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Complexity Of Antibodies Associated With *JK*01W.01*

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INTRODUCTION

- More than thirty alleles encoding altered or silenced expression of Jk in multiple ethnicities are known.
- The *JK*A* variant, *JK*01W.01,* with c.130G>A encoding p.Glu44Lys has been reported in all populations but has a higher frequency in persons of Asian, 0.3931 or African, 0.2003, descent (gnomAD).
- These RBCs can type weaker than expected with anti-Jk^a.
- There are several reports of anti-Jk^a and/or -Jk3 in Jk(a+) individuals with *JK*01W.01* but the clinical significance of these antibodies with regard to pregnancy or transfusion is unclear.

OBJECTIVES

- We investigated the reactivity characteristics of anti-Jk^a associated with *JK*01W.01* in:
  - A pregnant female with an apparent anti-Jk^a but with a serological Jk(a+b–) phenotype.
    - Family members were also tested.
  - A child with Sickle Cell Disease (SCD) whose RBCs were predicted Jk(a+b+) by DNA with apparent anti-Jk^a in the plasma.

MATERIALS AND METHODS

- Serological testing was by standard methods.
  - Manual tube testing
  - Column agglutination technology (CAT, Ortho)
- Adsorptions were done with autologous or allogeneic Jk(a–) RBCs.
- Eluates were made with Gamma Elu-Kit II (Immucor).
- Genomic DNA was isolated from WBCs (Qiagen).
  - HEA PreciseType (Immucor) was performed.
  - *JK* coding exons 3-8, including flanking splice sites were amplified and Sanger sequenced.

CASE STUDIES

Case 1:
- A 31 year-old pregnant (G2P1) woman with a previous negative antibody screen and no history of transfusion.
- Anti-Jk^a was identified in her plasma by IAT, but RBCs typed Jk(a+b–).
- She delivered a full-term infant without complication or evidence of HDFN.

Case 2:
- A multiply transfused female child with SCD presented after receiving an RBC exchange (5 units).
- Anti-Jk^a reactive by IAT was identified in her plasma but her RBCs were predicted Jk(a+b+) by HEA.

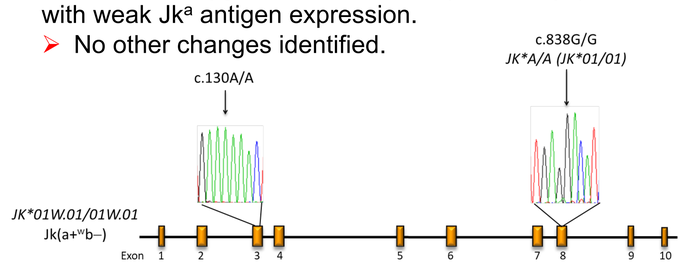
SEROLOGY RESULTS

Case 1
- **RBCs**
  - Typed Jk(a+b–).
  - DAT– with anti-IgG, but 1+/3+ with anti-C3.
- **Plasma**
  - Anti-Jk^a micro+ by PEG IAT; 2+ ficin IAT; 2+ by CAT.
  - Autologous control micro+ by PEG IAT.
  - Incompatible with RBCs from *JK*01W.01/01W.01* siblings and with other *JK*A* variants.
- **Eluate**
  - Anti-Jk^a micro+ by PEG IAT.
- **Plasma Adsorption Studies**
  - Autoadsorption removed most, but not all anti-Jk^a reactivity.
  - Alloadsorption with Jk(a–b+) RBCs did not remove anti-Jk^a.
- **Baby's sample**
  - RBCs were DAT–.
  - Typed Jk(a+b+).
  - Eluate contained anti-Jk^a from baby's DAT– RBCs.

Case 2
- **RBCs**
  - DAT–.
- **Plasma**
  - Anti-Jk^a micro+ by PEG IAT and 1+ by CAT.
- **Eluate**
  - Anti-Jk^a micro+ by PEG IAT.

JK SEQUENCE RESULTS

Case 1
- Exon 8: confirmed *JK*01/01 (JK*A/A).*
- Exon 3: homozygous for c.130G>A (p.Glu44Lys) associated with weak Jk^a antigen expression.
  - No other changes identified.



Case 2
- Exon 8: *JK*01/02 (JK*A/B)*
- Exon 3: heterozygous for c.130G>A (p.Glu44Lys) associated with weak Jk^a antigen expression.
  - No other changes identified.

CASE 1 FAMILY PHENOTYPE, GENOTYPE AND X-MATCH RESULTS WITH PROBAND PLASMA

Sample	Phenotype	JK genotype	X-Match IAT
Proband	Jk(a+^{w}b–)	*JK*01W.01/01W.01*	micro+
Brother	Jk(a+^{w}b–)	*JK*01W.01/01W.01*	3+
Sister	Jk(a+^{w}b–)	*JK*01W.01/01W.01*	3+
Sister	Jk(a+^{w}b+)	*JK*01W.01/02*	2+
Baby	Jk(a+^{w}b+)	*JK*01W.01/02*	3+
Jk^a variant 1	Jk(a+^{w}b–)	*JK*01W(134C)/02N.08*	2+
Jk^a variant 2	Jk(a+^{w}b–)	*JK*01W.01/02N.01*	1+
Jk^a variant 3	Jk(a+^{w}b+)	*JK*01(350C)/02*	1+^{w}

CONCLUSIONS

- We describe anti-Jk^a with auto and allo characteristics in a pregnant woman (case 1) and apparent allo anti-Jk^a in a patient with SCD (case 2).
- Both patients had altered Jk^a due to *JK*01W.01*.
- For case 1, the baby's RBCs were DAT– but anti-Jk^a was found in the cord eluate indicating low level IgG on the baby's RBCs and that the anti-Jk^a crossed the placenta.
- Only Jk(a–) RBCs were compatible with the maternal antibody, but transfusion with Jk(a–) RBCs introduces risk of sensitization to Jk^b.
- For case 2, of the 5 transfused RBC units, 3 typed Jk(a+).
  - Surprisingly, only one unit was incompatible post transfusion, but DNA from the Jk(a+) donors was not available for genotyping to investigate for the presence of *JK*01W.01.*
- The patient will be transfused with Jk(a–b+) units in the future.
- Providing transfusion support for patients with *JK*01W.01*, especially Jk(b–) patients, is challenging.
- This study highlights the complexity of anti-Jk^a reactivity in patients with *JK*01W.01.*
- Previously reported cases (Velliquette et. al. Transfusion 2015) showed that patient care is enhanced when donors, matched for *JK*01W.01* were used.
- Case 1 is unusual in that genotype matched RBCs are incompatible and this reflects that there are allo and autoantibodies components to the anti-Jk^a.