Immunohematology Case Studies 2020 - #7

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Clinical History

58 year old female with no information about clinical history

Serologic History

- Referring laboratory had a weak positive antibody screening and a weak positive DAT
- A sample was sent to the national reference laboratory for further antibody identification with a request of two blood units for the same evening

Current Sample Presentation Data

ABO/Rh: A RhD positive

DAT: anti-IgG weakly positive, anti-C3d negative

Antibody Screen Method: LISS-IAT

Antibody Screen Results: weakly positive

Antibody Identification Method: LISS-IAT with untreated and papain treated cells on NaCl card

Antibody Identification Preliminary Results:

All panel cells reacting weak positive in both milieus, C^{W} positive cell stronger positive

In-house test cells on Bio-Rad LISS/Coombs Cards

Panel Sample

	Rh	MNSs	P	Lutheran	Kell	Lewis	Duffy	Kidd	Xg	Colton	Cartwr.	Sid	Bg	HTLA	Dombrock	Vel	mit s.p AK	Auberger	Gerbich
Trypsin		- -		- -					-		+ +		+ +	- - - - -	-			-	-?
Papain		- - - -		-/± - / +			- -		-		- -			- / + - -		+			-

		C	D	E	c	e	Cw	M	N	S	s	P1	Lua	Lub	K	k	Kpa	Kpb	Lea	Leb	Fya	Fyb	Jka	Jkb	Xga	Coa	Cob	Yta	Ytb	Sda	Bga	Bgb	Kna	McC	Yka	Csa	Ch	Rg	Doa	Dob	Vel	Vel	Aub	Ge	IAT	Pap.	T/C
1	R1R1	+	+	-	-	+	-	+	+	+	-	+	-	+	-	+	-	+	+	-	-	(+)	-	+	-	+	-	+	-	-	-	-	+	+	+	-/±	+	+	+	+	+	-	+	-	1	2 DP	1
2	R2R2	-	+	+	+	-	-	+	-	+	+	+	-	+	+	+	-	+	-	+	+	-	+	-	±	+	-	+	-	-	-	?	+	+	+	+	+	+	+	+	+	-		1	2 DP	1
3	R1wR1	+	+	-	-	+	+	+	+	-	+	+	-	+	-	+	-	+	+	-	-	+	-	+		+	-	+	-	-	?	-	(±)	+	+	±	+	+	+	+	+	+			3	4 DP	nd
4	rr	-	-	-	+	+	-	+	-	-	+	+	+	+	-	+	-	+	-	+	+	-	-	+	+	+	+	+	-	-	-	-	+	+	+	±	-	+	+	+	(±)	-	+		1	2 DP	nd
5	r'r	+	-	-	+	+	-	-	+	-	+	+	-	+	-	+	-	+	-	+	+	-	+	+	+	+	-	+	+	-	-	-	±	-	±	-	±	+	-	+	+	-	-		1	2 DP	nd
6	r"r	-	-	+	+	+	-	+	+	+	-	-	-	+	-	+	-	+	-	+	-	+	+	-	+	+	-	+	-	±	+	-	(+)	+	-	±	+	(+)	+	±	+	+	-	(±)	1	2 DP	nd
7	rr	-	-	-	+	+	-	+	+	+	+	+	-	+	-	+	+	+	+	-	+	+	+	-	-	+	+	+	-	-	-	-	(±)	±	(±)	+	(±)	±	-	+	+	+	-		1	2 DP	nd
8	rr	-	-	-	+	+	-	+	-	-	+	-	-	+	+	+	-	+	-	+	-	+	+	+	+	+	-	+	-	-	-	-	±	±	-	±	+	+	+	±	+	+	-	nb	1	2 DP	nd
																																													Autocontrol		neg.	

DP= double population
nd= not determined
T/C= trypsin/IAT

Challenge with the Current Presentation

- All panel cells were positive, autocontrol negative, DAT weakly positive
- Panagglutinin or an antibody against high prevalence antigen?
- Phenotype: C+E-c-e+ K-

Panel Sample

	Rh	MNSs	P	Lutheran	Kell	Lewis	Duffy	Kidd	Xg	Colton	Cartwr.	Sid	Bg	HTLA	Dombrock	Vel	mit s.p AK	Auberger	Gerbich
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		C	D	E	c	e	Cw	M	N	S	s	P1	Lua	Lub	K	k	Kpa	Kpb	Lea	Leb	Fya	Fyb	Jka	Jkb	Xga	Coa	Cob	Yta	Ytb	Sda	Bga	Bgb	Kna	McC	Yka	Csa	Ch	Rg	Doa	Dob	Vel	Vel	Aub	Ge	IAT	Pap.	T/C
1	R1R1	+	+	-	-	+	-	+	+	+	-	+	-	+	-	+	-	+	+	-	-	(+)	-	+	-	+	-	+	-	-	-	-	+	+	+	-/±	+	+	+	+	+	-	+	-	1	2DP	1
2	R2R2	-	+	+	+	-	-	+	-	+	+	+	-	+	+	+	-	+	-	+	+	-	+	-	±	+	-	+	-	-	-	?	+	+	+	+	+	+	+	+	+	-		1	2DP	1
3	R1wR1	+	+	-	-	+	+	+	+	-	+	+	-	+	-	+	-	+	+	-	-	+	-	+		+	-	+	-	-	?	-	(±)	+	+	±	+	+	+	+	+	+			3	4DP	nd
4	rr	-	-	-	+	+	-	+	-	-	+	+	+	+	-	+	-	+	-	+	+	-	-	+	+	+	+	+	-	-	-	-	+	+	+	±	-	+	+	+	(±)	-	+		1	2DP	nd
5	r'r	+	-	-	+	+	-	-	+	-	+	+	-	+	-	+	-	+	-	+	+	-	+	+	+	+	-	+	+	-	-	-	±	-	±	-	±	+	-	+	+	-	-		1	2DP	nd
6	r"r	-	-	+	+	+	-	+	+	+	-	-	-	+	-	+	-	+	-	+	-	+	+	-	+	+	-	+	-	±	+	-	(+)	+	-	±	+	(+)	+	±	+	+	-	(±)	1	2DP	nd
7	rr	-	-	-	+	+	-	+	+	+	+	+	-	+	-	+	+	+	+	-	+	+	+	-	-	+	+	+	-	-	-	-	(±)	±	(±)	+	(±)	±	-	+	+	+	-		1	2DP	nd
8	rr	-	-	-	+	+	-	+	-	-	+	-	-	+	+	+	-	+	-	+	-	+	+	+	+	+	-	+	-	-	-	-	±	±	-	±	+	+	+	±	+	+	-	nb	1	2DP	nd
																																													Autocontrol		neg.	

DP= double population
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Interim Antibody Identification
Possible Answers and Next Steps

All test cells are positive, the reactions with papain or trypsin treated cells does not enhance the reaction strength markedly. The C^W positive cell reacts strongly with the patient serum; hence an anti-C^W is most likely present.

In order to exclude antibodies against stabilization solution, a panel with fresh donor test cells was used.

Fresh donor test cells without stabilization solution

	C	D	E	c	e	Cw	M	N	S	s	P1	Lua	Lub	K	k	Kpa	Kpb	Lea	Leb	Fya	Fyb	Jka	Jkb	Cob	ID/IAT	Tube /IAT	Tube w/o LISS
1	+	+	-	-	+	+	+	+	+	-	/	/	/	-	+	-	+	/	/	+	-	+	-		2	2	nd
2	-	+	+	+	-	-	+	-	+	-	/	-	+	-	+	-	+	/	/	+	-	-	+		w+	w+	nd
3	+	+	-	+	+	-	-	+	+	+	+	-	+	-	+	+	+	-	+	+	+	+	+	+	w+	w+	1
4	+	+	+	+	+	-	+	-	-	+	+	-	+	+	+	-	+	+	-	-	+	+	+		w+	w+	nd
5	-	-	-	+	+	-	+	+	-	+	-	+	+	-	+	-	+	-	-	-	+	+	-		w+	w+	nd
6	-	-	-	+	+	-	+	+	-	+	-	-	+	-	+	-	+	-	+	+	-	-	+		w+	1	nd

Interim Antibody Identification
Possible Answers and Next Steps

The reactions with fresh donor test cells are similar to the normal test cells. Even in tube without addition of LISS. Thus, the presence of an antibody against a high prevalence antigen is likely.

Further Testing Results and Interpretations

In Switzerland the most “common” antibodies against high prevalence antigens are anti-k, -Kp^b, -Vel, -Yt^a and -Co^a. Cells lacking these high prevalence antigens are always ready to be used.

IAT	k neg.	Kp(b-)	Vel neg.	Yt(a-)	Co(a-)
Patient serum	1+	w+	w+	1+	1+

Unfortunately, the patient serum reacted with all cells.

Further Testing Results and Interpretations

Looking closer at the reaction strengths in the different techniques, antibodies against Cs^a or an antigen in the KEL, LAN, DI or JR blood group system is most likely.

Our experience is that anti-Lan and anti-Jr^a antibodies show mixed field (double population) reactions with our in-house papainized test cells.

Further Testing Results and Interpretations

With two Jr(a-) negative cells ready in the fridge, these cells were chosen first, as Lan negative cells had to be thawed first.

IAT	Jr(a-) 2017/3569	Jr(a-) 0049S #12
Patient serum	neg.	neg.

Additionally, the patient was confirmed to be negative for both the C^W and the Jr^a antigen.

Updated Clinical Information

In the patient serum an anti-Jr^a could be identified and due to the stronger reactivity with papainized test cell an anti-C^W was presumed.

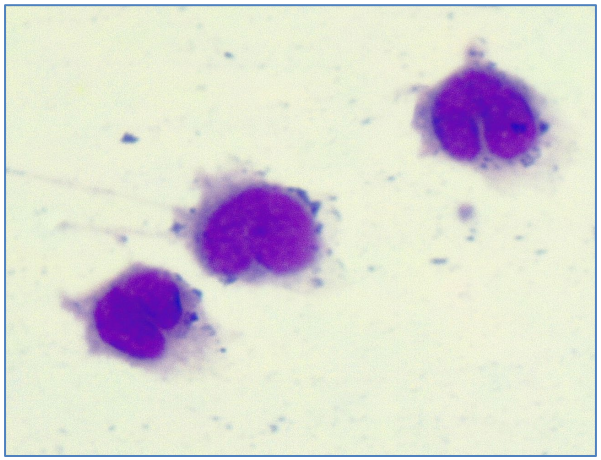
The request of two Jr(a-) units could unfortunately not be met. In the past the monocyte monolayer assay (MMA) has been used to estimated the clinical significance of anti-Jr^a antibodies and in 12 out of 13 cases the test indicated the antibody to be clinically insignificant. With this knowledge, it was decided to transfuse, in case of an emergency, Jr(a+), c-, E-, K-, C^W- blood units.

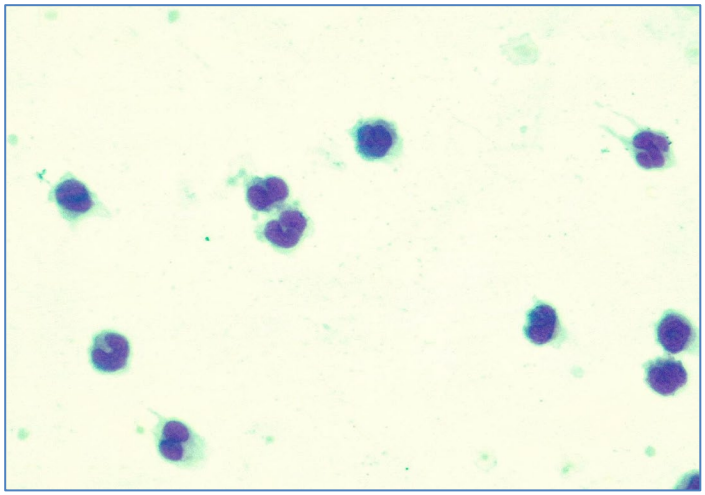
Genotyping Results

Using SSP-PCR the patient was shown to be homozygous for the allele *JR*01N.02* (*ABCG2*01N.02*).

Further Testing Results and Interpretations

The MMA showed 1.7 % reactive monocytes, indicating that the anti-Jr^a was not clinically significant.





Non-reactive monocytes (negative MMA result)

Updated Clinical Information

The patient presented herself in the emergency ward with increasing back pain, despite extended analgesic therapy. On the following day the blood culture showed the presence of Staphylococcus aureus. The MRI showed a pronounced epidural abscess. The indication for emergency abscess evacuation was given. The surgical procedure was performed the following day without complications. No transfusion was needed. The patient was operated a second time. Also, this time without the need of a blood transfusion.

Conclusions

- An anti-C^W and an anti-Jr^a was identified in the patient's serum
- Jr(a-) blood is very rare and no such donors are known in Switzerland
- Fortunately, the MMA indicates that the antibody is not clinically significant

Summary of Case Challenges

- The patient's serum reacted with all test cells, while the autocontrol was negative
- Panagglutinin or an antibody against high prevalence antigen?

Lessons Learned by the Case

When the patient's serum reacts with all panel cells and the autocontrol is negative, it is important to exclude the presence of antibodies against the stabilization solution.

The use of enzyme treated panel cells can give valuable information about the antibody characteristics and narrow down the search.

If the clinical significance of the antibody is not clear, the MMA can give guidance for transfusion recommendations.

ISBT Terminology of the JR System

ISBT symbol (number): JR (032)

CD number: CD338

Number of antigens: 1

High prevalence Jr^a

Brief Review of the Blood Group System or Antibody

In 2012 the Jr^a antigen was promoted from the 901 series of high-incidence antigens to a system. The Jr(a-) phenotype is defined by *ABCG2* null alleles. To date 28 *ABCG2* null alleles have been described.

Anti-Jr^a may be clinically significant as it has been implicated in hemolytic disease of the fetus and newborn (HDFN) and hemolytic transfusion reactions (HTR). In the literature reports of delayed and acute HTR have been made, as well as incompatible transfusions with no symptoms of HTR. A study on clinical significance using the MMA reported that only one of eight anti-Jr^a samples showed clinical significance.

References

Reid ME, Lomas-Francis C, Olsson ML. The Blood Group Antigen FactsBook, 3rd ed. San Diego, CA, Elsevier, 2012.

Castilho L and Reid ME. A Review of the JR blood Group system. Immunohematology 2013; 29:63-68