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Case Report

Intraperitoneal and intracardiac transfusion of recurrent fetal erythroblastosis due to anti-M alloimmunization with unfavorable outcome

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Abstract

Objective: To present intensive intrauterine treatment of recurrent early onset fetal erythroblastosis due to anti-M alloimmunization.
Case Report: A 33-year-old woman, gravid 3, para 1, had anti-M IgG antibody, which caused alloimmunization of her previous pregnancies. This time she visited our hospital for intensive intervention. No evidence of fetal hydrops was found during ultrasound examination at 12 weeks of gestation. Plasmapheresis was given from 17 weeks of gestation but fetal erythroblastosis still developed 1 week later. Two intraperitoneal transfusions and one intracardiac transfusion were given within three days but fetal erythroblastosis still progressed to fetal bradycardia and occasional asystole. Epinephrine resuscitation could only temporarily improve the fetal heart rate and fetal death was inevitable.
Conclusion: Serial measurements of fetal middle cerebral artery peak systolic velocities, advanced plasmapheresis, intrauterine blood transfusion, and, if needed, intravenous immunoglobulin supplement, may be the appropriate treatment for early onset fetal erythroblastosis resulting from alloimmunization.

Keywords: anti-M alloimmunization; fetal erythroblastosis; hydrops fetalis; intracardiac transfusion; intraperitoneal transfusion; plasmapheresis

Introduction

Most cases of fetal erythroblastosis are caused by Rhesus alloimmunization, which was firstly reported by Levine et al in 1941 [1]. Maternal prophylaxis with RhoGAM successfully decreases the incidence of erythroblastosis fetalis. However, there are still some other blood-type incompatibilities, such as Kell, Duffy, Kidd, and the MNS system, that may be the cause of fetal erythroblastosis but are without treatment consensus. Antibodies with anti-M specificity, usually IgM, have been reported to be detected in 10% of pregnant women with a positive antibody screen. However, 0.01% to 0.7% of pregnant women would trigger anti-M IgG that can cross the placenta, resulting in variable degrees of hemolysis in fetuses [2,3]. Only sporadic cases of anti-M isoimmunization have been reported during past few decades. We report a case of recurrent early-onset fetal erythroblastosis due to anti-M alloimmunization that was treated with fetal intraperitoneal and intracardiac transfusion but still resulted in intrauterine fetal death.

Case report

The patient was a 33-year-old female. Her first male baby was born at 40 weeks gestational age complicated with cardiomegaly and congenital hemolytic disease of the newborn and who became healthy after blood transfusion 3 years before this admission. Serological tests of congenital infection including pavovirus B19, toxoplasma, cytomegalovirus, rubella, and herpes simplex were all negative. An irregular anti-M antibody (IgG) was identified by antibody screening

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test of the newborn. In addition, a positive Kleihauer-Batke test revealed evidence of fetal–maternal hemorrhage. Thus, the subsequent hemodynamic changes of the newborn were caused by anti-M alloimmunization. Plasmapheresis and intravascular transfusion via cordocentesis were planned for the patient's second pregnancy. However, the pregnancy ended in unexpected early-onset hydrops with intrauterine fetal death at gestational age 18 weeks 1 year before this admission.

This third pregnancy received combined care by obstetric and hematologic physicians. The treatment plan was thoroughly explained to the patient and her family. The first trimester nuchal translucency examination at gestational age 12 weeks did not disclose any hydropic sign (Fig. 1). Plasmapheresis starting from 17 weeks' gestation was advised by hematologic physicians, with the frequency depending on the level of antibody titer. The anti-M IgG antibody titer decreased from 1:32 to 1:8 thereafter. However, hydrops fetalis developed 1 week later. Gestational age prior to 20 weeks made it difficult to gain fetal intravascular access for transfusion. A 20-gauge needle was placed into the fetal hydropic abdominal cavity for slowly transfusion of 5 mL donor blood under direct ultrasound guidance with informed consent. Care was taken to avoid the liver and the kidneys. Three days later, at gestational age 19 weeks and 2 days, the hydrops fetalis progressed to generalized skin edema, pericardial effusion, pleural effusion, and massive ascites (Fig. 2). Fetal heart rate decreased to 100 beats/minute. Fetal blood was obtained by cordocentesis. The fetal hemoglobin concentration and hematocrit were 1.1 g/dL and 3.2%, respectively, indicating severe anemia. Attempts to perform an intravascular transfusion were unsuccessful. Afterwards, intrauterine intraperitoneal/intracardiac transfusion of 7 mL and 17 mL donor blood were given urgently. Intravenous immunoglobulin (1 g/kg/day) was also given. Persistent fetal bradycardia and occasional asystole were temporarily improved after serial intracardiac 0.1 mL epinephrine (1:10,000) resuscitation; however, intrauterine fetal death 3 hours later was inevitable.

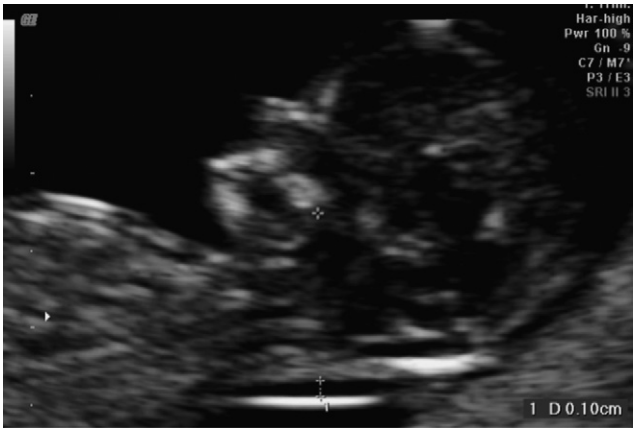

Fig. 1. Ultrasound picture for measurement of nuchal translucency at gestational age 12 weeks. There was no evidence of fetal erythroblastosis at this time.

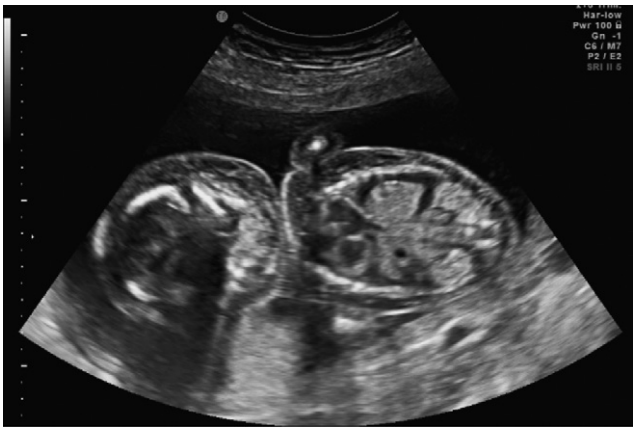

Fig. 2. Ultrasound picture at gestational age 19 weeks, showing fetal generalized skin edema, pericardial effusion, pleural effusion, and massive ascites.

Discussion

Antigen M incompatibility between mother and fetus is an extremely rare cause of red-cell alloimmunization. Considering the low frequency of anti-M alloimmunization, routine prenatal screening of anti-M antibody is unnecessary.

Fetal surveillance using either middle cerebral artery peak systolic velocity measurements or fetal hemoglobin results obtained by fetal blood sampling is important for management of alloimmunized pregnancies. Intravascular routes, superiority to intraperitoneal route for blood transfusion has been demonstrated in a previous case-controlled study [4], but the route of treatment prior to 20 weeks' gestation is limited by technical aspects. Hence early-onset fetal hemolytic disease continues to be a challenging clinical entity.

Von Kaisenberg et al treated a hydropic monochrionic twin by both intraperitoneal and intracardiac transfusions [5], However, Lewis et al reported that hydropic fetuses were unable to absorb red cells from their peritoneal cavity [6]. To overcome this, early intraperitoneal transfusion before there is evidence of erythroblastosis fetalis should be a better way for treatment of early-onset isoimmunized pregnancies. David et al reported five cases experience of serial intraperitoneal transfusion starting before the onset of hydrops and continuing until 20 to 22 weeks of gestation and all of them had favorable prognosis [7].

An alternative route to the fetal intravascular space is by direct puncture of the fetal heart, but this is potentially dangerous. Six patients with pregnancies of 19 to 31 weeks' duration displaying evidence of erythroblastosis fetalis were treated with a total of 25 times with fetal intracardiac blood transfusions. The live birth rate was 66.7% [8]. Complications included bradycardia, asystole, and hemopericardium. However, the fetal cardiac structure cannot be clearly identified before 18 weeks of gestation. We cannot convince ourselves to use a potentially high-risk procedure to treat the fetus before hydrops develop. Intracardiac transfusion should be preserved as a second-line treatment of choice.

Van Kamp et al illustrated an overall intrauterine therapy procedure-related fetal loss rate of 5.6% [9]. It should be higher

when performed before 20 weeks' gestation, which gives us a reason to search for a noninvasive treatment for the fetus in these circumstances. Most experiences and reports are from treatment of patients with Rh alloimmunization. Plasmapheresis aims to decrease the target antibody titer by direct plasma replacement. Intravenous immunoglobulin (IVIG) blocks the Fc receptors of the fetal reticulo-endothelial system, thereby reducing the degree of phagocytosis of sensitized fetal red cells. Both plasmapheresis and IVIG have been utilized individually for their effect of prolongation of gestation prior to the need for intrauterine therapy. Combined plasmapheresis and IVIG therapy has also been utilized in a variety of antibody-mediated diseases. Only 16 patients have been reported in the literature using combined treatment in maternal red cell alloimmunization, and all had favorable outcome [10−12]. The dosage of IVIG is 1 g/kg, and administration interval ranged from 3 times/week to every 20 days according to the patients' antibody titer. The cost of IVIG is extremely expensive, and cost-benefit efficiency requires a further larger study evaluation.

In summary, anti-M alloimmunization was the cause of our case's fetal hemolytic anemia and intrauterine fetal death. Although the highest anti-M IgG titer was only 1:32, the fetal erythroblastosis still appeared too rapidly and we were caught unawares. Based on the previous reports and literature reviews, combined treatment of plasmapheresis, IVIG, and intrauterine blood transfusion may have been appropriate for our patient. Plasmapheresis may start as soon as possible right after pregnancy is confirmed to lower the anti-M IgG titer. Serial ultrasonograhic examinations every 1 to 2 weeks and measured middle cerebral artery Doppler peak systolic velocities can provide us more information about fetal hemodynamic status. Treatment should be given before the onset of hydrops with serial intraperitoneal transfusion and continuing until 20 to 22 weeks of gestation when intravascular transfusion is feasible. IVIG can also provide an additional protection, but the cost-benefit efficiency should be discussed with the patient and her family. Intracardiac blood transfusion may be associated with potentially severe complications and should be reserved until previous methods failure.

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