Respiratory Distress Following Transfusion

M.S., a 48-year-old female with acute myelogenous leukemia (AML), received induction chemotherapy consisting of daunorubicin and cytosine arabinoside. On day 21 of therapy, her hemoglobin was 8 g/dL, her platelet count was 800 u/dL, and her white blood cell count was 100 mm³. Her oncologist ordered two units of leukoreduced red blood cells and four units of leukoreduced platelets. She had no history of prior transfusion reactions; therefore, premedications were not ordered.

M.S.’s pretransfusion vital signs were temperature 98.6°F; pulse 90 and regular; respirations 14, regular, and symmetrical; and blood pressure 110/80 mm Hg. Her 24-hour intake was 2,800 ml and her output was 2,700 ml. Her heart rate and rhythm were regular, and her lungs were clear to auscultation. No peripheral edema was noted.

The RN initiated the first unit of red blood cells to run over three hours. Vital signs were assessed at the initiation of the transfusion, 15 minutes after initiation, and then hourly. Two hours after the transfusion was initiated, M.S. put her call light on and stated, “I am having problems breathing.” The RN stopped the transfusion and started 0.9% normal saline at a keep-open rate. The patient’s vital signs were temperature 102°F, pulse 120 and regular, respirations 30 and shallow, and blood pressure 90/70. Her oxygen saturation on room air was 85% by pulse oximetry. She had decreased breath sounds bilaterally. Her skin and mucous membranes were pale, and no peripheral edema was noted.

The RN notified the physician and blood bank. In addition to the blood reaction work-up, the physician ordered:
- 60% oxygen via a mask
- Chest x-ray
- Continuous IV of 0.9% normal saline at a rate to maintain the systolic blood pressure > 100 mm Hg and urine output > 100 ml/hour
- Diphenhydramine 30 mg via IV push
- Hydrocortisone 100 mg via IV piggyback injection.

The direct Coombs test was negative. The chest x-ray revealed bilateral pulmonary infiltrates with evidence of cardiac compromise or fluid overload. Based on the patient’s symptoms and the negative Coombs test, the physician determined that the patient had experienced transfusion-related acute lung injury (TRALI). The patient continued to receive antihistamines, corticosteroids, and respiratory and blood pressure support until her condition was stabilized.

Clinical Problem Solving

Responding to this clinical challenge are Maureen Knippen, DNscc, RN, and Laurel Stark, RN, BSN. Dr. Knippen is from the Office of Compliance and Biologic Quality at the Center for Biologics Evaluation and Research of the U.S. Food and Drug Administration (FDA) in Rockville, MD. Ms. Stark is the chief operating officer of Hematology-Oncology Centers of the Northern Rockies, P.C., in Billings, MT.

How do the clinical findings of TRALI differentiate it from other transfusion reactions?

M. Knippen: The symptoms of TRALI may be indistinguishable from adult respiratory distress syndrome; however, TRALI typically manifests within one to two hours, but always within one to six hours, after transfusion of a plasma-containing blood component. The patient develops acute respiratory distress, hypotension, hypoxemia, noncardiac pulmonary edema, and fever. A chest x-ray often reveals a “white out” picture of the lungs. TRALI necessitates supplemental oxygen and, often, mechanical ventilation.

What laboratory tests can help establish the diagnosis of TRALI?

M. Knippen: Tests for TRALI should include measurement of antigranulocyte antibodies and antihuman leukocyte antibodies (HLA). TRALI has been associated with infusion of granulocyte or HLA class I antibodies, but a recent report cited a case of TRALI in which donor HLA class II antibodies were directed against the recipient’s phenotype (Kopko et al., 2001). Multiparous women have a higher likelihood of HLA sensitization, which increases with each subsequent pregnancy. Donors who themselves have had multiple transfusions are at risk for developing anti-HLA or antigranulocyte antibodies.

Should TRALI be reported to anyone other than the physician and blood bank?

M. Knippen: TRALI cases should be reported to the blood center that supplied the blood component. The remaining product should be returned and tested for anti-HLA or antigranulocyte antibodies in the donor. Fatalities from TRALI should be reported to the FDA’s Center for Biologics Evaluation and Research in accordance with 21 CFR 606.17(b). The FDA encourages voluntary reporting of TRALI as a serious adverse reaction to transfusions. Reports can be filed via MedWatch by phone (800-FDA-1088), fax (800-FDA-0178), U.S. Postal Service (Medwatch, HF-2, 5600 Fishers Lane, Rockville, MD 20852), or the World Wide Web (www.fda.gov/medwatch).

TRALI is a relatively unfamiliar blood reaction to many healthcare professionals. What can be done to increase awareness and educate healthcare professionals about this potentially fatal blood reaction?

L. Stark: The incidence of TRALI is unknown. This certainly is affected by the lack of knowledge regarding this syndrome. I have worked in the blood collection facility in our community and have seen the education, testing, and quality control that are required for collecting a unit of blood. I also have worked in a stem cell transplant center and administered many units of red blood cells, fresh frozen plasma, and single donor platelet products. Yet, even with this background, I was not aware of TRALI. When I consider that TRALI...
Clinical Highlights: Transfusion-Related Acute Lung Injury

**Definition:** Transfusion-related acute lung injury (TRALI) is a nonhemolytic transfusion reaction characterized by acute respiratory distress in the form of severe hypoxemia and bilateral pulmonary edema, tachycardia, fever, hypotension, and cyanosis following the recent transfusion of plasma-containing blood products. TRALI has an immunologic basis related to anti-human leucocyte antibodies (HLA) and antigranulocyte antibodies most often found in the blood product donor (Popovsky, 1996).

**Incidence:** The actual incidence is unknown. It is believed to be the third leading cause of transfusion-related death (American Association of Blood Banks [AABB], 2001; Zoon, 2001).

**Risk factors:** No specific demographic risk factors related to age, gender, or history of previous transfusions have been identified (AABB, 2001; Zoon, 2001). Popovsky, Chaplin, and Moore (1992) reported that 89% of donors in TRALI cases were positive for anti-HLA and antigranulocyte antibodies.

**Treatment:** If TRALI is suspected, what appropriate actions for the RN caring for the patient to take?

**Pathophysiology:** The cause of TRALI is unknown; however, it may be attributed to the presence of anti-HLA or antigranulocyte antibodies found in the plasma of multiparous females and donors who have received previous transfusions (Zoon, 2001). This reaction may cause the activation of complement and the release of histamine, leading to increased pulmonary capillary permeability resulting in pulmonary edema, impaired perfusion, and hypoxia.

**Clinical findings:** Dyspnea, hypotension, and fever begin one to two hours after the transfusion and are fully manifested within one to six hours. Radiologic findings include bilateral pulmonary infiltrates without cardiac compromise or fluid overload.

**Incidence:** TRALI is believed to be the third leading cause of transfusion-related death, a lack of knowledge on the part of physicians and nurses is of serious concern.

Education of healthcare professionals regarding this adverse effect of transfusions is extremely important to ensure that the transfusion is stopped, appropriate treatment is immediately initiated, and the incident is properly reported. The need for education regarding TRALI is widespread because knowledge of this condition is uncommon and because any blood product containing plasma can cause TRALI. These products include packed red blood cells, fresh frozen plasma, cryoprecipitate, platelet concentrates, apheresis platelets, and, in rare instances, IV gamma globulins. This means that patients in many areas of the healthcare environment are at risk. Education must be disseminated to blood bank personnel, nurses, physicians, and transfusion recipients. Institution-based required education often includes transfusion-related information. TRALI should be added to this education in all institutions. Journal features that reach specialty nurses who perform transfusions, plasma exchanges, or other blood product procedures as part of their patient care are an excellent strategy. Full-length articles that reach physicians and medical technologists also would be helpful.

As nurses, we are all educated regarding transfusion reactions. Clearly, TRALI must be included in this education. Education regarding TRALI should detail its pathophysiology, clinical findings, and management. The signs and symptoms of TRALI are easily recognizable, and nurses should explain them to their patients as transfusions are initiated. In my current position as the manager of an outpatient chemotherapy area where we also give transfusions on nearly a daily basis, I can say that I have added TRALI to the transfusion-related education required for the RNs in our office.

**If TRALI is suspected, what are appropriate actions for the RN caring for the patient to take?**

L. Stark: TRALI can be mild, moderate, or severe. A severe case of TRALI may present as an emergency situation that could require intubation and mechanical respiration. In all cases of suspected TRALI, the transfusion should be discontinued immediately because TRALI is believed to be attributed to the presence of anti-HLA and antigranulocyte antibodies in the blood product. The line should be kept open with normal saline at a keep-open rate. The blood product should be sent to the blood bank for testing, and this serious adverse reaction to the transfusion should be reported appropriately.

Patient assessment should include vital signs, pulse oximetry, and auscultation of breath sounds. Evaluation for signs and symptoms of fluid overload and allergic reaction can help to narrow the diagnostic possibilities. The physician should order a chest x-ray. If TRALI actually is the diagnosis, bilateral infiltrates without cardiac compromise or fluid overload would be evident. Appropriate treatment then could be initiated.


For more information, see the AABB Web site (www.aabb.org).