ABID CASE #24,ANSWERS

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1. What hypothesis can you make regarding what antibody or antibodies might be present? How would you investigate this?

   Negative reactions with cells I and II (both routinely R1R1 cells) in the first panel immediately suggests anti-c, but then one notices that the other R1R1 cells, screening cell I and panel cell #11 are reactive. "Crossing out" on the nonreactive cell #1 and #2 of the panel fails to rule out anti-E, anti-K, anti-Fy^a, anti-Jk^b, and anti-Le^b. Of these, only anti-K could cause reactions with both screening cell I and panel cell #11 so by the principle of Occam's razor (the simplest explanation is the most likely) one could make the hypothesis that alloanti-c and alloanti-K are present. One might also note that panel cells #1 and #2 have a "single dose" of Jk^b and Fy^a respectively are non-reactive making these antibodies less likely.
   Since anti-c plus anti-K could explain all of the reactions the next step would be to select "rule out" cells for anti-E, anti-Fy^a, anti-Jk^b, and anti-Le^b. It would also be useful to phenotype the patient for the corresponding antigens if appropriate typing sera are readily available.

2. Now which antibodies do you think are present? What alloantibodies cannot yet be excluded?

   If our previous hypothesis (anti-c plus anti-K) had been correct all 3 selected cells would have been non-reactive and anti-E, anti-Fy^a, anti-Jk^b, and anti-Le^b would have been ruled out. (Anti-E would only have been ruled out on a single dose RzR1 cell, but double dose E+c- RzRz cells are rarely available except in specialized laboratories.) Since only cell #18 is non-reactive, only anti-Le^b is, in fact, ruled out. Various combinations of the other three possibilities could explain the two positive reactions. Moreover, the patient's antigen phenotype does not help to rule out any of the other antibodies since he lacks E, Fy^a, and Jk^b; instead it shows he indeed could have made anti-E, -Fy^a, and/or -Jk^b

3. What does this selected cell panel tell us? In the comment column of the antagram above indicate what each selected cell result tells us in terms of ruling out (indicate "R/O") or ruling in (indicate "R/I") one of the possible antibodies in this case. Taking all of the reactions together, what antibodies are proven? What cells are still needed to prove all of the antibodies? In the blank rows above list their phenotypes and the reactions expected if your hypothesis is correct.

Selected cells

		Rh system						Kell						Duffy		Kidd		Lewis		P	MNSs				Lutheran		Xg	Gel	Comment
Cell	Rh	D	C	c	E	e	V	K	k	Kp^a	Kp^b	Js^a	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P1	M	N	S	s	Lu^a	Lu^b	Xg^a		
1	R1R1	+	+	0	0	+	0	+	+	0	+	0	+	0	0	+	+	+	0	+	0	+	0	+	0	+	0	3+	Not helpful
2	R1R1	+	+	0	0	+	0	0	+	0	+	0	+	+	0	+	0	0	+	+	+	+	0	+	0	+	+	0	Rules out anti-Fy^a
3	RzR1	+	+	0	+	+	0	0	+	0	+	0	+	0	+	+	0	0	+	+	0	+	0	+	0	+	0	4+	Rules IN anti-E
4	R1R1	+	+	0	0	+	0	+	+	0	+	0	+	0	+	+	0	0	+	0	+	0	+	+	0	+	+	4+	Rules IN anti-K
5	R2R2	+	0	+	+	0	0	0	+	0	+	0	+	+	0	+	+	0	+	+	0	+	0	+	0	+	+	4+	Not helpful
6	R1wR1	+	+	0	0	+	0	0	+	0	+	0	+	+	+	0	+	+	0	0	+	+	+	0	0	+	+	w+	Rules IN weak anti-Jk^b given anti-Fy^a ruled out
7	R1R1	+	+	0	0	+	0	0	+	0	+	0	+	+	+	0	+	+	0	+	+	0	+	0	0	+	+	w+	Rules IN weak anti-Jk^b given anti-Fy^a ruled out
8	RzR1	+	+	0	+	+	0	0	+	0	+	0	+	0	+	+	0	0	+	+	+	0	+	+	0	+	0	4+	Rules IN anti-E
9	R1R1	+	+	0	0	+	0	+	+	0	+	0	+	0	+	+	0	0	+	+	+	+	+	0	0	+	0	4+	Rules IN anti-K
	rr	0	0	+	0	+		0								+	0												Rules IN anti-c
	R1R1	+	+	0	0	+		0								0	+												Rules IN weak anti-Jk^b
	RzR1	+	+	0	+	+		0								+	0												Rules IN anti-E

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Our four criteria that must be met to prove that an alloantibody is present include: 1) 3 cells react which express the corresponding antigen but not other antigens for which an antibody is present ("rule-in" cells); 2) 3 cells lacking the corresponding antigen fail to react; 3) other common clinically significant antibodies are ruled out (in this case anti-D, -C, -e, -k, -Fya, -Fyb, -Jka, -Lea, -Leb, -M, -N, -S, -s, and -P1) either by failure to react with an appropriate cell or because the patient expresses the corresponding antigen; 4) the patient fails to express the corresponding antigen.

Taking the results of the initial panel and two selected cell panels together, criteria #2 is met by the negative reactions of cells #1 and #2 of the initial panel, cell #18 of the 1st selected cell panel (rules out anti-Le^b), and cell #2 of the 2nd selected cell panel (rules out anti-Fy^a). Criterion #4 is also met by the patient's phenotype. Criterion #1 is only met for anti-K (cells #11 on the initial panel and #4 and #9 on the 2nd selected cell panel). There are only 2 rule in or "proof" cells for anti-E (cells #3 and #8 on the 2nd selected cell panel) and anti-c (cells #5 and 10 on the initial panel). There are 2 rule-in cells for anti-Jk^b (cells #6 and #7 on the 2nd selected cell panel), and these are only rule-in cells once anti-Fya was ruled out..

4. What percentage of donors is expected to be compatible with this recipient given the probable combination of antibodies present? Perform the calculation for European-American (E-A) and African-American (A-A) donors.

Although we still need 3 reactive rule-in cells to prove that the patient had anti-c, -K, -E, and –Jk^b if we assume that is the case the frequency is 0.19 (R1R1) x 0.91 (K-) x 0.26 (Jk^{b-}) = 0.045 or 4.5% for E-A donors and 0.02 (R1R1) x 0.98 (K-) x 0.51 (Jk^{b-}) = 0.01 or 1% for A-A donors. Note that in making this calculation one cannot multiply the frequency-compatible for c- and E- individuals in the population because Rh alleles are in "linkage disequilibrium". One has to use the frequency for the R1R1 phenotype. Had we made that error we would calculate the compatible E-A donor frequency as .04 (c-) x 0.71 (E-) x 0.91 (K-) x 0.26 (Jk^{b-}) = 0.034 or 3.4%.

Of interest to many of our readers 7% of donors of South Asia background are estimated to have a compatible phenotype.