Delayed hemolytic reaction due to anti Jk<sup>a</sup> alloimmunization

Sheetal Malhotra, Gagandeep Kaur, Lakhwinder Singh, Sabita Basu, SS Lehl

ABSTRACT

Introduction: Kidd blood group system has a special importance in transfusion medicine as the antibodies to Kidd antigens tend to go down to undetectable levels but show an anamnestic response on exposure through pregnancy or blood transfusion and cause hemolytic transfusion reaction, most commonly delayed transfusion reaction. Case Report: We report a patient who developed alloantibodies to ‘Kidd a’ antigen leading to delayed hemolytic transfusion reaction. Conclusion: We emphasize the steps for detecting these antibodies and the precautions to be taken once these antibodies are identified.

Keywords: Alloimmunization, Kidd blood group system, Delayed hemolytic transfusion reaction, Dosage phenomenon, Anamnestic response

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INTRODUCTION

Alloimmunization by Kidd (Jk) blood group system is uncommon. These antibodies are often immune in nature and are produced in response to pregnancy or transfusion. Owing to their weak serological nature and their tendency to show dosage phenomenon, these antibodies are difficult to detect. Dosage phenomenon refers to the fact that antibodies of certain blood group systems react more strongly with homozygous (double dose antigen) red cells and may not react when both antithetical antigens are present on red cells (heterozygous red cells). Moreover these antibodies often occur in combination with other antibodies which further complicates the case work up. We report a case of delayed hemolytic transfusion reaction (HTR) due to alloimmunization by Jk<sup>a</sup> antigens.

CASE REPORT

A 14-years-old female presented with complaints of fever with chills, rash all over the body, bleeding from mouth for the past 20 days. There was history of typhoid three months back. The patient had been transfused one unit of packed red blood cells (PRBC) from an outside hospital 15 days back. In addition, she had also received two units of blood components (?platelets ??FFP, definite information could not be
obtained) 14 days back. Both these transfusions were uneventful. Clinically, possibilities of systemic lupus erythematosus (SLE) and thrombotic thrombocytopenic purpura (TTP) were considered. As such, her sample was sent to the blood bank for direct Coombs test, indirect Coombs test and a requisition was received for one unit of PRBC and two units of platelet concentrate.

Complete blood count of the patient showed anaemia (Hb - 4.4 g/dl), leucopenia (Total leucocyte counts - 2400/μl) and thrombocytopenia (Platelet count - 10,000/μl) with increased reticulocyte count (6.8%) and peripheral smear showed marked anisocytosis and poikilocytosis with microcytes, normocytes, few macrocytes, few macro-ovalocytes, fragmented cells, elliptical cells and bite cell, features which were consistent with hemolytic anaemia. Liver functions revealed hyperbilirubinemia (S. bilirubin - 2.3 mg/dl) with mild transaminitis. Renal parameters were within normal limits. Her hemoglobin prior to the above mentioned transfusion was 5.2 g/dl.

Blood group of the patient was A Rh(D) positive. The direct antiglobulin test (DAT) was positive (2+ on gel and 1+ on tube) with polyspecific anti-human globulin (anti-IgG and anti-C3d) and with monospecific anti-IgG. With anti-C3d, it was negative on tube and very weakly positive on gel. The indirect antiglobulin test was negative on immediate spin phase and positive on AHG phase. Autocontrol was negative on immediate spin phase and showed a mixed field reaction on anti-human globulin (AHG) phase. Antibody screen and identification panel was put on gel (using commercially prepared red cell antigens from DiaMed lab) and the results confirmed the presence of anti-Jka antibodies (table 1). It was noted that the strength of the reactions were stronger in the cells carrying a double dose of Jka antigens as compared to cells which were heterozygous for Jka, thereby demonstrating dosage phenomenon. An eluate was obtained from patient’s red cells (by heat elution method). An antibody screen and identification panel of the eluate was put up confirming anti-Jka antibodies. Alloabsorption with Jka positive cells was performed. On elution, Jka antibodies were confirmed. Enzyme treatment with 1% papain was done. Papanicolas cells were prepared and reactivities were checked with the patient’s serum. The strength of the reaction was increased as Jk blood group system is known to be enhanced after enzyme treatment. Antibody titres were 1:2 on tube. Patient’s phenotype could not be done because of recent transfusion 15 days back. After Dithiothreitol (DTT) treatment, strength of the reactions remained same; confirming IgG nature of antibodies. So the final inference drawn was IgG type warm reacting Jka alloantibody, showing dosage phenomenon. As mentioned earlier, autoantibody could not be ruled out because of the presence of transfused donor cells in circulation. Two random cross matches done by the technician before identification of the antibody were found to be compatible on immediate spin phase at 4°C, 22°C and 37°C. These units were checked for Jka phenotype and compatibility by AHG phase. One unit which was homozygous for Jka, Jk(a+b-) gave a stronger reaction (+) than the other unit (weak +) which was heterozygous Jk (a+b+). Thereafter, six units of packed red blood cells, blood group A Rh(D) positive were phenotyped for Jka of which one was Jka negative. It was transfused under close monitoring and there was a reported rise of Hb by 1g/dl next day. Two units of platelet concentrate were transfused on the same day.

**DISCUSSION**

In 1951, Kidd Blood Group System, ISBT Symbol: Jk and ISBT Number: 009, was discovered. It was named after Mrs. Kidd in whom an antibody, not previously recognised caused hemolytic disease of newborn and fetus (HDFN) in her sixth child. The antigens in this system are well developed at birth with Jk(a) appearing at 11 weeks and Jkb at 7 weeks of intrauterine life. The antigens are also found on neutrophils and in kidney cells. The prevalence of Jk antigens has been variably estimated in different studies. Thakral found Jk(a+b-) to be present in nearly 33%, Jk(a-b+) in 17%, Jk(a+b+) in 49% and Jk(a-b-) in 0% of the 1420 donors [1]. In another study by Nanu et al, the relative frequencies of these antigens was estimated as 29%, 22%, 48% and 0.5% respectively among more than 6334 donors [2].

These antibodies are more commonly implicated in hemolytic transfusion reactions and sometimes in hemolytic disease of fetus and newborn (HDFN). There are very few case reports of anti-Jka causing HDFN in contrast to 13 published case reports of HDFN due to anti-Jkb. Franco et al. scrutinized records of all alloimmunized pregnancies at their center from 1959 to 2008 and in 20 pregnancies, anti-Jka was identified. Of these, one had severe disease due to anti-Jkb which was diagnosed using maternal antibody titer (1:32) and middle cerebral artery peak systolic velocity (MCA PSV). This pregnancy required 4 intravenous transfusions for fetal anaemia [3]. One of the authors have reported a case of HDFN due to anti-Jkb antibody in a woman with high risk pregnancy [4].

The index case described above elucidates anti-Jka alloimmunization following a blood transfusion. In this case, anti-Jka antibodies could be missed had the AHG crossmatch and antibody screen not been performed. This highlights the importance of serological compatibility testing at AHG phase and the necessity for performing the antibody screen using appropriate panel cells. There are a few case reports in literature demonstrating anti-Jka as an allo or auto antibody [5-10]. Sedlmayer et al. reported a case of HTR due to Jka antibody. In routine cross matching, the antibody was missed in both saline and 22% bovine serum albumin after incubation at 4°C, 20°C and 37°C and was detected at AHG crossmatch [7]. Sosler reported a case of acute hemolytic anemia associated with a chlorpropamide-induced apparent auto-anti-Jkb [8]. Recently Munoz et al. also reported presence of auto Jka antibodies to complicate a case of common variable immunodeficiency and Evan’s syndrome. The patient
had a positive DAT with C3d and a serum auto-antibody with anti-Jkα specificity in the eluate prepared from his red blood cells. Indirect anti-globulin test (IAT) was also positive [10].

The present case showed a drop in hemoglobin levels from 5.2 g/dl to 4.4 g/dl after her previous transfusion with peripheral blood picture suggestive of hemolytic anaemia. It can be inferred that she had a delayed HTR due to the alloimmunization to Jkα antigen through blood transfusion. The nature of antibody was IgG, reacting at body temperature and was clinically significant. Alloimmunization is an immune response due to exposure of foreign antigens through pregnancy or blood transfusion in an immunocompetent host leading to development of corresponding antibodies.

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Since Jkα has been identified uncommonly as a cause of alloimmunization, universal implementation of antibody screening in all cases may not prove to be cost effective. However, it cannot be overemphasized that screening for such uncommon but clinically significant antibodies including anti-Jkα should be carried out at least in all cases with a prior history of transfusion and/or pregnancy. The results also emphasize the fact that whenever anti-Jkα antibodies are suspected, use of red cells homozygous for Jkα antigen in antibody screen and identification panel is essential for their detection as they may give a weak or a negative reaction with Jk(a+b+) cells. A special immunohematology card was issued to our patient stating the presence of Jkα antibodies, as levels of these antibodies are known to go down to undetectable levels even after a severe HTR and she was advised to show the card before any subsequent transfusion. Once anti-Jkα antibody is identified, it is of utmost importance to review the previous transfusion records of the patient for all future transfusions. Such patients should always be transfused Kidd negative blood units as these antibodies are known to show an anamnestic response after transfusion of Kidd positive blood units leading to severe transfusion reaction.

**CONCLUSION**

It is well established that pre transfusion compatibility testing by AHG crossmatch technique is more sensitive compared to immediate spin in detecting clinically significant IgG antibodies. However, in a resource poor setting like ours, primarily because of the

**Table 1: Results of antibody screen and identification panel on the patient’s serum.**

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Abbreviations: SC – screening cell; ID –identification; IS – immediate spin; AHG – anti human globulin.
financial constraints and also due to lack of awareness, the personnel engaged in transfusion services may omit this important step of AHG crossmatch and thus increase the risk of alloimmunization. So we recommended that the indirect Coombs test, which is able to reveal such irregular antibodies, should be routinely performed as a part of serological compatibility testing.

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Author Contributions
Sheetal Malhotra – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
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Sabita Basu – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
SS Leh – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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REFERENCES