Transfusion-Associated Lung Injury (TRALI)

What is TRALI?
TRALI is a syndrome characterized by the development of acute respiratory distress with hypoxemia during or up to 6 hours after completion of a blood transfusion. TRALI is a clinical diagnosis based on patient symptoms that has been associated with all types of blood products.

What are the clinical signs and symptoms of TRALI?
The diagnosis of TRALI should be based on clinical and radiologic findings. The most frequent signs and symptoms include: dyspnea, hypoxemia, bilateral pulmonary edema. Other reported findings have been hypotension, tachycardia and fever (1-2˚C rise). Characteristic chest X-ray results show evidence of bilateral patchy infiltrates, with alveolar and/or interstitial patterns. The chest x-ray may indicate non-cardiogenic pulmonary edema without cardiac enlargement or other evidence of fluid overload. In 2004, a Consensus Conference held in Toronto, Canada determined the definition and criteria for TRALI (Table 1)

In cases where an alternative etiology for the development of pulmonary edema exists, TRALI should be diagnosed with caution. The use of Brain Natriuretic Peptide (BNP) test results may indicate a diagnosis of cardiogenic pulmonary edema but may not conclusively eliminate a diagnosis of TRALI. Alternative etiologies could include myocardial damage, valvular heart disease, or volume overload or when there is a co-existing risk factor for acute lung injury (ALI). Risk factors for ALI may include aspiration, pneumonia, inhalation injury, lung contusion, near drowning, severe sepsis, shock multiple trauma, burn injuries, cardiopulmonary bypass, and acute pancreatitis. Other causes of dyspnea (pulmonary embolus, severe allergic reaction) should also be excluded.

When do the symptoms of TRALI appear?
Symptoms typically begin during the transfusion, but can occur up to 6 hours after transfusion.

How should a patient with suspected TRALI be managed?
Treatment of patients with suspected TRALI is supportive: supplemental oxygen and mechanical ventilation for severe hypoxemia. Fluid administration for hypotension may be beneficial in some patients. Diuretics have not been shown to be effective in treating TRALI, as the edema is due to microvascular injury, not volume overload.

The majority of patients recovery quickly – many patients begin to show clinical improvement within the first few hours of onset with complete resolution within 96 hours. Infiltrates resolve within 96 hours in about 80% of affected patients but may persist for 7 days or more. Mortality has been reported to be 5-35%, highlighting the importance of early recognition.

If additional transfusions are needed for the patient with suspected TRALI, no change in transfusion practice or modifications of the blood product are needed.

What blood components are implicated in TRALI?
All blood products have been associated with TRALI. Plasma content appears to be associated with increased risk. Since the voluntary implementation of TRALI reduction strategies, the incidence of TRALI related to plasma product transfusions has decreased according to the 2010 FDA Annual Summary.

What is the incidence of TRALI?
The incidence of TRALI has been reported between 1 in 2000 to 1 in 7500 transfusions in the United States. It is felt that TRALI remains under-recognized and under-reported. By minimizing the number of transfusions to patients, the incidence of TRALI can be reduced. In the most recent data on FDA reported deaths following blood transfusion, TRALI
remains the most common cause, representing 45% of all such deaths. Since 2008, approximately 16 fatal cases of TRALI have been reported annually to the FDA.

**What are the possible causes of TRALI?**
The causes of TRALI are not well understood. Two theories on the pathogenesis of TRALI have been proposed: (1) antibodies to white blood cell antigens (HLA, granulocyte and monocyte) and (2) two-event model that includes the clinical condition of the patient. In the first theory, it is proposed that white blood cell antibodies present in the donor’s plasma bind to the white cells of the recipient which results in activation of complement and neutrophils. The aggregation of white cells within the lungs, and subsequent adhesion to the capillary endothelium produce endothelial damage, capillary leakage and the development of pulmonary edema.

The second theory accounts for the clinical condition of the patient (e.g. sepsis, trauma, etc) which causes sequestration of primed neutrophils in the activated pulmonary endothelium. The transfused blood product contains either anti-HLA or anti-HNA antibodies directed against the neutrophils or biologic modifiers (lipids) caused by storage of blood products which activate the primed neutrophils. This results in endothelial damage, capillary leakage and the subsequent development of pulmonary edema. The two-event theory may explain the development of TRALI when there is no evidence of donor HLA/HNA antibodies. Further studies are required to clarify the exact pathogenesis of TRALI.

**What should I do if I suspect TRALI in one of my patients?**
Once your patient is stabilized, immediately notify the hospital Transfusion Service. Because the diagnosis of ALI can be difficult and may be due to an alternative cause, it is important that there be communication between the patient’s physician and Transfusion Service physician. After discussion and review of the patient’s medical record including pre and post transfusion chest x-rays, BNP and other laboratory test results, if TRALI or possible TRALI is suspected, the Transfusion Service Medical Director will begin the investigation process and notify BloodCenter of Wisconsin. The investigation is not considered diagnostic but rather assists in identifying and deferring implicated donors involved in TRALI reactions, possibly preventing TRALI in future recipients. If your patient has suffered a fatal reaction thought to be TRALI, federal regulations require Transfusion Services to notify the FDA within 24 hours. Therefore such cases should be reported to the Transfusion Service as soon as possible after they occur.

**What testing will typically be done for a suspected TRALI investigation?**
Samples from the patient will be collected for HLA typing and a serum sample set aside for possible HLA antibody testing. Ordering and collection of patient samples is done under the direction of the Transfusion Service physician. Testing is performed at BloodCenter of Wisconsin.

The associated donors are interviewed and those with a history of pregnancy and/or transfusion will be tested for HLA and granulocyte antibodies. If an HLA or granulocyte antibody is identified, correlation with the typing of the recipient is completed to aid in determining if a donor is implicated in the suspected TRALI. Since donors are asked to return for collection of blood samples, testing and interpretation of results may take up to 10 weeks to complete. The results of the findings are forwarded to the Transfusion Service physician who will communicate the findings to the attending physician(s). If additional information is needed, the hospital Transfusion Service Medical Director may be contacted by BloodCenter of Wisconsin.

**References:**

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