ABID CASE #29, ANSWERS

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1. What can you say about the initial test results? Are there any hypotheses you would like to test?

   This patient has a weakly positive antibody detection test ("screen") by the "gel" column agglutination test, a negative DAT, and the plasma reacts with all cells in an antibody panel. The latter reactions are weak and somewhat variable.

   Lack of reactivity with SCII may simply reflect the weak nature of the antibody rather than any particular specificity, so we appear to be dealing with an alloantibody directed against a high prevalence antigen. Gel-method-dependent reactivity may present this picture as may reactivity due to daratumumab treatment. The latter is ruled out by the history of lymphoma rather than multiple myeloma. To rule out gel-dependent reactivity we could try an IAT by a tube method.

2. What did we learn from the PEG panel? (Hint: Note the mixed field reactions.) What would you like to do next?

   The first thing we learn from the PEG panel is that we are not dealing with gel-dependent reactivity. In addition, the pattern of variable, mixed field reactivity with most RBCs is characteristic of anti-Sd^a. Note that the mixed field reactivity was not evident by the gel method but was only detected when we tested in tubes. Tube testing frequently reveals hints to an antibody's identity are not evident with more modern methods, and many reference labs start cases "in tubes".

   Anti-Sd^a is neutralized by urine, so a urine-neutralization test should be done.

3. What did the neutralization test show? How is the neutralization done? What does the saline control demonstrate? Is any further workup needed?

   Neutralization of this patient's serum by urine demonstrates that the antibody is anti-Sd^a.

   In the urine neutralization test the unknown serum is incubated for 15 minutes at room temperature with at a 1:1 ratio with boiled, dialysed urine containing Sd^a. Urine is obtained from guinea pigs, from individuals known to have strong expression of the antigen, or pooled from multiple individuals. A tube of the urine is placed in boiling water for 10 minutes and then dialysed against saline to produce an isotonic solution containing the antigen. The dilution control demonstrates that the loss of reactivity in the treated plasma is not simply due to the 1:1 dilution. In this case it also rules out other alloantibodies, as the PEG IAT is a sensitive test, even with the dilution.

4. Does this antibody cause hemolytic transfusion reactions? Hemolytic disease of the fetus and newborn? How would you provide compatible RBCs in this case?

   Anti-Sd^a is reported to have caused hemolysis in two cases in which the donor RBCs had very strong expression of the antigen (Daniels, 2013). The antigen is not expressed on the RBCs of newborns and has not been reported to cause HDFN. A "Coombs" crossmatch would be done to prevent transfusion with RBCs strongly expressing Sd^a. As seen in the last table, the patient's serum failed to react in an IAT using saline-suspended donor RBCs.

5. What is the biochemical nature of the antigen?

   Sd^a or "Sid" antigenicity is carried by oligosaccharides expressed on a variety of tissues in addition to RBCs, particularly on kidney tubule cells. It is present on the Tamm-Horsfall glycoprotein secreted into urine, but can also be detected in serum, milk, and meconium. Sd^a is named "Sid" after the head of the maintenance department at the Lister institute whose RBCs were strongly positive. Sid expression on RBCs is characterized by its variability between individuals, and the frequency of anti-Sd^a detection depends on the RBCs used; one family from Mauritania, the "Cad" family, express Sid so strongly that their cells appear polyagglutinable (agglutinated by all or most human sera), as well as being agglutinated by Dolichos Bifloris lectin which has anti-A_1 activity. In this regard, the Sd^a gene product is a transferase for N-acetylgalactosamine, the group A immunodominant sugar. About 91% of Europeans express Sid on their RBCs, but expression is about 95% in urine tested by sensitive inhibition methods.