Immunohematology Case Studies 2018 - #7

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Clinical History

Female, Caucasian, 64 years old

Has been pregnant twice and delivered three healthy children (over 30 years ago)

Has received a transfusion 9 years ago (two units) without complications.

Now planned for knee surgery. There is a small chance of need for units of red cells.

Serologic History

Several times tested as:

A RhD positive

Last antibody screen performed 9 years ago, was negative (as were all performed before).

Current Sample Presentation Data

ABO/Rh: A RhD positive

CcDee (R_1r)

DAT: negative

Antibody Screen Method: LISS, gel card

Antibody Screen Results: positive (1 out of 3 cells)

Antibody Identification Method: LISS, gel card

Initial panel

	D	C	E	c	e	C w	K	k	Fy a	Fy b	Lu a	Lu b	Jk a	Jk b	M	N	S	s	Le a	Le b	P 1		LISS gel	
1	+	+	0	0	+	+	0	+	+	0	0	+	+	0	0	+	0	+	0	+	+		w+	
2	+	+	0	0	+	0	+	+	0	+	0	+	0	+	+	0	+	0	0	+	+		0	
3	+	0	+	+	0	0	0	+	0	+	0	+	+	+	0	+	0	+	0	0	w		0	
4	0	+	0	+	+	0	0	+	+	0	0	+	+	0	+	0	0	+	0	+	0		1+	
5	0	0	+	+	+	0	0	+	+	+	0	+	0	+	+	+	0	+	+	0	+		0	
6	0	0	0	+	+	0	+	+	+	0	0	+	0	+	+	+	+	0	0	+	0		1+	
7	0	0	0	+	+	0	0	+	+	0	0	+	+	0	0	+	0	+	0	+	+		0	
8	+	0	0	+	+	0	0	+	0	0	0	+	+	+	0	+	0	+	0	0	+		0	
9	0	0	0	+	+	0	0	+	0	+	+	+	0	+	+	0	+	+	0	+	s		0	
10	0	0	0	+	+	0	0	+	0	+	0	+	0	+	0	+	+	0	+	0	+		0	
11	0	0	0	+	+	0	0	+	+	0	0	+	+	0	+	+	0	+	0	+	+		w+	
auto																							0	

Challenge with the Current Presentation

Weak positive reactions are seen with several cells tested.

No clear pattern can be seen.

Initial panel

	D	C	E	c	e	C w	K	k	Fy a	Fy b	Lu a	Lu b	Jk a	Jk b	M	N	S	s	Le a	Le b	P 1		LISS gel	
1	+	+	0	0	+	+	0	+	+	0	0	+	+	0	0	+	0	+	0	+	+		w+	
2	~~+~~	~~+~~	0	0	~~+~~	0	~~+~~	+	0	~~+~~	0	~~+~~	0	~~+~~	~~+~~	0	~~+~~	0	0	~~+~~	~~+~~		0	
3	~~+~~	0	~~+~~	~~+~~	0	0	0	~~+~~	0	~~+~~	0	~~+~~	+	+	0	~~+~~	0	~~+~~	0	0	w		0	
4	0	+	0	+	+	0	0	+	+	0	0	+	+	0	+	0	0	+	0	+	0		1+	
5	0	0	+	~~+~~	+	0	0	~~+~~	+	+	0	+	0	~~+~~	+	+	0	~~+~~	~~+~~	0	~~+~~		0	
6	0	0	0	+	+	0	+	+	+	0	0	+	0	+	+	+	+	0	0	+	0		1+	
7	0	0	0	+	~~+~~	0	0	+	~~+~~	0	0	+	~~+~~	0	0	~~+~~	0	+	0	~~+~~	+		0	
8	+	0	0	+	+	0	0	+	0	0	0	+	+	+	0	+	0	+	0	0	+		0	
9	0	0	0	+	+	0	0	+	0	+	~~+~~	+	0	+	~~+~~	0	+	+	0	+	s		0	
10	0	0	0	+	+	0	0	+	0	+	0	+	0	+	0	+	~~+~~	0	~~+~~	0	+		0	
11	0	0	0	+	+	0	0	+	+	0	0	+	+	0	+	+	0	+	0	+	+		w+	
auto																							0	

Challenge with the Current Presentation

Weak positive reactions are seen with several cells tested.

No clear pattern can be seen.

Most of the specificities can be excluded.

An enzyme (papain) treated panel is also tested (direct agglutination, no anti IgG used), and found negative.

Additional panel

	D	C	E	c	e	C w	K	k	Fy a	Fy b	Lu a	Lu b	Jk a	Jk b	M	N	S	s	Le a	Le b	P 1		Pap ain gel	
1	+	+	0	0	+	+	0	+	+	0	0	+	+	0	0	+	0	+	0	+	+		0	
2	+	+	0	0	+	0	+	+	0	+	0	+	0	+	+	0	+	0	0	+	+		0	
3	+	0	+	+	0	0	0	+	0	+	0	+	+	+	0	+	0	+	0	0	w		0	
4	0	+	0	+	+	0	0	+	+	0	0	+	+	0	+	0	0	+	0	+	0		0	
5	0	0	+	+	+	0	0	+	+	+	0	+	0	+	+	+	0	+	+	0	+		0	
6	0	0	0	+	+	0	+	+	+	0	0	+	0	+	+	+	+	0	0	+	0		0	
7	0	0	0	+	+	0	0	+	+	0	0	+	+	0	0	+	0	+	0	+	+		0	
8	+	0	0	+	+	0	0	+	0	0	0	+	+	+	0	+	0	+	0	0	+		0	
9	0	0	0	+	+	0	0	+	0	+	+	+	0	+	+	0	+	+	0	+	s		0	
10	0	0	0	+	+	0	0	+	0	+	0	+	0	+	0	+	+	0	+	0	+		0	
11	0	0	0	+	+	0	0	+	+	0	0	+	+	0	+	+	0	+	0	+	+		0	
auto																							0	

Interim Antibody Identification Possible Answers and Next Steps

Anti-Fy^{a} and anti-Jk^{a} appear to have been excluded but almost fit the pattern of reactivity observed.

The presence of anti-C and anti-E has also been excluded once, but they do not fit the pattern and the enzyme panel is non-reactive.

A second panel (combined from several other panels) is tested to confirm the presence of anti-Fy^{a} and/or anti-Jk^{a}, and to exclude the presence of other antibodies.

Follow-up Panel

	D	C	E	c	e	C w	K	k	Fy a	Fy b	Lu a	Lu b	Jk a	Jk b	M	N	S	s	Le a	Le b	P 1		LISS gel	
1	+	+	0	0	+	+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	+		0	
2	+	+	0	0	+	0	+	0	0	+	0	+	0	+	+	0	+	0	0	+	+		0	
3	+	0	+	+	0	0	0	+	0	+	+	+	0	+	0	+	0	+	0	0	0		0	
4	+	0	+	+	0	0	0	+	0	+	0	+	0	+	+	0	0	+	0	+	+		0	
5	+	0	+	+	0	0	0	+	0	+	0	+	0	+	+	+	0	+	+	0	0		0	
6	+	0	+	+	0	0	+	+	0	+	0	+	0	+	+	+	+	0	0	+	+		0	
7	+	+	0	0	+	+	0	+	+	0	0	+	0	+	0	+	0	+	0	+	+		1+	
8	+	+	0	0	+	0	0	+	+	0	0	+	0	+	0	+	0	0	0	0	+		0	
9	0	0	0	+	+	0	0	+	+	0	0	+	0	+	+	0	+	+	0	+	+		w+	
10	0	0	0	+	+	0	0	+	0	+	0	+	+	0	0	+	+	0	+	0	0		0	
11	0	0	0	+	+	0	0	+	0	+	0	+	+	0	+	+	0	+	0	+	+		0	
12	+	+	0	+	+	0	+	+	0	+	0	+	+	0	+	+	0	+	0	+	0		0	

Challenge with the Current Presentation

The follow-up panel showed only a few reactions.

The presence of anti-C, -E, -K and -Jk^a can be excluded several times.

Anti-Fy^a can be excluded only once, and the two positive reactions are with Fy(a+b-) cells.

Follow-up Panel

	D	C	E	c	e	C w	K	k	Fy a	Fy b	Lu a	Lu b	Jk a	Jk b	M	N	S	s	Le a	Le b	P 1		LISS gel	
1	+	~~+~~	0	0	+	~~+~~	0	+	0	+	0	+	0	+	0	+	0	+	0	+	+		0	
2	+	~~+~~	0	0	+	0	~~+~~	0	0	+	0	+	0	+	+	0	+	0	0	+	+		0	
3	+	0	~~+~~	+	0	0	0	+	0	+	~~+~~	+	0	+	0	+	0	+	0	0	0		0	
4	+	0	~~+~~	+	0	0	0	+	0	+	0	+	0	+	+	0	0	+	0	+	+		0	
5	+	0	+	+	0	0	0	+	0	+	0	+	0	+	+	+	0	+	+	0	0		0	
6	+	0	+	+	0	0	~~+~~	+	0	+	0	+	0	+	+	+	+	0	0	+	+		0	
7	+	+	0	0	+	+	0	+	+	0	0	+	0	+	0	+	0	+	0	+	+		1+	
8	+	+	0	0	+	0	0	+	~~+~~	0	0	+	0	+	0	+	0	0	0	0	+		0	
9	0	0	0	+	+	0	0	+	+	0	0	+	0	+	+	0	+	+	0	+	+		w+	
10	0	0	0	+	+	0	0	+	0	+	0	+	~~+~~	0	0	+	+	0	+	0	0		0	
11	0	0	0	+	+	0	0	+	0	+	0	+	~~+~~	0	+	+	0	+	0	+	+		0	
12	+	+	0	+	+	0	+	+	0	+	0	+	~~+~~	0	+	+	0	+	0	+	0		0	

Further Work

The patient cells where typed for several antigens:

K negative, Fy(a-), Jk(a+)

This typing indicates that it is possible for the patient to make alloanti-Fy^a

Further Work

There is no explanation for the 2 non-reactive cells with the Fy(a+b-) phenotype.

Both show an additional typing (not shown on previous slides)

	D	C	E	c	e	C w	K	k	Js a	Js b	Fy a	Fy b	Jk a	Jk b	M	N	S	s	Aditional typing		LISS gel	
7	0	0	0	+	+	0	0	+	+	+	+	0	+	0	0	+	0	+	V+		0	
8	+	+	0	0	+	0	0	+	0	+	+	0	0	+	0	+	0	0	U-		0	

Both cells are most likely from donors with African background, based on their typing. The donor from the first panel is Js(a+) and V positive, while the donor from the second panel is negative for S, s and U.

Fy antigens

In donors of African descent the frequency of the Duffy antigens is different.

%	Caucasians	Africans
Fy^a	66	10
Fy^b	83	23
Fy(a+b-)	17	9
Fy(a+b+)	49	1
Fy(a-b+)	34	22
Fy(a-b-)	0	68

Fy antigens

In Africans the *FY*0* allele (*FY* null, no expression) is very common.

Africans with a Fy(a+b-) phenotype often do not have a homozygous expression of the Fy^a antigen.

More often they have the genotype *FY*A/FY*0*, instead of *FY*A/FY*A* as found in Caucasian donors with the Fy(a+b-) phenotype.

The holds true for the Fy^b antigen.

Genotyping Results

Of donor 7 (the first panel) no DNA could be retrieved for testing.

DNA of donor 8 (follow-up panel) was tested and the presence of one *FY*0* allele could be confirmed.

The genotype was *FY*A/FY*0*, leading to a Fy(a+b-) phenotype with only single dose expression of Fy^a (comparable with a Fy(a+b+) donor).

Other examples

There are several antigens with different frequencies from that observed in Caucasian donors.

The following low prevalence antigens have a higher frequency in African donors; He, Dantu, V, VS, Go^a, Crawford, DAK, Rh32, Rh42, STEM, Js^a, Ls^a, Tc^b

The presence of one of these antigens on a panel cell points to the origin of the donor (African). This can be a warning to the fact that these cells probably will not have a double dose expression of Fy^a/Fy^b antigens, when appearing Fy(a+b-) or Fy(a-b+).

Other examples

The absence of the following high prevalence antigens on a panel cell, can also point to the African origin of the donor;

U, Js^b, Cr^a, Tc^a, Hy, Jo^a, McC^a, Sl^a, At^a

This also can be a warning to the fact that these cells probably will not have a double dose expression of Fy^a/Fy^b antigens, when appearing Fy(a+b-) or Fy(a-b+).

Other examples

This situation, hemizygous expression is seen most often for Fy^a/Fy^b antigens but almost all other blood group systems also have null alleles (genotype positive, phenotype negative).

This situation is also seen within the Rh, MNS and Kidd (JK) blood group systems. Where a donor does not show double dose when expected.

Exclusion of the presence antibodies based on non-reactivity with these cells can lead to wrong conclusions.

Conclusions

This case shows a woman who had a weak-reactive anti-Fy^a antibodies (only reactive with cells with double dose expression of the antigen).

This antibody is probably made after transfusion (9 years ago) or at the time of her pregnancies.

In case of a transfusion, Fy(a-) negative red cells need to be selected.

Because she has shown to be an antibody producer one can consider extended matching for E and K antigens, to prevent further antibody formation.

Summary of Case Challenges

In case of weak reactions and unexplained reactions, a second (or third) round of exclusion can help determine the specificity of the antibody.

Lessons Learned by the Case

- Panels of RBCs with homozygous expression of an antigen do not always express this antigen in double dose as could be expected

- The "two-times exclusion rule" is therefore a wise thing to do

- Particular blood group phenotypes can provide a strong indication of the most likely ethnic origin of the donor, this information can help the technician to interpret the different reactions found

References

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