A Case of Hyporegenerative Anemia and Direct Hyperbilirubinemia Complicating Hemolytic Disease of Newborn Secondary to Rhesus Alloimmunization

Htay Aung , Folasade Kehinde

Introduction

Rhesus hemolytic disease of the newborn (Rh-HDN) is rare but continues to occur after the implementation of anti-D immunoglobulin prophylaxis. The severity of the disease depends on the type and the quantity of maternal antiRh antibodies. Severe entities of this disease usually require exchange transfusion and multiple blood transfusions which can lead to subsequent hematologic complications such as hyporegenerative anemia and cholestatic hyperbilirubinemia. There are a few cases reported in literature in terms of its complications, however the timeline of when these complications arise is quite variable which makes it challenging to safely discharge and follow these patients. We discuss an early term infant with severe Rh-HDN and its complications.

Case Description

An early term male infant was born to a 22 year old G2P1 mother who was positive for anti-Rh D antibodies, via vaginal delivery induced due to increasing maternal antibody titers from 1:16 to 1:152 during the pregnancy. The delivery was uncomplicated. The infant's birth weight was 2344 g (symmetrically small for gestational age) and the Apgar were 9 and 9 at 1 and 5 mins of life respectively. At 4 hours of life (HOL), his total serum bilirubin was elevated at 19.5 mg/dl and he was also anemic (Hemoglobin [Hb] 9.2 g/dl) with reticulocyte count [Retic] of 22%. His blood group was O positive and his direct antiglobulin test was positive as well. Intensive phototherapy was initiated immediately followed by two doses of IV immunoglobulin followed by a double-volume exchange transfusion (DVET) at 60 HOL for serum bilirubin of 22 mg/dl. The infant required two successive DVET. Though indirect hyperbilirubinemia improved post-exchange transfusion, direct hyperbilirubinemia persisted for which ursodiol was started. MRI of the brain performed prior to discharge to rule out kernicterus was unremarkable. He was discharged on DOL 16 with serum total/direct bilirubin level of 8.3/ 4.3 on ursodiol. One week later, he was readmitted to the hospital with severe anemia, noticed during the follow up outpatient visit (Hb 6.8 g/dl with Retic 0.4%) with persistent indirect hyperbilirubinemia. The anemia was not accompanied by reticulocytosis. He received two packed red cell transfusions at 3 and 5 weeks of age during the second admission. Erythropoietin (EPO) was considered due to his hyporeactive marrow to anemia. His serum erythropoietin level resulted normal for his age (20.9 mlU/ml) and Hb stabilized around 9-10 g/dl after two transfusions two weeks apart without any other intervention. At discharge, Hb was 8.4 g/dl with improved reticulocyte of 5.2%. The persistent direct

hyperbilirubinemia showed no satisfactory response to ursodiol, a brief course of phenobarbital, DEKAs vitamins and fish oil. Therefore, extensive cholestasis workup was performed including liver ultrasound, cholestasis panel, alpha-1 antitrypsin level and phenotype, and intraoperative cholangiogram with liver biopsy. Liver biopsy showed cholestatic hepatitis without identifiable primary etiology and no anatomical obstruction in the biliary system was identified. He was continued on ursodiol and being followed up outpatient every 2-3 weeks with his primary pediatrician, hematologist, and gastroenterologist. All his labs including Hb, Reticulocyte count, Bilirubin level normalized by 3 months of age. The infant has been growing and developing well otherwise.

Discussion

It is important to look out for complications such as prolonged anemia and cholestatic hyperbilirubinemia in infants with alloimmune hemolytic disease of the newborn. These complications can lead to prolonged hospital stay, increase risk of readmission and complicate safety discharge for the infants. This case illustrates that prolonged anemia can present as early as 3 weeks and last up to 8 weeks after onset and then normalize by 10-12 weeks of age. It is likely that the affected infants may need additional blood transfusions during 3-8 weeks of age. Erythropoietin may be needed to correct hyporegenerative anemia. Post-exchange transfusion cholestatic/ direct hyperbilirubinemia can persist up to 10-12 weeks of age as well and routine medical management of cholestasis does not seem to work well in such cases.