A Rare Case of Anti-Jk3 Antibody Detected on Pre-Transfusion Investigation

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Abstract We report a 47-year-old Malay lady, para 4 + 1, with known medical history of hypertension whom presented at Emergency Department with severe anaemia, most likely secondary to menorrhagia caused by uterine fibroids. Her haemoglobin was 5.5 g/dl and she was transfused with three units of packed cell without any adverse reaction, her haemoglobin level increased to 9.8 g/dl. She was then planned for total abdominal hysterectomy and bilateral salpingo-oophorectomy later. Four months later when she came for the elective surgery, her pre transfusion investigations showed blood group as B Rh D positive, with a probable R1R1 phenotype. Her antibody screening was positive in all the three panel cells. Further testings showed a negative Direct Coomb's test and negative autocontrol, antibody identification showed pan-agglutination reaction on all 11 panel cells with enzyme enhancement. Patient's red cell phenotype was Jk(a–b–). Anti-Jk3 was suspected and further confirmed in the reference laboratory by phenotyping as well as negative urea lysis test. This case report highlights an extremely rare but clinically significant anti-JK3 antibody detected during pretransfusion testing. This phenotype is rare in the white population, more commonly seen in various polynesians. Increased awareness among the blood bank personnel regarding the variability of the blood group phenotype and the capricious nature of the Kidd antibodies may contribute to the better management of these patients.

Keywords Kidd blood group · Anti-Jk3 · Pan-agglutination · Urea lysis test

Introduction

Kidd blood group system is a major antigenic system, discovered in 1951 [1] which consists of two antithetical antigens Jk^a and Jk^b that defines three phenotypes, Jk(a+b+), Jk(a+b–) and Jk(a–b+) among different population [2]. The null phenotype Jk(a–b–) is extremely rare and was first detected in a Philippine women with alloantibody that reacts with all available donor cell [3]. People with rare Jk null phenotype lack Jk^a and Jk^b antigen and associated with the homozygous inheritance of a rare 'silent' allele Jk at the JK locus. This phenotype has been described among the Asian and Polynesian population. There is another genetic explanation for the null phenotype present among Japanese population, reported by Okubo et al. (1986). He mentioned that inheritance of a dominant inhibitor gene *In(Jk)*, unlinked to the JK locus causes the dominant suppression of kidd antigens and expressed as null phenotype [4, 5].

Red cell alloantibodies against Kidd system are significant as they can cause severe immediate and delayed haemolytic transfusion reaction as well as haemolytic disease of the fetus and newborn [6]. These antibodies are formed secondary to pregnancy, transfusion or needle sharing, and they can fix the complements and cause the development of diffuse intravascular coagulation [7]. These antibodies are often not detected due to the tendency to remain in low titre or undetectable in the plasma [8].

Individuals with inheritance of silent Jk allele can form haemolytic antibodies known as anti-Jk3 where anti-Jka and anti-Jkb specificities are inseparable [7]. The other Jk(a–b–) phenotype that results from the inheritance of a dominant inhibitor do not make anti-Jk3. They can express the antigens very weakly and their Jk(a–b–) red cells can adsorb and elute anti-Jk3 and anti-Jka and/or anti-Jkb depending on the gene inherited [2]. Like other Kidd

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antibodies, anti-Jk3 antibody can be detected by the anti-globulin test with enzyme enhancement [8].

Case Report

We report a 47-year-old Malay lady, para 4 + 1, with known medical history of hypertension for 10 years, presented at Emergency Department with severe symptomatic anaemia secondary to menorrhagia caused by uterine fibroid. Her haemoglobin was 5.5 g/dl and she was transfused with three units of packed cell without any adverse reaction and her post transfusion haemoglobin level had increased to 9.8 g/dl. She was then planned for total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAHBSO) later. Four months later, she was admitted for elective TAHBSO and 2 units of packed cell was requested for the surgery. On pre transfusion investigations, she was grouped as B Rh D positive with a probable R1R1 phenotype. The antibody screening was positive in all the three panel cells. The Direct Coomb's test and the autocontrol were negative. Further testing with antibody identification by the antiglobulin test on a Diamed 11 cells panel showed the same strength of pan-agglutination reactions in all 11 cells, which were all enhanced by enzyme treatment. Similar findings were seen on CSL 10 cells panel. The antibody reacted equally with Jk(a+b-), (a-b+), and (a+b+) panel cells. Nevertheless, anti-Jk3 was suspected and supported by the patient's phenotype as Jk(a-b-). Subsequently the patient's sample was sent to the Reference Laboratory (National Blood Center) and was confirmed as anti-Jk3. As Jk(a-b-) blood is very rare, the patient's sample was sent to the Reference Laboratory to request for two units of Jk(a-b-) packed cells. The operation was done successfully and the patient was transfused with the 2 units of cross-matched compatible Jk (a-b-) blood, and post operative recovery was uneventful. Patient was discharged well on day 8 post operation.

Discussion

This case report highlights an extremely rare but clinically significant anti-Jk3 antibody detected during pre-transfusion testing. The clinical significance of Jk null phenotype individuals is that they readily form alloantibodies on exposure to Jka and/or Jkb antigens.

When this patient was first presented to the Emergency Department with severe symptomatic anaemia, no significant findings detected during the pre-transfusion testing and she was transfused with 2 units of packed red cells without any delayed transfusion reactions. Her anti-Jk3 that was detected during the pre-transfusion testing for elective

TABSHO is most likely as a result of the sensitization to the Kidd antigen from the recent transfusion of group specific crossmatched compatible blood 4 months earlier. However, there is another possibility that she might have been sensitized during her previous pregnancies some years ago and the antibody titre has become too low to be detected by the indirect antiglobulin tests and cross-matched, and subsequently stimulated the secondary immune response upon exposure to the antigens presence in the donor units. In patients who developed the secondary immune response to anamnestic antibody such as Kidd antibodies, they will usually present with delayed haemolytic transfusion reaction. However, in this patient, she did not develop any uneventful event following the transfusion of the two units of packed cells. Therefore, it is more likely that the anti-JK3 that the patient has developed was the result of the recent exposure to the antigen positive blood during the blood transfusion.

Prevalence of Jk null phenotype, Jk(a-b-) is less than 1 % among the white population. However, this phenotype has been recorded in many ethnic groups, most abundant among people originating from the Polynesian Islands and Finland. Among the Polynesians, the prevalence is as high as 1.4 % [7]. Among Indian population, the frequency is 0.58 % [9]. In Taiwan, 1.2 % among the Paiwan tribe and 1 % among the Rukai tribe were detected as Jk null phenotype [10]. This rare phenotype has also been detected among the ethnic population of the Brazil, and Japan [5]. Among Thai blood donors, 0.025 % were found positive for Jk(a-b-) [11]. Study in Malaysia showed that out of 594 blood donors, Jk(a-b-) phenotype was found in seven Malay donors and 2 Indian donors giving the incidence of 3.5 and 1.7 % respectively [12].

Anti-Jk3 antibody reacts with all Jk(a+) and Jk(b+) red cell but not with Jk(a-b-) red cells. This gives rise to the pan-agglutination reaction except the auto control in the antibody identification panel because the panel red blood cells are either Jk(a+) or Jk(b+) [2, 8]. The anti-Jk3 detected in our patient also gives the similar pan-agglutination reactions with all panel cells in two different antibody identification panels except the auto control.

One of the laboratory test that is helpful in identifying Jk null phenotype is urea lysis test. Red cells of Jk null individuals exhibit an increased resistance to lysis in aqueous 2 M urea. Olive et al. (1995) has evidenced that the urea transporter molecule known as human urea transporter 11 (HUT11) is the product of the Kidd locus and both genes are co-localized to chromosome 18q12-q21. The Kidd (JK) blood group is carried by an integral membrane glycoprotein which transports urea through the red cell membrane. Jk(a-b-) red cells lack the entire urea transport protein and showed a selective defect in urea transport [13]. In the urea lysis test, red cells are placed in 2 M urea

to see the red cell haemolysis. Normal red cells are rapidly lysed because the urea transported into the cells makes them hypertonic and the cells burst as a result of water influx due to osmosis. In Jk(a–b–) individuals, the cells do not haemolysed because of the absence of urea transporter. [11]. In this patient, her urea lysis test was negative which is consistent with the Jk(a–b–) phenotype.

For transfusion in these patients with anti-Jk3, Jk(a–b–) phenotyped red cells are recommended. These patients often face problem of getting the suitable JK(a–b–) blood for surgery, more so during emergency situation. Additional time is required to obtain the JK(a–b–) red cells due to the high prevalence of these Kidd antigens in most of the donor population [11]. It is very important for the blood bank to maintain the list of the rare blood group donor pools in order to provide the suitable blood when necessary; and also to maintain a complete record of the transfusion histories of such patients' to prevent haemolytic transfusion reaction in future transfusion due to the amanaestic effect of these antibodies.

Conclusion

This case report highlights an extremely rare anti-Jk3 antibody that was detected during a pre-transfusion blood testing. Anti-Jk3 should be suspected in a previously pregnant or transfused patient during the antibody screening and identification when it shows the pattern of an antibody reacting to all cells in the panel i.e. reacting to a high frequency antigen, but with negative autocontrol. Increased awareness among the blood bank personnel regarding the variability of the blood group phenotype and the capricious nature of the Kidd antibodies may contribute to the better management of these patients.

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