Bahrain Medical Bulletin, Vol. 29, No.4, December 2007

Transfusion-Related Acute Lung Injury (TRALI) and Strategies for Prevention

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Background: Transfusion-Related Acute Lung Injury (TRALI) is a serious complication of blood transfusion. In recent years, TRALI has been reliably shown to be the most common cause of transfusion-related fatalities in the United States and in the United Kingdom. Its prevalence is about 1 in 1323 transfused components; however, it is often under diagnosed. Classically, TRALI present as non- cardiogenic pulmonary oedema. Management is mainly supportive with 72% of cases requiring ventilatory support.

Objective: The aim of the study was to highlight the condition, discuss the pathophysiology of the disease and the preventive measures.

Design: Retrospective study.

Setting: Haematology/Oncology department, Salmaniya Medical Complex, Kingdom of Bahrain.

Method: Two patients with documented and proven TRALI were encountered at our department from January 2004 till end of December 2006. The records of these patients were reviewed for personal characteristics, clinical settings, the components transfused, time onset of the complication, and management and outcome.

Result: Two female patients were found, one 20 years old, was transfused 2 units of packed red blood cells (PRBC) because of low haemoglobin, she developed (TRALI) during the transfusion. The second case was 38 years old lady; she developed (TRALI) two hours following platelets transfusion for thrombocytopenia. Both were managed conservatively.

Conclusion: TRALI is a rare and serious disease, however, we reported two critical cases to raise the awareness of the problem and build a high index of suspicion for these cases especially where the practice of transfusion is common. We also propose some recommendations for prevention.

Bahrain Med Bull 2007; 29(4):

Transfusion-Related Acute Lung Injury (TRALI) is a life threatening complication of blood transfusion often underdiagnosed and underreported. The incidence of Serious Hazards of Transfusion (SHOT) in U.K was reported as 1 in 250000 units transfused in 1997/1998 report; however, an incidence of .02% was reported from a hospital in USA with a particular interest in TRALI[3]. Both males and females are equally affected and TRALI has been reported in all age groups.

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TRALI has been associated with transfusion of blood components which contain different quantity of plasma and include: whole blood (WB), packed red blood cell (PRBC), fresh frozen plasma (FFP), cryoprecipitate, and platelets concentrates[4].

We are likely to come across this complication frequently in our region due to the excessive practice of blood transfusion because of the presence of hereditary haemolytic disorders namely sickle cell disease and thalassaemia. However, lack of awareness of this condition, and failure to adhere to proper usage and guidelines will pose an obstacle to the detection and prevention of this serious complication of blood transfusion.

In this study, we are presenting two cases of TRALI to highlight this problem, aiming for early detection and timely appropriate interventions. We would also like to draw strategies for preventions.

CASE ١

A twenty years old female, a known case of sickle cell disease, was admitted with lower limbs pain for two days. There was no history of fever, chest pain or shortness of breath. On examination, she was pale, jaundiced, but not in distress. Temperature was 37^0 C; blood pressure was 120/75mmHg with a pulse rate of 100 beats/minute. Examination of respiratory, cardiovascular, central nervous system and abdomen was unremarkable.

Her investigations showed: haemoglogin (Hb) of 6.5 g/dl, white blood cells (WBC) $9.5X10^9$/L, platelets count of $335X10^9$/L, reticulocytes count of 12%. Liver function tests (LFT) showed indirect hyperbilirubinaemia. Renal function test was normal.

The patient was diagnosed as sickle cell disease with painful crisis and low Hb. Thus, she was transfused two units of packed red blood cells (PRBC). During the transfusion, she developed acute respiratory distress; her arterial blood gases showed hypoxaemia with oxygen saturation of 80%, chest x-rays showed bilateral infiltrate consistent with Transfusion-Related Acute Lung Injury (TRALI). Consequently, the patient was intubated and transferred to the Intensive Care Unit (ICU) where she was managed conservatively. She recovered and was transferred to the normal ward.

CASE 2

A thirty-Eight years old female, not known to have any medical illness, was referred from the gynaecology clinic as she was found to have thrombocytopenia on routine follow up. She was asymptomatic and had no complaint. On examination, she was not pale or jaundiced. The vital signs were stable and physical examinations were unremarkable. Her blood investigations were as follow: Complete blood count (CBC) showed Hb of 9.8g/dl, WBC of $4.3X10^9$/l and platelets count of $20X10^9$/l. Her Liver function (LFT) and Renal

function tests were normal. She was diagnosed as thrombotic thrombocytopenic purpura (TTP).

Due to her thrombocytopenia, she was transfused 6 units of platelets. Two hours later, she developed acute respiratory distress and became febrile. Chest examination showed bilateral crepitations, her arterial blood gases showed hypoxaemia with oxygen saturation of 82%, Chest x-rays demonstrated bilateral lung infiltrates. TRALI was suspected; hence, she was intubated and transferred to ICU on supportive care. Patient recovered and was discharged from the ICU.

DISCUSSION

Transfusion-Related Acute Lung Injury (TRALI) is a life-threatening complication of transfusion, presenting as non-cardiogenic pulmonary oedema. Recently, TRALI has been recognized as the most common cause of transfusion-related fatalities in the United States and United Kingdom. Recent studies suggest that it has a prevalence of one in 1323 components transfused.

The underlying mechanisms are still not completely understood. However, two models have been proposed. The first model supports the notion that TRALI is an immune-mediated reaction caused by the interaction between leucocytes and HLA or granulocyte antibodies, usually of donor origin[2]. The second model considers TRALI as a two-event phenomenon, where both the patient predisposition and factors in the transfused component play an important role[2].

TRALI is mainly diagnosed clinically. Classically, patient present with dyspnoea, cyanosis, hypotension, fever, chills and cough along with physical findings of bilateral pulmonary edema and hypoxaemia confirmed by new bilateral lung infiltrate in chest X-rays, with the absence of volume overload or cardiac malfunction. These findings often develop within 4 hours and up to 24 hours of a transfusion. These features usually resolve within 96 hours and are indistinguishable from Acute Respiratory Distress Syndrome (ARDS). Our first patient developed the classical symptoms during transfusion of Packed Red Blood Cells (PRBC), while the second one presented two hours following platelets transfusion.

Severity of TRALI is related to degree of hypoxaemia with significant morbidity (72% mechanical ventilation) and mortality rate of 6%[1]. Both of our patients were critical and required ventilatory support.

TRALI is mostly associated with transfusion of white blood cells, red blood cells and fresh frozen plasma. However, albeit, rare, TRALI has been reported following platelets and cryoprecipitate transfusions even in small amount, as seen in our patients.

Although, diagnosis is mainly clinical, laboratory tests consisting of finding White Blood Cells (WBC) antibodies (leucoagglutinating and/or lymphocytotoxic antibodies) in the plasma of the donor, usually from multiparous donors directed against the WBC of the recipient confirm the diagnosis. Occasionally, antibodies in the recipient against the WBC of donor, and rarely inter donor TRALI have been reported.

Various drugs have been used for treatment of TRALI including corticosteroids, epinephrines and diuretics, however, studies showed treatment with diuretics can lead to

decrease in cardiac output and hypotension might be detrimental. On the other hand, the use of corticosteroids remain controversial. Furthermore, albumin may increase mortality in critically ill patients compared with crystalloid. Therefore, maintenance of haemodynamic status is the most beneficial and appropriate therapy with ventilatory support and saline infusion are probably the only standard therapies. As such, both patients were managed conservatively. It is important to stress on the conservative management and avoidance of drug therapy which can do more harm but with no proven benefit.

Finally, prevention of TRALI is the most important aspect in the patient care because of the seriousness of the disease and lack of specific and effective therapy.

We would like to stress on the preventive measures for such a serious illness, particularly in our region, where transfusion practice is common due to presence of hereditary haemolytic disorders namely sickle cell disease and thalassaemia. Firstly, there should be a clear indication for the transfusion, for instance in the second case, platelets transfusion was not needed, in fact it is contraindicated. Secondly, we require treating the cause, for example in case number two, treatment is by plasma exchange rather than platelets transfusion.

Thirdly, implicated donors should be prohibited from blood donation. Particular caution should be taken in cases of patient-directed donation of relatives' blood, particularly if the donor is the mother of the recipient. Theoretically, donation of blood from a woman to the father of her children could also result in TRALI. Therefore, the gender of the donors of all components transfused within the six hours prior to the reaction should be determined, and all female donors are questioned and tested regarding pregnancy and transfusion history.

Lastly, screening of the donors for the presence of HLA antibodies is expensive and time consuming. However, presence of antibodies in donor serum not necessarily translates into TRALI in a recipient. HLA antibodies test is not available in our centre; therefore, our diagnosis was based on the clinical presentation.

Finally, reporting of any reactions and excluding of the suspected donor is helpful to prevent any future reactions from the same donor. We would recommend formation of a vigilant system, similar to the British Serious Hazards of Transfusion (SHOT), in which all transfusion reactions are reported.

CONCLUSION

TRALI is a serious transfusion reaction that is often underdiagnosed. We are presenting two cases to highlight the problem and suggest various therapeutic and preventive measures.

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