ABID CASE #12, ANSWERS

Case study by Jim Perkins, M.D. (© 2006)

1. What is the identity of this antibody? What are the possibilities when all cells in the initial panel are reactive?

   Anti-Kp^b, an antibody directed against a high prevalence antigen in the Kell blood group system..

   When all cells in the initial panel are reactive, classically there are 3 initial differential diagnoses including:
   1) an autoantibody (most auto-antibodies are pan-agglutinins reacting with most RBCs),
   2) an antibody against a high prevalence antigen, and
   3) antibodies of multiple specificities.
   Today however, one might add additional scenarios. Method-dependent pan-agglutination may occur with column agglutination ("gel") or solid phase technique. Also anti-cancer antibody administration, particularly with daratumumab which reacts with all adult RBCs, may present as a panagglutinin.

   Confronted with a panagglutinin many reference labs would immediately test RBCs treated with proteolytic enzymes (ficin or papain, others) or sulfhydryl reducing agents (DTT or AET) to gain a hint as to the identity of the target antigen. In this case the sensitivity to DTT and resistance to enzymes could have pointed to a specificity within the Kell blood group system and avoided the need to thaw, and waste, the rare JMH-, Cs^a-, and Yt^a-negative RBCs, all of which show a different pattern of sensitivity to these reagents.

2. Is any further workup needed to prove it? Are other antibodies ruled out as required by our procedure manual?

   Anti-E and anti-K are not ruled out. However, Kp^b negative, K positive RBC samples do not exist (all Kp^a alleles also determine k and Js^b, see below), and our rare cell library simply did not contain a Kp^b neg, E pos cell. Note that anti-N and anti-S are ruled out by the patient's phenotype.

3. Is this an example of primary or secondary immunization?

   The fact that there are still Kp^b positive cells circulating at 14 weeks suggests that this is primary immunization.

4. Does this antibody cause hemolytic transfusion reactions? Hemolytic disease of the newborn?

   Yes to both.

5. What percentage of donors is expected to be compatible with this recipient? How would we select compatible blood for this patient?

   About 1 in 10,000 Caucasians are expected to be Kp^b negative. Since anti-Kp^b is not routinely available, it would not be possible for all blood banks to type donor cells for Kp^b, but a Coombs' crossmatch would still be performed with recipient plasma. For an antibody such as this, one typically would depend on frozen RBCs at the blood center or acquired through the rare donor registry. Such units are known to be negative for the blood group in question and ideally a sample from the unit would be crossmatched prior to thawing. One would also want to investigate the possibility of using autologous blood or RBCs from a sibling.

6. What is the biochemical nature of the antigen? What are the genetics? (Include a discussion of DTT and ficin)

   The Kp^a/Kp^b polymorphism is carried by the Kell protein, a single pass membrane glycoprotein. It is a zinc endopeptidase which converts "big endothelin-3" to its vasoconstrictor form endothelin-3. Kell antigens are destroyed by sulfhydryl reducing agents (AET, DTT, 2-ME), because the protein is tightly folded with internal disulphide bonds. It is resistant to ficin and other proteases. Because they are all part of one gene, the K/k, Kp^a/Kp^b, and Js^a/Js^b polymorphisms are in tight linkage disequilibrium, and no alleles have been observed that direct formation of both K and Kp^a or Js^a, or both Kp^a and Js^a. Therefore, an individual who was Kp^a/Kp^a, such as this patient, would be expected to be K negative.