Immunohematology Case Studies 2017 - 11

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Clinical History

- 81 year old female
- Ethnicity: African descent
- Unspecified anemia
- Hemoglobin 6.2g/dL
- Hematocrit 19.1%
- Previously transfused 2 units of packed red blood cells November 2006
- Previous pregnancies unknown
- Medications: unknown

Serologic History

- Hospital reports an anti-Fy^a identified in 2006
- Reference laboratory identified an additional anti-C, -E in 2006
- No additional serologic history available

Current Sample Presentation Data Hospital Results

ABO/Rh: O positive

DAT: Negative

Antibody Screen Method: Gel column agglutination

Antibody Screen Results: Positive

Antibody Identification Method: Gel column agglutination

Antibody Identification Preliminary Results: Panagglutination with negative autocontrol

Sample referred to reference laboratory for additional testing

Current Sample Presentation Data Reference Lab Results

ABO/Rh: O positive

DAT: Negative (polyspecific)

Antibody Identification Method: PEG-IAT

Antibody Identification Preliminary Results: Panagglutination with negative autocontrol

Challenge with the Current Presentation

Both hospital and reference laboratory panels showed an antibody reactive 3+ with all reagent red cells tested.

Selected C-, E-, Fy(a-) cells were also reactive 3+

Initial Panel

	D	C	c	E	e	Cw	K	k	Fya	Fyb	Jka	Jkb	Lea	Leb	P1	M	N	S	s		PEG IAT	
1	+	+	0	0	+	0	+	+	+	+	+	+	0	0	0	+	0	+	0		3+	
2	+	+	0	0	+	+	0	+	+	0	+	+	0	+	+	0	+	0	+		3+	
3	+	0	+	+	0	0	0	+	+	+	+	+	+	0	+	0	+	+	+		3+	
4	+	0	+	0	+	0	0	+	0	0	+	0	0	0	+	0	+	+	0		3+	
5	0	+	+	0	+	0	0	0	0	+	0	+	0	+	+	+	+	+	+		3+	
6	0	0	+	+	+	0	0	+	+	+	0	+	0	+	+	+	+	+	+		3+	
7	0	0	+	0	+	0	+	+	0	+	+	+	+	0	+	+	+	+	0		3+	
8	0	0	+	0	+	0	0	+	+	0	+	0	0	+	+	0	+	+	+		3+	
9	0	0	+	0	+	0	0	+	0	+	+	+	+	0	+	+	0	0	+		3+	
10	+	0	+	+	0	0	0	+	+	+	+	0	+	0	0	+	+	+	+		3+	
11	0	0	+	0	+	0	+	+	0	+	0	+	+	0	+	+	+	0	+		3+	
AC																					0√	

Selected Cell Panel

	RhHr							MN				P	Lewis		Kell				Duffy		Kidd		X	Result
	D	C	E	c	e	f	Cw	M	N	S	s	P1	Lea	Leb	K	k	Kpa	Jsa	Fya	Fyb	Jka	Jkb	Xga	PEG-IAT
1	0	0	0	+	+	+	0	+	0	+	0	+	+	0	0	+	0	0	0	0	+	0	+	3+
2	0	0	0	+	+	+	0	+	+	+	+	0	+	0	0	+	0	0	0	+	0	+	+	3+
3	+	0	0	+	+	+	0	+	+	+	0	+	0	+	+	+	0	0	0	0	+	0	+	3+
4	0	0	0	+	+	+	0	+	+	+	+	+	+	0	0	+	0	0	0	0	+	+	+	3+
AC																								0√

Note: PEG, or polyethylene glycol, is a potentiator used to enhance red cell and antibody reactions. PEG works by excluding water molecules from the red cell surface, concentrating antibodies, and accelerating antibody binding.

Interim Antibody Identification Possible Answers and Next Steps

- Similar strength of reactivity with all cells tested
- Possible antibody to a high prevalence antigen
- Next steps:
  - Run cells negative for selected high prevalence antigens, especially those more often found in individuals of African descent
  - Perform patient phenotype

High Prevalence Antigen Negative Selected Cell Panel

Cell Type	PEG-IAT
k-	4+
Kp(a+b-)	4+
Js(a+b-)	4+
U-	0v
Lu(a+b-)	4+
Yt(a)-	4+
Vel-	4+

Selected U- Panel

	RhHr							MN					Lewis		Kell		Duffy		Kidd		X	
	D	C	E	c	e	f	Cw	M	N	S	s	U	Lea	Leb	K	k	Fya	Fyb	Jka	Jkb	Xga	PeG
1	0	0	0	+	+	+	0	+	0	0	0	0	+	0	0	+	0	0	+	0	+	0√
2	0	0	0	+	+	+	0	+	+	0	0	0	+	0	0	+	0	+	0	+	+	3+
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	+	+	+	0√
AC																						0√

- Probable anti-U
- Possible antibody to low prevalence antigen?
  - U-negative phenotype is most often found in individuals of African descent
  - Low prevalence antigens more common in donors of African descent: V, VS, Js^{a}, others

Patient Phenotype

D	C	E	c	e
+	0	0	+	+

K	Fy^a	Fy^b	Jk^a	Jk^b	M	N	S	s	U
0	0	0	+	+	+	+	0	+	+

Phenotype vs.
Antibody Investigation

- Patient is s+ and U+
- Should not be able to form anti-U
  - Autoanti-U have been reported
  - Our patient has a negative autocontrol and DAT, so autoantibody is unlikely

- Consider other high prevalence antigens
  - Patient is Fy(a-b-)
  - Possible anti-Fy3?

Revisiting Selected U- Panel

	RhHr							MN					Lewis		Kell				Duffy		Kidd		X	
	D	C	E	c	e	f	Cw	M	N	S	s	U	Lea	Leb	K	k	Kpa	Jsa	Fya	Fyb	Jka	Jkb	Xga	PEG
1	0	0	0	+	+	+	0	+	0	0	0	0	+	0	0	+	0	0	0	0	+	0	+	0√
2	0	0	0	+	+	+	0	+	+	0	0	0	+	0	0	+	0	0	0	+	0	+	+	3+
3	+	0	0	+	+	+	0	+	+	0	0	0	0	+	+	+	0	0	0	0	+	0	+	0√
4	0	0	0	+	+	+	0	+	+	0	0	0	+	0	0	+	0	0	0	0	+	+	+	0√
AC																								0√

- Cell 2 is Fy(b+), therefore Fy3+
- Cells 1, 3 and 4 are Fy(a-b-) and Fy3-

Selected Fy(a-b-) Panel

	RhHr							MN					Lewis		Kell				Duffy		Kidd		X	
	D	C	E	c	e	f	Cw	M	N	S	s	U	Lea	Leb	K	k	Kpa	Jsa	Fya	Fyb	Jka	Jkb	Xga	PEG
1	+	0	0	+	+	+	0	+	+	+	0	+	0	+	0	+	0	0	0	0	+	+	+	3+
2	+	0	0	+	+	+	0	0	+	0	0	0	0	+	0	+	0	0	0	0	+	0	+	0√
3	+	0	0	+	+	+	0	+	+	0	+	+	0	+	0	+	0	+	0	0	0	+	+	0√
4	+	0	0	+	+	+	0	0	+	0	+	+	0	+	0	+	0	0	0	0	0	+	0	0√
5	0	0	0	+	+	+	0	+	0	0	+	+	+	0	0	+	0	0	0	0	0	+	+	0√
6	0	0	0	+	+	+	0	0	+	0	+	+	+	0	0	+	0	0	0	0	+	0	+	0√

- Anti-U is excluded
- Cell 1 is reactive – this is the only cell on this selected cell panel that is S+
- Additional testing confirmed anti-S
  - See slide 8: selected cells 1, 3, 4 are S+, Fy(a-b-)

Additional Information

- S, s, Fy^a, and Fy^b antigens are destroyed by enzyme treatment, but U and Fy3 antigens are not. Enzyme treated cells were not tested in this case due to availability of Fy(a-b-) cells for rule-ins and rule-outs
- In the absence of sufficient Fy(a-b-) cells to complete antibody identification, anti-Fy3 can be adsorbed from the patient's plasma using cells positive for either Fy^a or Fy^b antigens

Further Testing Results and Interpretations

- Final antibody identification: Anti-C, -E, -Fy3, -S
- Anti-Fy^{a} reported in patient history was not evaluated due to presence of anti-Fy3
    - If desired, adsorptions studies can be used to confirm the presence of anti-Fy^{a} in sera containing anti-Fy3
    - A similar antibody, anti-Fy5, was also not evaluated.
    - Most U-negative donors are of African descent
    - Most common phenotype for U- donors is C-, E-, Fy(a-b-)
    - U- donors should type S-s-
    - The U- selected cells were coincidentally phenotypically similar to our patient
- Anti-Fy3 is considered a clinically significant red cell alloantibody and has been implicated in hemolytic transfusion reactions
- This patient should receive C-, E-, Fy(a-b-), S- red blood cells if transfusion is required

Anti-Fy3 vs. Anti-Fy5

- Like anti-Fy3, anti-Fy5 reacts with red cells expressing Fy^a or Fy^b
- Anti-Fy5 can be differentiated from anti-Fy3 by testing red cells of the Rh_{null} type
  - Anti-Fy3 will react with all cells except Fy(a-b-) cells
  - Anti-Fy5 will react with all cells except Fy(a-b-) cells and Rh_{null} cells
- Anti-Fy5 was not evaluated for this patient, as the recommendations for transfusion are the same for patients with anti-Fy3 and anti-Fy5

Anti-Fy3 vs. Anti-Fy5 Clinical Significance

	Anti-Fy3	Anti-Fy5
Immediate transfusion reaction?	Rare	No reports
Delayed hemolytic transfusion reactions?	Yes – mild to moderate in severity	Yes – mild in severity
HDFN?	Rare cases of mild HDFN have been reported	Insufficient data

Summary of Case Challenges

- Fy3 antigen is a high prevalence antigen in most populations. However, approximately 68% of African American individuals are Fy(a-b-) and likely Fy3-
    - Most Fy(a-b-) individuals inherit an allele with a GATA-box nucleotide change that prevents Fy^b expression on red blood cells. These individuals express Fy^b normally on non-erythroid cells (including tissues) and are not expected to make anti-Fy^b. However, numerous cases of anti-Fy3 have been reported in these individuals
- As with our patient, formation of anti-Fy^a commonly precedes the formation of anti-Fy3

Lessons Learned by the Case

- Apparent antibodies to high prevalence antigens can be due to a combination of antibodies in several blood group systems
- Patient phenotype and ethnicity can be useful in antibody identification, especially if an antibody to a high prevalence antigen is suspected
- When testing cells negative for high prevalence antigens, consider the full phenotype of the cells tested as high and low prevalence antigens present or absent in specific ethnic populations can be misleading

References

AABB Technical Manual, 18th Edition

The Blood Group Antigen FactsBook, 3rd edition by M.E. Reid, C. Lomas-Francis, and M.L. Olsson