

Case report

A Case Report of Haemolytic Disease of Foetus and Newborn due to Anti-E Antibody in a Primigravida Patient

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Abstract:

Anti-E antibody is one of the frequently encountered alloantibody of the Rh blood group system; however, it is seldom implicated in haemolytic disease of the foetus and newborn (HDFN). This case report describes a mild HDFN due to anti-E antibody in a full term baby-girl born to a primigravida patient. The baby developed jaundice on the first day-of-life. Blood group of both mother and the baby was B positive and Rh phenotype was CDe/CDe (R1R1) and CDe/cDE (R1R2) respectively. Anti-E and anti-c was identified in the mother while baby's blood showed weak positive Direct Antiglobulin Test with anti-E identified from the baby's serum. The baby was started on phototherapy and was discharged well on day -6. Although this was a mild HDFN, we would like to highlight the importance of antenatal screening for pregnant mothers. The antibody screening for Rh positive mothers is not a routine practice in many centers in Malaysia due to cost-benefit constraints. However, we would like to suggest to include the antenatal red cell antibody screening test for all pregnant mothers at least during the 1st antenatal booking to enable early detection of alloantibody which may cause HDFN, thus enable close monitoring of foetus and initiate early management as needed.

Key Words: allo antibody; anti-E; HDFN; antenatal antibody screening

Bangladesh Journal of Medical Science Vol. 15 No. 01 January'16. Page : 139-141

Introduction:

Haemolytic disease of the foetus and newborn (HDFN) is a condition where the red cell of the foetus is shortened by antibodies produced by the mother¹. Since the introduction of anti-D prophylaxis for RhD-negative women in 1968, the incidence of HDFN due to anti-D has been decreasing². Currently, other alloantibody towards Rh and non-Rh red cell antigens have become relatively more important and responsible for the greater proportion of HDFN³. The frequency of clinically significant alloantibodies other than anti-D such as anti-E, anti-K, and anti-c is 1:300 pregnancies and risk of HDFN caused by these antibodies is 1:500⁴. Anti-E antibody is one of the potent antibodies of

the Rh-blood group system, found after anti-D in general population as well as in pregnant mothers¹⁻⁵; however, it seldom causes HDFN¹. This case report describes a case of HDFN due to anti-E in a primigravida patient and to reinforce the importance of antenatal antibody screening during pregnancy.

Case Report:

We report here a case of HDFN caused by anti-E antibody in a full-term baby girl delivered through the vacuum delivery due to foetal distress by a 32-year-old Chinese primigravida. The mother's antenatal history was uneventful and she was on regular follow-up in a local clinic. She was admitted to Universiti Kebangsaan Malaysia Medical Centre (UKMMC) at the time of delivery. On laboratory

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investigation, her blood group was determined as B Rh-D positive and Rh phenotyped as CDe/CDe (R1R1). Her antibody screening and identification at the time of delivery was positive with anti-E and anti-c identified.

The neonate's birth weight was 3.69 kg with Apgar score of 8/9. The baby was noticed to have jaundice at about 10 hours-of-life. Her total bilirubin was 78 μ mol/l with direct bilirubin 8 μ mol/l. The bilirubin was found to be in an increasing trend up to 191 μ mol/l on day 4 with direct bilirubin up to 12 μ mol/l. The baby had a normal G6PD activity and sepsis had been excluded. The baby's blood group was B Rh-D positive with Rh genotype CDe/cDE (R1R2). Direct Agglutination test (DAT) was weakly positive at polyspecific AHG phase and monospecific anti-IgG phase. In view of the positive DAT, the Rh genotype result was interpreted cautiously. In this case the test was validated with a negative control that showed a negative reaction. The antibody screening and identification using baby's plasma revealed only anti-E and no anti-c. However, red cell elution study from the baby's red cell was negative. Her full blood picture did not show any obvious evidence of haemolysis with Hb of 14g/dl which was normal for age. With the presence of anti-E in both mother's and baby's serum and positive DAT with the underlying clinical jaundice, a diagnosis of anti-E antibody causing mild HDFN was made. The baby recovered well with phototherapy and was discharged on day 6-of- life.

Discussion:

It has been found that anti-E is the most common alloantibody detected in pregnant mothers though the frequency is very low^{5,6}. This antibody can be naturally occurring and sometimes detectable only with enzyme-treated red cells¹. Anti-E has been reported occasionally as rare cause of HDFN⁴.

In a report of alloantibody cases in pregnancy, data over 45 years showed anti-E alloantibody was identified in 283 pregnancies where 32 pregnancies in 27 women were identified at risk of HDFN. Among these 32 pregnancies, 50% had high antibody titre equal to or greater than 1:32, 15% fetuses had Hb less than 10 g/dL and 1 fetus had hydrops fetalis⁷. Another large scale study over 29 years assessing the HDFN due to anti-E showed the presence of anti-E in 122 pregnancies in 118 women where 62 infants (51%) to 59 mothers suffered HDFN where 48 cases were classified as mild, 8 were moderate; five were severe and one was very severe. The very severely affected case had anti-E titre of 1/1 or positivity at the neat undiluted serum only, highlighting the disparity between anti-E titre and disease severity. However, co-existent, non-immune cause for anaemia was not excluded in that particular case³. These two reviews suggest that HDFN due to anti-E is mainly of mild to moderate type. However, there was no general agreement regarding critical antibody titer for monitoring of the fetus⁸. Joy et al (2005)⁷ has shown the critical titer of anti-E as 1:32 while Moran et al (2000)³ found that lack of co-relation between anti-E titers and HDFN severity.

Red blood cell (RBC) alloimmunization occurs due to sensitization by pregnancy or blood transfusion⁵. However, in this case the mother has developed allo- antibody in her first pregnancy without known prior sensitization due to abortion or blood transfusion. The possible explanation on how the mother has developed the clinically significant antibodies could probably be due to the sensitization from sub-clinical fetomaternal haemorrhage during her current first pregnancy. However, there was no antenatal antibody screening to confirm this possibility. Another possibility is that there could be an unrecognized or silent miscarriage earlier that the mother was not aware of. The possibility of naturally occurring anti-c is unlikely as the anti-c needs sensitization event for its development unlike anti-E which could be a naturally occurring antibody¹. The antigen positivity in the baby also supports the possibility of sensitization in the mother leading to the development of maternal allo-antibody. In the laboratory findings, the anti-E antibody showed strong reaction (4+) in both LISS and enzyme treated panel cells whereas the anti-c was detected in the enzyme phase only (3+ reaction strength) with no reaction in the LISS, indicating the anti-E titer is stronger than anti-c, thus able to cross the placenta and caused the HDFN.

In this case, DAT test of the baby was weakly positive; however the antibody specificity was not identified from the eluate. This negative elution test in the baby could be explained by the weak DAT in the baby. In HDFN, mother's IgG antibodies cross the placenta and coat the antigens on the baby's red cells. DAT detects the coated antibody and by doing the elution, the antibodies from the sensitized red cells are recovered. By incubating the eluate with the reagent panel cells, the specificity of the eluate can be determined. However, depending on the strength of the DAT, i.e. with low concentration of IgG, the

eluate may not react with any of the panel cells⁹. This may explain the negative antibody specificity from the eluate in this present case.

Although this is a mild HDFN, we would like to highlight the importance of antenatal screening for all pregnant mothers. In some centers, the antibody screening is only carried out for Rh D negative pregnant mothers due to the cost-benefit constraints. Thus, there is every chance of missing the clinically significant alloantibodies apart from anti-D that can cause HDFN. Therefore, it is very important to perform the antenatal screening test at least once for all pregnant mothers. In this

case, although the antenatal history of the mother during this pregnancy was unremarkable, for her subsequent pregnancy the antenatal screening and monitoring the anti-E titre is vital, as the anti-E can result in severe HDFN in her subsequent pregnancies due to anamnestic reaction.

Conclusion:

This case report highlights the necessity of performing antibody screening for all pregnant women at least once during their antenatal follow up to detect the presence of clinically significant allo-antibody and thus to be able to take necessary measures to manage the HDFN cases as needed.

References:

1. Klein HG, Anstee DJ. Mollison's Blood Transfusion in Clinical Medicine. UK, John Wiley & Sons Ltd, 2014: 499-548 <http://dx.doi.org/10.1002/9781118689943>
2. Kennedy MS, Krugh D. Hemolytic Disease of the Newborn and Fetus. In Harmening DM, ed. Modern Blood Banking and Transfusion Practices, 5th Edition, Philadelphia, USA, F. A. Davis Company, 2005: 383-395
3. Moran P, Robson SC, Reid MM. Anti-E in pregnancy. *BJOG* 2000;**107**:1436-1438. <http://dx.doi.org/10.1111/j.1471-0528.2000.tb11662.x>
4. Usman AS, Mustaffa R, Ramli N, Diggi SA. Hemolytic disease of the fetus and newborn caused by anti-E. *Asian J Transfus Sci.* 2013;**7**(1): 84-85. <http://dx.doi.org/10.4103/0973-6247.106750>
5. Smith HM, Shirey RS, Thoman SK, Jackson JB. Prevalence of clinically significant red blood cell alloantibodies in pregnant women at a large tertiary-care facility. *Immunohematology* 2013;**29**(4):127-130.
6. Hassan MN, Noor NHM, Noor SRJ, Sukri SA, Mustafa R, Luc Aster HVR. Hemolytic disease of fetus and newborn due to maternal red blood cell alloantibodies in the Malay population. *Asian J Transfus Sci.* 2014;**8**(2):113-117. <http://dx.doi.org/10.4103/0973-6247.137449>
7. Joy SD, Rossi KQ, Krugh D, O'Shaughnessy RW. Management of pregnancies complicated by anti-E alloimmunization. *Obstet Gynecol.* 2005;**105**(1):24-8. <http://dx.doi.org/10.1097/01.AOG.0000149153.93417.66>
8. Kumawat V, Jain A, Sharma RR, Marwaha N. Hemolytic disease of fetus and newborn due to anti-E alloantibody in a newborn of Rh (D)-positive mother. *Asian J Transfus Sci* 2012;**6**(2):187 <http://dx.doi.org/10.4103/0973-6247.98946>, www.apip.com/Reference/Commentary/2008Bbbank.pdf