, diagnosis was based on clinical criteria and chest radiograph findings and non-invasive mechanical ventilation was used. Both cases were treated in a Pediatric Intensive Care Unit and they had a favorable outcome. Hippokratia 2011; 15 (2): 184-186

Key words: transfusion-related acute lung injury, mechanical ventilation, pediatric intensive care

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Transfusion-related acute lung injury (TRALI) is a serious clinical syndrome associated with the transfusion of blood or blood-components. It is characterized by acute non cardiogenic pulmonary edema with hypoxia occurring within a few hours of transfusion[1]. In the majority of cases, TRALI is a self-limited condition. In mild or severe cases supportive care with mechanical ventilation in intensive care unit may be sufficient for treatment[2]. We present two severe TRALI cases with differences in both diagnosis and mechanical ventilation procedures. Both cases were treated in a Pediatric Intensive Care Unit (PICU) and achieved a full recovery.

Case 1

A 13-year old girl suffered by beta-thalassemia, was on a regular transfusion regimen since the age of 2 when thalassemia was diagnosed. One hour after transfusion initiation, having received 125 mL of a single unit of leukocyte depleted, ABO compatible, packed red blood cells, she developed cough, respiratory distress, cyanosis and hypotension. Low oxygen saturation (<80%), tachycardia (>160/minute), tachypnea (>45/minute) were also noted. Chest auscultation revealed bilateral moist rales without bronchospasm and the patient was managed with oxygen, intravenous fluids, steroids and adrenaline. Urgent chest radiograph revealed bilateral coarse alveolar infiltrates with normal cardiac silhouette. Hemodynamic parameters progressively worsened with onset of respiratory distress and increased body temperature (T=39.7°C). Arterial blood gases are shown at Table 1. In the setting of a deteriorating clinical condition, she was transferred to the PICU. The patient was supported with invasive mechanical ventilation in a pressure-regulated volume control model using low tidal volume of 6 mL/kg, alveolar plateau pressure of ≤30 cmH_2O and positive end expiratory pressure (PEEP) of 7 mmHg. The patient was treated with multi-agent hemodynamic support (dopamine, dobutamin and noradrenaline) in addition to diuretics, midazolam and antibiotics. A normal electrocardiogram (EEG) with a normal echocardiogram (ECHO) ruled out the possibility of cardiopathy. In addition, ECHO performed annually had been also normal. All the cultures received from the patient were negative, so the diagnosis of transfusion related septic shock was excluded. The patient's condition progressively improved and the chest radiograph on the 4th day of hospitalization returned to normal. Serum samples from the patient were tested and showed anti-leukocyte and anti-platelets antibodies, while donor's serum showed anti-leukocyte antibodies in low titers and the diagnosis of TRALI was established[3]. The blood donor was a multiparous woman who was subsequently excluded from the donor pool. After 4 days of hospitalization in PICU the patient was clinically full recovered and discharged to the Pediatric department.

Case 2

A 5.5-year old girl suffered by Blackfan-Diamond syndrome, was on a regular transfusion regimen since the age of 8 months when the syndrome was first diagnosed. During the transfusion of a single unit of leukocyte depleted, ABO compatible, packed red blood cells, having received 55 mL, she developed respiratory distress, cy-

anosis and hypotension. A falling oxygen saturation was noted (<80%), in addition to tachycardia (>160/minute) and tachypnea (>50/minute). Chest auscultation revealed bilateral diffuse crackles. Treatment with oxygen, intravenous fluids, steroids and diuretics was initiated. An urgent chest radiograph was ordered and showed extensive bilateral pulmonary infiltrates with normal cardiac silhouette. Arterial blood gasses shown at Table 1. Despite treatment, her condition rapidly deteriorated, she developed fever (39ºC) and she was transferred to the PICU. Non-invasive mechanical ventilation with *Bussignac* mask at 15 liters/minute (PEEP=5 mmHg) was applied, in parallel to vasopressor (dopamine) to maintain adequate perfusion and empirically antibiotics. Diagnosis of transfusion related septic shock and cardiopathy could not be excluded in that time. Laboratory findings revealed decreased neutrophils (4320/μL) and platelets (132000/μL) as compared to the findings before the transfusion (neutrophils 16500/μL, platelets 304000/μL). The EEG and ECHO did not confirm any cardiopathy in addition to her annually performed tests which where also normal. Blood culture, urine and swab throat were negative. She remained on non-invasive mechanical ventilation with *Bussignac* mask for 36 hours and she presented progressive clinical and radiographic recovery. No investigation of the patient's and donor's serum for anti-leukocyte antibody was performed due to technical reasons of the laboratories. However, the clinical symptoms, the chest radiograph and the laboratory findings can establish the diagnosis of TRALI. Similarly to the previous case, the blood donor was a multiparous woman who was excluded from the donor pool. The patient was discharged from the hospital after a total of 4 days staying, 3 days in the PICU and one day in the Pediatric department.

Discussion

TRALI is a life threatening complication of blood transfusion often underdiagnosed. The estimate for TRALI occurrence ranges from 1/5,000 to 1/100,000 for all transfusion components[2,4]. Although the exact etiology of TRALI remains unclear, two distinct mechanisms have been proposed[5]. The traditional theory suggests the notion that TRALI is an immune mediated reaction caused by the interaction between recipient leukocytes and anti-leukocytes antibodies from donors. By the non-immune hypothesis an alternative mechanism was suggested, in which biologically active lipids of cell membranes called lysophosphatidylcholines, contained in the transfused product, may induce leukocyte priming and activation in the recipient resulting in endothelial cell damage[5].

TRALI is defined as any case of acute dyspnoea with hypoxia and bilateral pulmonary infiltrates occurring dur-

Table 1: Summary of investigations done in the two TRALI cases

		Case 1	Case 2
Age (y)		13	5.5
Gender		Female	Female
Indication of transfusion		Beta-thalassemia	Blackfan-Diamond syndrome
Occurrence of the adverse reaction		1h after transfusion initiation, having received 125mL of a single unit of leukocyte depleted, ABO compatible, packed red blood cells	40min after transfusion initiation, having received 55mL of a single unit of leukocyte depleted, ABO compatible, packed red blood cells
Initial arterial blood gas		(O_2 flow rate of 10 liters/ minute)	(O_2 flow rate of 10 liters/ minute)
	pH	7.55	7.35
	pCO_2	46.8mmHg	43.8mmHg
	pO_2	41mmHg	61mmHg
	HCO_3	25.1mmol/L	23.4mmol/L
	SBE	-3.1mmol/L	-1.8mmol/L
Initial blood pressure (mmHg)		Systolic 68, diastolic 47	Systolic 59, diastolic 41
Chest radiograph		Bilateral coarse alveolar infiltrates	Extensive bilateral pulmonary infiltrates
Mechanical ventilation type		Invasive (pressure-regulated volume control model)	Non-invasive (*Bussignac* mask)
Mechanical ventilation duration		3d	36h
Diagnosis of TRALI		Anti-leukocyte antibodies in donor's and receiver's serum	1. clinical criteria 2. chest radiograph 3. laboratory findings
Outcome		Favorable within 4d	Favorable within 3d
Blood donor			
	Gender	Female	Female
	Age (y)	42	36.5
	Characteristics	Multiparous	Multiparous
	No. of pregnancies	5 (2 children)	4 (4 children)

Table 2: Criteria for the clinical diagnosis of transfusion-related acute lung injury.

Definition of TRALI[a] according to the European Haemovigilance Network
Acute respiratory failure
Bilateral pulmonary infiltrate on X-rays
Ocurrence during or within 6 h after transfusion
No evidence of transfusion-related circulatory overload
Criteria for the diagnosis of TRALI[a] according to the Consensus Conference Committee in Toronto, 2004
Hypoxemia (PaO_2/FiO_2[b] < 300, oxygen saturation < 90% or other clinical evidence)
New acute respiratory failure and no other risk factor for acute respiratory failure present, including aspiration, multiple trauma,pneumonia, cardiopulmonary bypass, burns, toxin inhalation, pulmonary contusion, acute pancreatitis, drug overdose, drowning, shock and sepsis
If one or more risk factors for acute respiratory failure are present, possible TRALI could be diagnosed

[a]TRALI: transfusion-related acute lung injury

[b]PaO_2/FiO_2: arterial oxygen tension/fraction of inspired oxygen

ing or within 6 hours of transfusion not due to circulatory overload or other likely cause. The common clinical presentation of TRALI consists of dyspnoea, cyanosis, hypotension, fever, rigors and cough along with physical findings of bilateral pulmonary edema and hypoxia, confirmed by new bilateral interstitial pulmonary infiltrates in chest radiographs, in the absence of volume overload or cardiac malfunction (Table 2)[6,7].

The only routine laboratory parameter that has been associated with TRALI is leukopenia, as was found in the second presented case in addition to thrombocytopenia, as the cells were trupped in the lungs. Protein measurements of the oedema fluid and a matched plasma sample can be diagnostic of increased permeability pulmonary oedema. However, investigations of the donor and recipient for passively transfused anti-leukocyte antibodies confirm the diagnosis, as happened in the first presented case[1,3,6].

Management of TRALI is mainly supportive, as in any other case of adult respiratory distress syndrome. If a case is suspicious for TRALI during the transfusion of a blood-component, transfusion should be immediately discontinued. In 70% of severe cases of TRALI mechanical ventilation is required, 80% of cases recovering within 4 days and less than 1/5 of cases within 7 days[1,8]. In severe cases of TRALI either invasive or non-invasive mechanical ventilation may be necessary. This depends on patient's clinical condition and the degree of respiratory distress. It is more appropriate to use non-invasive mechanical ventilation to avoid the adverse effects that invasive mechanical ventilation can cause. However, for patients requiring invasive mechanical ventilation, a low tidal volume lung protective strategy has been advised in line with treatment of acute lung injury[1,9,10]. Although optimal tidal volume and plateau pressure are not known, a limited tidal volume of 6 mL/kg ideal body weight and alveolar plateau pressure of ≤30 cmH_2O has been associated with a lower mortality rate compared to higher values[9].

Diuretics and corticosteroids have been used, although there is no evidence of benefit and their use remain controversial. Therefore, maintenance of haemodynamic status with ventilatory support and fluid infusion are probably the only standard therapies. Prevention of TRALI seems to be the most important aspect in the patient care because of the seriousness of the disease with reported in-hospital mortality ranged between 5% to 15%[10]. In order to avoid any future reactions from the same donor, the suspected donor should be excluded from the donor pool[8].

TRALI constitutes a serious complication of blood transfusion needing awareness and high index of suspicion of practitioners working with transfusions. Management of severe TRALI case requires mechanical ventilation, either invasive or non-invasive. However, non-invasive mechanical ventilation procedures can be safer and should preferred in selected cases for an uncomplicated outcome.

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