ABID CASE #31; ANSWERS

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1. How would you interpret the initial test results? What do you want to do next?

   The patient is group A Rh positive with a positive antibody detection test. To identify the specificity of the antibody(ies) in the patient's plasma it should be reacted with an antibody identification panel.

2. Based on the results of the antibody detection test and initial panel, what antibody(ies) do you suspect? Is any further workup needed to prove your hypothesis? Is there any hint that this might not be the entire story?

   All of the E+ cells are reactive with the patient's plasma and all of the E- cells are non-reactive.. There are more than 3 E+ cells reactive and more than 3 E- cells that are non-reactive. In addition, antibodies directed against D, C, c, e, K, k, Jk^a, Jk^b, Fy^a, Fy^b, M, N, S, s, Le^a, Le^b, and P1 are all ruled out. The only additional test to prove the presence of anti-E, required by our procedure manual in the United States, is a negative E antigen typing result on the patient.

   Of note however, one single dose E+ cell (R1R2) in the antibody screen reacted more strongly than the double dose (R2R2) cell, and this cell is Mi(a+). Therefore, the presence of anti-Mi^a must be considered, particularly as it is a common antibody in this population. In a series from Taiwan (Lin. J, et al. Transfusion 2009;49:125A) anti-Mi^a was present in the plasma of 819 out of 1573 patients with alloantibodies; the next most common antibody was anti-E, present in 473 cases. In this case, to rule in anti-Mi^a the patient's plasma must be reactive with three cells that are E- Mi(a+). To rule anti-Mi^a out, the plasma must be non-reactive with one cell that is E-, Mi(a+). Finally, we would like to demonstrate that the patient LACKS any antigens against which we think she has made antibodies.

3. Is your hypothesis proven? What is the result?

   The patient's plasma reacts with three Mi(a+), E- cell samples. Moreover, the patient lacks the E and Mi^a antigens, demonstrating that she can form the corresponding alloantibodies. As a result the presence of allo-anti-E plus anti–Mi^a is proven.

4. How would you select RBCs for transfusion? How many units of blood would need to be screened to find four compatible units?

   The patient requires group A or O, Rh positive RBCs, lacking E and Mi^a because she has made antibodies against these antigens. The incidence of E and Mi^a in the Chinese population is 39% and 15% respectively. Thus the incidence of the combined antigen negative phenotype for these antigens is:

   $$0.61 \times 0.85 = 0.52\ (52\%)$$

   To find four units of E- and Mi(a-) RBCs we are likely to need to screen eight group A or O units as follows:

   $$52/100 = 4/N$$
   $$N = 4(100/52) = 8$$

5. Briefly describe the characteristics of the antibody(ies) discovered in the patient's plasma and the nature of the corresponding antigens?

   Anti-E is usually IgG, does not bind complement, reacts in the antiglobulin phase, and is produced in response to transfusion. Such examples of anti-E are clinically significant as they have been associated with mild to severe transfusion reaction, and HDFN. Non-red-cell-stimulated examples of anti-E are also described which are IgM and of questionable clinical significance.

   The E antigen (RH3) is coded by the RHCE gene, and is expressed on a non-glycosylated multipass RBC membrane protein closely related to RHD.

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Anti-Mi^a was first described in 1951 in the serum of Mrs. Miltenberger, and the corresponding antigen bears her name. Anti-Mi^a frequently occurs in mixtures of different antibody specificities, and it has been questioned whether it represents a specific entity. However, monoclonal antibodies are described which define Mi^a as a discrete antigen (Chen, V. et al. Vox Sang. 2001;80:230-233). In actual practice sera identified as having "anti-Mi^a" specificity are probably usually heterogenous mixtures. Anti-Mi^a is regarded as clinically significant. It has been associated with mild to severe HDFN, but transfusion reactions are uncommon.

The Mi^a antigen (NS7) is expressed on several glycophorin variants that are hybrids between the usual forms of glycophorin A and B. This places Mi^a and related antigens in the MNS blood group system. Various systems of nomenclature have been used to describe these variants, but the current system is based on designating the particular Mi^a related glycophorin variant present (e.g. GP.Hut, GP.Mur). The Mi^a antigen appears to be formed when one of two 11 amino acid sequences is present. These two sequences differ by a single amino acid. The prevalence of Mi^a antigen in Chinese and SE Asian populations may be as high as 15% (Reid M, Lomas-Francis C. Antigen Facts Book, 2nd ed. 2003)

6. Comment on the lessons of this case for selection of antibody detection cell sets.

In order to detect the blood group alloantibodies frequently formed by pregnant women and transfused patients in a given population, antibody detection cell sets must include at least one cell which expresses each of the corresponding antigens. From the data in answer #2 it is clear that antibody detection cells used for an ethnic Chinese population, and possibly other East Asian populations, should include at least one cell bearing the Mi^a antigen. Thus, screening a Taiwanese population entirely with cells sourced from European donors that were all Mi(a-) would miss the most common alloantibody in this population. Similar examples are present elsewhere in the world. For instance, screening for anti-Di^a may be appropriate in population with a high frequency of donors of Mexican origin (Thompson, C. Clin Lab Sci 2006;19:203).

In order to make decisions regarding the antigens that should be present on screening cells, one must know what alloantibodies are being made by gravid women and transfused patients in the population in question, as well as how frequent and how clinically significant the antibodies are. Unfortunately this data may not be available for some populations, and is only recently being published for India. Moreover, attempts to do such studies have the same methodological limitation as the antibody detection test, namely that alloantibodies can only be detected and identified when the cells used to do so have the relevant antigens. For this reason such studies should include cell panels made from individuals of the same population.

Finally, note that the antibody detection cells used in this case were not optimal for the population being screened. If anti-E and anti-Mi^a are the two most common antibodies present in the population, it would be useful if the corresponding antigens were not present on the same screening cell. That is, it would be useful if the Mi(a+) cell were E- (R1R1 or rr). For example, in the population served by the second author's hospital, the most common antibodies are anti-K and anti-E. Our screening cell I is usually E- (R1R1), K+ and screening cell II is E+,K-. This combination immediately suggests whether there is anti- E or anti-K present, or if the two antibodies are present together.