CASE #17, ANSWERS
Case Study by Jim Perkins, MD (©2019)

Indian Immunohematology Initiative

1. What antibody(ies) appear to be present? What are possible causes of the observed reactivity? What tests could you do to investigate these?

   As in case #16, the reactions of this donor's antiserum do not fit any obvious specificity or combination of specificities. This time there are fewer non-reactive cells, but several antibody specificities are ruled out by conventional criteria including anti-D, -C, -c, -e, -K, -k, -Fy^b, -Jk^a, -Jk^b, -Le^b, -S, -s, and –P1. Inspection of the reactive cells does not suggest commonality between them. Thus this reactivity is non-specific.

   Possible explanations for this non-specific pattern as discussed in the previous case (Case #16) include:

   A. *A weak cold-reactive autoantibody (cold agglutinin). Again this could be investigated by running a "cold panel", and it would have been useful to have performed an autocontrol.*
   B. *The nonspecific pattern if reactivity could be due to one or more weak alloantibodies. In particular this pattern of variable weak reactions suggests a so called "High-Titer, Low-Avidity" (HTLA) antibody. HTLA antibodies are a loosely defined group of relatively-frequently encountered antibodies directed against antigens in several different blood group systems. They are distinguished by their behavior, specifically by reacting weakly in the indirect antiglobulin test (IAT) using undiluted serum/plasma, but nonetheless continuing to react to a higher titer than might be expected from their initially weak reaction strength (see cases #26 and #27). The blood group antigens they define are generally of relatively high prevalence (e.g. JMH, McCoy^a, Chido/Rogers). This could be investigated by performing a titration tested against one of the more strongly-reactive cells by the same technique that demonstrated the reactivity.*
   C. *Again, the gel method may show weak, non-specific reactivity which cannot be replicated using other methods. This could be investigated by using another sensitive IAT method. In some case such "gel-dependant" antibodies may also be demonstrated by washing a few drops of reactive panel cells with saline and then re-suspending them in the same number of drops of the buffer the manufacturer provides for making suspensions of donor cells for crossmatching.*

2. What do the "cold antibody screen" tell us? What is this antibody's titer? Does the antibody screen with enzyme (ficin) treated cells help us? How?

   These tests rule out possibilities A and B. That is, the cold panel results make it very unlikely that the non-specific reactivity is due to cold autoantibody; although there is a cold agglutinin detected on incubation of the reaction at 4^{o}C, most individuals have such reactivity, and it is unlikely to have caused the reactivity in the gel antibody screen and panels.

   The antibody titer is the reciprocal of the highest dilution showing a weak positive reaction. In this case only the undiluted plasma reacted, so the titer is 1. This is not consistent with an "HTLA".

   The negative screen with enzyme-treated cells helps rule out a weak Rh antibody or antibody combination.

3. What do the PEG/tube and LISS/tube panel results tell us?

   The fact that these panels are completely non-reactive strongly suggests that the gel reactivity is an artifact of the gel method and not due to an autoantibody or true blood group alloantibody. When non-specific reactivity is encountered in gel or solid phase testing many laboratories simply run an antibody screen by the PEG method, and if the latter is negative they consider the initial results as false positive.

4. Why did the technologist perform the selected cell panel by the gel test? What does it tell us?

   The tech was seeking reassurance that the gel reactions weren't due to true RBC alloantibody(ies), and the results were indeed reassuring.

5. How would you use this donation?

   We elected to discard the donor's plasma but did make her RBCs available for transfusion without washing.

6. Does knowing the donor's phenotype help us?

   It helps to some degree. It rules out the presence of all of the alloantibodies with specificities for which she expresses the antigen. This may help us interpret future workups.