ABID CASE #26, ANSWERS

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1. What can be said about the nature of this antibody(ies)?

   The initial findings suggested the presence of a warm-reactive autoantibody with all donor cells reactive with the serum and a positive DAT. But when no autoantibody was recovered in the eluate, the positive DAT and serum panagglutinin appeared to be unrelated phenomena. This suggested that the antibody was instead directed against a high frequency antigen.

2. What further workup would you do to identify it?

   Definitive identification of an antibody directed against a high frequency antigen involves demonstration of its lack of reactivity against rare cells lacking the corresponding antigen, and use of rare sera to type the patient for the antigen. A common approach to such an antibody is to determine how it reacts with RBCs treated with any of a variety of enzymes and with sulfhydryl-reducing agents; this may allow one to narrow down the possibilities based on the know effects of these agents, and to allow conservation of such rare RBC samples and sera. Because several of the more commonly-encountered antibodies directed against high-frequency antigens exhibit "high-titer, low avidity" behavior, many technologists would perform a titration as well. Attention to the patient's ethnic background may also suggest certain possibilities such as anti-Jk^3 or anti-Di^b in individuals of Pacific island origin or anti-U in individuals of African heritage.

3. What is the identity of this antibody?

   The antibody appears to be anti-JMH based on the failure of the patient's serum to react with 3 JMH-negative RBC samples.

4. What results prompted the selection of the rare cells in the last panel?

   Failure of previously-reactive RBCs to react after ficin and AET (a sulfhydryl reducing agent) treatment suggested that the antibody might be directed against JMH.

5. What do the titration results demonstrate?

   The titration results are consistent with the "high-titer, low-avidity" antibody phenomenon. That is, the neat serum reacted 2+ at the AHG phase of testing and the strength of reactivity did not diminish when the serum was diluted 8 fold. A example of a typical blood group alloantibody that reacted 2+ on the neat serum would usually be non-reactive or only weakly reactive if diluted 8-fold.

6. Comment on the difference in reactivity using the Gamma AHG versus the Ortho and IMMUCOR reagents.

   The Gamma reagent does not react with IgG4 and will not agglutinate IgG4-coated RBCs. Anti-JMH is most often restricted to the IgG4 subclass. This is the reason the DAT and the antibody screen was negative with the Gamma AHG

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7. Is the patient at risk for an immediate hemolytic transfusion reaction? A delayed hemolytic transfusion reaction? How is this related to the answer to the previous question?

   Anti-JMH does not typically cause immediate or delayed hemolytic transfusion reactions although slightly accelerated clearance of JMH+ RBCs in patients with anti-JMH has been reported. This correlates with the IgG4 subclass restriction mentioned above, since IgG4-coated RBCs do not activate complement, nor are they destroyed by macrophages.

8. Review the characteristics of the blood group system involved in this case.

   The JMH antigen is carried by a GPI-linked (glycosylphosphatidylinositol-linked) "semophorin" signaling protein, Sema7A (CD108), and it is not expressed on complement-sensitive PNH RBCs. Although the JMH-negative phenotype may be inherited, it is more frequently an acquired phenotype. Some individuals with anti-JMH may retain some expression of the antigen and have a weak positive DAT, in which case it can be considered to be an autoantibody. JMH is weakly expressed on RBCs of neonates (see cord cell reactions in the selected cell panel on page 4). It is destroyed by proteases including papain, ficin, trypsin and chymotrypsin, as well as by certain phospholipases. The glycoprotein contains many cysteine residues, and the antigen is destroyed by disulfide reducing agents. High frequency JMH+ variants are described in individuals with alloantibodies that do not react with JMH1-negative RBCs.

   Patients with anti-JMH frequently have not been transfused or pregnant.