Anti Kp\(a\) alloantibody: Development of a rare alloantibody in a non-Hodgkin’s lymphoma patient of Indian origin

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Abstract:
The Kell blood group system is complex, contains many antigens, highly immunogenic, and potent in triggering immune reactions. Antibodies to Kell blood group system are the most common immune red cell antibodies, following ABO and Rh. However, among the anti-Kell antibodies; anti-Kp\(a\) is extremely rare. We report an interesting case of Anti-Kp\(a\) in a 59-year-old female patient of Non-Hodgkin’s Lymphoma, post radiotherapy, who first developed warm autoantibody and later developed anti-Kp\(a\) alloantibody on multiple transfusions.

Keywords:
Anti-Kp\(a\) antibody, alloantibodies, Kell blood group system

Introduction

The Kell blood group system is complex, contains 35 antigens that are highly immunogenic and potent in triggering immune reactions.[1] Kp\(a\) antigen (KEL3) is found in about 2% population of European lineage[2] and 0%–0.01% population of Asian ancestry.[1,3] Antibodies to Kell blood group system are the most common immune red-cell system following ABO and Rh systems[2] but anti-Kp\(a\) antibody is extremely rare in the Asian population. Kell antibodies are usually IgG type, predominantly IgG1.[4] These are clinically significant antibodies, capable of causing Hemolytic Disease of Fetus and New Born and Hemolytic Transfusion Reactions (HTRs). Anti-K and anti-Ku are capable of causing a severe reaction, but milder reaction is caused by anti-k, anti-Kp\(b\), anti-Kp\(a\), Anti Js\(a\), and anti-Js\(b\). On review of literature, three cases of anti-Kp\(a\) antibody were found in Indian Literature,[5–7] of which two cases of anti-Kp\(a\) antibody are reported in multi-transfused thalassemic patients.[5,6] We report a case of anti-Kp\(a\) antibody in a Non-Hodgkin’s Lymphoma patient who first developed warm autoantibody and later developed rare anti-Kp\(a\) alloantibody on multiple transfusions.

Case Report

A 59-year-old female patient follow-up case of Non-Hodgkin’s Lymphoma (Low grade, stage 4) was admitted to medicine department of our institute with presenting complaints as generalized weakness, cough with expectoration, and shortness of breath. On examination, there was facial puffiness and pallor. Her hemoglobin was 5.5 g/dL. Blood sample received for pretransfusion testing showed her blood group as ‘O’ Positive. Two units of leukodepleted, packed red blood cell (PRBC) transfusion was uneventful, and the patient was discharged. After a gap of 10 months, the patient was admitted again with generalized weakness, joint pains, loose motions, and melena. Her investigation revealed hemoglobin as 6.7 g/dL. Direct Agglutination Test (DAT) was positive (3+) with positive auto control. Her Rh phenotype was CCeeK(DCe/DCe; R1R1). Antibody

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screening using 3-cell panel on Solid Phase Red Cell Adherence (SPRCA; Capture, Immucor Inc., Norcross, GA, USA) was positive, and 14-cell identification panel using SPRCA showed pan positivity with a diagnosis of warm autoantibody. No alloantibody was detected at this stage. Two units of leukodepleted, PRBC transfusion were uneventful.

The patient was admitted twice again in a gap of 4–6-weeks time with repeated fall of hemoglobin to 4.5 g/dL. Four and five units of leukodepleted PRBC were transfused, respectively. During her third admission, DAT and antibody screening using 3-cell panel were negative. Blood sample received for pre-transfusion testing on the fourth admission revealed positive antibody screening with 3-cell panel on SPRCA [Table 1]. 11-cell and 14-cell identification panels using SPRCA technique showed positivity leading to the conclusion of Anti-Kp<sup>a</sup> alloantibodies [Table 2] which was confirmed with three different lots of 14 cell panels. Kp<sup>a</sup> antigen presence on patient’s red cells could not be excluded due to strong DAT positivity. There was no evidence of extravascular hemolysis in any of admissions.

**Discussion**

Kp<sup>a</sup> antigen is a low-frequency antigen of Kell system. Kp<sup>a</sup> antigen is found in about 2% population of European lineage<sup>[3]</sup> but extremely rare in the Asian population. The development of antibody to this rare antigen of low frequency is rare in Indian population due to limited exposure. Antibodies to Kp<sup>a</sup> usually develop following transfusion or fetomaternal immunization. However, original example of this rare antibody was naturally occurring.<sup>[8]</sup> A low rate of red cell alloimmunization has been reported in general patients ranging from 0.49% to 2.4%.<sup>[7,9]</sup> This could be due to homogeneity of red cell antigens between blood donors and recipients.

In our case, DAT was initially negative, became positive with the development of warm autoantibody which turned negative again before the development of rare anti-Kp<sup>a</sup> alloantibody which is of IgG class, no complement binding and can be detected by Indirect Antiglobulin Test (IAT). There was no problem in finding compatible units with IAT crossmatch. This could be due to the extremely low prevalence of Kp<sup>a</sup> antigen in Indian population.

Spanos et al.<sup>[10]</sup> have shown a direct relationship between number of transfusions and the alloimmunization rate. Although the relation between number of units of blood transfused and antibody formation is unknown, it is an important factor for increased alloimmunization. Earliest sensitization appears after ten transfusions.<sup>[10]</sup> In our case also, red cell alloimmunization developed after ten transfusions.

To summarize, regular screening for the development of alloantibodies should be included in pretransfusion testing protocol. With the identification of antibodies, patients should be given corresponding antigen negative donor unit which would help in effective red cell survival and desired effects of transfusions by minimizing antibody-mediated destruction of transfused cells. Singer et al.<sup>[10]</sup> also observed that patients who received blood matched for Rh and Kell systems from their first transfusion, rate of alloimmunization was found to be very low.<sup>10</sup> The significance of transfusion of phenotypically matched blood in multi-transfused patients cannot be overemphasized in preventing alloimmunization. Less number of phenotypically matched transfusions would reduce the financial burden and psychological trauma to the patient and family.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

**Conflicts of interest**
There are no conflicts of interest.

**Table 1: Antibody Screening Using 3 Cell Panel**

| Expired: 2016/09/21 | Rh-Hr | Kell | Duffy | Kidd | Lewis | P | MN | Lutheran | Xg | Patient's Test Results |
|---------------------|-------|------|-------|------|-------|---|----|----------|----|------------------------|
| LOT NO: E211        | Donor | D | C | c | e | e | V<sup>+</sup> | Cw | k | Kpa | Kpb | Jsa<sup>*</sup> | Jsb | Fya | Fyb | Jka | Jkb | Lea | Leb | P1 | P1 | M | N | S | s | Lu<sup>r</sup> | Lu<sup>r</sup> | Xg<sup>*</sup> | Patien<sup>’</sup>s Test Results |
| 1                   | R1wR1 | + | 0 | 0 | 0 | 0 | + | 0 | 0 | + | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | 0 | + | 1 | 0 |
| 2                   | R2R2  | + | 0 | 0 | 0 | 0 | + | 0 | 0 | + | 0 | 0 | + | 0 | + | 0 | 0 | + | 0 | + | 0 | + | 2 | 3 |
| 3                   | rG1547 | 0 | 0 | 0 | 0 | + | + | 0 | + | 0 | 0 | + | 0 | 0 | 0 | 0 | + | 0 | 0 | + | 0 | 0 | + | 3 | 0 |
Table 2: Antibody Screening Using 14 Cell Panel

| LOT NO: ID313 | Rh - Hr | Kell | Duffy | Kidd | Lewis | P | MN | Lutheran | Xg | Cells | Patient's test Results |
|--------------|---------|------|-------|------|-------|---|----|----------|----|-------|------------------------|
| Special Type | Donor   | D    | C    | c    | E     | e | V* | Cw      | k | Kpa   | Kpb                    |
|              |         | Ksa* | Jab  | Fya  | Fyb   | Jka| Jkb| Lea     | Leb| P1    | M | N | S | s | LuaLubXga* |
| 1            | Di (a+) | +    | 0    | +    | 0     | 0 | +  | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 0 |
| 2            | RzR1 A4474 | +  | + | 0    | +    | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 2 | 0 |
| 3            | R2R2 C5437 | +  | 0    | +    | 0     | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 3 | 0 |
| 4            | Ror D986  | +  | 0    | +    | 0     | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 4 | 0 |
| 5            | r'r E998  | +  | +    | 0    | +    | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 5 | 0 |
| 6            | r'r F869  | +  | +    | +    | 0     | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 6 | 0 |
| 7            | r'H592    | +  | 0    | +    | 0     | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 7 | 0 |
| 8            | r'G1476   | +  | 0    | +    | 0     | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 8 | 0 |
| 9            | Co (b+)   | +  | 0    | +    | 0     | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 9 | 0 |
| 10           | r'H388    | +  | 0    | +    | 0     | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 10 | 0 |
| 11           | r'N4247   | +  | 0    | +    | 0     | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 11 | 0 |
| 12           | r'H857    | +  | 0    | +    | 0     | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 12 | 0 |
| 13           | Yt (b+)   | +  | 0    | +    | 0     | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 13 | 0 |
| 14           | r'R1783   | +  | +    | 0    | +    | 0 | + | 0       | + | 0    | + | 0 | + | 0 | + | + | 1 | 14 | 0 |
| 15           | POSITIVE CONTROL | / | / | / | / | / | / | / | / | / | / | / | / | / | / | / | / | / | PC | 3 |
| 16           | NEGATIVE CONTROL | / | / | / | / | / | / | / | / | / | / | / | / | / | / | / | / | / | NC | 0 |
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