CORRESPONDENCE

ABO Hemolytic Disease of Fetus and Newborn; Still a Diagnostic Dilemma: A Case Report

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Dear Editor

The incidence of ABO HDFN is reported 0.33–2.2% [1]. ABO-HDFN occurs almost exclusively in neonates of blood group A or B who are born to group O mothers [2] because IgG anti-A or -B occurs commonly in group O than in group A or B [2]. Severe ABO HDFN is relatively rare, minor degrees of red cell destruction are common, evident by incidence of neonatal jaundice and slight lowering of the hemoglobin in ABO-incompatible compared with ABO-compatible neonates [2]. The A and B antigens are not fully developed at birth and these are not confined to the red cells only, so that a small fraction of IgG anti-A/anti-B crossing placenta combines with neonate's red cells [3]. Anti-A and anti-B from pregnant women are at least partly IgG2 and Fcγ receptors in placental tissue bind IgG1 with higher affinity than IgG2 [3]. IgG2 anti-A and -B play a part in red cell destruction in those infants with ABO HDN whose macrophages carry the high-affinity FcR2a receptor [3].

A male neonate born to a 28 year, primigravida at 35 weeks gestation weighing 1.56 kilograms, by vaginal delivery after prolonged rupture of membranes was admitted to neonatal intensive care unit due to prematurity and respiratory distress. Neonate was managed symptomatically as per protocol for prematurity. Neonatal CBC showed Hb = 16.3gm/dl, platelet = 420,000/μl and blood group was B Rh D positive. The CRP was <2.8 mg/L and blood culture at 48 h of life was negative. On Day 3 of life, neonate showed signs of severe sepsis with CRP of 81 mg/dl, Hb dropped to 10.9gm/dl and total serum bilirubin was 8.7 mg/dl (unconjugated 7.3 mg/dl). Blood culture was positive for *Klebsiella Pneumoniae* with sensitivity to third generation cephalosporin. Neonate was ventilated and IV antibiotics upgraded accordingly. Neonate received ABO identical fresh frozen plasma and platelet concentrate due to deranged coagulation (INR 1.5) and low platelet count (18,000/μl). On Day6, Hb dropped to 8.5gm/dl with TSB 6.1 mg/dl and direct anti-globulin test (DAT) was 4+ (Polyspecific IgG + C3d, column agglutination technology, Ortho clinical diagnostic, USA). The mother blood group was O Rh D positive with negative 3 cell antibody screening panel (Surgiscreen, Ortho clinical diagnostic, USA). The nonspecific DAT showed presence of IgG and absent complement. The neonatal serum showed presence of anti- A anti- B isoagglutinins reacting (4+) with in-house pooled A1 and B cells at 37 °C in AHG phase on polyspecific IgG + C3d gel card but nonreactive in saline phase. Elute prepared by heat and acid elution methods [4] showed presence of anti- AB antibody coating neonatal red cells. Maternal titer for anti- A and anti- B isoagglutinins in AHG phase were 1:1024. Double volume exchange transfusion with reconstituted blood (O Rh D positive PRBC + AB

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positive FFP) was performed. Neonate recovered and extubated to continuous positive airway pressure on Day 8 and no further drop in Hb noted.

The clinical course of ABO HDFN is relatively benign, characterized by high serum bilirubin, moderately severe anemia, reticulocytosis and spherocytosis. Hydrops caused by ABO-HDFN is extremely rare, and very occasionally exchange transfusion for the prevention of kernicterus is indicated. ABO HDFN predominantly results in hyperbilirubinemia, without significant anemia [5], but there are reported ABO incompatibility cases resulting in severe anemia [6]. Index case presented with severe anemia and modest increase in bilirubin. DAT positivity has been reported up to 30% [7] but lower percentage of DAT positivity has been reported in preterm newborns attributed to low placental IgG transport in early gestation period [8]. The newborn presented with a positive DAT (4+). DAT is usually positive due to IgG component and even in severe ABO hemolytic disease the neonate's red cells do not react with anti-C3d. This is due partly to the weak expression of A/B antigens and also relatively low level of complement in neonates [9]. In ABO HDFN, when the DAT is only weakly positive or even negative, elutes from the neonate's red cells may give strong indirect antiglobulin test (IAT) reactions with adult A1 and B red cells. The incompatible high titer (>256) IgG antibody in maternal serum in absence of elution or serum studies on a blood sample from neonate, supports that neonate may be suffering from ABO HDFN [10]. It was predominantly anti- AB responsible for hemolysis in index case as evident by elute reacting to both A1 and B cells. The O group mothers should routinely be screened for ABO system antibody (ies) titer and neonates of high titer mother (IgG $\geq$ 256) should be screened and monitored for evidence of hemolysis.

Compliance with Ethical Standards

Conflict of interest None for all authors.

Informed Consent Obtained from parents of index case.

References

1. Dufour DR, Monaghan WP (1980) ABO hemolytic disease of the newborn: a retrospective analysis of 254 cases. *Am J Clin Pathol* 73:369–373
2. Rosenfield RE (1955) A-B hemolytic disease of the newborn. Analysis of 1480 cord blood specimens, with special reference to the direct anti-globulin test and to the group O mother. *Blood* 10:17–28
3. Haemolytic disease of fetus and newborn. In: Harvey GK, David JA (eds) *Mollison's blood transfusion in clinical medicine*, 11th edn (2005). Blackwell, pp 496–545
4. Glycine-HCl/EDTA elution procedure (method 4-2) & heat elution procedure (method 4-3), general laboratory methods. In: Fung MK, Grossman BJ, Hillyer CD, Westhoff CM (eds) *Technical manual*, 18th edn (2014). American association of blood bank, Bethesda, Maryland, USA
5. Murray NA, Roberts IA (2007) Haemolytic disease of the newborn. *Arch Dis Child Fetal Neonatal Ed* 92:F83–F88
6. Ziprin JH, Payne E, Hamidi L, Roberts I, Regan F (2005) ABO incompatibility due to immunoglobulin G anti-B antibodies presenting with severe fetal anaemia. *Transfus Med* 15:57–60
7. Desjardins L, Blajchman MA, Chintu C, Gent M, Zipursky A (1979) The spectrum of ABO hemolytic disease of the newborn infant. *J Pediatr* 95:447–449
8. Yogeve-Lifshitz M, Leibovitch L, Schushan-Eisen I, Taran C, Strauss T (2016) Maayan metzger. Indication of mild hemolytic reaction among preterm infants with ABO incompatibility. *Pediatr Blood Cancer* 63(6):1050–1053
9. Brouwers HAA, Overbeeke MAM, Huiskes E et al (1988) Complement is not activated in ABO-haemolytic disease of the newborn. *Br J Haematol* 68(3):363–366
10. Li Ping, Pang Li-Hong, Liang Hai-Feng, Chen Hong-Yan, Fan Xiao-Jing (2015) Maternal IgG anti-A and anti-B titer levels screening in predicting ABO hemolytic disease of the newborn: a meta-analysis. *Fetal Pediatr Pathol* 34(6):341–350