Management of a Pregnant Woman with Anti-Holley Alloantibody

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Keywords

Anti-Holley alloantibody · Hemolytic disease of the fetus and newborn · HDFN · Pregnancy

Summary

Background: Holley (Hy) is a high-incidence antigen of the Dombrock blood group system (ISBT 014), present in almost 100% of most populations and more than 99% of Blacks. Since anti-Hy is an extremely rare antibody, data on its clinical relevance and in particular on a possible hemolytic disease of the fetus and newborn (HDFN) are scarce. **Case Report:** The pregnant patient underwent two autologous whole blood collections at weeks 17 and 19 of gestation with cryopreservation. In our case autologous whole blood collection was well tolerated. There were no signs of HDFN in the healthy newborn. **Conclusion:** Our case improves our understanding of anti-Hy alloantibodies during pregnancy. Additionally, autologous whole blood collection of RBC units with cryopreservation is a safe and feasible way to manage pregnancies in women with rare alloantibodies, when no compatible donor can be found.

Introduction

Holley (Hy) is a high-incidence antigen of the Dombrock blood group system (ISBT 014), present in almost 100% of most populations and more than 99% of Blacks. Since anti-Hy is an extremely rare antibody, data on its clinical relevance and in particular on a possible hemolytic disease of the fetus and newborn (HDFN) are scarce.

Case Report

A 29-year-old, native Nigerian female patient was taken care of during her 4th pregnancy at our institution. In the past medical history, the patient had three induced abortions in 2007, 2009, and 2010. Further medical history was unremarkable; in particular, the patient did not receive any transfusions. The first routine testing was performed at her 14th gestation week and revealed a blood group A₁ ccDEe.

Antibody screening in the gel system (indirect antiglobulin test; Bio-Rad, Cressier, Switzerland) was positive. Patient's serum reacted with all panel red blood cells (RBCs) in the subsequently disposed antibody identification panel, except her own. Blood samples of the patients were sent to the national reference laboratory for further testing, and an anti-Hy (Holley, DO4) alloantibody was identified. Genotyping with DNA chips (HEA beadchips v1.2; BioArray Solutions, Immucor, Rödermark, Germany) confirmed that the patient showed the c.323G>T and c.793A>G mutations at the homozygous state in the *ART4* gene, consistent with an Hy⁻ (DO⁻:4) rare phenotype. During follow-up an additional anti-Bg^a alloantibody was detected in one testing at the 5th month of gestation. Bg (Bennett-Goodspeed) antigens are RBC HLA antigens that are occasionally expressed strongly enough to be detected by conventional blood grouping techniques. Bga represents HLA-B7 [1]. HLA antibodies have very rarely been responsible for hemolytic transfusion reactions and not for HDFN.

Regular monitoring of the fetus was done. Fetal middle cerebral arterial (MCA) doppler assessment showed no signs of fetal anemia. In the allo-antibody screening during the 5th and 7th month of gestation, the anti-Hy alloantibody could no longer be detected.

The pregnancy was otherwise uneventful. We searched for compatible blood in case of need at delivery or in the post-partum period. Although the siblings and the parents of the patients were theoretically available for antigen testing and possibly for directed blood donation, the patient did not give her consent to contact her relatives. Thus, two autologous whole blood collections at her 17th and 19th gestation week were performed. After agreement of the French National Immunohematology Reference Laboratory (National Institute of Blood Transfusion, Paris, France), the RBC units were sent for cryopreservation at –80 °C and storage at the French National Rare Blood Bank (French National Blood Service, Créteil, France).

Because of low ferritin level of 11 µg/l (normal range: 10–200 µg/l) without anemia during her 19th and 34th gestation week the mother was given intravenous iron (iron-III-hydroxide-polymaltose complex 500 mg twice).

A cesarean section was carried out in the 40 + 5 week of gestation after spontaneous rupture of the membranes and unsuccessful medical induction of labor as well as laboratory signs of infection with vaginal colonization with group B *Streptococcus*. The two autologous RBC units were retrieved for transfusion. With the intraoperative use of a Cell Saver device the total perioperative blood loss was 600 ml, with no need of transfusions. A healthy boy was born with blood group A positive, negative direct agglutination test, and no signs of hemolysis. A molecular testing revealed the presence of the Hy antigen (Holley, DO4) in the newborn. The molecular testing was performed by DNA extraction using SIGMA Extract-N-amp (Sigma-Aldrich, St. Louis, MO, USA) and SSP-PCR detection of the SNP for DO*4(Hy).

Discussion

Hy (DO4) is a high-incidence antigen belonging to the Dombrock blood group system (ISBT 014), present in almost 100% of most populations and more than 99% of Blacks [2–4]. Thus, anti-Hy is an extremely rare antibody and Hy-negative RBC concentrates are very difficult to obtain. Furthermore, antibodies in the Dombrock blood group system can be difficult to identify [5].

At least one published transfusion reaction due to anti-Hy antibodies with biphasic destruction of Hy antigen-positive RBCs has been reported [6]. Other rare moderate hemolytic transfusion reactions were also reported. Data on HDFN in women with anti-Hy alloantibody are scarce [7].

Autologous RBC collection and cryopreservation of RBC units is a safe and feasible way to manage pregnancies in women with rare alloantibodies, when no compatible donors are available.

In our case autologous blood collection during pregnancy was well tolerated. In comparison to a possible directed blood donation from matched sibling's donors, there is no additional risk of further alloimmunization and no need to irradiate the RBC products.

Although molecular testing performed in the newborn was consistent with a Hy-positive phenotype, there were no signs of anemia and hemolytic disease in the fetal monitoring during pregnancy as well as after birth.

Disclosure Statement

The authors declare that they have no conflicts of interest relevant to this article.

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