ABID CASE #8

Case study by Jim Perkins, M.D. (© 2005)

Indian Immunohematology Initiative

1. What is the probable identity of this antibody?

   Cold-reactive anti-M. The pre-warmed test demonstrates that the antibody does not react at 37°C.

2. Why aren't many of the antigen positive cells reacting?

   Because of the "dosage effect"; that is, the antibody only reacts with double dose M-positive cells by the gel method. We would say the antibody "shows dosage". Essentially all anti-M antibodies show dosage.

3. Is any further workup needed to prove it? Why were the selected cells from the second panel run?

   The antibody is considered proven. (Three antigen positive cells react, three antigen negative cells fail to react, other antibodies are ruled out as required by protocol, and the patient is M antigen negative.) One could possibly show reactivity with all M-positive cells by testing at a lower temperature or by acidifying the serum and retesting. The pre-warmed testing was performed to determine how units would be selected (see below).

4. What would we require to consider a unit of RBCs compatible for this patient? (See the procedure "Blood Component Compatibility Requirements".)

   The unit should be compatible by the routine IAT crossmatch. No special antigen typing is required because anti-M antibodies that fail to react at 37°C or in the antiglobulin phase of a pre-warmed test are considered to be clinically INsignificant..

5. What would you expect to find after dithiothreitol (DTT) treatment of the serum and rerunning the panel (DTT denatures sulfhydryl bonds)? What about after ficin or papain treatment of the panel RBCs?

   DTT denatures IgM antibodies, and this antibody is likely of the IgM class, so the serum would be expected to become non-reactive. Ficin and papain cleave glycophorin A, so again the test would become non-reactive.

6. Is the patient at risk for an immediate hemolytic transfusion reaction?

   No, because the antibody is cold-reactive.

   A delayed hemolytic transfusion reaction?

   Rarely, due to anti-M antibodies that become reactive at 37°C after antigen stimulation.

7. Would this antibody be expected to cause hemolytic disease of the fetus and newborn?

   Although anti-M that is reactive at 37°C has rarely be reported as causing severe HDFN, an antibody with these in vitro characteristics would not be expected to. Since cold-reactive anti-M can rarely become reactive at 37°C if one were conservative one could recheck the patient in 3rd trimester.

8. What is the biochemical nature of the antigen? What is the basis for the polymorphism between this and its antithetical antigen?

   The M and N antigens are carried by glycophorin A, a single pass membrane glycoprotein carrying 60% of the negative charge on the RBC. The MN genes are closely linked to the S/s genes, so they are considered to be part of the same system (along with many other polymorphisms). M varies from N by two amino acids separated by a short sequence of 3 others that are the same. M and N are sensitive to proteases. Anti-N is uncommon and is not considered clinically significant.