Red blood cell transfusion in a patient with anti-AnWj: a case report

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Anti-AnWj (Anton) has been associated with clinically significant hemolytic transfusion reactions. More than 99 percent of studied populations have RBCs that express the antigen. Reported here is a patient with anti-AnWj who was transfused with antigen-positive RBCs without adverse reaction. *Immunohematology* 2007; 23:55–58.

Key Words: RBC, anti-AnWj

The AnWj antigen is located in the ISBT 901 series of high-incidence antigens. It has a more than 99 percent occurrence in all populations. As such, the clinical significance of an anti-AnWj has to be interpreted carefully as RBC units negative for this antigen are extremely rare. Limited evidence exists to help guide transfusion practice in patients with this antibody; we describe a single case in which a patient whose serum contained anti-AnWj was successfully transfused with serologically incompatible RBCs without an adverse reaction. The signs and symptoms of an adverse reaction include fever or chills or both, nausea or vomiting, pain (at infusion site or flank), dyspnea, hypotension or tachycardia or both, renal failure, disseminated intravascular coagulation, jaundice, hemoglobinemia, hemoglobinuria, inadequate increase in posttransfusion Hb, increase in bilirubin (e.g., indirect bilirubin), increase in LDH, and decreased haptoglobin.

Case Report

The subject was a 57-year-old Caucasian male (of German, Irish, and French descent) with a history of autoimmune hemolytic anemia (AIHA) that was diagnosed at a different institution in March 2005 and was treated with prednisone and azathioprine. He was admitted on July 25, 2005, to the coronary care unit at our institution with a 40-pound weight loss and unstable angina. He was diagnosed with a myocardial infarction, and he was found to be anemic with a Hb of 8.3 g/dL. Cardiac catheterization showed three-vessel coronary artery disease with high-grade stenosis of the mid left anterior descending coronary artery. During hospitalization, the following complications occurred: hyperglycemia—probably related to steroid therapy—*Aspergillus fumigatus* infection of the lower lobe of the right lung, and bronchial bleeding during bronchoscopy. The bronchial hemorrhage was associated with a drop in Hb to 7.2 g/dL; RBC transfusion was considered to be clinically indicated owing to the patient's coronary artery disease (CAD), chest pain (rated at 5 of 10), pain on inspiration, and electrocardiographic changes.

Materials and Methods

**Historical serologic investigation**

The American Red Cross (ARC) North Central Blood Services (St. Paul, MN) had identified an anti-AnWj in this patient's serum in March 2005. They documented it as reactive by IAT in saline and albumin. According to the ARC report, the serum of the patient reacted weakly using PEG-IAT with all RBCs tested, including those that were either AnWj– or Lu(a–b–) and the patient's own RBCs. This panagglutinin was detectable only in PEG-IAT. The ARC testing excluded antibodies to common blood group antigens by using test RBCs that were negative for AnWj or were Lu(a–b–) and the patient's own RBCs. This panagglutinin was detectable only in PEG-IAT. The ARC testing excluded antibodies to common blood group antigens by using test RBCs that were negative for AnWj or were Lu(a–b–) by using both saline-IAT and albumin-IAT. The DAT was positive (ARC did not specify strength) with anti-human IgG and negative with anti-human C3b, C3d. The ARC performed an elution because of the positive DAT with anti-IgG and the resulting eluate reacted with all RBCs tested, including those that were AnWj– or Lu(a–b–). The patient's RBC phenotype performed by the ARC before any transfusion was as follows: group O, D+, C+E–c–, M+N+S–s+, P1–, K–k+.
Kp(b+), Fy(a–b+), Jk(a–b+), AnWj−; the ARC did not
provide the Lutheran phenotype of the patient. These
results were interpreted to indicate the presence of an
antibody to the high-prevalence antigen AnWj plus a
warm autoantibody. The immune stimulus for
developing the anti-AnWj was unknown.

In light of observed evidence of the association
with delayed hemolytic transfusion reactions,2 the ARC
(St. Paul, MN) recommendation was to transfuse AnWj−
RBCs (if available) or RBCs with the dominant Lu
(a–b–) phenotype encoded by In(Lu).

Current serologic investigation

The patient arrived at our institution on July 25,
2005, after receiving two units of phenotypically
similar [E–, K–, Lu(a–b–)] group O, D+ RBCs provided
by the ARC and infused at another institution. Three
additional group O, D+ RBC units were transferred to
our facility by the ARC. These latter three units were
phenotypically similar (E−, K−) but the units were
Lu(a–b+) and thus AnWj+. Units were negative for E
and K as a precaution.

It is known that Lu(a–b–) RBCs have poor
expression of the AnWj antigen.1 Therefore, reagent
RBCs negative for AnWj were used in conjunction with
Lu(a–b–) reagent RBCs to evaluate for the presence of
antibodies to other major blood group antigens.
Testing in the immediate spin phase using the patient’s
plasma (collected in EDTA) revealed no reactivity with
reagent RBCs and 1+ reactivity against the autologous
RBCs. Testing was then carried into the PEG-IAT phase,
which showed 2+ and 3+ reactivity with AnWj+ and
Lu(a–b+) RBCs, respectively, w+ reactivity with AnWj−
and Lu(a–b−) RBCs, and 3+ reactivity with autologous
RBCs. A DAT showed 2+ reactivity using monoclonal
anti-human IgG (Ortho-Clinical Diagnostics, Raritan,
NJ) and was negative when tested with anti-human
C3b, C3d (Ortho-Clinical Diagnostics). Using the acid/
EDTA method, an elution was performed. The eluate
showed no reactivity at PEG-IAT against the same
antibody identification panel of RBCs described earlier.
Although our eluate results were puzzling, the rest of
our results were consistent with those reported by the
ARC in St. Paul when testing in PEG-IAT.

The rarity of the antibody also presents problems
when trying to locate antisera for typing the patient’s
RBCs. The AnWj typing sera at our institution failed to
react with the control RBCs, and we were unable to
locate additional antisera from outside sources. A
phenotype was performed for the common blood
group antigens, and, where indicated, the patient’s
RBCs were treated with acid/EDTA to remove antibody
that could interfere with antigen typing. The
phenotype performed in our facility was in agreement
with the ARC with the following additional antigen
typings: e+, CW+, Le(a–b+).

It was concluded through RBC antibody identifi-
cation testing and antigen typing that the patient
lacked alloantibodies to the major blood group
antigens, and it was inferred through testing performed
at our facility and the ARC that the patient had made
anti-AnWj. As previously mentioned, we could not
confirm the AnWj because of a lack of antisera, but the
ARC typed the patient’s RBCs and determined that they
were AnWj−. Autoanti-AnWj has been reported as a
result of transient suppression of the AnWj antigen, and
therefore we could not definitively rule out that
possibility.1 Testing in LISS decreased the panreactive
autoantibody’s strength to nonreactive macroscopically.
An allogeneic adsorption was performed on the
patient’s serum using intact RBCs in an attempt to
remove the anti-AnWj to rule out all antibodies to
common blood group antigens using our test
methodology of choice, PEG-IAT. The adsorption was
performed on a phenotypically similar (matched for
antigens as described earlier—except AnWj) RBC
aliquot. The allogeneic adsorption was successful, and
there was no evidence of alloantibodies against any of
the major blood group antigens using PEG-IAT. Left
behind in the absorbate was an autoanti-e. We can
speculate that a warm autoantibody with specificity
other than anti-e exists, as well as one with anti-e
specificity.

The clinical service was made aware of the diffi-
culty in obtaining serologically compatible, antigen-
negative RBC units. Based on assessment of clinical
need by the patient’s service, an order for one unit of
RBCs was received. A unit known to be Lu(a–b−) was
crossmatched. This unit was serologically incompatible
(2+) using our routine PEG-IAT methodology,
presumably because of the warm autoantibody (as it
reacted 2+) but was compatible using LISS-IAT. This
unit was transfused without clinically evident
complications. Samples from the patient’s available
siblings (a total of four) were also crossmatched with
the patient’s plasma and were found to be incompatible
using both PEG-IAT and LISS-IAT methods. RBC antigen typing was not performed on
the samples from the patient’s siblings as a result of this
incompatibility.
Requests for Lu(a–b–) RBC units could not be filled through the American Rare Donor Program (ARDP). Because of this, it was considered necessary to assess the likely clinical significance of the patient’s anti-AnWj. A sample of the patient’s serum was sent to the National Reference Laboratory for Blood Group Serology of the ARC for performance of a monocyte monolayer assay (MMA). Concurrently, an in vivo radiolabeled (In-111) RBC survival study was performed at our institution.

The MMA is an in vitro diagnostic evaluation of the hemolytic potential of an antibody. It has been shown previously through multiple studies to be a predictor of RBC antibody clinical significance.\(^3\)\(^-\)\(^5\) It was performed using group O AnWj– RBCs and group O AnWj+ RBCs. Pooled monocytes from two normal blood donors were used. The AnWj+ RBCs reacted strongly positive by DAT after incubation with the patient’s serum. AnWj– RBCs were negative by the DAT after incubation with the patient’s serum. The percentages of reactive monocytes, after incubation with the patient’s serum, with and without fresh complement, were 19.0 percent and 37.5 percent, respectively, with AnWj+ RBCs. AnWj– RBCs, after incubation with the patient’s serum, with and without fresh complement, displayed 0.5 percent and 0.3 percent of reactive monocytes, respectively. Between 0 percent and 3 percent of reactive monocytes is considered within the normal range. Values above this range suggest that the antibody in question may cause accelerated clearance of antigen-positive RBCs. Again, the ARC recommendation was to transfuse AnWj– RBCs.

In the radiolabeled survival study,\(^6\)\(^,\)\(^7\) an intravenous infusion of 10 mL of indium 111-labeled Lu(a–b+) RBCs (2+ crossmatch incompatible at PEG-IAT and w+ crossmatch incompatible at LISS-IAT) was administered, and samples were obtained at specified intervals to determine the percentage of radiolabeled RBCs persisting in the circulation. The intervals were 3 hours, 20 hours, 47 hours, and 70 hours after infusion. The results at the specified intervals were 95 percent, 87 percent, 81 percent, and 80 percent, respectively. Data from this particular test suggested that RBCs of this phenotype were unlikely to undergo a clinically relevant degree of hemolysis within 3 days of transfusion.

**Clinical outcome**

Because of clinical necessity and despite the conflicting predictive test results, a decision was made to transfuse two available units of Lu(a–b–) RBCs that were 1+ and 2+ crossmatch incompatible in PEG-IAT phase but compatible in LISS-IAT phase of testing. The transfusions were without any clinically apparent adverse outcomes, and 2 days later the patient’s Hb level had risen from 7.2 g/dL to 8.6 g/dL. Subsequent to that transfusion, no more Lu(a–b–) units were available at our institution, and the ARDP was unable to supply additional units. The patient required further transfusion and was transfused two (1+ incompatible at PEG-IAT and compatible at LISS-IAT) units of Lu(a–b+) RBCs, again without any clinical adverse reaction. Our transfusion service recommended premedication with IVIG (1 g/kg) and IV hydrocortisone to reduce the possibility of an acute hemolytic reaction and its clinical effects. The patient’s Hb increased from 8.1 g/dL before transfusion to 11.2 g/dL after transfusion. Owing to the nature of his warm AIHA, anti-AnWj, and compounding myocardial infarction and CAD, the patient’s clinical service limited blood loss from laboratory testing and phlebotomy. Because of this, there were few biochemical markers for hemolysis ordered. Results from those that were are summarized in Figure 1.

At another hospital, the patient later underwent coronary artery bypass graft surgery. He presented to our institution 10 months later, in September 2006, with gastrointestinal bleeding associated with the use of aspirin and other nonsteroidal anti-inflammatory medications. His Hb level on admission was 6.1 g/dL and dropped to 5.1 g/dL the next day. In addition to the anti-AnWj, an anti-Fya\(^a\) was found, further complicating the patient’s serologic workup. No serologically compatible units or units that were Lu(a–b–), Fy(a–) were available. Two units of Lu(a–b+), Fy(a–) RBCs were transfused (reactions were 2+ incompatible at
PEG-IAT and 1+ incompatible at LISS-IAT) without adverse reaction and his posttransfusion Hb stabilized at 6.1 g/dL.

Discussion

Although anti-AnWj has been reported to cause significant clinical hemolysis, there is clearly insufficient experience to reliably predict its potential for hemolysis in any particular case. The MMA and in vivo RBC survival testing in our case gave conflicting information, and the RBC survival study seemed to more accurately predict the clinical result in this case. It should be noted that, although it is unlikely, the MMA could have been influenced by an antibody to an unidentified low-prevalence antigen. Although RBC units negative for AnWj are virtually impossible to locate in the general population, it is slightly less difficult to find Lu(a–b–) units. The patient’s clinical condition led to a decision that RBC transfusion was necessary despite the inability to locate AnWj- or Lu(a–b–) RBC units for him. Based on the objective evidence provided by the in vivo survival study, we deemed Lu(a–b+) RBC units, in spite of serologic incompatibility, to be a relatively safe choice for transfusion. The patient suffered no apparent adverse clinical events after transfusion. One may wish to consider that this occurred because the initially reported alloanti-AnWj may, in fact, have been an autoanti-AnWj. However, this is only one case, and it is certainly possible that quite different results might be found in other cases. Similarly, caution should be taken with patients who have antibodies to high-prevalence antigens whose clinical significance is unknown. This case report should not be applied generally to all antibodies to high-prevalence antigens.

References


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