CASE REPORT

High Coombs Test Titers With No Fetal Anemia: Value of Middle Cerebral Artery Peak Systolic Velocity

Juan **PIAZZE**[1], Albana **CEREKJA**[1], Antonella **GIANCOTTI**[1], Anna **CASADEI**[2], Renato **LA TORRE**[1], Ermelando **COSMI**[2]

[1]*Institute of Gynecology, Perinatology and Child Health, Policlinico Umberto I, Rome, Italy*
[2]*Department of Pediatrics, Policlinico Umberto I, Rome, Italy*

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Abstract

Maternal Rh antibody titers increased progressively in a 26-years old black woman at her 4th pregnancy, but the stable and low middle cerebral artery peak systolic velocity (MCA PSV) suggested that the fetus did not develop anemia. Hemolysis did not occur. This case describes the ability of the MCA PSV in reflecting the not crossing-over of maternal antibodies to the fetus, even in the presence of high maternal anti-D antibodies titers.

Keywords: alloimmunization, fetal anemia, middle cerebral artery peak systolic velocity

Özet

Yüksek Coombs Test Titreleri Varlığında Orta Serebral Arter Maksimum Sistolik Akım Hızının Fetal Anemiyi Belirlemedeki Değeri

Yirmi altı yaşında zenci bir kadının 4. gebeliğinde maternal Rh antikor titrelerinin artmasına rağmen, tutarlı ve düşük orta serebral arter maksimal sistolik akım hızı (MCA PSV) fetuste anemi oluşmadığına işaret etmiştir. Hemoliz oluşmamıştır. Bu vaka, maternal anti-D antikor titresinin yüksekliğine rağmen, MCA PSV'nin maternal antikorların fetuse geçmeyiş yetisini yansıtmaktadır.

Anahtar sözcükler: alloimmünizasyon, fetal anemi, orta serebral arter maksimum sistolik akım hızı

Introduction

The fetus expresses Rh antigens on the red blood cells virtually as early in gestation as these are present. Once exposed, the mother mounts a competent antibody response against the fetal red blood cell antigens. With a first immune exposure to a given antigen, a primary immune response follows, in the form of the immunoglobulin M (IgM), which does not cross the placenta. The second exposure to that antigen results in the mature immune response. A sensitized woman is one with a detectable antibody. When this antibody is immunoglobulin G (IgG), it readily cross the placenta, as early as 10 weeks, and can cause fetal disease. As the antibody binds fetal red blood cells in circulation, it triggers fetal reticuloendothelial system digestion. With worsening anemia, the fetus compensates by maximising red blood cells production in the liver, spleen, intestinal wall and other sites to a minor extent, mediated by fetal erythropoietin. Amniotic fluid spectrophotometry (ΔOD_{450}) correlates with the amount of bilirubin present. Since bilirubin is the endproduct of fetal disposal of the waste products of hemolysis, amniotic fluid bilirubin estimation gives information on the amount of hemolysis degree, and therefore on fetal anemia degree. Bilirubin can be quantitated most accurately by spectrophotometric measurements of the optical density between 420-460 nm, the wavelength absorbed by bilirubin. Amniocentesis with ΔOD_{450} evaluation provides ongoing reassurance that more invasive fetal testing is not yet necessary but rarely may provide false reassurance (1). Ultrasound examination represents an important tool on the evaluation of the alloimmunized fetus. Anemia does not appear to bear any pathognomonic fetal physical signs, and a serious degree of fetal anemia may be present without frank

Corresponding Author: Dr. Juan Piazze
V.le Regina Elena, 324 00161 Rome, Italy
Phone : +39 63 938 73 55
E-mail : jjpiazze2000@hotmail.com

hydrops (2,3). Additional information is provided by Doppler ultrasound. The circulation of the anemic fetus is hyperdynamic. In anemia the blood viscosity decreases and the blood velocity increases (4). A marked increase in peak systolic velocity (PSV) of the thinner fetal blood has been documented in almost all fetal vessels detected by Doppler. Originally described in umbilical arteries, the correlation between severity of anemia and degree of Doppler anormality in the descending aorta, middle cerebral artery (MCA) and precordial veins has been clinically significant. MCA is short and straight, the Doppler angle (a zero degree angle between the ultrasound beam and the direction of blood flow) can be standardized easily and the measurement has low observer-dependent variation (5). In 1995, Mari et al. published the curve of MCA PSV (cm/s) plotted as a function of gestational age (GA) and subsequently the risk zones of fetal anemia (A, B, C, D) according to which an established follow up is recommended. In 1997 they reported that the trend of MCA is at least as effective as the Δ optical density at 450 nanometers (ΔOD_{450}) to predict fetal anemia (6) but the assesment of MCA is less expensive and less invasive than amniocentesis.

In this case, increasing anti D antibody titers were not associated to fetal anemia, manifesting with normal MCA PSV in the intrauterine life and with normal red blood cells counts, hemoglobin and bilirubin after birth.

Case

The mother was a 26-years-old African woman from Ivory Coast at her 4th pregnancy. Obstetrical history included a spontaneous delivery in 1996 at 30 week's gestation who died 9 hrs after birth for imprecise cause, a spontaneous abortion in 1999 at 8 weeks and a cesarean section at term in 2000 (blood group ABO and Rhesus positive, birthweight 2870 g) affected by anemia due to alloimmunization who underwent exchange transfusion and phototherapy. Only in last pregnancy anti Rh prophylaxis was administrated. At present pregnancy complete data regarding blood group of both fetus mother and father were obtained. Mother: group B, Rhesus negative, phenotype rhesus Ccddee, Du negative, Kell Ag negative; Father: group 0, Rhesus positive, ccDdee, K negative.

The indirect Coombs test was performed monthly at the Hematology Service and the anti-D antibody titer resulted repeatedly with 1:8 until 20 week's gestation. At 26 week's the titer increased to 1:128. It was decided to evaluate the MCA PSV. The measurements were performed by a single physician, with insonation angle <10° in both MCAs, and after a minimum of 15 minutes required for the analysis, the MCA PSV was related to a mean of five measurements (Figure 1). At 29 week's gestation the patient was admitted to our Department. There was evidence of regular fetal growth (50°-75° percentile) and normal amniotic fluid volume; and MCA PSV was at 34 cm/sec. This value was compared with the MCA PSV curves (5) and corresponded to the D risk zone (low risk) for fetal anemia suggesting repeat evaluation after 2-3 weeks. It was repeated weekly because of increasing anti D antibody titers (1:128 at 26 weeks, 1:256 at 28 weeks, 1:512 at 29 weeks). The MCA PSV was 40-43 cm/sec at 30 weeks, 44-53 cm/sec at 31 weeks, 44-46 cm/sec in repeated evaluations at 32 weeks and 43-47 cm/sec at 33 weeks, thus, remaining always in the D risk zone. The patient was discharged and monitored as outpatient. Doppler velocimetry at 34 weeks and 4 days showed oligohydramnios. Despite the elevated anti D antibody titer was stable at 1:512, the MCA PSV was still 47 cm/sec. On the same day, five fetal heart rate traces were performed with evidence of low variability and late decelerations after low intensity uterine contractions. Cesarean section was performed the next morning, at 34 weeks and 5 days due to fetal heart rate alterations. A male of 2430 g and with a 8/9 Apgar score at 1st and 5th minutes was born. The newborn presented a blood ABO 0 and positive Rhesus and a direct Coombs test ++++ (titer 1:256). However, neonatologists did not report anemia findings at all (hemoglobin 17.5 g/dl, hematocrit 54.3%, erythroblasts 50% of the nucleated cells, bilirubin 3.4 mg/dl). The neonate was discharged one week after caesarean section and after continuous hematologic evaluations. A control evaluation after one month showed again good neonatal conditions and blood analysis confirmed no signs of neonatal anemia.

Discussion

In every Rh D negative pregnant woman, anti-D antibodies, if present, can be revealed by the indirect Coombs test. Because of factors such as the Rh antibody binding constant or avidity of the antibody for the antigen in the red blood cells membrane, and therefore its ability to produce hemolytic disease, the amount of Rh antigen in the red blood cell membrane and the ability of the fetus to maintain adequate circulating red blood cell hemoglobin varies. There exists a relatively poor correlation between blood group antibody titrations and severity of hemolytic disease. The antibody titer below which there is no risk for hydrops fetalis or stillbirth before term is conventionally 1:16. In the case presented here, an anti-D antibody titer at 1:128 prompted the decision to perform MCA PSV evaluation since it has the same effectiveness as ΔOD_{450} (6). The MCA PSV values measured weekly matched with the D low risk zone, indicating that the fetus was not anemic. All ultrasound examinations were normal. At third trimester evaluation, evidence of moderate oligohydramnios followed by fetal heart rate trace alterations were found. All ultrasound and fetal heart rate recordings were not related to maternal alloimmunization. Why the fetus did not develop anemia despite the high maternal anti-D antibody titer remains open. Possibly the maternal anti-D antibodies did not cross-over with fetal Rh antigens in the fetal circulation. Maternal Rh antibody titers increased progressively but

the stable and low MCA PSV suggested that the fetus did not develop anemia. Therefore, it was concluded that hemolysis did not occur. In fact, the newborn presented normal hemoglobin and bilirubin values. However, this is just a hypothesis that may just help us to explain and understand why the newborn did not develop anemia. Late decelerations of the heart rate are not related to hematological conditions since they appeared after uterine contractions in the environment of a non-reactive fetal heart trace monitoring.

This case describes the ability of the MCA PSV in reflecting the not crossing-over of maternal antibodies to the fetus, even in the presence of high maternal anti-D antibodies titers.

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