

A case of D alloimmunization in pregnancy: successfully treated solely with therapeutic plasma exchange (TPE)

This article was published in the following Dove Press journal:
Journal of Blood Medicine

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Abstract: One of the most common causes of fetal anemia is red cell alloimmunization. The standard treatment in fetuses with anemia is intrauterine transfusion (IUT); but this approach may have adverse effects, or sometimes it is not available or even possible. Therefore, immune modulating approaches such as therapeutic plasma exchange (TPE) and the use of intravenous immunoglobulin should be implemented to avoid or delay IUT. We report here the successful management of a case of D alloimmunization in pregnancy solely with TPE, without the need for IUT. The patient was a 33-year-old G4, L2, and D1, who had a history of alloimmunization in her previous pregnancy. TPE was initiated at 17 weeks gestation and was repeated weekly. Altogether, 20 times of plasma exchange were performed and a normal fetus was delivered at week 37.

Keywords: alloimmunization, therapeutic plasma exchange, hemolytic disease of the newborn

Case presentation

The patient was a 33-year-old G4, L2, and D1. Her blood type was A RhD negative, and the blood group of her husband was known to be A, Rh (D) positive. Her first pregnancy produced a healthy female infant, delivered at the 38th week of gestation by natural delivery. Her second pregnancy produced a healthy male infant, delivered at the 38th week by natural delivery. Her third pregnancy had been terminated at the 35th week of pregnancy by cesarean section due to severe preeclampsia. The newborn died a few minutes afterbirth because of hydrops fetalis. There was no history of blood transfusion or blood product exposure. She had never received anti-D immunoglobulin and she was unaware of the blood groups of her two first children.

In her fourth pregnancy, the Nuchal Translucency ultrasound and the anomaly scan were both normal. Due to bad memories of her unfortunate previous pregnancy, she was referred to perinatologist for further management of her pregnancy. The indirect combs test was positive. D alloimmunization was detected in this pregnancy, with a corresponding Rh (D) titer of 1:128 at 17 weeks of gestation.

Fetal ultrasound examinations and Doppler study of middle cerebral artery (MCA) was normal at 17 weeks of gestation, so therapeutic plasma exchange (TPE) was initiated and then repeated weekly. Plasma exchange (PE) was performed by HAEMONETICS PCS2, Model NO, 6002 (400 Wood Road, Braintree,

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Massachusetts 02184, USA) by peripheral venous access. During PE, in each procedure 500 cc plasma (250 cc twice) was removed and was replaced by 0/9% normal saline. The anticoagulant used was 4% sodium citrate. Fetal heart rate was monitored before and after the procedure. The patient was placed in lateral position, especially in the third trimester. She was controlled with Doppler sonography every 3 weeks. All ultrasound examinations were normal and PEs were tolerated without any complications. At 35 weeks of gestation, ultrasound examinations reported an increase in MCA peak systolic velocity (PSV MCA: 72 cm/s) that was suggestive of mild anemia.

She was admitted at 37 weeks of gestation due to the initiation of labor. She inclined to have vaginal delivery after her previous cesarean section (VBAC), but due to fetal distress and prolonged deceleration, cesarean section was performed. A healthy male infant weighing 2,520 g, with APGAR scores of 7 at 1 min, and 8 at 5 mins was born. The blood group of the infant was O Rh positive. Direct antiglobulin testing was negative. The infant's hemoglobin was 13.8 g/dL and stable. Both mother and infant were discharged on day 3.

The patient provided written informed consent for the publication of the case details. The ethical committee of Mashhad University of Medical Sciences approved the publication of this case report.

Discussion

One of the most common causes of fetal anemia is red cell alloimmunization in which fetal red cells are destroyed due to the transplacental passage of maternal antibodies. This leads to the overproduction of immature fetal and neonatal red cells (erythroblastosis fetalis); a condition referred to as hemolytic disease of the fetus and newborn (HDFN). In severe cases, hydrops fetalis and intrauterine death may occur.¹

In D alloimmunization, an RhD-negative pregnant woman who is exposed to fetal D positive red cells is at risk for developing anti-D antibodies.² Those diagnosed to have anti-D antibodies should be managed based on measurement of the maternal blood antibody titers and also Doppler ultrasonography of the fetal MCA. A Doppler flow velocity study of the fetal MCA is a replacement for amniocentesis which was an invasive method for fetal anemia determination.³ An anti-D antibody titer of 1:16 to 1:32 is reported to be associated with risk for fetal hydrops.⁴

The standard treatment in fetuses with anemia is intrauterine transfusion (IUT); but this approach may have adverse effects, especially if undertaken before the 20th week of

pregnancy.² Since hydrops might develop before week 20 in severe cases of D alloimmunization, immune modulating approaches such as TPE and the use of intravenous immunoglobulin (IVIG) should be implemented to avoid or delay IUT.⁵ Plasmapheresis is undertaken with the aim of reducing the levels of maternal anti-D which will destroy the fetus's red cells after passing through the placenta.⁶

Different combinations of IUT, plasmapheresis and IVIG have been reported to be effective in treating an alloimmunized pregnant women. Our patient who had a history of alloimmunization in her previous pregnancy was managed solely with TPE in her current pregnancy.

In 2006, Palfi et al reported a case of severe Rh (D) alloimmunization who was treated by intensive PE, high-dose IVIG and IUT. Their patient had a history of two pregnancies resulting in hydrops despite the use of IVIG and IUT. But her last pregnancy was successfully managed by performing PE for 35 times and IUT for 2 times.⁷

Isojima et al performed plasmapheresis at the 15th week of gestation followed by high-dose IVIG treatment in a severe Rho incompatible pregnancy. They concluded that the early application of plasmapheresis and IVIG treatment in this patient eliminated the need for weekly plasmapheresis.⁸

Another case report of a D alloimmunized pregnant woman treated with plasmapheresis followed by IVIG has been presented in which IUT was not necessary. Treatment was initiated at 28 weeks of gestation in this patient.⁶

Our patient was managed only with PE; initiated at week 17 and continued until delivery. The sole use of plasmapheresis in the management of a case of Rh (D) in compatible pregnancy with previous HDFN has been reported by Kamei et al in 2015. Their patient was treated with double-filtration plasmapheresis (DFPP) without the need of transfusion. But in the pregnancy prior to her last one, her incompatibility status was managed using DFPP, IVIG and also IUT.⁹

The American Society for Apheresis recommends that therapeutic plasmapheresis should be considered early in alloimmunized pregnancies from the 7th to 20th week and be continued until about the 20th week of gestation; when IUT can safely be administered.¹⁰ The principal of plasmapheresis in Rh alloimmunization is the removal of maternal alloantibodies which reduces their titer and subsequently reduces the placental transfer of harmful maternal alloantibodies.⁹ Some of the complications which might limit the implementation of plasmapheresis include the risk of catheter-related infection and thrombosis, hemodynamic instability and severe resource utilization.¹¹ Fortunately, our patient developed none of the above and

received 20 PEs without any complications from 17 to 36 weeks of gestation.

To our knowledge, this is the first case report of D alloimmunization in pregnancy managed by implementing PE only, without the need for IUT or the use of any other immune modulating treatments; neither in the current pregnancy nor in previous ones.

Conclusion

TPE can successfully be used in the management of pregnancies affected by Rh (D) alloimmunization, without the need for IUT or the use of any other immune modulating treatments.

Disclosure

The authors report no conflicts of interest in this work.

References

- Cunningham FG. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill Medical; 2014:xviii, 1358.
- Zwiers C, Lindenburg ITM, Klumper FJ, de Haas M, Oepkes D, Van Kamp IL. Complications of intrauterine intravascular blood transfusion: lessons learned after 1678 procedures. *Ultrasound Obstet Gynecol*. 2017;50(2):180–186. doi:10.1002/uog.17319
- Mari G, Deter RL, Carpenter RL, et al. Noninvasive diagnosis by Doppler ultrasonography of fetal anemia due to maternal red-cell alloimmunization. Collaborative Group for Doppler Assessment of the Blood Velocity in Anemic Fetuses. *N Engl J Med*. 2000;342(1):9–14. doi:10.1056/NEJM200001063420102
- Moise KJ Jr. Management of rhesus alloimmunization in pregnancy. *Obstet Gynecol*. 2008;112(1):164–176. doi:10.1097/AOG.0b013e31817d453c
- Colpo A, Tison T, Gervasi MT, et al. Personalized treatment with immunoabsorption and intravenous immunoglobulin in a case of severe Rh alloimmunization during pregnancy unresponsive to plasma - exchange. *Transfus Apher Sci*. 2017;56(3):480–483. doi:10.1016/j.transci.2017.05.024
- Fernandez Alba JJ, Leon R, Gonzalez-Macias C, et al. Treatment of D alloimmunization in pregnancy with plasmapheresis and intravenous immune globulin: case report. *Transfus Apher Sci*. 2014;51(1):70–72. doi:10.1016/j.transci.2014.02.026
- Palfi M, Hilden JO, Matthiesen L, Selbing A, Berlin G. A case of severe Rh (D) alloimmunization treated by intensive plasma exchange and high-dose intravenous immunoglobulin. *Transfus Apher Sci*. 2006;35(2):131–136. doi:10.1016/j.transci.2006.07.002
- Isojima S, Hisano M, Suzuki T, Sago H, Murashima A, Yamaguchi K. Early plasmapheresis followed by high-dose gamma-globulin treatment saved a severely Rho-incompatible pregnancy. *J Clin Apher*. 2011;26(4):216–218. doi:10.1002/jca.20288
- Kamei K, Yamaguchi K, Sato M, et al. Successful treatment of severe rhesus D-incompatible pregnancy with repeated double-filtration plasmapheresis. *J Clin Apher*. 2015;30(5):305–307. doi:10.1002/jca.21372
- Schwartz J, Winters JL, Padmanabhan A, et al. Guidelines on the use of therapeutic apheresis in clinical practice-evidence-based approach from the Writing Committee of the American Society for Apheresis: the sixth special issue. *J Clin Apher*. 2013;28(3):145–284. doi:10.1002/jca.21276
- Houston BL, Govia R, Abou-Setta AM, et al. Severe Rh alloimmunization and hemolytic disease of the fetus managed with plasmapheresis, intravenous immunoglobulin and intrauterine transfusion: A case report. *Transfus Apher Sci*. 2015;53(3):399–402. doi:10.1016/j.transci.2015.07.010

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