Management of pregnancy complicated by anti-hrB/anti-HrB

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Anti-hrB and anti-HrB are rare alloantibodies found predominantly in people of Black African descent. It has been assumed that strongly reacting examples of anti-hrB may cause hemolytic transfusion reactions, but precise information is limited. Anti-HrB is a clinically significant antibody and may cause hemolytic transfusion reactions and HDN. Selection of blood for transfusion support for patients with these alloantibodies, and especially with anti-HrB, imposes a special challenge in the United Kingdom. We report two antenatal patients (both patients were of the partial D phenotype DIII), one with anti-hrB, anti-Ce, and anti-D; the other, with anti-hrB and anti-D, who later formed anti-HrB. Transfusion support and the outcome of the pregnancies are discussed. A literature search confirms that, apart from some publications in abstract form, there is not much detailed clinical information available for either anti-hrB or anti-HrB. Further information and publications are warranted to gain more knowledge of these rare antibodies. Immunohematology 2007;23:143–5.

Key Words: Anti-HrB, anti-hrB, hemolytic transfusion reactions, hemolytic disease of the newborn

Patients of Black African descent with variant RHCE genes may make alloanti-e-like antibodies such as anti-hrB.1 There is scant information available regarding the clinical significance of anti-hrB, but it has been recommended that hrB– units be provided for potent anti-hrB.2 Transfusion of hrB– blood is often achieved by using R2R2 (e–, hrB–) blood. These patients may make anti-E (if E–), anti-HrB, or both.2,3 This, in turn, may lead to complications in antibody identification and provision of suitable blood. Anti-HrB is a clinically significant antibody against the high-prevalence HrB (Rh34) antigen and may cause HDN.4 We report two antenatal patients with the partial D phenotype DIII, one who made anti-hrB, anti-Ce, and anti-D, the other who made anti-hrB and anti-D, who later formed anti-HrB. Transfusion support and outcome of the pregnancies are discussed.

Case Reports

Patient 1

A 30-year-old woman of African-Caribbean origin was seen at the antenatal clinic at 19 weeks’ gestation. This was her second pregnancy. During her previous pregnancy weakly reacting anti-D, anti-Ce, and anti-hrB were identified in her serum. The International Blood Group Reference Laboratory (IBGRL), Bristol, United Kingdom, confirmed her blood group as A, probable Rh genotype Cce/DIIIce. Review of the case showed that there was no evidence of HDN during her previous pregnancy; the RBCs from her baby’s cord sample were negative in the DAT, with a Hb of 19 g/dL at delivery. The patient had not received a blood transfusion. At her initial antenatal visit for the second pregnancy, only weakly reacting anti-hrB and anti-D were identified in her serum. The patient missed her follow-up appointments, but revisited the clinic at 39 weeks’ gestation. Serologic investigation showed the presence of weakly reacting anti-hrB, anti-D, and anti-Ce. Rh phenotype rer” (ce/cE) RBCs were reserved to cover the delivery. The patient delivered a normal, healthy baby by vaginal route and did not require transfusion. The DAT on the RBCs from the cord sample was negative and the baby showed no clinical evidence of HDN.

Patient 2

A 29-year-old woman of West African origin, with sickle cell anemia (HbSS), was seen at 20 weeks’ gestation. Her sickle cell disease ran a mild course. She had a history of recurrent miscarriages and had no live children. She had been transfused previously on two occasions. Three years previously, at another hospital, “pan-reacting antibodies” had been identified in her serum, and the IBGRL confirmed the presence of weakly reacting anti-D and anti-hrB. Her blood was typed as group AB and the probable Rh genotype was reported as Cce/DIIIce. At presentation in the index pregnancy, only weakly reacting anti-hrB was detected in the serum. Although the pregnancy progressed satisfactorily, she experienced sickle-related pain, leading to short admissions. Her Hb was stable at approximately 7.0 g/dL, and transfusion was avoided. It was planned to provide rer”, K– RBCs should the patient need transfusion support. At 32 weeks’ gestation, unexpectedly,
anti-HrB was detected in her serum, resulting in the need for Rhnull or HrB– or units from a donor with the same unusual blood type. Units of HrB– RBCs would have to have been imported from South Africa. We were able to reserve two units of Rhnull RBCs at the National Frozen Blood Bank (NFBB), United Kingdom, for the patient. At 35 weeks’ gestation, the patient experienced acute sickle chest syndrome. She was treated supportively, and the infant was delivered by cesarean section under spinal anesthesia. The two frozen units of Rhnull RBCs were thawed, and transfused preoperatively and postoperatively. Her Hb the day after delivery was 7.8 g/dL. The infant’s RBCs typed as group B, D+. The DAT was positive (anti-IgG 2+, anti-C3d 1+). The infant’s Hb at delivery was 15.2 g/dL, with a bilirubin level of 157 µmol/L (normal range, 5–180 µmol/L). No therapy was required.

Materials and Methods

Column agglutination technology (DiaMed-AG, Cressier sur Morat, Switzerland) was used at National Blood Service (NBS)-Tooting Centre, using standard serologic methods. To establish whether other clinically significant alloantibodies were underlying the anti-hrB or anti-HrB present, multiple differential alloadsorption studies were undertaken with papain-treated R1R1, R2R2, and rr RBCs (NBS Reagents, Cambridge, UK).

In the serum of Patient 1, the apparent anti-Ce gave significantly more avid reactions than did the anti-hrB (i.e., more avid reactions were detected with RBCs expressing the Ce haplotype, with or without a ce haplotype in the trans position, than those expressing the ce haplotype only, even in presumed homozygous expression). Samples from both patients were referred to the IBGRL, which confirmed the presence of anti-hrB, anti-D, and anti-Ce in the serum of Patient 1 and anti-HrB in the serum of Patient 2, respectively. Extensive Rh typing was undertaken by the IBGRL for both patients.

Results

Patient 1

The RBCs of the patient were typed as group A; M+, N+, S–, s+; P1+; Lu(a–b+); K–, k+, Kp(a–b+); Le(a–b+); Fy(a–b–); and Jk(a+b–). The Rh phenotype was determined to be C+, c+, DIII, E–, e+, V–, VS+, hrB–, and hrS+. The probable genotype was CceS/DIIIce. Anti-D, -Ce, and -hrB were identified in her serum.

Patient 2

The RBCs of the patient were typed as group AB; M+, N–, S+, s+; P1+; Lu(a–b+); K–, k+, Kp(a–b+); Le(a–b+); Fy(a–b–); and Jk(a+b–). The Rh phenotype was C+, Ce–, c+, DIII, E–, e+, V–, VS+, hrB–, and hrS+. The probable genotype CceS/DIIIce. Initially, weakly reacting anti-hrB was identified in her serum. Toward the end of her pregnancy, however, the patient developed a strongly reacting anti-HrB. Weakly reacting anti-D, identified in her serum in a previous pregnancy, was not detectable.

Discussion

We describe two patients with the probable Rh genotype CceS/DIIIce and the VS+, hrB– phenotype; both formed weakly reacting anti-hrB and weakly reacting anti-D. Interestingly, with regard to Rh genotypes, Vege and Westhoff5 have postulated that the loss of expression of the hrB epitopes on RBCs may be a dominant phenotype, as they report that the majority of their hrB– donors were heterozygous, with some even carrying conventional alleles. Individuals who are hrB– often have variant D alleles.5 Patients who make anti-hrB and have a DIII partial D phenotype are at risk of making anti-D.5 Although there are no data available regarding hemolytic transfusion reactions in association with anti-hrB,1,2 the selection of hrB– RBCs has been recommended for transfusion in cases of potent anti-hrB.2 Once anti-hrB is identified, transfusion of hrB– RBCs can be achieved by providing RBCs that are R2R2 (c–, hrB–).

In the case of Patient 1, weakly reacting anti-hrB, anti-D, and anti-Ce were identified, and so r”r” (cdE/cdE) RBCs were selected for transfusion support. As far as we are aware, there is only one case report of anti-hrB in pregnancy (in abstract form).6 In that study, the patient’s serum contained anti-hrB, weakly reacting anti-D, and anti-Ce (serologic findings that are similar to those seen in our Patient 1), and r”r” RBCs were provided for delivery, but the patient did not require blood. The DAT on the RBCs from that infant’s cord sample was positive, and anti-hrB+D+Ce was eluted from the RBCs, with no evidence of HDN.6 In our Patient 1, the DAT on the RBCs from the cord sample was negative, with no evidence of HDN and the hospital failed to investigate the infant’s hrB type.

In our Patient 2, anti-hrB broadened into anti-HrB during the latter part of the pregnancy. Recent studies from South Africa have confirmed that anti-HrB is a clinically significant antibody that may cause HDN, and transfusion of HrB– RBCs was recommended for patients.
with anti-HrB. Provision of suitable blood for Patient 2 imposed a special challenge, as HrB- RBCs cannot be easily obtained from the existing UK donor population. There were two options, either to import extremely rare D- or DIII, HrB- RBCs from South Africa, or to provide Rhnull RBCs. We were able to locate two units of Rhnull RBCs through the UK Rare Donor Register. The patient received these Rhnull RBCs, and the transfusions were uneventful. Although the DAT on the infant’s RBCs was positive, there was no clinical evidence of HDN. The reference laboratory did not receive the infant’s sample for HrB typing. A literature search confirms that, apart from some publications in abstract form, there is not much detailed clinical information available for either anti-hrB or anti-HrB. The information obtainable from abstracts is limited, and further case reports are warranted to gain further knowledge concerning these antibodies.

Acknowledgment
We are grateful to Ms. Joyce Poole and her team at the IBGRL, Bristol, for Rh, HrB, and hrB typing and serologic confirmations.

References