FEATURED CASE #19-07; ANSWERS
(Case study by Jim Perkins, © 201)

Indian Immunohematology Initiative

Questions:

1. What is the cause of the positive antibody screen? Can we identify a specificity for the patient's antibody? If not, can we make guesses? What do you think might be going on here? What testing would you like to do to clarify this case?

   The patient has a new positive antibody screen over 2 weeks after transfusion of 2 units of RBCs and another transfusion over a week earlier suggesting that the patient might have had a delayed hemolytic transfusion reaction (DHTR) or a delayed serologic transfusion reaction (DSTR)."Crossing out" on the screening and panel cells eliminates common, clinically significant antibodies. However, inspection of the phenotype of the two reactive cells reveals that both are K positive, although a third K+ cell is nonreactive. The next step would probably be to test additional K+ and K- cells including double-dose K+ cells (K+k-) if available.

2. What is the specificity of the patient's antibody? Is it proven? Is there anything notable about this patient's antibody compared to other antibodies of this specificity? What additional testing would you like to do to investigate this case?

   The additional results meet the criteria for proof that the patient has alloanti-K (3 K+ cells reactive, 3 K- cells nonreactive, "everything else" ruled out, patient is K-). This example of anti-K is a little out of the ordinary in that it appears to "show dosage"; that is, it reacts more strongly with double-dose than single-dose K+ cells.

   Again, given the presence of a new antibody 17 days after the last transfusion (day 25 overall), we should investigate the possibility of a DHTR including determining whether any of the previously transfused units were K+ and repeating the previous antibody screens to see if a weak positive was missed.

3. Do you think that we can say there has been a DHTR? If so, what is unusual about it as a DHTR?

   To call this a DHTR we need to show not only that there is a new, potentially causative antibody as we have already, but also that there has been hemolysis of the K+ donor RBCs. Given the patient's bleeding, the course of his hemoglobin levels is an unreliable guide to whether he had hemolysis. However, note that on the day his antibody was discovered (D25) his K phenotype was negative, so RBCs from the 2 K+ units were not detected by this method. Moreover, his DAT was negative, again suggesting that K+ RBCs were not circulating 17 days after transfusion.

   Calculating his total blood volume from his height and weight (6.4L), his total RBC volume by multiplying this by his hematocrit (6.4L x 27.4% = 1.75L), and assuming 180mL of RBCs per units, on day 9 immediately after transfusion K+ donor RBCs should have represented 20% of his total. One would not expect these RBCs to have become undetectable over 17 days just on the basis of normal senescence, suggesting that the K+ cells were differentially destroyed.

   Typically we think of DHTRs as being caused by an anamnestic or secondary antibody response in a person who was previously immunized against a blood group antigen, but whose antibody has fallen below a detectable level due to the passage of time. On exposure to the same blood group again at a later date antibody appears over just a few days, so that it encounters RBCs bearing the offending antigen and destroys them. However, in a primary immune response we typically expect appearance of an antibody to take up to 3 months, by which time few antigen positive donor RBCs are still circulating and at risk of hemolysis.

   In this case the patient denied previous transfusion on careful questioning, and he had never had a surgical procedure that might have caused him to be transfused without his knowledge. He was very cooperative with this questioning, and he was not cognitively impaired at the time.

   There are very few reports of DHTRs due to a primary antibody response, but this case appears to represent one.

Take home points

Delayed hemolytic transfusion reactions are generally thought of as due to a secondary immune response but this case suggests that they can occasionally be caused by a primary immune response.
Anti-K can occasionally show dosage if the proper cells are tested (both (K+k- and K+k+)