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Transfusion-related Acute Lung Injury (TRALI) Complicating Colectomy for Ulcerative Colitis

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TRANSFUSION-RELATED acute lung injury (TRALI) is a life-threatening complication that presents as adult respiratory distress syndrome after recent blood transfusion. The diagnosis may not be immediately obvious, especially if another systemic illness complicates the clinical picture. The immune basis of this transfusion reaction usually is caused by an incompatibility of recipient white cells and donor human leukocyte antigen (HLA) antibodies. Therefore, routine transfusion reaction evaluations, which explore erythrocyte incompatibilities, will fail to confirm the diagnosis. We report a case of TRALI, complicating colectomy for active ulcerative colitis. Postreaction immunologic evaluation clarified the pathogenesis of this event. Our findings point to the role of donor and recipient mediators. When transfusing blood during active inflammatory disease, minimizing potential white blood cell and serum interactions may be considered.

Case Report

A 12-yr-old, 53.6-kg girl with ulcerative colitis, which was unresponsive to medical therapy, was scheduled for colectomy. Preoperative course was notable for febrile episodes coincident with bowel preparation and for a hemoglobin level of 7.7 g/dl. The child received 500 cc irradiated, packed erythrocytes the evening before surgery, with no posttransfusion complications.

Induction and maintenance of general anesthesia with pentothal, fentanyl, hydromorphone, vecuronium, and isoflurane were uneventful. Approximately 5 h after the start of the case, the patient's hemoglobin level decreased from 8.1 to 6.1 g/dl. A transfusion of whole blood was administered. After completion of the blood transfusion, the patient's peak airway pressure suddenly increased from 23 to 45 cm water, and copious secretions were noted issuing from the endotracheal tube. Pulmonary auscultation revealed distant bilateral breath sounds, but no expiratory wheezes. The endotracheal tube was suctioned repeatedly for large amounts of clear, frothy fluid. Arterial blood gas revealed the following: *p*H: 7.21; P_{O2}: 69 mmHg; P_{CO_2}: 66 mmHg; HCO_3^-, 25.2 meq/L; base excess: 3 meq/L. The patient was administered furosemide, hydrocortisone, and diphenhydramine. Oxygen (100%) was administered with 10 cm water positive-end expiratory pressure. Systolic blood pressure decreased to 70 mmHg, necessitating several bolus doses of epinephrine to restore a normal blood pressure. Central venous cannulation was performed, revealing a central venous pressure of 14 mmHg. Chest radiography showed diffuse bilateral pulmonary infiltrates.

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Key words: Blood; HLA; inflammatory bowel disease; transfusion; transfusion reaction; transfusion-related acute lung injury; ulcerative colitis.

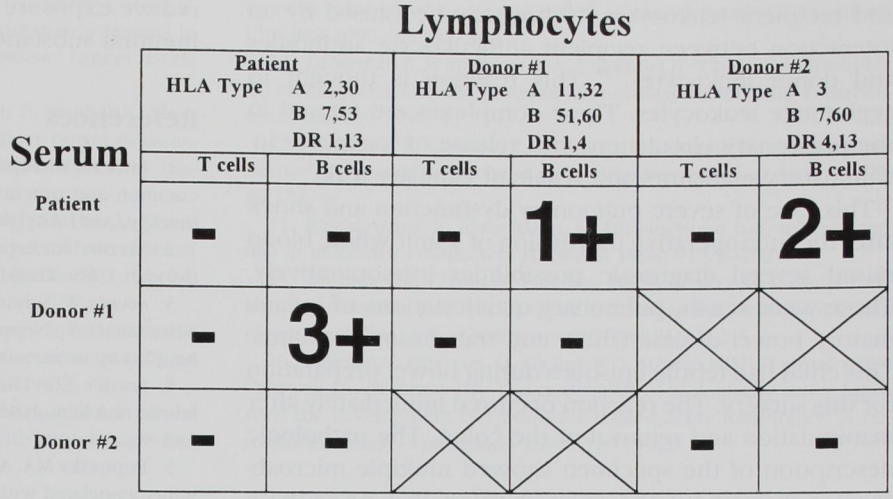

Fig. 1. Results of posttransfusion lymphocytotoxic cross-matching of patient and blood donor. The donor possesses an anti-human leukocyte antigen antibody of A2 specificity. Although the patient's leukocytes contain the A2 antigen, this antibody only reacts with the B cells. The patient's serum is found to have no anti-T-cell reactivity (anti-HLA class I antibodies) but reacts weakly with the B lymphocytes of the donor.

3+ strong positive:100% cell death
2+ positive: 50% cell death
1+ weakly positive: 10-20% cell death

Postoperatively, the patient received a dobutamine infusion (10 $\mu g \cdot kg \cdot min$) and required mechanical ventilation. Her condition improved rapidly, and she was weaned from the dobutamine infusion and extubated 48 h after surgery. Postextubation chest radiography showed evidence of rapid clearing of the pulmonary infiltrates. She was discharged to home on postoperative day 7.

Postoperative Evaluation

Blood cultures failed to grow an organism; however, the patient received antibiotics immediately before surgery. Pathologic evaluation of the resected colon revealed severe inflammation with numerous crypt abscesses. Transfusion reaction evaluation showed no evidence of immune-mediated erythrocyte reaction. Histocompatibility testing and cross-matching were performed to determine whether HLA antibodies were involved. The patient and her intraoperative donor were tested to determine their HLA types and the extent of sensitization (if any) to HLA antigens. Lymphocytotoxicity cross-matches were performed (in the forward and reverse directions) to determine whether the patient's serum had antibodies directed against HLA (class I or class II) antigens possessed by the donor or, conversely, whether the intraoperative donor's transfused unit had antibodies directed against the patient's HLA antigens (fig. 1).

Postreaction investigation revealed that the donor possessed an HLA antibody that reacted against the patient's B lymphocytes. This donor antibody was identified as an anti-A2 antibody.

Discussion

Because of the acute, severe, but rapidly reversible, clinical course temporally associated with heterologous transfusion, the possibility of some type of transfusion reaction must be considered. ABO incompatibility reactions may present with fever and shock, but they are not usually accompanied by adult respiratory distress syndrome and usually show signs of renal impairment, acute hemolysis, or diffuse intravascular coagulation (all of which were absent in this case). Posttransfusion cross-matching showed no evidence of erythrocyte incompatibility. Although a febrile transfusion reaction cannot be eliminated, the clinical course was more severe than that usually seen with this type of reaction. Allergic transfusion reaction is attributable to an immunoglobulin (Ig) E immune response to foreign donor proteins, characterized by urticaria and occasionally bronchospasm, which were not present. Allergic reaction to intraoperative drugs is unlikely because these drugs were administered either at a constant infusion or by bolus injection many hours before the event. Although congestive failure secondary to volume overload is a possibility, it does not explain the exudative nature of the pulmonary edema fluid, nor does it account for the other systemic inflammatory manifestations (fever and shock).

Transfusion-related acute lung injury comprises a constellation of symptoms that explains the process that occurred in this patient. Usually, TRALI is caused by an HLA-mediated reaction between donor HLA antibodies

and recipient leukocytes,[1-6] but may be caused by an interaction between recipient antileukocyte antibodies and donor leukocytes.[7,8] This reaction is thought to agglutinate leukocytes. These complexes are filtered in the pulmonary circulation with release of leukocyte inflammatory mediators and resultant capillary leak.

This case of severe pulmonary dysfunction and shock after the intraoperative transfusion of 1 unit whole blood raised several diagnostic possibilities intraoperatively. These were sepsis, pulmonary manifestations of inflammatory bowel disease (IBD), and transfusion reactions. This child had febrile episodes during bowel preparation for this surgery. The reaction occurred immediately after manipulation and removal of the colon. The pathologic description of the specimen showed multiple microabscesses throughout the excised colon that provided a potential source of bacteria and inflammatory mediators associated with ulcerative colitis.[9-11] A sudden and high fever was a component of this reaction. Although the patient was administered antibiotics, the inability to grow an organism from the blood does not support a diagnosis of septicemia.

There are many extracolonic manifestations of IBD.[12-25] However, these reports describe chronic extraintestinal inflammatory manifestations readily identified as a component of IBD. Pulmonary complications of IBD also are reported, but these appear to represent a chronic inflammatory manifestation of the extraintestinal tissue[21] or methotrexate pulmonary toxicity.[15]

A recent study showed the presence of lipid substances with "polymorphonuclear priming activity" in patients with TRALI.[26] The additional observation that these patients were more likely to have systemic inflammation or tissue damage supports the notion that TRALI develops because of an HLA incompatibility and a predisposition brought on by systemic inflammation. The coexistence of active ulcerative colitis and TRALI in this case report suggests a similar mechanism in view of the many inflammatory mediators described in IBD.[9] Lymphocytotoxicity observed in the patient's serum (see fig. 1) may be caused by this type of inflammatory mediator. Unfortunately, a method to identify these lipid substances was not available at the time of the reaction.

This case of TRALI, complicating active ulcerative colitis, suggests that donor anti-HLA antibodies may be responsible for the systemic and pulmonary manifestations. Interaction between donor leukocytes and inflammatory mediators produced by the recipient may have contributed to the reaction. In either event, when performing transfusion for such a patient, one may wish to reduce exposure to potential interacting leukocytes and humoral substances.

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Secretion of Dantrolene into Breast Milk after Acute Therapy of a Suspected Malignant Hyperthermia Crisis during Cesarean Section

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IMMEDIATE intravenous administration of dantrolene is the pharmacologic first line treatment of malignant hyperthermia (MH) crisis.[1] There exist extensive data about its pharmacology and its placental transfer when administered during pregnancy and delivery.[2,3,4] However, it was unclear whether and for what duration dantrolene is detectable in human breast milk after intravenous administration of therapeutic doses.[5]

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Key words: Dantrolene; infant breast-feeding; pharmacokinetics.

Case Report

Tachycardia, respiratory acidosis, and hyperthermia (39.8°C) developed in a 37-yr-old pregnant woman (62 kg body weight) shortly after the induction of general anesthesia for urgent cesarean section because of oblique fetal position. Succinylcholine and thiopental were used for the induction of anesthesia, which was maintained with oxygen/nitric oxide and isoflurane, 0.4%. Despite immediate discontinuation of isoflurane administration and hyperventilation with oxygen, 100%, the symptoms did not vanish, and an MH crisis was suspected.

Intravenous dantrolene (160 mg) was administered after the umbilical cord was clamped and after the delivery of a healthy and obviously unaffected newborn (birth weight, 3.1 kg; gestational age, 36 weeks; Apgar score, 8 at 1 min of age, 10 at 5 min of age) was accomplished. Postoperatively, the patient was transferred to the intensive care unit, where intravenous dantrolene was continued in decreasing doses for 3 days until full recovery (560 mg on day 1, 320 mg on day 2, and 80 mg on day 3). Because of potential exposure of the newborn to dantrolene, on day 1 after delivery the question arose of whether breast feeding could be allowed. Because reliable data were not found in the literature, written informed consent was obtained from the mother to determine dantrolene concentrations in her breast milk. Dantrolene concentrations were measured using an HPLC-technique according to