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REVIEW ARTICLE

Transfusion-related Acute Lung Injury in Obstetrics and Gynecology

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ABSTRACT

Transfusion-related acute lung injury (TRALI), a type of non-cardiogenic pulmonary edema related to blood transfusion, is gaining prominence as a common adverse event related to blood transfusions in hospitals. It is typified by dyspnea, cough, hypoxemia and pulmonary edema within 6 hours of transfusion.

Without any 'gold standard', the diagnosis of TRALI relies on a high index of suspicion and on excluding other types of transfusion reactions. As our understanding of TRALI deepens, risk reduction or prevention may become possible.

The management of TRALI is early diagnosis and good supportive care with, occasionally ventilator support. With the increasing use of blood products in obstetrics and gynecology, awareness of this complication is desirable to prevent one of the commonest and most frequently under-recognized transfusion related adverse event of the present day.

Keywords: TRALI, Blood transfusion, Fresh frozen plasma, Obstetrics, Gynecology.

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INTRODUCTION

Transfusion-related acute lung injury (TRALI) has become one of the leading causes of transfusion-related morbidity and mortality, especially since the transmission of infectious diseases through blood transmission has diminished. The true incidence of TRALI is unknown partly, because a standard definition is not available.[1] In 1983, Popovsky recognized a pattern of acute pulmonary compromise in a series of five patients and termed it TRALI.[2]

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With the increasing use to blood components in all medical fields including obstetrics and gynecology, it is imperative that we be aware of this uncommon but potentially fatal adverse reaction to transfusion of plasma containing blood components.[3]

DEFINITION

The European Haemovigilance Network (EHN) defines TRALI as a clinical entity consisting of acute shortness of breath during or in the first 6 hours after blood transfusion, combined with the new appearance of bilateral pulmonary infiltrates (pulmonary edema) on chest X-ray, and in the absence of evidence of heart failure due to volume overload.[4]

The EHN has suggested that the following be the minimum requirement for a clinical diagnosis of TRALI:[5]

- The occurrence of acute respiratory distress during or within 6 hours of transfusion.
- Absence of signs of circulatory overload.
- Radiographic evidence of bilateral pulmonary infiltrates.

The Canadian Consensus Conference in Toronto in 2004, suggested a somewhat restricted definition.[6] These are as follows:

Criteria for TRALI are as follows:

- Acute lung injury (ALI)
  - Acute onset
  - Hypoxemia: Ratio of PaO_2/FiO_2 < or equal to 300 or SpO_2 < 90% on room air
  - Bilateral infiltrates on frontal chest radiograph
  - No evidence of left atrial hypertension (i.e. circulatory overload).
- No pre-existing ALI before transfusion
- During or within 6 hours of transfusion, and
- No temporal relationship to an alternative risk factor for ALI.

Criteria for 'possible TRALI' are as follows:

- Acute lung injury
- No pretexting ALI before transfusion
- During or within 6 hour of transfusion, and
- A clear temporal relationship to an alternative risk factor for ALI.

Pathogenesis

The mechanism of TRALI is multifactorial and may vary from patient to patient. An immune antibody-mediated mechanism is commonly implicated in up to 85% of cases, although a nonimmune mechanism and a combination of both also been demonstrated.[7,8]

In the immune-mediated hypothesis, antibodies in the transfused product, commonly human leukocyte antigen (HLA) or human neutrophil antigen induce neutrophil activation in the recipient. Most of these antibodies have been observed in multiparous women who became alloimmunized during pregnancy. The antibody bound neutrophils are sequestrated in lung capillaries, where compliment activation and release of neutrophil bioactive products result in endothelial damage and capillary leak.[9]

According to the nonantibody hypothesis, biological response modifiers, such as lipids or cytokines contained in the transfused product, may induce leukocyte priming and activation in the recipient, causing endothelial cell damage.[10]

Since TRALI has been noted to occur more often in patients in poor clinical condition at the time of implicated transfusion, this had led to the proposition of 'two-hit hypotheses.' The first hit is the predisposing condition and second is the transfusion of biologically active lipids, cytokines, or leukoagglutination alloantibodies.[11]

Differential Diagnosis

Because transfusions typically are given to sick patients, it is important to consider all entities that might cause acute respiratory distress. Transfusion-associated circulatory overload (TACO) is chief among these entities. Reports of incidence of TACO vary from less than 1 to 11% in critically ill medical patients.[3] Clinically, patients with TACO have tachypnea, dyspnea, cyanosis, tachycardia and hypertension. They also have signs of circulatory overload, such as jugular venous distension and elevated pulmonary artery occlusion pressure. Such signs may be present before the initiation of transfusion, and review of the patient's intake and output will likely add evidence for the diagnosis. Transfusion associated circulatory overload usually responds to diuresis and ventilatory support.[3]

Respiratory distress is a major symptom in anaphylactic transfusion reactions as well. These typically include tachypnea, cyanosis and wheezing. Hypotension is also frequently a component. These symptoms typically arise from laryngeal and bronchial edema instead of interstitial pulmonary involvement. Skin manifestations include urticarial, erythema and edema of face and trunk.[3]

Bacterial contamination of transfused blood products should also be considered. Sepsis usually manifests as hypotension, fever, and even circulatory collapse, often accompanied by respiratory distress. Finally, an acute hemolytic transfusion reaction should also be considered and ruled out, because the signs and symptoms may include respiratory distress.[3]

Diagnosis

The central principle in diagnosing TRALI is exclusion of cardiogenic causes of pulmonary edema. A high index of suspicion is necessary to accurately identify TRALI. Any patient experiencing dyspnea, hypoxemia, pulmonary edema, hypotension and fever temporally related to transfusion should be suspected of having TRALI. To aid in diagnosis and management, the hospital transfusion services should be notified immediately.[3]

Brain natriuretic peptide (BNP) is recently postulated as a adjunct in differentiating TRALI from TACO. Brain natriuretic peptide is a polypeptide released by ventricles and atria in response to volume pressure overload.[12] Brain natriuretic peptide is elevated in cardiogenic pulmonary edema or volume overload, but under 100 pg/ml in TRALI.[13] Atrial natriuretic peptide is another peptide marker for TACO.

Acute transient neutropenia has been reported in TRALI, and is an inexpensive reliable marker.[14] If the suspected case of TRALI proves fatal, autopsy of the lung will reveal diffuse edema, and microscopic examination will identify an increased number of leukocytes in the microvasculature and alveolar spaces.[15]

Treatment

The mainstay of treatment for TRALI remains supportive care. If the suspected blood product is still being transfused, it should be immediately discontinued.[16] Hospital blood bank has to be notified immediately. Repeat the ABO typing, the cross-match, obtains complete blood count. Arterial blood gas (ABG), blood cultures and chest radiograph. Return all the component bags recently transfused. The patient requires intensive care management in most of the cases.

Ventilator support is frequently required, and although optimal ventilation strategy for TRALI is not specifically studied, smaller tidal volumes and optimization of positive end-expiratory pressure seem to improve outcome in acute lung injury.[17]

Proper diagnosis of TRALI and exclusion of TACO are also important. There are reports of TRALI being treated with diuretics. Fluid replacement is crucial to

treat the hypotension and respiratory signs as evidenced by immediate improvement in oxygenation and hemodynamics observed after administration of large volumes of 5% albumin.[18]

Preventing TRALI

Transfusion of any blood product poses a risk of TRALI as fllows:.[7]

- Transfuse blood or blood components only if absolutely necessary—this is the best strategy.[19] Consultation with a hematologist is helpful for guidance in high-risk situations.
- Institutional protocols should be set for guidance of healthcare professionals for the appropriate use of blood products.[19]
- Use of fresh cellular components—as biologically active lipids accumulate in blood products with storage, fresh cellular components may reduce the risk.[20]
- Avoidance of multiparous female FFP donors.
- Donor screening for leucocyte antibodies.[16]
- Leukodepletion and use of solvent detergent plasma.[21]

DISCUSSION

Obstetrics and gynecology has since long been known as a 'bloody-branch' since its association with hemorrhage and blood transfusions. The use of blood and components is on a steady rise due to increasing occurrence of medical complications in obstetrics. Severe pre-eclampsia complicated by HELLP (hemolysis, elevated liver enzymes and low platelet count), eclampsia, Postpartum hemorrhage, placenta previa, and placenta accreta is few common indications where transfusion of blood and components is required in obstetrics. Many of these patients require massive transfusion of fresh frozen plasma and blood, and hence they are at risk of developing TRALI.

With the reduction in the transmission of infectious diseases through blood transmission, the incidence of transfusion-related complications due to TRALI and TACO is on the rise.[1]

Without any 'gold standard', the diagnosis of TRALI relies on a high index of suspicion and on excluding other types of transfusion reactions. Treatment is mainly supportive with oxygen supplementation and, in most cases, with ventilatory support. In contrast with other cases, patients with TRALI tend to recover faster and the mortality rate is 5 to 10%.[9] With early diagnosis and prompt intervention, morbidity and mortality of this complication can be reduced.

CONCLUSION

Transfusion-related acute lung injury is a rare but serious complication of transfusion therapy. Since the first description, a great deal of insight has been gained into its pathogenesis, and yet lot many answers remain elusive.

Rapid recognition whenever a case of TRALI occurs remains crucial for proper treatment and understanding of this complication.

With the increasing trend of 'high-risk obstetrics', the incidence of use of blood components is on the rise. But, it is mandatory for the consultant in obstetrics and gynecology to be aware of this commonest and most frequently under-recognized transfusion-related adverse event.

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