CLINICAL VIGNETTE

A Change in Rh Blood Typing Status in the Pregnant Mother and the Risk of Hemolytic Disease of the Fetus and Newborn (HDFN)

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A 34-year-old woman had her first pregnancy with a full-term uneventful delivery. Her blood type was type A and RhD negative and her husband was RhD positive and she received a standard 300 mcg of anti D immune globulin at the end of the second trimester to minimize the risk of hemolytic disease of the fetus and newborn (HDFN) and after delivery to minimize the chance of allogeneic anti D developing affecting future pregnancies.[1] She gave birth to a blood type A positive daughter by vaginal delivery without evidence of HDFN. At age 36, she became pregnant and underwent repeat laboratory testing with her blood type now reporting as type A but weak D positive. She had not received any blood products prior to her first pregnancy, nor between the 2 pregnancies. She was scheduled for repeat anti D immune globulin at the end of her second trimester and was referred for hematology evaluation to assess the risks to the mother of the anti D immune globulin and the risk of HDFN.

At hematology evaluation she was referred for specialized serologic and molecular weak D testing. She was found to have a weak D type 1 variant which is considered RhD positive for clinical purposes. She hence should not receive anti D immune globulin since she was not at risk for forming allogeneic anti-D antibodies.

Discussion

HDFN can occur when the mother develops IgG antibodies to red blood cell membrane antigens (RBC), either pre-existing or acquired during pregnancy, since IgG antibodies can cross the placenta. Allogeneic antibodies (allo-antibodies) can occur to A or B blood types, which generally causes only mild hemolysis, or to RhD, which is much more common and causes more severe hemolysis, or to other RBC antigens, causing variably severe hemolysis.[2,3] Anti D immune globulin is quite effective in reducing the risk of HDFN in RhD negative women with RhD positive partners if the baby is RhD positive by minimizing allo immunization with slight fetal blood exposure to the mother.[2,3] Allo immunization to RhD in the pregnant mother will often lead to severe fetal hemolysis. A French study of 30 years of patient experience reported, 62 percent of RhD positive newborns of mothers with RhD alloimmunization underwent exchange transfusion.[2] More severe fetal and newborn hemolytic anemia correlates with higher titers of anti D antibody.[3] In severe cases, intrauterine fetal hemoglobin measurements and even intrauterine fetal transfusions might be required and have been performed successfully.[3] In addition a combination of plasmapheresis and intravenous immunoglobulin have been used in pregnant allo D immunized pregnant women to reduce the severity of HDFN.[4]

Serologically weak RhD positive tests occur in 0.2 to 1 % of type and screen testing.[5,6] Weak D by serologic testing involves a 2 + or lower anti D reactivity score and positivity for anti-human globulin.[5] In the past, weak D positive patients were considered to be RhD positive as blood product donors and RhD negative as blood product recipients or when pregnant.[5,6] The RhD protein is comprised of 487 amino acids and has a complex RBC membrane associated structure with 12 transmembrane domains.[5] Molecular studies have identified numerous mutations which have demonstrated 4 distinct genotypes of weak D serologic patients.[5,6] Types 1 through 3, which occur mainly in Caucasians, should be considered RhD positive and Type 4, which occurs mainly in patients of African ancestry, should be considered RhD negative for clinical purposes. Therefore, our patient did not need anti D immune globulin with her second pregnancy and her first RhD positive child was at no risk of anti RhD HDFN.

The use of anti D immune globulin to treat RhD positive patients with immune thrombocytopenia (ITP) can induce significant intravascular hemolysis in less than 1% which can rarely be fatal.[4] There was essentially no risk in our patient since the dose of anti D immune globulin for ITP is 50 mcg/kg,[4] or approximately 3000 mcg if it had been given, as opposed to the 300 mcg standard non weight based obstetrical dose that she received. In addition, serological weak D RBC would be much less sensitive to intravascular hemolysis compared to normal RhD RBC given a much lower antigen density.

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