Educational Topic 19: Alloimmunization

Rationale: The incidence of maternal D alloimmunization has decreased in the past few decades. Awareness of the red cell antigen-antibody system is important to help further reduce the morbidity and mortality from alloimmunization.

Intended Learning Outcomes:
A student should be able to:

• Describe the pathophysiology and diagnosis of alloimmunization
• Describe the use of immunoglobulin prophylaxis during pregnancy for the prevention of alloimmunization
• Discuss the management of a patient with Rh-D sensitization in pregnancy

TEACHING CASE

CASE: A 32 year-old P1101 woman and her new husband present for prenatal care at 20 weeks gestation. Her past obstetric history is significant for a first child delivered at term following an abruption. Her second child died of complications of prematurity following in utero transfusions for Rh alloimmunization. Her initial prenatal labs this pregnancy indicate her blood type as A negative and an antibody screen positive for anti-D with a titer of 1:256. You discuss any additional evaluation needed, her risks in this pregnancy, and the plan of management with her and her husband.

COMPETENCY-BASED DISCUSSION & KEY TEACHING POINTS:
Competencies addressed:
• Patient Care
• Medical Knowledge
• Practice-Based Learning
• Systems-Based Practice

1. What is Rh alloimmunization and what are the red cell antigens involved?

   • Occurs when any fetal blood group factor (in this case the Rh antigens) inherited from the father is not possessed by the mother. Antepartum or intrapartum fetal-maternal bleeding may stimulate an immune reaction in the mother
   • Most cases of Rh alloimmunization causing significant hemolytic disease in the fetus or newborn are the result of D antigen incompatibility
2. What are the risk factors for Rh alloimmunization?

- Any clinical situation that could lead to fetal-maternal hemorrhage:
  - Obstetric procedure: pregnancy termination, chorionic villus sampling, amniocentesis, external cephalic version
  - Threatened abortion, ectopic pregnancy, abortion
  - Delivery of an Rh+ neonate to an Rh- mother (cesarean or vaginal delivery)—most common cause of alloimmunization
  - Multifetal gestation
  - Abdominal trauma
  - Bleeding placenta previa or abruptio
  - Manual removal of placenta
- Spontaneous fetal-maternal hemorrhage has been detected to 10% of cases of alloimmunization.

3. What is the mechanism for RhoGAM prophylaxis against Rh disease? What is the dose of RhoGAM? What is the recommended schedule for RhoGAM administration?

- Exogenous IgG (Rho(D) immune globulin) suppresses the maternal immune response through central inhibition. The Rh D IgG coated fetal RBCs are sequestered in the maternal spleen and these antigen-antibody complexes inhibit the primary immune response (B cell transformation to plasma cells) and antigen-specific B cell proliferation.
- 300 micrograms of anti-D immune globulin can prevent Rh D alloimmunization after an exposure to up to 30 mL of Rh D-positive blood or 14 mL of fetal cells
- In the U.S. for Rh-mothers, the recommended immunoprophylaxis regimen using anti-D immunoglobulin is:
  - 300 mcg dose at 28 week EGA
  - Second 300 mcg dose should be given if delivery has not occurred within 12 weeks of the initial dose
  - Within 72 hours after delivery of an Rh+ neonate
  - After first trimester pregnancy loss, threatened abortion, or elective termination
  - After invasive antepartum procedures
  - Following external cephalic version or trauma
  - After second or third trimester bleeding

4. Could this patient’s Rh alloimmunization have been prevented? What are the ways in which alloimmunization might be diagnosed? Is there any further blood work that should be obtained before you counsel this patient on her risks in this pregnancy? What are some ultrasound findings that may suggest Rh disease?

- Administration of an adequate dose of RhoGAM within approximately 72 hours prevents an active maternal antibody response to the fetal antigens. The extent of fetal to maternal hemorrhage can be estimated using the Kleihauer-Betke test.
- Maternal antibody screen is recommended at the first prenatal visit, at 28 weeks gestation, at the time of any event in pregnancy associated with possible fetal-maternal hemorrhage, and postpartum. Positive antibody screens should be evaluated for strength of antibody response (titer) and type of antibody. A critical titer that may be associated with fetal hemolytic disease is most often between 1:16 and 1:32.
- The paternal antigen status for the specific maternal antibody should be assessed to determine if the fetus is at risk. This assessment is accomplished by performing direct genotype testing of the father. If paternal testing is not possible, fetal antigen assessment can be accomplished through genetic analysis of fetal cells obtained through amniocentesis.
• Ultrasound findings consistent with severe fetal anemia include elevated peak velocity of the middle cerebral artery and evidence of hydrops fetalis (fetal subcutaneous edema, pleural and/or pericardial effusions, and ascites).

REFERENCES


