Anti-E as a Cause of Hemolytic Disease of the Newborn

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Abstract

A case of HDN caused by anti-E antibody is reported. A group A, E-positive, hemoglobin E trait female infant was born from a group A, E-negative, ß-thalassemia / hemoglobin E mother. Hyperbilirubinemia was noted at the first day of life. The DAT was positive. Anti-E was detected in the maternal serum. Jaundice and anemia occurring to the baby were severe enough to require phototherapy intervention for 9 days and 50 ml of group A, E-negative packed red blood cells was transfused. The baby's condition improved. She was discharged at 12 days of age. Follow-up of the baby at 1 year old showed that she was alive and in good health.

Alloimmune hemolytic disease of the newborn results from the transplacental passage of maternal antibody active against red blood cell antigens of the infant, leading to an increased rate of red cell destruction[1]. It is an important cause of anemia and jaundice in infants. A few reports have described hemolytic disease of the newborn (HDN) in Thai infants due to incompatibility in the Rh system. Of all the Rh antigens, D is the most antigenic. Other antigens in the Rh system such as C, E and c are also potent immunogen although less potent than D[2,3]. HDN due to anti-D, anti-C and anti-e have been observed in Thai infants[4,5]. Spence et al reported a case of HDN due to anti-E antibody[6]. Anti-E in particular caused the infant severe enough to require intervention and treatment. Rh E HDN is rarely found in Thailand. The purpose of this report was to present a study of the first case found in Chiang Mai of HDN due to anti-E antibody.

CASE REPORT

A 28-year-old woman, gravida 1, para 0, 37 weeks gestation gave birth to a 1,900 g female infant. She was ß-thalassemia/hemoglobin E and had been splenectomized 21 years ago. She had occasionally received blood transfusions before she was pregnant. During pregnancy, she was anemic, so packed red blood cells 1, 2, 2 and 2 units were transfused at 20, 27, 35 and 37 weeks' gestation,

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respectively. At 30 weeks' gestation, ultrasound was performed. The fetus showed intrauterine growth retardation. Non stress test (NST) was reactive. At 37 weeks' gestation, ultrasound was performed again. The fetus was termed. NST was reactive. She had no labor pain. The pregnancy was terminated by intravaginal misoprostol (Cytotec). The infant was born by normal delivery with Apgar score of 9 and 10.

Physical examination of the infant revealed asymmetrical-small-for-gestational-age. The body weight was the 8th percentile, the body length was the 15th percentile and the head circumference was the 12th percentile on gestational growth curve. The liver and spleen were not enlarged. Neither anemia nor jaundice was noted. Within the first day of life, the infant developed jaundice (total bilirubin 14.8 mg/dL, indirect bilirubin 13.6 mg/dL). The hematocrit decreased from 49 per cent to 42 per cent. The direct antiglobulin test (DAT) was positive with broad-spectrum, anti-IgG and anti-C3 reagent. The elution was not performed due to insufficient infant's red blood cells. The glucose-6-phosphate dehydrogenase (G6PD) was normal. The laboratory data after delivery are shown in Table 1.

Serological studies were performed on the blood of this family. The antibody screening of maternal serum showed strong reaction at the antiglobulin test against R_1R_2 (CDe/cDE) red blood cells but no reaction with R_1R_1 (CDe/CDe) red blood cells. At this time, a strong reactive anti-E was identified in her serum.

The ABO, Rh genotypes of the members of the family are shown in Fig. 1. The infant's blood type was group A, R_1R_2. The father and mother's blood types were group O, R_1R_2 and group A, R_1R_1, respectively. HDN due to anti-E antibody was diagnosed. Phototherapy was administered.

At 5 days old, the infant was markedly pale. The hematocrit was 30 per cent. Twenty milliliter of packed red blood cells group A, E-negative was transfused. Phototherapy was continued. On the ninth day of life, the jaundice had improved. The bilirubin declined (total bilirubin 11.3 mg/dL, indirect bilirubin 7.8 mg/dL). Phototherapy was discontinued. One day later, the hematocrit was 33 per cent. Thirty milliliter of packed red blood cells group A, E-negative was subsequently transfused. After blood transfusion, the hematocrit was 44 per cent. The infant recovered and was discharged at the twelfth day of life.

At home, the baby appeared well. No jaundice was noted. Blood tests at the age of one year revealed negative direct and indirect antiglobulin test. The mother still had anti-E in her serum with a titer of 64. The adsorption and ether elution between maternal serum and baby's red blood cells were performed. Anti-E was found in the eluate with titer 64. The eluate analysis using sandwich enzyme-linked immunosorbent assay (ELISA) revealed IgG antibody. Both the eluate and serum antibody were resistant to denaturation by 2-mercaptoethanol showing them to be IgG.

Table 1. Laboratory data after delivery.

Day of life	HCT (%)	DAT	Bilirubin (mg/dL)		G6PD	Treatment
			Total	Indirect		
0	49					
1	42	3+	14.8	13.6	normal	On phototherapy
2	41	3+	21.7	18.2		
3	36		17.0	13.3		
4	34		19.2	16.0		
5	30		16.4	11.7		PRC 20 ml
6	40		15.7			
7	36		12.1			
8	35		11.5	8.1		
9	35		11.3	7.8		Off phototherapy
10	33		11.7	8.3		
11	33					PRC 30 ml
12	44					

Hemoglobin typing of members of this family was performed. The baby's hemoglobin was AE (hemoglobin A=74%, E=26%). The mother's hemoglobin was EF (hemoglobin E=42.2%, F= 57.8%). The father's hemoglobin was normal (hemoglobin A=97.4%, A_2 = 2.6%). The hemoglobin typing of members of this family is shown in Fig. 1.

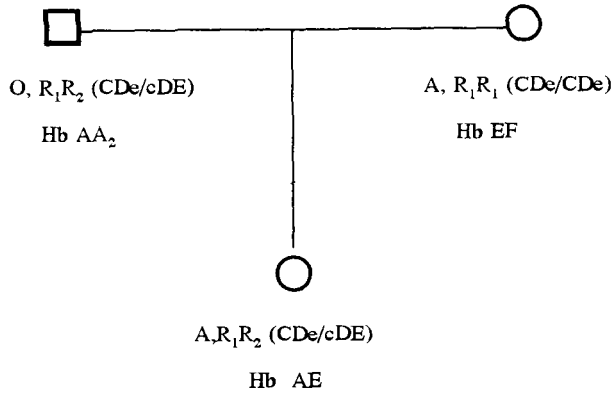

Fig. 1. The ABO, Rh genotypes and hemoglobin typing of the members of the family.

DISCUSSION

Hyperbilirubinemia in the newborn can be classified into physiologic and pathologic jaundice. The diagnosis of physiologic jaundice can be established only by excluding known causes of jaundice on the basis of the history, clinical manifestations and laboratory findings. In general, a search to determine the cause of jaundice should be made if it appears in the first 24 hours of life, serum bilirubin is greater than 12 mg/dL and serum bilirubin is rising at a rate greater than 5 mg/dL/day[1]. In our case, the baby's indirect bilirubin was 13.6 mg/dL in her first day of life. Therefore, pathologic jaundice should be considered. The G6PD was normal. The DAT was positive and maternal serum showed strongly reactive anti-E antibody. Thus, the hemolytic disease of the newbown due to anti-E antibody was diagnosed. The mother had ß-thalassemia/hemoglobin E disease and had received blood transfusion before delivery. Thus, she might be immunized to form anti-E antibody by previous transfusion.

Indirect bilirubin is neurotoxic for infants[3]. If left untreated, it can cause kernicterus or permanent damage to parts of the brain. Phototherapy is beneficial. Bilirubin in the skin absorbs light energy, which by photoisomerization converts the toxic native unconjugated 4Z, 15Z-bilirubin into the unconjugated configurational isomer, 4Z, 15E-bilirubin. The latter product is excreted in the bile without the need for conjugation. Phototherapy also converts native bilirubin to the structural isomer lumirubin, which is excreted by the kidney in the unconjugated state[1]. If HDN is severe, exchange transfusion is indicated. Removing the infant's plasma reduces the load of accumulated bilirubin and the number of unbound antibody molecules. Replacement with donor plasma restores albumin and any deficient coagulation factors. Antibody-coated cells, whose destruction would further raise the bilirubin load, are removed and replaced with red blood cells compatible with the maternal antibody. In this case, phototherapy was administered for 9 days. 50 ml of packed red blood cells group A, E-negative was transfused. The infant recovered without requiring exchange transfusion and was discharged on the twelfth day of life.

At the age of one year, the baby appeared well. DAT was negative. The mother still had anti-E in her serum. Maternal anti-E isolated by adsorption and elution was IgG. This IgG antibody may actively transport across the placenta and bind to the fetal E-positive red blood cells. The sensitized red blood cells may be destroyed by the fetal reticuloendothelial system, resulting in anemia. The hemoglobin typing of the baby was AE. The hemoglobin E trait is asymptomatic and causes no anemia[7]. So, it was not a relevant problem in this situation.

The HDN can be caused by other blood group antibodies such as anti-K, anti-Fy^a and anti-Jk^a[2,8]. Almost all IgG red blood cell antibody is capable of causing HDN. Therefore, all pregnant women with IgG red blood cell antibodies should be followed closely when giving birth to a child with HDN.

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โรคเม็ดเลือดแดงแตกในทารกแรกคลอดที่เกิดจาก anti–E

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รายงานโรคเม็ดเลือดแดงแตกในทารกแรกคลอดที่เกิดจาก anti–E ผู้ป่วยทารกเพศหญิงหมู่เลือด A, E บวกและฮีโมโกลบินเป็นชนิด E trait กำเนิดจากมารดา ซึ่งเป็นโรค ß–thalassemia /ฮีโมโกลบิน E และมีหมู่เลือด A, E ลบ ทารกมีอาการตัวเหลืองในวันแรก พบ anti–E ในซีรั่มของมารดา ทารกซีดและเหลืองมาก ได้ให้การรักษาด้วย phototherapy เป็นเวลา 9 วันและได้ให้เม็ดเลือดแดงเข้มข้น หมู่ A, E ลบ จำนวน 50 ml. ทารกมีอาการดีขึ้น และออกจากโรงพยาบาลเมื่ออายุได้ 12 วัน ได้ติดตามผู้ป่วยเมื่ออายุได้ 1 ปี พบว่าสบายดี

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