Brief Comunication

Anti-Lewis alloimmunization: report of seven cases

L.M.M. Nardozza, G.R. Lobo, A.F. Moron, L. Camano, E. Araujo, Jr., H.A. Guimarães Filho

Fetal Medicine Sector, Obstetrics Department, São Paulo Federal University-Paulista Medical School (UNIFESP-EPM), São Paulo (Brazil)

Summary

Objective: The purpose of this study was to investigate the perinatal results of seven pregnant women with anti-Lewis antibodies and evaluate the need to screen for these antigens during routine prenatal care. *Setting:* São Paulo Universtity Hospital, São Paulo, Brazil. *Population:* 200 Rh-negative pregnant women with a positive indirect Coombs test, managed during a 6-year period. *Methods:* The charts of all patients were reviewed to collect pertinent data and the variables were analyzed. *Main outcome measures:* Indirect Coombs test titer, intrauterine transfusion, mode of delivery, gestational age at birth, birthweight, neonatal transfusion, duration of neonatal hospitalization and perinatal mortality. *Results:* All newborn infants were classified as adequate for gestational age at birth and none needed intrauterine or neonatal transfusions. All infants, except one, were discharged in good health on the third day after birth. *Conclusions:* Alloimmunized pregnancies (Levis antigens) have good perinatal results.

Key words: Anti-Le^a; Anti-Le^b; Alloimmunization in pregnancy; Antenatal screening; Hemolytic disease of the newborn.

Introduction

Red cell alloimmunization is an immune disorder caused by incompatibility between maternal and fetal red blood cell antigens [1]. Due to its high prevalence and immunogenicity, D-antigen incompatibility is the most frequent cause of significant perinatal hemolytic disease (PHD).

However, red blood cells have over 300 other surface antigens and at least 43 of these are capable of producing hemolytic disease [2]. The following blood group system (and antigens) are the most frequently associated with PHD: Rh (D, C, E, c, e, f, Cw), Kell (K, k-celano, Kp^a, Kp^b, Js^a, Js^b), MNS (M, N, s, S), Kidd (JK^a, JK^b), Duffy (Fy^a, Fy^b) and Lutheran [3]. The Lewis system is represented by two red cell antigens: Le^a and Le^b. Since most species of anti-Lewis antibodies are exclusively immunoglobulin M (IgM), which cannot cross the placenta, they rarely cause perinatal hemolytic disease (PHD) [4].

In Brazilian laboratories, when the indirect Coombs test is positive, the patient's serum is routinely tested using a panel of antigens which include the following systems: Rh: (D, C, E, c, e, f, Cw, variants), Lewis (Le^a, Le^b), Kell (K, k (celano), Kp^a, Kp^b, Js^a, Js^b), MNS (M, N, s, S), Kidd (JK^a, JK^b), Duffy (Fy^a, Fy^b), Diego (DI, Di^a, Di^b). While it is scientifically correct to try to identify exactly the specific antibodies present in the maternal blood, for clinical practice, only the detection of antibodies capable of producing hemolysis would be relevant. Motivated by the economic aspects of this question, we decided to study the prevalence of women sensitized to the Lewis system in our obstetric population and review the perinatal results of these pregnancies.

Revised manuscript accepted for publication January 25, 2008

The purpose of this study was to investigate the perinatal results of seven pregnant women with anti-Lewis antibodies and evaluate the need for screening of these antigens during routine prenatal care.

Methods

This was a retrospective observational descriptive study of all (200) Rh-negative pregnancies with a positive indirect Coombs test managed at the Prenatal Unit of São Paulo Federal University (UNIFESP-EPM) during a 6-year period (2000-2005). These 200 pregnant women with a positive Indirect Coombs test were screened for Rh system antibodies and also for others red cell antibodies. In 15 of these women, other red cell antibodies were detected: seven Lewis, three MNS, three Kell and two Diego.

The charts of patients with anti-Lewis antibodies were reviewed and the following information was collected: indirect Coombs test titer, intrauterine transfusion, mode of delivery, gestational age at birth, birthweight, neonatal transfusion, duration of neonatal hospitalization and perinatal mortality. The study was approved by the Ethics Committee of the São Paulo Federal University (protocol no. 1407/05).

Results

Table 1 presents the results of the seven patients. All newborn infants were classified as adequate for gestational age at birth and none needed intrauterine or neonatal transfusions. All infants, except case 7, were discharged in good health on the third day after birth.

Discussion

The relative frequency of non-D alloimmunized pregnant patients has been rising in the last decades. A large study involving over 18,000 pregnant women reported 1.6% (299) had irregular antibodies. In this study, there were seven pregnant women sensitized to the Lewis antigens in a group of 200 Rh-negative pregnant patients managed at our tertiary center over a 6-year period [3].

Table 1. — *Perinatal results of seven pregnant women with anti-Lewis antibodies.*

Case	Indirect Coombs titer	MCA Doppler	Delivery	GA (weeks)	Weight (g)	Apgar score (1st and 5th minute)
1	1/8	Normal	Vaginal	38	3440	9/10
2	1/2	Normal	C section	40	3660	7/9
3	1/8	Normal	Vaginal	37	3510	8/10
4	1/4	Normal	C section	38	2890	9/9
5	1/4	Normal	Vaginal	39	3600	9/10
6	1/8	Normal	C section	38	3350	9/9
7*	1/8	Normal	Vaginal	25	650	–

MCA: middle cerebral artery. GA: gestational age.
* Fetal death at 25 weeks.

Anti-E antibodies are the most common cause of non-D alloimmunization in pregnancy. In a retrospective study (1959 to 2004), Joy *et al.* [5] identified 283 pregnant patients with anti-E antibodies, 32 of them at risk for PHD. According to these authors, five of the 16 cases with indirect Coombs titers > 1:32 needed intrauterine or neonatal transfusions and there was one case of fetal hydrops and one perinatal death attributed to the anti-E antibodies. Additionally, two cases with titers > 1:32 had elevated middle cerebral artery peak systolic velocity.

There are no reports of PHD related to anti-Lewis alloimmunization. This may be attributed to two factors: most red blood cells express this antigen only after birth and most, if not all, antibodies against these antigens are IgM, which do not cross the placenta. In this study, as expected, the women with anti-Lewis antibodies had excellent perinatal results, with normal healthy infants who did not need transfusions.

The only fetal death was unrelated to anti-Lewis sensitization and occurred in a patient who had lost a previous child due to severe muscular dystrophy.

In summary, we believe this study contributed to reinforce the argument against ordering anti-Lewis antibody screening in routine prenatal care. This is especially true in developing countries, such as Brazil, where public health resources are limited and the money spent on this exam could be used in other more relevant tests to identify significant maternal and fetal disorders.

References

[1] Choavaratana R., Uer-Areewong S., Makanantakosol S.: "Feto-maternal transfusion in normal pregnancy and during delivery". *J. Med. Assoc. Thai*, 1997, *80*, 96.
[2] Moise K.J. Jr.: "Non-anti-D antibodies in red-cell alloimmunization". *Eur. J. Obstet. Gynecol. Reprod. Biol.,* 2000, *92*, 75.
[3] Smith B.D., Haber J.M., Queenan J.T.: "Irregular antibodies in pregnant women". *Obstet. Gynecol*., 1967, *29*, 118.
[4] Beal R.W.: "Non-rhesus (D) blood group isoimmunization in obstetrics". *Clin. Obstet. Gynaecol*., 1979, *6,* 493.
[5] Joy S.D., Rossi K.Q., Krugh D., O'Shaughnessy R.W.: "Management of pregnancies complicated by anti-E alloimmunization". *Obstet. Gynecol*., 2005, *105,* 24.

Address reprint requests to:
L.M.M. NARDOZZA, M.D.
Av. Lopes de Azevedo, 888
Morumbi
05603-001 São Paulo, SP (Brazil)
e-mail: lunardozza@ud.com.br