Overt immediate hemolytic transfusion reaction attributable to anti-Wr

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Wr is a low-prevalence antigen. Anti-Wr is a relatively common antibody present in approximately 1 in 100 healthy blood donors. Anti-Wr is reported to cause different degrees of hemolysis in transfusion and in HDN, ranging from benign to severe. This report describes an acute overt hemolytic transfusion reaction in a patient whose serum contained anti-Wr and who received a Wr(a+) RBC component. Immunohematology 2008;24:113–115.

Key Words: low-prevalence antigens, Wr, anti-Wr, hemolytic transfusion reaction

In 1953, Holman described an RBC antibody, which was named anti-Wr, that detects a rare antigen, Wr. In 1995, Wr was shown to be part of the Diego system, which is controlled by the SLC4A1 (DI) gene on chromosome 17. The prevalence of Wr is 1 in 1000 in the White British population and 1 in 785 in the White Spanish population. Although far fewer people have been tested, Wr has not been found in Blacks, Australian Aborigines, natives of New Guinea, or other non-European populations. Wr antigens on RBCs are resistant to treatment with proteolytic enzymes, including trypsin, α-chymotrypsin, papain, and pronase, or neuraminidase and to treatment with 2-aminoethylisothiouronium bromide.

Anti-Wr is a relatively common antibody with an incidence of 1.06 to 4.3 percent in the sera of healthy individuals and is more frequent (4 to 10%) in patients with autoimmune hemolytic anemia and in pregnant and recently postpartum women. Anti-Wr can be isotype IgM reactive at less than 37°C or IgG reactive by IAT. Wr is well developed in newborns; however, HDN attributable to anti-Wr is very rare. Although anti-Wr is common, it is seldom detected in contemporary antibody-screening tests as Wr(a+) RBCs are not present on commercial reagent screening RBCs.

The routine use of the immediate spin compatibility test and computer matching of units for patients in whom antibody screening tests are negative may result in some patients with anti-Wr receiving Wr(a+) RBCs. However, the probability of incompatibility and hemolytic transfusion reaction is very low. This report describes an acute overt hemolytic transfusion reaction in a transfusion-dependent adult whose serum was nonreactive with reagent screening RBCs and who received a transfusion of Wr(a+) packed RBCs that were compatible at immediate spin. Because of the low probability of a transfusion reaction attributable to the presence of a low-prevalence antigen, an immediate spin or computer crossmatched transfusion can be considered safe. However, if during the transfusion there are any complaints from the patient or changes in vital signs, the transfusion must be terminated immediately.

Case Report

An 83-year-old White man with large granular T-cell lymphoproliferative disorder was diagnosed with aplastic anemia and became transfusion-dependent. The patient received 17 units of packed RBCs during the 3 months before the present episode. The patient had presented for transfusion with Hb of 8.7 g/dL. His RBCs typed as group A, D+; the auto-control and screening tests for unexpected antibodies by IAT were negative. One group A, D+ RBC unit was crossmatched using the immediate spin technique and found to be compatible. During transfusion of the RBC unit, the patient complained of chills and rigors. He received an antipyretic and the transfusion was continued. Posttransfusion hemoglobin was not measured. The patient returned in 2
days feeling profoundly weak, with a blood pressure of 84/50 mm Hg (pretransfusion blood pressure was 135/86 mm Hg). His Hb had fallen to 7.8 g/dL, his creatinine rose from 2.2 mg/dL before transfusion to 3.3 mg/dL, his LDH level was elevated at 681 IU/L, his total bilirubin was increased from 0.5 mg/dL to 2.3 mg/dL, and his haptoglobin was low normal. Troponin was elevated, which is consistent with a silent myocardial infarction. His DAT was negative and no elution was performed. The ABO group of the transfused unit was reconfirmed, and a serologic workup with panel RBCs was negative. Other possible causes of hemolysis, including medication, were excluded. When IAT crossmatches were performed on the retained donor blood segments with the patient's pre- and posttransfusion serum, both were strongly positive (3+). The specimens were sent to a reference laboratory (New York Blood Center, immunohematology laboratory). When the serum was tested against RBCs with low-prevalence antigens, the Wr(a+) RBC samples reacted. No other unexpected antibodies were detected using IAT that included albumin, papain-modified RBCs, and PEG. The Wr(a) typing was performed using single-donor-source antibodies, and the RBCs from the donor unit were Wr(a+).

**Discussion**

Holman first described anti-Wr as a cause of HDN and named it after the family (Wright) in which it was found. Later the antigen was assigned to the Diego blood group system. Anti-Wra is not uncommon as a naturally occurring or secondary antibody to RBC transfusion or pregnancy. Anti-Wr was found in 7.3 percent of pregnant women and 7.9 to 10.2 percent of hospital patients without other RBC antibodies. Only the rare IgG anti-Wr may cause HDN.

Despite the fact that the antibody could cause hemolysis in vitro, only one case of hemolytic transfusion reaction in an adult patient attributable to anti-Wra was reported and an additional case was described as part of a survey.

In the present case, the antibody screen was negative owing to the lack of Wr on the reagent RBCs. In addition, the immediate spin crossmatch was compatible because of the IgG nature of the circulating antibody. A transfusion reaction was noticed during the RBC transfusion but ignored as a trivial observation. Two days later the patient presented with symptoms and laboratory evidence highly suggestive of a hemolytic transfusion reaction. The screening for a low-prevalence antigen and antibody showed that the patient has an IgG anti-Wr reactive by the IAT and the donor unit was Wr(a+).

The use of an immediate crossmatch may allow transfusion of incompatible RBCs. Because the
prevalence of Wr is 1 in 1000, the occurrence of the antibody is 7 to 10 percent, and most of the antibody isotype is IgM, the probability of incompatibility and hemolytic transfusion reaction is calculated to be 7 to 10 in 100,000. As a result of this low probability of a transfusion reaction in patients with antibodies directed at low-prevalence antigens, an immediate spin transfusion can be considered safe.\textsuperscript{9–11} However, if during the transfusion any complaint from the patient or change of vital signs occurs, the transfusion must be terminated immediately.

Acknowledgments
We thank the staff of the Laboratory of Immunohematology, New York Blood Center, New York, NY, for performing the low-prevalence antigen and antibody testing and Drs. Marion E Reid and Harold H. Harrison for reviewing the manuscript. We also thank Dr. D. Phillips at Sound Shore Medical Center, New Rochelle, NY, and Elisa Steinbacher at Geisinger Medical Laboratory for secretarial assistance.

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