INDIAN IMMUNOHEMATOLOGY INITIATIVE
CASE OF THE MONTH, ANSWERS: November, 2010
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1. What is your impression from the initial test results? (Hint: what is the differential diagnosis when all of the cells on the antibody identification panel are reactive?) What would you do next?

Seventeen days after transfusion the patient has a new blood group antibody or antibodies which cause his plasma to agglutinate all of the 13 donor cells tested. The relatively short post-transfusion interval is consistent with an anamnestic response, and the patient might have been transfused at the time of the previous surgeries.

When all cells react the most common explanation is an autoantibody. However, the negative direct antiglobulin test (DAT) is against this diagnosis, particularly given the strong serum reactivity. Reactivity with all cells could also be due to antibody directed against a high frequency antigen or to antibodies with multiple specificities. The slight variation in strength of reactivity with different cells might suggest the latter. Such variation might be more apparent in tube tests with different phases of reactivity.

If multiple antibodies are suspected, one response might be to simply react the patient's plasma with more panel cells. Alternatively the patient's phenotype for the antigens against which antibodies are frequently encountered might be determined in order to determine what antibody specificities he could make. Interpretation of phenotyping tests is complicated by the possible presence of RBCs from the recent transfusion, but if the patient had eliminated the transfused cells in a delayed hemolytic transfusion reaction (DHTR), this would not be an issue. Finally, if an antibody against a high frequency antigen is suspected, cells lacking such antigens can be selected.

2. Do these reactions help? What antibody(ies) do you think is(are) present now? Now what would you do?

At this point a non-reactive cell is very helpful, allowing us to eliminate several possible antibodies. We cannot choose between multiple antibody specificities and an antibody against a high frequency antigen, since cell #2 could fortuitously lack a high frequency antigen that is not depicted in the antigram, but if we hypothesize that multiple antibodies are present, we can determine their possible specificities and select cells to prove our hypotheses.

Of note, the non-reactive cell has the phenotype D+C+c-E-e+ or "R1R1", raising the possibility that anti-c or anti-c + E is present. Either of these possibilities would explain much of the reactivity with the previous cells. Our attention should then turn to the other R1R1 cells. If you "crossed out" antigens present in "double-dose" (apparent homozygous expression) on cell #2, in addition to anti-D, anti-C, and anti-e, you were able to eliminate anti-Fy^b, anti-Jk^b, and, in the conventional manner anti-Le^a, and anti-P1. By our procedures we would also rule out anti-K even though it is only present in "single-dose" on cell #2. Although you could not completely eliminate anti-k, and anti-M, -N, -S, and –s, all of which were present in single-dose on the cell, these are less likely. Instead, the fact that the cell lacks Jk^a and Fy^a should focus your efforts on ruling out or ruling in these specificities. Further inspection of the other reactive R1R1 cells reveals that they were all positive for Jk^a and/or Fy^a.

Therefore, the next step might be to select and test R1R1 cells with Fy^a, Jk^a, Kk, and MNSs phenotypes which would allow you to rule these specificities in and out. One might also select rr, Jk(a-) and Fy(a-) cells that could prove the presence of anti-c.

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3. What antibody(ies) do you think is(are) present now? Is your hypothesis proven? If not, what is missing?

Anti-k, anti-s, anti-N are ruled out on double-dose cells. Anti-M and anti-S are not ruled out to this level of certainty, but there are additional non-reactive cells that have these antigens in single-dose and which were tested by another technique that might have been more sensitive to their presence (in particular anti-M might have been detected at "immediate spin" in the LISS/tube test. Finally there is one E+e+c- cell that is non-reactive, suggesting that there is no anti-E.

More importantly, we now have 4 reactive R1R1, Jk(a+), Fy(a-) cells which rule-in anti-Jk^a ("proof cells") and one reactive R1R1, Jk(a-), Fy(a+) cell to rule-in anti-Fy^a. Anti-c appears to be ruled in based on weak reactivity of three rr, Jk(a-), Fy(a-) cells. Moreover the phenotype demonstrates that the patient is susceptible to formation of anti-c, anti-Jk^a, and anti-Fy^a.

We would like to be able to rule out anti-S and anti-M more certainly, but did not have cells available to do so. Phenotyping the patient for M and S might have helped, but that was not done. One would not be likely to find a RzRz, Jk(a-), Fy(a-) cell to rule out anti-E, but to do so would have little consequence as R1R1 cells will undoubtedly be selected for transfusion. Finally, no additional anti-Fy^a proof cells were available for testing.

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

We selected group O, R1R1 RBCs (D+C+c-E-e+) that were Jk^a and Fy^a negative. In the European origin population of most of our donors, 14 in 1000 donors (1.4%) would be expected to be compatible. Only 1 in 1000 African-Americans would be expected to be compatible. Approximately 10 in 1000 cosmopolitan North Indian donors would be compatible (Thakral et al. Trans & Aph Sci, 2010).