

Leukocyte reduction of red cells when transfusing patients with autoimmune hemolytic anemia: a strategy to decrease the incidence of confounding transfusion reactions

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Autoimmune hemolytic anemia (AIHA) presents a difficult challenge to clinicians and blood bankers alike. Autoantibodies in the serum significantly complicate serologic evaluation, and necessitate performing procedures such as adsorptions to eliminate the possibility of underlying alloantibodies. In many instances the blood that is issued may be phenotypically similar but remains crossmatch incompatible, generating a considerable degree of anxiety among the clinical staff who are responsible for transfusing the patient. We report a case of warm autoimmune hemolytic anemia (WAIHA) in which the transfusion of red cells was complicated by a febrile transfusion reaction. Evaluation of the reaction resulted in a significant delay in transfusion therapy. Subsequent administration of leukocyte-poor red cells resulted in uneventful transfusions with a good therapeutic response. Retrospective analysis of the pretransfusion sample demonstrated significant levels of anti-neutrophil antibodies. This case resulted in the establishment of our policy to administer all red cell transfusions to patients with autoantibodies (warm or cold) as leukocyte-poor red cells. *Immunohematology* 1996;12:84-86.

The autoimmune hemolytic anemias are a group of disorders with the underlying clinical feature of anemia, resulting from a shortened red blood cell (RBC) survival caused by circulating autoantibodies directed against RBC antigens.¹ The most prominent laboratory feature of AIHA is a positive direct antiglobulin test (DAT) due to the presence of immunoglobulin or complement coating the RBCs.¹ Combined, warm and cold autoimmune hemolytic anemia afflicts an estimated 1 in 25,000 persons per year, with WAIHA afflicting 1 in 41,000 to 80,000 per year.¹ The clinical presentation of AIHA may be quite variable. Patients may be well compensated and relatively asymptomatic with a gradual onset of fatigue and anemia. Alternatively, the presentation may be acute, with rapid onset of symptoms ranging from fatigue and

pallor, to palpitations and dyspnea, to congestive heart failure and central nervous system abnormalities.² Because individuals afflicted with AIHA tend to be older¹ and may have an underlying disease state (such as infection or malignancy) in association with their autoimmune disorder,^{3,4} the degree of hemolysis is often quite severe and the clinical situation may be grave.

Therapy for AIHA varies depending on the degree of severity of the illness and the underlying nature of the autoantibody (warm or cold, IgG or IgM, respectively).⁴ Corticosteroids are frequently employed in patients with warm AIHA, while treatment of cold AIHA is based on treatment of the underlying disease that is associated with the cold agglutinin or the hemolysis. Independent of the underlying cause or autoantibody subgroup, the treatment of any form of severe AIHA may require the transfusion of RBCs.

Transfusion of these patients is problematic from several perspectives. Proper serologic evaluation requires eliminating the presence of an alloantibody masked by the autoantibody. Although some data suggest that patients with WAIHA do not have a higher incidence of forming alloantibodies,⁵ the possibility of previous alloimmunization always exists in patients who have had transfusions or pregnancies.

A second complication centers around the need to transfuse units of blood that are incompatible by cross-match. By definition, persons with AIHA have RBC

autoantibodies and/or complement on their erythrocyte membranes, which often interfere with routine serologic compatibility testing. Even when a complete phenotype is known and phenotypically similar blood is available for transfusion, clinicians are often reluctant to assume responsibility for transfusing blood that is serologically incompatible. This hesitance to transfuse patients may, on occasion, overshadow the patient's critical, often life-threatening need for RBC support.

A third complication arises if the patient happens to have a reaction to the RBC transfusion. There is frequently a higher index of suspicion concerning transfusion reactions in these cases because of the need to transfuse "incompatible" blood. The transfusion is terminated and a transfusion reaction evaluation often ensues. A phenotypically specific unit of rare blood may be wasted. The patient is not likely to receive additional units until the transfusion reaction evaluation is complete, and the staff is assured that the reaction was not the result of the "incompatibility."

We report in this article the case of a patient with warm AIHA in which transfusion therapy was complicated by a febrile transfusion reaction, and further transfusion of RBCs was significantly delayed.

Case Report

The patient was a 31-year-old Caucasian woman with a 5-year history of WAIHA. Acute hemolytic crises had resulted in four previous hospitalizations, all at outside institutions. She had been multiply transfused for these crises (most recently 7 months ago), and she had had one pregnancy. She had not had a splenectomy. An evaluation by a regional reference laboratory, performed at the time of her last hospitalization, concluded that the patient was blood type O, Rh-positive. Further antigen typing was as follows: D+C-E+c+e+; S+s-; K-; Fy(a-b+); Jk(a+b+). No alloantibodies had been detected.

The patient presented to an outside institution with complaints of fatigue and dyspnea. She was transferred to The Johns Hopkins Hospital because of reluctance to transfuse incompatible units of blood.

Materials and Methods

Routine serologic studies were performed using appropriate guidelines.⁶ Direct antiglobulin testing was performed using monospecific anti-IgG (Organon-Teknika, West Chester, PA) and anti-C3 (Gamma Biologicals, Houston, TX). Antibody identification was

performed using a standard LISS technique and monospecific anti-IgG for the antiglobulin phase. An acid eluate (Gamma Biologicals) was prepared according to manufacturer's instructions.

An assay for anti-neutrophil antibodies was performed as described by Loomis et al.⁷ The bedside leukocyte reduction filters (RCXL-1) used at our institution are manufactured by Pall Biomedical Incorp., Fajardo, PR.

Results

Laboratory values on admission included a hemoglobin of 4.2 g/dL, a hematocrit of 12 percent, and a reticulocyte count of 16.1 percent. Her serum chemistries were remarkable for a total bilirubin of 3.5 mg/dL, a direct bilirubin of 0.6 mg/dL, and an LDH of 509 IU/L. Serologic studies performed revealed a strong (3+) panagglutinating warm autoantibody (IgG) in her serum and in her red cell eluate. The DAT was positive with monospecific anti-IgG and negative with anti-C3. Phenotypically similar units were obtained from the American Red Cross for transfusion. Five minutes into the infusion of the first unit, the patient developed a temperature elevation from 37°C to 39°C, shaking chills, diaphoresis, chest pain, and a decrease in systolic blood pressure of 20 mm Hg. The transfusion was immediately discontinued, and Demerol was administered for relief of the rigors. A transfusion workup on a post-transfusion blood sample by the blood bank did not reveal any discrepancies from the pretransfusion testing. However, as is our protocol when evaluating a febrile transfusion reaction, an assay for anti-neutrophil antibodies was performed and found to be positive. Therefore, subsequent units were administered through a leukocyte reduction filter. The patient tolerated these transfusions well and had a good therapeutic response. Transfusion therapy was discontinued after transfusion of a total of nine units of RBCs. The patient was concomitantly started on IV methylprednisolone. Her clinical response to therapy was quite impressive, and she was discharged in good condition.

Discussion

Transfusion of crossmatch-incompatible units of blood to patients with RBC autoantibodies is frequently met with reluctance by the clinical staff. This situation is significantly worsened should the patient suffer a febrile reaction during the course of the transfusion. Febrile, non-hemolytic reactions, while clinically signif-

icant, are not the feared consequence of transfusing incompatible units of blood. Rather, they are a nuisance-type reaction, unrelated to the red cell serology, and may result in a critical delay in transfusion. In addition, the blood bank may be required to defend the suitability of the donor RBCs that have been selected for transfusion.

Administration of leukocyte-poor RBCs by any of the various modalities has been shown to eliminate febrile, non-hemolytic transfusion reactions in patients alloimmunized to neutrophil antigens.⁸ Administering leukocyte-reduced products to a patient with RBC autoantibodies makes inherent sense. Any patient who has been previously transfused may have been sensitized to leukocyte antigens that were passively administered.

Moreover, since both hemolytic transfusion reactions and febrile non-hemolytic transfusion reactions are characterized by the primary symptom of fever, a fever occurring in a patient receiving leukocyte-reduced products may more likely result from a hemolytic reaction. Removal of the white cells from an RBC product to avoid a febrile reaction is preferable to premedicating the patient with antipyretics, which may mask a hemolytic transfusion reaction.

Salama et al.⁵ reported that the incidence of both alloimmunization to RBC antigens and adverse hemolytic transfusion reactions is less in patients with warm AIHA.⁵ Their data indicate that fears of alloimmunization or aggravated hemolysis should not be deterring factors when considering transfusing patients with warm AIHA. This case emphasizes the importance of administering leukocyte-reduced RBC products to all patients with AIHA in order to decrease the frequency of febrile, non-

hemolytic transfusion reactions. This results, overall, in more speedy and efficient transfusion of critically needed RBCs.

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