Acute Lung Injury Syndrome (TRALI) in a Dog Possibly Triggered by Blood Transfusion

Vinicius Gonzalez Peres Albernaz1, Natache Arouca Garofalo2, Francisco José Teixeira Neto1, Isabella de Almeida Fabris1 & Juliany Gomes Quitzan1

ABSTRACT

Background: Acute Lung Injury (ALI) and the Acute Respiratory Distress Syndrome (ARDS) are clinical syndromes, differing in severity, characterized by bilateral noncardiogenic pulmonary edema, usually associated with an underlying cause. Diagnosis is given by thoracic radiography and PaO2/FiO2 ratio <300. The possible Transfusion Related Acute Lung Injury (TRALI) occurs when ALI or ARDS signs (i.e. hypoxemia and bilateral pulmonary infiltrates) are found in patients without preexisting ALI that have received transfusion in the last 72 h. This case report describes a case of a canine patient that developed possible TRALI after a forelimb amputation and a whole blood transfusion.

Case: A 10-year-old female dog, with necrotic and infected bite injuries on left forelimb was initially treated conservatively with topical and systemics antibiotics. Eventually, a forelimb amputation was required, due to the soft tissue necrosis. Pre-operative complete blood count, serum biochemistry and venous blood gas analysis showed mild changes, including anemia, leukocytosis, metabolic acidosis, and increases in blood urea nitrogen, alkaline phosphatase, alanine transaminase. The patient was stable before surgery but required a post-operative whole blood transfusion to treat severe anemia. A crossmatch test was performed to reduce the possibility of transfusion reaction. Despite both surgery and hemotherapy went as expected, approximately eight hours after the transfusion, the patient developed deterioration of all vital signs, including hypotension and severe hypoxemia, with PaO2/FiO2 <126 and oxyhemoglobin saturation (SpO2) < 90% on room air. Thoracic radiographies showed mixed pattern of bilateral pulmonary infiltration. The patient’s condition worsened with signs of respiratory failure, cyanosis and severe hemodynamic impairment. There was no improvement after administration of furosemide, hydrocortisone, vasoactives, supplemental oxygen and mechanical ventilation. The patient died quickly after the diagnosis, despite cardiopulmonary resuscitation efforts.

Discussion: The term possible TRALI was created due to the difficulty in diagnosing the condition in patients with other risk factors for lung injuries. TRALI usually follows a two-hit model in which an underlying illness activates the endothelial cells and the transfusion activates the neutrophils causing lung damage. In this case, all four mandatory criteria for veterinary ALI occurred, namely the acute onset, systemic inflammation, pulmonary infiltrates on thoracic radiographs, PaO2/FiO2 ratio < 200 and SpO2 < 90%. The absence of cardiopathy and preexisting ALI supports the diagnosis of TRALI, which is the most frequent cause of transfusion related death in humans. Nevertheless, there are few reports of TRALI in animals making impossible to draw any conclusion about the incidence of this syndrome in veterinary patients. Differential diagnosis for TRALI is circulatory overload, anaphylaxis, bacterial contamination and acute hemolytic transfusion reaction. The treatment of ALI is focused on supportive care and on the underlying cause rather than focusing ALI as a distinct condition. The best therapeutic approach is oxygen supplementation and mechanical ventilation. Any non-ventilatory treatment approach is currently controversial. All ventilatory and pharmacological attempts in this case had no result and the patient condition declined rapidly. Since TRALI seems to be a real life-threatening entity in canine patients, a restrictive strategy for transfusion medicine should be considered.

Keywords: lung, distress, respiratory, acute, gasometry.
INTRODUCTION

Acute lung injury (ALI) is a clinical syndrome, characterized by bilateral noncardiogenic pulmonary inflammatory edema, causing hypoxemia (PaO2/FiO2 ratio < 300), hypotension, tachycardia, cyanosis, and acute respiratory failure [9,30]. Severe cases of ALI can lead to acute respiratory distress syndrome (ARDS), which is characterized by greater oxygenation impairment (PaO2/FiO2 ratio < 200) [3,9,31].

An ALI/ARDS related to a blood transfusion, is termed as Transfusion-Related Acute Lung Injury (TRALI) [18,30]. TRALI can occur from 6 to 72 h after a blood transfusion and is often associated with preexisting risk factors for ALI [18,30]. Several criteria are used to define TRALI in humans, including the acute onset, hypoxemia, bilateral pulmonary infiltrates, no evidence of left atrial hypertension, and no preexisting ALI [18,30]. Sepsis, pneumonia, near-drowning, disseminated intravascular coagulation, pulmonary contusion, bone fractures or burns are risk factors for developing TRALI [18,22,30]. In people, TRALI is underrecognized and underreported, mainly due to nonspecific, variable or unrecognizable clinical signs [23]. Signs of acute respiratory distress or death can be mistaken for circulatory overload secondary to transfusion, pneumonia, or other reactions to the blood products [28]. Despite its close relation to transfusion, it may be impossible to determine that patients suffered from TRALI instead of ALI secondary to other illness [28].

To our knowledge, few reports have been published about possible TRALI in dogs and cats until this moment [28]. This report describes a rare case of fatal TRALI following whole blood transfusion in a canine patient.

CASE

A 10-year-old intact female mixed breed dog, weighting 17 kg, was referred to the veterinary hospital, due to an infected and necrotic wound on the left forelimb. The animal suffered a severe bite injury from another dog during an epileptic crisis and his wound was sutured 7 days before. Three days after the first wound care the animal developed apathy, anorexia, lateral recumbency, and necrosis of the skin followed by intense signs of infection and purulent content.

Upon admission to the veterinary hospital, the animal underwent anesthesia for surgical debridement, in which free necrotic tissue was resected, exposing bone extremities, muscle, tendons and ligaments (Figure 1). The necrosis extended from the distal phalanx to the proximal shoulder. The wounds were washed with chlorhexidine gluconate 0.05% followed by topical sugar application and bandages. Bandages were changed every 3 h in the first day to promote fast decrease of infectious content. After that, bandage changing occurred twice daily. The animal was treated with levofloxacin (10 mg/kg intravenous every 24 h), dipyrone (25 mg/kg subcutaneous every 8 h), ranitidine hydrochloride (2.2 mg/kg subcutaneous every 12 h), morphine (0.5 mg/kg intramuscular, every 8 h) and ketamine (0.5 mg/kg intramuscularly, every 8 h).

Admission venous blood gas analysis revealed hypokalemia (K+ 2.92 mmol/L), mild metabolic acidosis and respiratory alkalosis (pH 7.377; HCO3(act) 14.3 mmol/L; BE(ecf): -10.6 mmol/L; PaCO2 25.2 mmHg). Complete blood count showed moderate anemia (Hct: 29%; Hb: 9.4 g/dL; RBC: 4,460,000 cels/µL) and mild leukocytosis (18,930 cels/µL) due to neutrophilia (14,200 cels/µL). Serum urea (78.8 mg/dL), alanine transaminase (87 mg/dL), and alkaline phosphatase (533 UI/L) were also increased.

Figure 1. A massive bite injury on the left forelimb after suture, infection, and dehiscence. Note the large area of deep necrosis involving several tissue layers.
Five days after admission, the wound progressed with less infected tissue and the animal improved its general status. At that time, forelimb amputation was performed since soft tissue damage could not be repaired. The animal received morphine (0.5 mg/kg, IM) as premedication. After induction of anesthesia with propofol (3 mg/kg, IV) and ketamine (0.5 mg/kg, IV), orotracheal intubation was achieved and anesthesia was maintained with isoflurane in association with a brachial plexus blockade (2 mg/kg, bupivacaine 0.5%). Surgery was carried out without complications, with mild blood loss and hypotension, successfully treated with dopamine constant rate infusion (7.5-10 µg/kg/min).

However, at the end of surgery, the animal presented pale oral mucous membrane, mild tachypnea and tachycardia. Complete blood count revealed severe anemia (Hct: 10%; Hb: 2.8 g/dL; RBC: 1,280,000 cels/µL) with normal WBC count. A whole blood transfusion was carried out after negative major and minor cross-match test. The animal had no history of previous blood transfusions and received 340 mL of whole blood (Hct: 45%) in approximately 3 h. The patient was monitored for changes in temperature, arterial blood pressure, heart and respiratory rates and signs of peripheral edema. No immediate signs of reaction to blood products could be noted and the animal showed improvement of vital signs.

Eight hours after blood transfusion, an increase in all hematologic parameters (Hct: 26%; Hb: 9.0 g/dL; RBC 3,710,000 cels/µL) and leukocytosis (WBC: 39,400 cels/dL) with neutrophilia (35,000 cels/dL) was observed. However, deterioration of vital signs, including tachypnea, was noticed. Approximately 12-h after blood transfusion, the animal showed signs of respiratory failure, cyanosis, SpO₂ < 90% and hemodynamic impairment (i.e. absent peripheral pulse, tachycardia, hypothermia, decreased mental status, and lateral recumbency). Arterial blood gas analysis revealed respiratory alkalosis (pH 7.47; PaCO₂ 29.4 mmHg; BE (ecf) -3.0 mmol/L), severe hypoxemia (PaO₂ 26.6 mmHg), in addition to mild hypokalemia (K+ 2.97). The PaO₂ / FiO₂ ratio just before oxygen supplementation (FiO₂ 21%) was 126.6. Triple thoracic radiography confirmed severe bilateral diffuse mixed alveolar and interstitial lung pattern (Figure 2).

One hour later, the patient remained hemodynamically unstable and non-responsive to resuscitation efforts, including endotracheal intubation, intermittent positive pressure ventilation (tidal volume, peak airway pressure and respiratory rate adjusted to maintain normocapnia: ETCO₂ 35-45 mmHg), 100% oxygen supplementation, Fluid challenges with lactated Ringer’s solution (15 mL/kg during 15 min, guided by noninvasive arterial pressure monitoring), constant rate infusion of dopamine (7.5-15 µg/kg/min, IV) and norepinephrine (0.1-1.0 µg/kg/min, IV), high doses of furosemide (8 mg/kg, IV) and hydrocortisone (40 mg/kg, IV). The endotracheal tube had to be changed frequently due to expectoration of a frothy light red respiratory fluid. The patient evolved to a non-responsive cardiorespiratory arrest and after 3 cycles of reanimation, the tutor opted for no further reanimation maneuvers.

**DISCUSSION**

Despite the criteria for TRALI, the term “possible TRALI” was coined because of difficulties in establishing a definite diagnosis of TRALI in patients with other risk factors for lung injury [13], such as systemic inflammatory response syndrome, sepsis, disseminated intravascular coagulation, burns, trauma or drugs [25,32]. To our knowledge, there are few reports of TRALI in veterinary medicine [1,5,28], which encouraged us to report this case, in view of the clear association between the blood transfusion and development of ALI. In veterinary patients, possible TRALI should be suspected in any patient developing acute respiratory distress during or after blood transfusion [25].

The patient of this report met all four obligatory criteria of veterinary ALI [32] and human TRALI...
developing ALI/ARDS without transfusion [21,28] making it impossible to draw conclusions about the actual incidence of the syndrome in canine patients.

The treatment of ALI/ARDS/TRALI focuses on supportive care [9]. Most patients require oxygen therapy and mechanical ventilation with positive pressure [1,11,15]. Any other non-ventilatory treatment modality is currently controversial [6,7]. Furosemide has been described in human literature for treatment of ALI, and some authors describe some success cases in veterinary patients [7,19]. The best therapeutic approach is made by addressing the underlying cause, rather than focusing in ALI as a separate entity [7]. Nevertheless, the use of corticosteroids and high-dose furosemide showed no effect in the present case report.

Some studies suggested that the risk-benefit of transfusion may not be favorable in all cases, increasing the acceptance of a restrictive transfusion policy [8,18,24]. The absence of a consensus in hemoglobin concentration to trigger transfusion in veterinary patients and miscomprehension of oxygenation markers to guide transfusion decisions turns difficult to incorporate a conservative strategy [25].

This case report highlights the importance of a restrictive strategy for transfusion medicine, since TRALI seems to be a real entity in canine patients and should be considered as a life-threatening condition following blood transfusion in critically ill animals. A large, systematic, multi-centric review of patients receiving blood transfusion should be carried out to define the actual importance of both TRALI and a restrictive transfusion policy in canine population.

**REFERENCES**


24 Pierrakos C. & Vincent J.L. 2012. The changing pattern of acute respiratory distress syndrome over time: a comparison


