Immunohematology Case Studies 2019 - #10

Anu Korhonen, M.Sc
Immunohematology Reference Laboratory
Finnish Red Cross Blood Service, Finland
anu.korhonen@bloodservice.fi

Clinical History

- A 60 year old Finnish woman, with a Caesarean Section and one RBC transfusion previously
- She needed hand surgery because of a trauma.
- Two RBC units were transfused
- After the operation, she got post-operative infection and needed another surgery
- After the second operation Hgb was 83g/l

Serologic History

- Antibody screening was negative before the first operation
- After the second operation antibody screening was positive and all antibody identification panel cells were positive at the university hospital laboratory
- A sample was sent to the national reference laboratory for further antibody identification with an urgent need of blood transfusion

Current Sample Presentation Data

ABO/Rh: O RhD negative

DAT: weakly positive

Antibody Screen Method: IAT gel column

Antibody Screen Results: positive

Antibody Identification Method: gel column and tube, both with papain treated cells (direct aggl.) and untreated cells(IAT)

Antibody Identification Preliminary Results: all test cells reacted strongly

Challenge with the Current Presentation

- All panel cells were positive, autocontrol positive, DAT weakly positive
- Panagglutinin or an antibody against high prevalence antigen?
- Phenotype: C- E- c+ e+ K-, Jk(a+b+), P+
- Excluded anti-Jk3 and anti-P
- All crossmatched units (C- E- K-) were incompatible, but because the patient needed a transfusion, two of them were sent for transfusion

Basic panel
Gel and tube methods

	Rhesus							MNS				P	Lewis		Kell		Duffy		Kidd		Gel card		Tube	
	D	C	Cw	Cx	E	c	e	M	N	S	s	P1	Lea	Leb	K	k	Fya	Fyb	Jka	Jkb	pap	IAT	pap	IAT
1	+	+	0	0	0	+	+	0	+	0	+	+s	0	+	+	0	0	+	+	0	4+	3+	2+	1+
2	+	+	+	0	0	0	+	0	+	+	0	+	0	+	0	+	0	+	+	+	4+	2+	3+	1+
3	+	+	0	+	0	0	+	0	+	+	+	+w	0	+	0	+	+	+	+	0	4+	3+	2+	2+
4	+	0	0	0	+	+	0	+	0	0	+	+	0	0	0	+	+	0	0	+	3+	2+	2+	2+
5	+	0	0	0	+	+	0	0	+	+	0	+	0	+	0	+	+	+	+	0	4+	3+	2+	1+
6	0	+	0	0	0	+	+	+	+	0	+	0	0	+	+	+	+	+	+	+	4+	3+	3+	1+
7	0	0	0	0	+	+	+	+	+	+	+	0	0	+	0	+	0	+	0	+	4+	3+	2+	1+
8	0	0	0	0	0	+	+	+	+	0	+	+	0	+	0	+	+	+	+	+	4+	3+	3+	1+
9	0	0	0	0	0	+	+	+	+	+	+	+	0	+	+	+	+	0	+	+	4+	3+	2+	1+
10	0	0	0	0	0	+	+	0	+	+	+	0	0	+	0	+	0	+	+s	0	4+	3+	2+	2+
11	0	0	0	0	0	+	+	+	+	+	+	0	+	0	0	+	+	+	0	+	4+	3+	3+	1+
Auto																					1+	2+	(+)	(+)

Interim Antibody Identification
Possible Answers and Next Steps

- Anti-Jk3 and anti-P antibodies were excluded.
  - They are the most common antibodies against high prevalence antigens enhanced by papain treatment in the Finnish population
- Blood transfusion was needed urgently in night time and it was not possible to use any special methods for antibody identification at that time.
- Incompatible RBC units were sent to the hospital with a warning of a possible transfusion reaction

Updated Clinical Information

- After the transfusion of first incompatible RBC unit patient had a acute hemolytic transfusion reaction and needed intensive care

- A day after the transfusion reaction, a surgeon called to the reference lab to ask what kind of blood to transfuse and to tell about the transfusion reaction. He wanted to transfuse more blood before moving the patient to another hospital

Further Work

- k phenotype was performed to exclude K_0
- Patient's phenotype proved to be K-k-
- DTT-treated antibody identification panel cells were prepared and tested with patient's plasma

	Rhesus							MNS				P	Lewis		Kell		Duffy		Kidd		Gel card
	D	C	Cw	Cx	E	c	e	M	N	S	s	P1	Lea	Leb	K	k	Fya	Fyb	Jka	Jkb	DTT IAT
1	+	+	0	0	0	+	+	0	+	0	+	+s	0	+	+	0	0	+	+	0	0
2	+	+	+	0	0	0	+	0	+	+	0	+	0	+	0	+	0	+	+	+	0
3	+	+	0	+	0	0	+	0	+	+	+	+w	0	+	0	+	+	+	+	0	0
4	+	0	0	0	+	+	0	+	0	0	+	+	0	0	0	+	+	0	0	+	0
5	+	0	0	0	+	+	0	0	+	+	0	+	0	+	0	+	+	+	+	0	0
6	0	+	0	0	0	+	+	+	+	0	+	0	0	+	+	+	+	+	+	+	0
7	0	0	0	0	+	+	+	+	+	+	+	0	0	+	0	+	0	+	0	+	0
8	0	0	0	0	0	+	+	+	+	0	+	+	0	+	0	+	+	+	+	+	0
9	0	0	0	0	0	+	+	+	+	+	+	+	0	+	+	+	+	0	+	+	0
10	0	0	0	0	0	+	+	0	+	+	+	0	0	+	0	+	0	+	+s	0	0
11	0	0	0	0	0	+	+	+	+	+	+	0	+	0	0	+	+	+	0	+	0
Auto																					2+

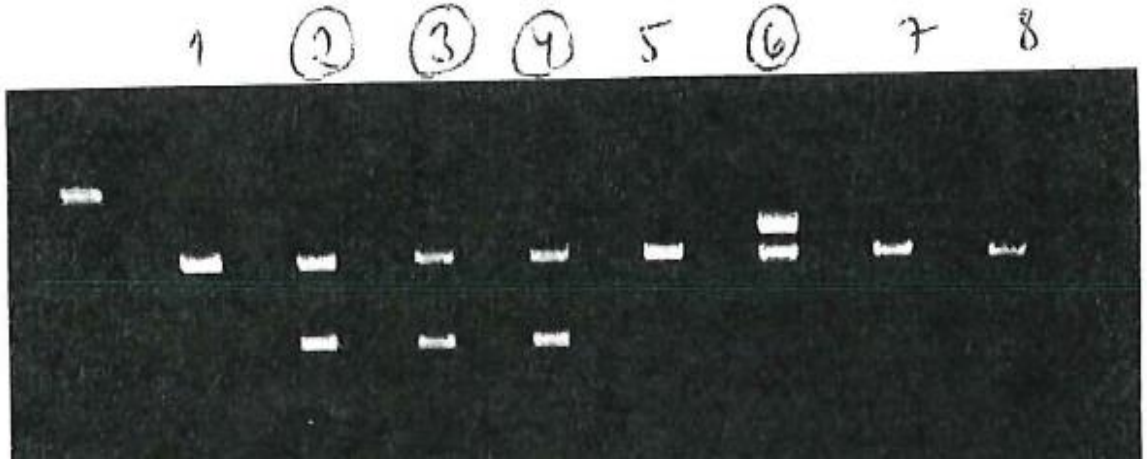
Further Work

- Anti-Ku (anti-KEL5) antibody was suspected, other antibodies excluded (with DTT treated cells only)
- One frozen O RhD pos K_0 RBC unit was crossmatched for the patient and it was compatible

Genotyping Results

- Genotype was tested with RBC-Ready Gene KKD (SSP), Innotrain and IDCORE^{XT}(SSO), Grifols kits
- *KEL*01* was neg but *KEL*02* pos with both kits

Reaction-No.	1	2*	3*	4	5	6	7	8#
PCR Product (Size in bp)	135	140	130	130	720	720	720	185
SNP	578C>T	578C	838A>G	838A	125A>G	125A	-67T>C 125A	265C>T 125A
ISBT Allele Name	KEL*01.01	KEL*02	JK*01 or JK*A	JK*02 or JK*B	FY*01 or FY*A	FY*02 or FY*B	FY*02N.01	FY*02W.01 FY*02W.02
ISBT Phenotype	K+k-	k+	Jk(a+)	Jk(b+)	Fy(a+)	Fy(b+) Fy(b+^{w})	Fy(a-b-)	Fy(b+^{w}), Fy^{x}



Further Testing Results and Interpretations

- Patient's two siblings and a daughter were tested
  - all were K- k+
- KEL sequencing revealed *KEL*02N.19* corresponding to the c.2023 C>T change, predicted to encode the p. Arg675Ter amino acid change
  - first described in Austria (Körmöczi et al 2007)
- K_0 phenotype was confirmed

Updated Clinical Information

- In Finland
  - only one other K_0 person, who is O RhD pos and unable to donate anymore
  - one frozen O RhD pos K_0 unit (→ could have been used for this patient in emergency)
- The patient needed another operation later
- One O RhD neg K_0 unit was received from Japan and frozen to wait for a possible transfusion
- Both K_0 units were crossmatched to confirm the antibody identification and they were compatible
- Before the operation the patient donated two times for herself and units were frozen

Summary of Case Challenges

- Antibody was undetectable before transfusion
- Positive autocontrols caused staff to think this was an autoantibody
- Only one other known anti-Ku reported in Finland →no one thought this case could be another one
- Used genotyping methods that did not recognize the *KEL*02N.19* mutation
- No O RhD neg K_0 donors available in Finland

Lessons Learned by the Case

- Alloantibodies can cause positive autocontrol, if a patient has received recent blood transfusions
  - Look for mixed field
    - Tube test is better at detecting mixed field than gel test
  - Eluate may help allo vs. auto antibody determination
- When suspecting an antibody against a high prevalence antigen, remember also null types

ISBT Terminology of the System

Kell Blood Group System

- ISBT symbol KEL (006)
- 36 antigens
- Chromosomal location 7q33
- Several null alleles

Brief Review of the Blood Group Antibody

- K_0 persons can make anti-Ku antibody
- Anti-Ku is potentially clinically significant
    - Hemolytic transfusion reactions reported
    - Hemolytic Disease of the Fetus and Newborn reported

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