Dyspnoea due to plasma transfusion-related acute lung injury

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ABSTRACT

We describe an unusual case of unexpected dyspnoea following transfusion of fresh frozen plasma (FFP) in a previously-well 72-year-old woman. Our patient was scheduled for an ultrasonographically-guided liver biopsy for work-up for autoimmune hepatitis. She was given FFP to correct a prolonged prothrombin time. Shortly after the transfusion was initiated, she started coughing and became progressively dyspnoeic. Clinically, she was tachypnoeic with diffuse bilateral crepitations, and rapidly went into respiratory failure. She was intubated and placed on mechanical ventilation. Her condition improved and she was extubated by the second day, with no long-term pulmonary sequelae. A diagnosis of transfusion-related acute lung injury (TRALI) was made, based on the rapidity of onset and association with transfusion. This was confirmed by the findings of anti-human leukocyte antigen antibodies in both the patient and recipient blood. Our case highlights this important but under-recognised condition. The incidence, diagnosis and management of TRALI are also discussed.

Keywords: dyspnoea, fresh frozen plasma, lung injury, plasma transfusion, transfusion reaction, transfusion-related acute lung injury

Singapore Med J 2006; 47(10):904-906

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INTRODUCTION

Transfusion reactions are not uncommon, and range from a mild rash to severe anaphylactic shock. One such manifestation affecting the lungs predominantly is transfusion-related acute lung injury (TRALI). TRALI is a syndrome characterised by the development of dyspnoea, hypoxaemia and pulmonary oedema secondary to transfusion of blood products[1], and can manifest as a life-threatening emergency. Mechanisms have been postulated as both immune and non-immune mediated[2]. While rarely reported in literature, prompt recognition and urgent action could help prevent fatality. To date, few confirmed cases of TRALI have been reported in Singapore[3]. We present and discuss a classic case, where prompt intervention has prevented morbidity and mortality, and where the diagnosis was supported by clinical findings, radiology and corroborated by blood immunology studies.

CASE REPORT

A 72-year-old Indian woman presented with elevated liver panel with alanine aminotransferase (ALT) of 340 U/L and jaundice (bilirubin of 328 μM) for assessment. Based on her initial biochemical investigations and history, a probable diagnosis of autoimmune hepatitis was suspected[4]. She was scheduled for percutaneous liver biopsy for confirming the diagnosis, and excluding other alternative causes. She was given 210 ml of fresh frozen plasma to correct a prolonged prothrombin time of 15.2s (normal <13s). 20 minutes post-infusion, she started coughing and rapidly became progressively dyspnoeic.

Physical examination revealed tachycardia (143 beats/minute), tachypnoea (28 breaths/minute) and diffuse bilateral crepitations throughout her lungs. Hypoxaemia was evident with a SpO_2 persistently below 90% and increasing oxygen requirements. Intravenous frusemide and hydrocortisone were administered acutely, but they did little to reverse the clinical situation. Urgent chest radiograph (Fig. 1) showed bilateral alveolar shadowing, and she was promptly intubated and placed on mechanical ventilation. An arterial blood gas analysis showed a PaO_2/FiO_2 of 98. There was no evidence of acute heart failure secondary to an ischaemic event (no acute changes on serial electrocardiographs nor elevated cardiac enzymes) or circulatory overload (initial CVP + 8, arterial blood pressure 125/76 mmHg). There was also no rash, clinical

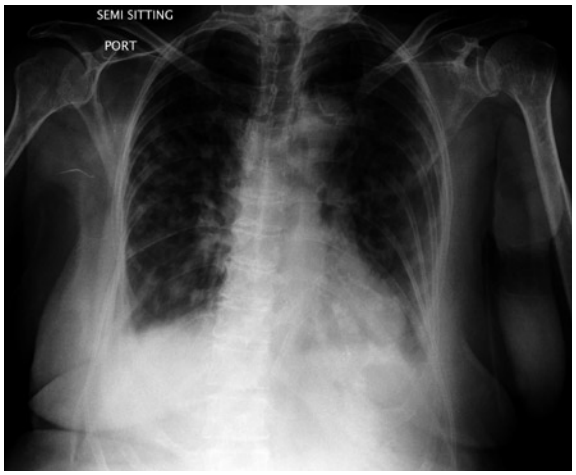

Fig. 1 Chest radiograph taken during the acute onset of dyspnoea shows bilateral pulmonary infiltrates.

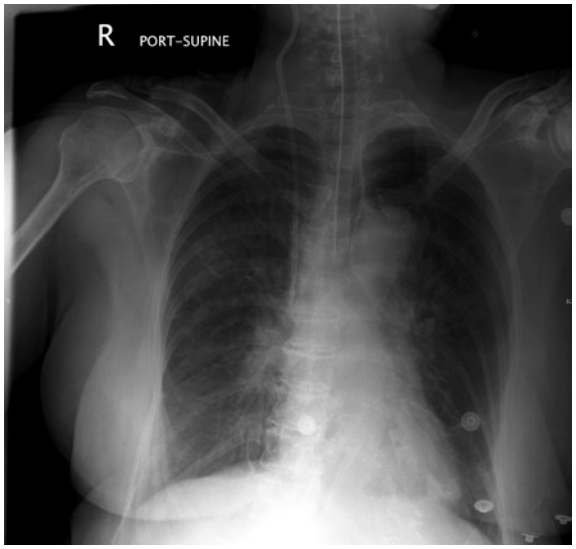

Fig. 2 Chest radiograph taken 18 hours post-event with the patient still intubated shows resolution of the pulmonary infiltrates seen earlier.

evidence of periorbital oedema, or perioral swelling. No other medication had been concomitantly administered with the transfusion.

The patient's pulmonary condition rapidly improved clinically and a radiograph taken just 18 hours post-event (Fig. 2) showed marked resolution of the airspace shadowing. She was extubated and transferred out of the intensive care unit one day later, with no further pulmonary sequalae. She was discharged seven days later, and remained well with no respiratory complaints. Though a liver biopsy was not done, a probable diagnosis of autoimmune hepatitis was made. With initiation of high dose prednisolone at 30 mg once a day, her jaundice and elevated ALT normalised at four weeks post-discharge. A diagnosis of TRALI was made based on the rapidity of onset, association with transfusion and subsequent presence of anti-HLA antibodies in both donor and recipient blood.

DISCUSSION

The first case of non-cardiogenic lung oedema was first described in the 1950s by Barnard[5], with the term TRALI being coined by Popovsky and Moore[6] in 1983, when they described the first large case series of 36 patients. Increasingly, TRALI has been recognised as an important adverse event of blood transfusion, and is now only second to ABO incompatibility as a cause of transfusion-related death[7]. Recently, the British Serious Hazards of Transfusion (SHOT) initiative identified TRALI as one of the common causes of transfusion-related major morbidity and mortality[8].

In the Singaporean context, there have to date been only two reported suspected cases of TRALI, and no cases in the first half of 2005[3]. Popovsky and Moore quoted the occurrence of immune TRALI at a rate of 1 in 5,000 units transfused[9]. More recently, Silliman et al in 2003 found that for non-immune TRALI, this rate was even higher at 1 in 1,120 units transfused[10]. Given the estimate of over 78,000 component units transfused in the first half of this year alone throughout healthcare institutions in Singapore[3], it is highly likely that TRALI has been under-reported. We postulate that this is likely to be due to a lack of recognition of this clinically important condition; with the clinical symptoms, especially of non-immune TRALI, being too mild to have been recognised, or having been wrongly ascribed to transfusion-related volume overload.

The definition of TRALI was established by the European Haemovigilance Network (EHN), defined as the occurrence of acute respiratory distress within six hours of transfusion, with radiological evidence of bilateral pulmonary infiltrates in the absence of transfusion-associated circulatory overload[1]. This definition was further honed by the TRALI Consensus Committee in 2004 to include clinical signs of hypoxaemia (defined as SpO_2 <90% or PaO_2/FiO_2 <300) and the absence of other acute lung injury risk factors, e.g. aspiration or sepsis[11]. The diagnosis of TRALI remains a clinical one, and our patient fulfilled all these diagnostic criteria.

Almost all blood products have been implicated in TRALI, including whole blood, red cell concentrates and FFP. The pathogenesis is believed to involve both immune and non-immune mechanisms[2]. Immune TRALI is a leukocyte antibody mediated reaction, commonly against human neutrophil antigens (HNA) and human leukocyte antigens (HLA). The ability of these antibodies to induce

transfusion-related pulmonary reactions was already described in 1957 by Brittingham, where infusion of leucoagglutinin into a healthy individual produced a respiratory reaction marked by pulmonary infiltrates on radiographs[12]. In non-immune TRALI, the pathogenesis is believed to be a "two-hit model", where the transfused product contains neutrophil-priming factors, believed to be biologically-active lipids, enters into a host with a predisposing risk factor, usually an underlying malignancy, on-going infection or trauma[10]. The final pathway is similar for both, where the activated neutrophils release radicals and enzymes in the capillaries of the lung, damaging the endothelium and causing leakage of fluid into the alveoli. Our patient clearly has the immune-mediated form of TRALI, confirmed by the presence of HLA antibodies in the donor FFP retrospectively.

Management of TRALI is largely supportive, with ventilatory support, if necessary intubation, and mechanical ventilation being the mainstay. There is, to date, no proven role for immunosuppressants and the role of diuretics is debatable[2]. Significantly, non-immune TRALI is milder in manifestation, has a lower fatality, and often requires only oxygen supplementation and close observation. Our patient was sufficiently hypoxaemic to require mechanical ventilation, and with good supportive management and monitoring, could be weaned off the ventilator once the pulmonary oedema resolved.

The question that remains is how can we prevent or reduce the occurrence of TRALI. Popovsky and Moore postulated[9] and Palfi et al[13] proved that the blood products in immune-mediated TRALI commonly came from multiparous female donors. HLA antibodies were found in up to 40% of parous women, arising from sensitisation by the foetus during pregnancy, and this number rose with each consecutive pregnancy. A logical conclusion would therefore be to exclude all multiparous women from the donor pool, but this would result in an untenable loss of valuable blood donors. A more rational approach would be to screen for relevant leukocyte antibodies in this subgroup of patients and exclude them from FFP and platelet concentrate donations. In preventing non-immune TRALI, Silliman et al proposed the use of fresh or washed blood products for at-risk recipients[10]. A prudent approach would ultimately be the judicious use of blood products in patients and balancing the benefits versus the risks of transfusion-related reactions.

In conclusion, we showed a case of TRALI with a classical presentation. With prompt endotracheal intubation, respiratory and intensive care support, our patient recovered without sequelae. Prompt recognition of the syndrome, and immediate intervention upon desaturation are the keys to successful management of patients with TRALI.

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