Immunohematology Case Studies 2017 - 1

Edmond Lee MSc, FIBMS, FRSM
Red Cell Immunohaematology, NHSBT, UK

Clinical History

- A 73 year old male
- Referred for redo vascular surgery on Jun 2016
- Osteomyelitis 2 years ago (May 2014)
- Antibody screen (ABID) was negative
- Transfused 3 occasions on Nov 2015 (a total 15 units during surgery)
- ABID positive (Jun 2016)
- Sample referred to Reference Laboratory after routine hours for investigation for following date surgery
- Patient is from Philippines & speaks Tagalog

Serologic and Transfusion History

Antibody screen negative on:

- 18 May 2014
- 05 Oct 2015
- 26 Nov 2015

Patient was transfused the following:

- 28 Nov 2015 9 units red cells transfused
- 23 Nov 2015 4 units red cells transfused
- 26 Nov 2015 2 units red cells transfused

Current Sample Presentation Data

- ABO/Rh: A, D+C+c+E+e+,K-
- DAT: negative
- Antibody Screen Method: using IH1000
- Antibody Screen Results: Panel reactive
- Antibody Identification Method: Bio-Rad IAT (3+), Bio-Rad enzyme IAT (4+) and Tube LISS-IAT (2+)

Antibody Identification Preliminary Results:

- Pan reactive suggestive of antibody to a high frequency antigen

Challenge with the Current Presentation

- Extended phenotyping was performed as this appeared to be antibody to a high prevalence antigen
- M+S+s+ excluded anti-U
- Lu(a-b+), Kp(a+b-) excluded anti-Lu^b or anti-Kp^b
- Fy(a+b-) excluded anti-Fy^3
- Jk(a-b-) suggestive the presence of anti-Jk3

Panel Sample

	D	C	c	E	e	Cw	K	k	Fya	Fyb	Jka	Jkb	Lea	Leb	P1	M	N	S	s	Gel IAT	Gel Enz IAT	Tube IAT
1	+	0	+	+	0	0	0	+	0	+	+	+	0	+	+	0	+	0	+	3+	4+	2+
2	0	+	0	0	+	0	0	+	0	0	+	+	0	0	+	+	+	0	0	3+	4+	2+
3	0	+	+	0	+	0	0	+	0	+	0	+	0	+	+	+	+	+	+	3+	4+	2+
4	0	0	+	+	+	0	0	+	0	w	+	0	0	+	+	+	0	+	+	3+	4+	2+
5	0	0	+	+	0	0	0	0	0	+	0	+	0	+	+	+	+	+	+	3+	4+	2+
6	0	0	+	0	+	0	+	+	+	+	+	+	0	+	+	+	+	+	0	3+	4+	2+
7	0	0	+	0	+	0	+	+	0	+	+	0	0	+	+	+	0	0	+	3+	4+	2+
8	0	0	+	0	+	0	0	+	+	0	+	+	+	0	+	0	+	0	+	3+	4+	2+
9	0	0	+	0	+	0	0	+	+	0	+	+	+	0	0	+	0	+	0	3+	4+	2+
10	0	0	+	0	+	0	0	+	0	0	+	0	0	0	+	0	+	+	0	3+	4+	2+
11	0	0	+	0	+	0	0	+	+	0	0	+	0	+	0	+	+	+	+	3+	4+	2+
12	0	0	+	0	+	0	0	+	+	+	+	0	0	+	0	0	+	0	+	3+	4+	2+

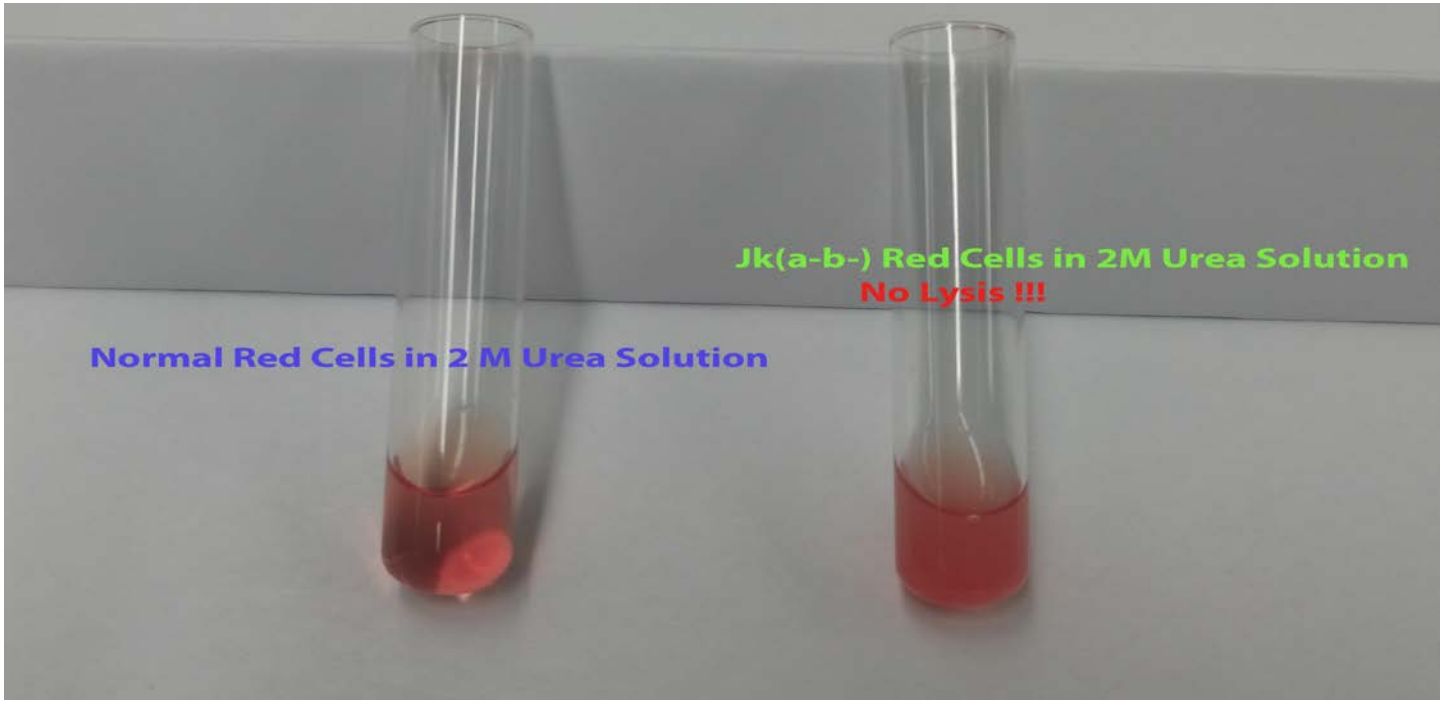
Jk(a-b-) panel

	D	C	c	E	e	Cw	K	k	Fya	Fyb	Jka	Jkb	Lea	Leb	P1	M	N	S	s	Gel IAT			Tube IAT
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

Further Work

Testing for 2M Urea lysis

Jk(a-b-) cells lack the Urea Transporter (UT-B1) encoded by the SLC14A1 gene, and therefore are not lysed with 2M urea solution



Jk(a-b-) phenotype

- Jk_{null} or Jk(a-b-) first reported by Pinkerton *et al* (1959) from a Filipino woman of Chinese & Spanish ancestry
- Cases of Jk(a-b-) are more frequent in the Polynesian & Finns
- Other populations, Chinese, Japanese, Asian Indians, Native Brazilians, African American, Tunisian, and European descent

Anti-Jk3

- Reacted optimally by IAT
- Enhanced by enzyme treated RBC
- Usually IgG, less common to be than IgM antibodies
- Complement binding
- Found in a non-transfused male
- No preference for Jk(a+b-) or Jk(a-b+)
- Not a mix of anti-Jk^{a} and anti-Jk^{b}
- No to severe/immediate or delayed transfusion reaction
- No to mild HDFN
- Auto anti-Jk3 has been reported

Transient Jk(a-b-) phenotype

Case report of a transient Jk(a-b-) phenotype

- Russian woman with myelofibrosis who made anti-Jk3 at the time her RBCs typed Jk(a-b-)
- Severe transfusion reaction
- Five weeks later typed as Jk(a+^{w}b-)
- Anti-Jk^{b} was detected
- One year later typed as Jk(a+b-) with no anti-Jk3 and/or anti-Jk^{b} detected

Summary of Case Challenges

- Jk(a-b-) donations are rare
- Frozen and recovery donations were required for transfusion purpose
- Only anti-Jk3 was identified post transfusion in this case, using Jk(a-b-), Fy(a-b+) RBCs (exclusion of anti-Fy^b in the Fy(a-b+) patient)
- No confirmation of the presence of additional anti-Jk^a or anti-Jk^b

Lessons Learned by the Case

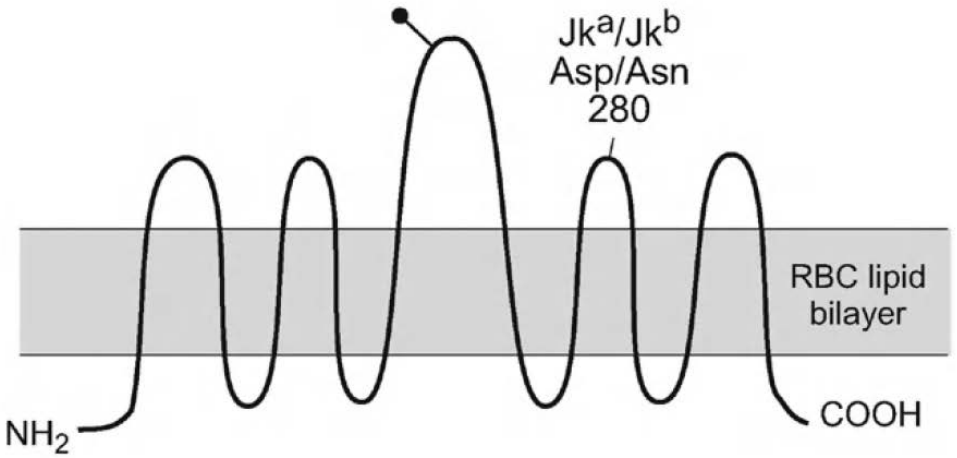
- Molecular basis of the Jk(a-b-) phenotype are diverse among the different populations
- 2M Urea solution is considered easier and cheaper than genotyping to mass screen Jk_{null} blood donors in countries with a significant prevalence of this phenotype
- The ethnic origin and/or spoken language of the patient can give very important information about the putative rare blood type. In this case, the patient spoke Tagalog which is a Filipino dialect and quickly provided the clue for the antibody to a high prevalence antigen to be a likely anti-Jk3

Molecular basis for JK phenotype

- *JK* gene (*SLC14A1*, *HUT11A*)
- Located at chromosome 18q12.3
- Jk^a antigen: p.Asp280 (c.838G)
- Jk^b antigen: p.Asn280 (c.838A)

Carrier molecule

Multi-pass glycoprotein.



From Reid, Lomas-Francis & Olsson, The Blood Group Antigen Factsbook, 3rd Ed 2012

Molecular based of some silencing of *JK*A* or *JK*B alleles*

Reference allele, *JK*02* (NM_015865), encodes Jk^b, Jk3

Allele name	Exon/ intron	Nucleotide	Amino acid	Ethnicity (prevalence)
*JK*01N.01*	4 & 5	Exons 4&5 deleted	Initiation Met absent	Tunisian, English, Bosnian (Rare)
*JK*01N.02*	5	202C>T	Gln68Stop	Caucasian, American (Rare)
*JK*01N.03*	7	582C>G	Tyr194Stop	Swiss, English (Few)
*JK*01N.04*	10	956C>T	Thr319Met	African American, (Rare)
*JK*01N.05*	7	561C>A	Tyr187Stop	African American (Rare) African Brazilian (Many)
*JK*01N.06*	Intron 5	IVS5–1 g>a	Exon 6 skipped; in frame	Asian Indian (Rare)

Allele name	Exon/ intron	Nucleotide	Amino acid	Ethnicity (prevalence)
*JK*02N.01*	Intron 5	IVS5–1 g>a	Exon 6 skipped; in frame	Polynesian, Chinese (Several)
*JK*02N.02*	Intron 5	IVS5–1 g>c	Exon 6 skipped; in frame	Chinese (Rare)
*JK*02N.03*	5	222C>A, 499A>G	Asn74Lys, Met167Val	Taiwanese (Rare)
*JK*02N.04*	Intron 7	IVS7+1 g>t	Exon 7 skipped; frameshift→ Leu223Stop	French (Rare)
*JK*02N.05*	8	723delA	Frameshift→ Ile262Stop	Hispanic American (Rare)
*JK*02N.06*	9	871T>C	Ser291Pro	Finns (Several)
*JK*02N.07*	9	896G>A	Gly299Glu	Taiwanese (Rare)
*JK*02N.08*	10	956C>T	Thr319Met	Indian, Pakistani (Rare)
*JK*02N.09*^	5	191G>A	Arg64Gln	Black (Rare)

From Reid, Lomas-Francis & Olsson, The Blood Group Antigen Factsbook, 3rd Ed 2012

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