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-Jkα.
- There are several reports of anti-Jkα 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-Jkα associated with JK*01W.01 in:
  - A pregnant female with an apparent anti-Jkα 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 HEA.

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-Jkα 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-Jkα 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-Jkα micro+ by PEG IAT; 2+ ficin IAT; 2+ by CAT.
  - Autologous control micro+ by PEG IAT.
  - Incompatible with RBCs from JK*01W.01W.01 siblings and with other JK*A variants.
- Eluate
  - Anti-Jkα micro+ by PEG IAT.

Case 2
- RBCs: DAT–.
- Plasma
  - Anti-Jkα micro+, by PEG IAT and 1+ by CAT.
- Eluate
  - Anti-Jkα micro+ by PEG IAT.

SEQUENCE RESULTS

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

Case 2
- Exon 8: JK*01/02 JK*A/B
- No other changes identified.

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

<table>
<thead>
<tr>
<th>Sample</th>
<th>Phenotype</th>
<th>JK genotype</th>
<th>X-Match IAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proband</td>
<td>Jk(a+b–)</td>
<td>JK<em>01W.01JK</em>01W.01</td>
<td>micro+</td>
</tr>
<tr>
<td>Brother</td>
<td>Jk(a+b–)</td>
<td>JK<em>01W.01JK</em>01W.01</td>
<td>3+</td>
</tr>
<tr>
<td>Sister</td>
<td>Jk(a+b–)</td>
<td>JK<em>01W.01JK</em>01W.01</td>
<td>3+</td>
</tr>
<tr>
<td>Sister</td>
<td>Jk(a+b+)</td>
<td>JK<em>01W.01JK</em>01W.01</td>
<td>2+</td>
</tr>
<tr>
<td>Baby</td>
<td>Jk(a+b+)</td>
<td>JK<em>01W.01JK</em>01W.01</td>
<td>3+</td>
</tr>
<tr>
<td>Jkα variant 1</td>
<td>Jk(a+b–)</td>
<td>JK<em>01W(134C)JK</em>02N.08</td>
<td>2+</td>
</tr>
<tr>
<td>Jkα variant 2</td>
<td>Jk(a+b–)</td>
<td>JK<em>01W.01JK</em>02N.08</td>
<td>1+</td>
</tr>
<tr>
<td>Jkα variant 3</td>
<td>Jk(a+b+)</td>
<td>JK<em>01(350C)JK</em>02</td>
<td>1+</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- We describe anti-Jkα with auto and allo characteristics in a pregnant woman (case 1) and apparent allo anti-Jkα in a patient with SCD (case 2).
- Both patients had altered Jkα due to JK*01W.01.
- For case 1, the baby’s RBCs were DAT– but anti-Jkα was found in the cord eluate indicating low level IgG on the baby’s RBCs and that the anti-Jkα crossed the placenta.
- Only Jk(a–) RBCs were compatible with the maternal antibody, but transfusion with Jk(a–) RBCs introduces risk of sensitization to Jkα.
- 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-Jkα 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(a–b+) RBCs 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-Jkα.