Hemolytic Disease of the Newborn Due to Anti-Jkb: Case Report and Review of the Literature

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Received: 17 August 2012 / Accepted: 20 September 2012 / Published online: 9 October 2012
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Abstract Although anti-Jkb is a well-defined cause of severe acute or delayed hemolytic transfusion reactions, it is rarely associated with severe Hemolytic Disease of the Newborn (HDN), even with high antibody titer. To date, only 13 cases have been reported, so the possible reasons for that still remain unclear. Most of HDN due to anti-Jkb are mild-to-moderate, and usually have a good prognosis. A 41-years-old woman, who had a positive antibody screening test in her 13th week of pregnancy, was sent to the blood bank for study before an amniocentesis. Antibody identification and red blood cell (RBC) phenotyping of the patient and his husband were performed, plus arrays study in the amniotic fluid. An anti-Jkb was identified in the patient's serum with a titer of 1:1, and her RBC phenotype was O Rh(D) positive, C(+), c(+), E(−), e(+), K(−), Jka(+), Jkb(−). The RBC genotype of the fetus was B Rh(D) positive, Jka(+), Jkb(+). Antibody titer remained stable and the pregnancy was uneventful. At birth, there was no need of phototherapy or exchange transfusion for the newborn and her Jk(b+) typing result was confirmed in a cord blood sample. Although most of HDN cases due to anti-Jkb have a good outcome, monitoring antibody titer should be done to prevent fatal complications. Furthermore, antenatal antibody screening should be performed in every pregnant woman irrespective of her

Rh(D) antigen status in order to detect red cell alloimmunization to other clinically significant blood group antigens.

Keywords Hemolytic · Newborn · Anti-Jkb · Kidd · Anemia · Pregnancy

Introduction

The primary system Kidd antigens (Jka and Jkb) play a key role in urea transport through the membrane of red blood cells (RBC) [1]. They are present in Kidd proteins, which are codified by codominant alleles of a gene expressed in erythrocytes, endothelial cells and other tissues. In 1951 Allen et al. [2] discovered the antigen Jka in a pregnant woman without transfusion history who delivered a newborn with mild hemolytic disease. The first case of alloimmunization during pregnancy by anti-Jkb was described 2 years later, in 1953, by Plaut et al. [3]. The frequency of both antigens is high in Caucasian population (77 % for Jka and 72 % for Jkb). Approximately 20–29 % of caucasian and asian population have the Jk (a+b−) phenotype. Moreover, people with phenotype Jk (a−b−) are usually Asiatic. Kidd antibodies are usually IgG, which means they are capable of going through the placenta and bind the complement, producing hemolysis both intra and extravascular. They are not always detected by the routine techniques due to their tendency to decrease after the antigenic stimulus ends (52 % of the anti-Jk antibodies disappear within first months after exposure) [4]. This is the reason why they may produce severe immediate or delayed hemolytic transfusion reactions because of a strong anamnestic response in subsequent re-exposure to similar antigen positive RBC. This occurs even when antibody levels are undetectable. Then, the alloimmunized individuals should be continued on lifelong transfusions of antigen-negative blood.

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Table 1 Summary of immunohematologic data of present case

Pregnant (February 2011)		Husband (February 2011)	
ABO/Rh(D) bloodtype	O positive	ABO/Rh(D) bloodtype	B positive
Antibody screening	Positive	Antibody screening	Negative
Direct antiglobulin test	Positive (2+)	Rh/Kell phenotype	C+, E–, c–, e+, K–
IgG	Positive	Jk system phenotype	Jka(–), Jkb(+)
C3d	Negative	Amniotic fluid (February 2011)	
Antibody identification	Anti-Jkb, Anti-I	Jk system phenotype	Jka(+), Jkb(+)
Antibody titer:		Newborn cord blood (August 2011)	
Anti-Jkb: 1/1 against Jka–, Jkb+ RBC in liss/coombs		ABO/Rh(D) bloodtype	B positive
Anti-I: 1/32 against adult bloodtype O RBC at 4 °C		Direct antiglobulin test	Negative
Rh/Kell phenotype	C+, E–, c+, e+, K–	Eluate	Negative
Jk system phenotype	Jka(+), Jkb(–)	Jk system phenotype	Jkb(+)

Case Report

We report a case of a 41-years-old healthy pregnant woman, gravida 3, para 2 who was sent to the blood bank for study because of a positive antibody screening test. She had no history of any blood derivatives transfusion. None of her two previous children presented data of hemolytic disease. Her husband was healthy and unrelated. Patient's bloodtype was O Rh(D) positive and routine antenatal antibody screening (Serascan Diana2, Grifols®, Barcelona, Spain) performed in 13th week of gestation was positive [cell I (–) and cell II (++)]. The direct antiglobulin test (DAT) on mother's RBC (DG Gel DC Scan cards, Grifols®, Barcelona, Spain) was positive (2+) with polyspecific antihuman globulin (anti-IgG and anti-C3d, BioClone®, Marrickville, Australia) and with monoclonal anti-IgG, but not with anti-C3d antihuman globulin. Maternal serum was tested against two commercial panels, of 11 and 16 RBC, both with known antigenic determination (Identisera Diana/Extend, Grifols®, Barcelona, Spain). Most cells were positive with this method, so the antibody could not be identified certainty. Then, a new patient blood sample was sent to Regional Transfusion Centre of Madrid (RTCM) to complete the study, since a positive DAT interferes with the antibody identification. An antibody against Jkb was identified with anti-human globulin titer of 1:1, using Liss/Coombs cards and commercial panels with 10 RBC (Bio-Rad®, Hercules, California, USA) and 20 RBC (Immucor®, Norcross, Georgia, USA). An additional antibody anti-I (titer 1/32) was also identified when patient's serum was tested against O bloodtype RBC incubated at 4 °C (with no clinically significance) (Table 1). All these findings were confirmed by genetic methods, concluding that the patient's erythrocytes phenotype was group O, D + C + c + E – e +, K– and Jkb–. Father's RBC phenotype was B, Rh(D) positive and Jk(a–b+). Moreover, an Arrays Blood-Chip test was performed in amniotic fluid of the

newborn, whose RBC extended typing showed blood group B, Rh(D) positive and Jk(a+b+).

Follow-up was continued and anti-Jkb titer remained low during whole pregnancy. No data of anemia were noted in the fetus, thus no intrauterine transfusion was required. At August 10th of current year, our patient delivered a female infant after 40 weeks gestation. Her weight was 3.15 kg. The baby had no complications at birth and she was a normal full-term infant, without jaundice or data of hemolysis.

Bloodtype B Rh(D) positive and phenotype Jkb+ were confirmed in cord blood sample, with DAT and eluate negatives.

Forty eight hours after birth total serum bilirubin was 8.6 mg/dL. No data of haemoglobin or reticulocytes were available. Neither phototherapy nor exchange transfusion was needed, and the newborn as well as her mother were discharged 2 days after birth. The patient gave her informed consent prior to her inclusion in the study.

Discussion

The most common route of sensitization against Kidd antigens is via blood transfusion. Antibodies are usually IgG able to cross the placenta, bind complement and produce rapid either intravascular and/or extravascular hemolysis. In those fetal RBC-maternal blood contact cases, the sensitization is rare but possible.

The vast majority of cases of fetomaternal incompatibility are due to ABO sensitization, although most of severe HDN are produced by anti-RhD. The proportion of cases that has been caused by Kell, Duffy, Kidd and other systems is just around 3 % [5–11]. Kidd antigens can be detected from the 7th week of gestation and are well developed at birth. When alloimmunization occurs it can potentially lead to a HDN which usually has a mild clinical course and a good outcome.

Table 2 Summary of the clinical and laboratory findings in published anti-Jkb incompatibility cases

	Kornstad et al.	Geczy et al.	Wagman et al.	Zodin et al.	Lange et al.	Kim et al.	Merlob et al.	Tomar et al.	Park et al.	Kim et al.	Ferrando et al.	Thakral et al.	Present case
GA (weeks)	41	Full-term	37	Full-term	Full-term	38	38	Full-term	37	37	25	37	Full-term
Onset of jaundice (hours)	4	Early (?)	2	Early (?)	NM	24	Birth	30	24	Early (?)	Birth	10	None
Day of peak T-bilirubin (day)	2	2	1	2	1	3	2	2	4	4	NM	2	2
Peak T-bilirubin (mg/dL)	10,3	9	4,9	8,4	8	24,5	16,8	14,4	24	46,1	NM	18,1	8,6
Hemoglobin (g/dL)	12	14,8	21,2	NM	17	13,1	12,4	18,8	9,7	11,4	NM	NM	12,3
Hematocrit (%)	NM	NM	61	60,5	NM	39	37,4	NM	28,1	36,8	NM	50	37,1
Reticulocyte (%)	6,4	4,6	NM	NM	NM	5,8	6,7	6	5	14,9	NM	10,42	NM
Treatment	None	None	None	None	None	PT	PT + TF	NM	PT	PT + ETF	TF	PT	None
Outcome	Good	Good	Good	Good	Good	Good	Good	Good	Good	Fatal	Fatal	Good	Good
Gravida-para	5-4	2-1	3-3	5-4	NM	1-0	3-3	4-3	2-1	4-2	4-3	7-0	3-3
Previous HDN siblings	2nd child	None	NM	None	NM	None	2nd child	None	None	Suspected 1st and 2nd child	None	Suspected 1st	None

GA gestational age, NM not mentioned, PT phototherapy TF transfusion, ETF exchange transfusion

There are only thirteen cases of anti-Jkb related HDN reported in medical literature (Table 2) [12–23]. Most of them (76.92 %) were mild and the newborn required either phototherapy (4 cases: 30.76 %) or no treatment at all. Only Merlob's case needed red blood cell transfusion. Despite of these data, 2 cases (15.38 %) had a fatal outcome. One of them developed hidrops fetalis and intra-uterine death [21], and the second one died of acute renal failure 4 days after birth in spite of intensive treatment with exchange transfusion and phototherapy for 3 days [17].

Our case differs from other good outcome cases on the absence of signs of hemolysis in the newborn. Unlike other reported cases, our patient's previous pregnancies were uneventful and her children had no jaundice at birth. Furthermore, antibody screenings were always negative until current gestation, so the certain moment of sensitization cannot be determined. Given the potential clinical significance of Kidd antibodies, periodical titer determinations were performed in our patient with the purpose of detecting the onset of fetal anemia early and performing intrauterine transfusion if necessary.

Although HDN of anti-Jkb incompatibility generally shows mild clinical symptoms and a favourable prognosis, severe anemia and hidrops fetalis can occur. Because of that antibody titer monitoring should be performed in every alloimmunized pregnant, and a high-risk-pregnancy management by an expert consultant is recommended.

We consider routine antenatal antibody screening as an essential strategy to be carried out in every pregnant woman, irrespective of her Rh(D) phenotype, in order to detect red cell alloimmunization to other clinically significant blood group antigens such as Kidd, Duffy or Kell.

Conflict of interest The authors of this article have no conflict of interest.

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