A rare case of naturally occurring allo anti-Jk(a) missed in manual screening test on tube method

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Abstract:
BACKGROUND: Antibodies to the Kidd blood group are mainly red blood cell (RBC) immune, but a few reports on naturally occurring antibodies have been documented.
AIM: The aim of this study is to study the anti-Jk(a) for its unusual reactivity with different serological methods.
MATERIALS AND METHODS: Donor’s plasma was tested with RBCs from in house donors and commercial panels by manual and automated devices.
RESULTS: A 36-year-old male blood donor with naturally occurring anti-Jk(a) is detected by solid-phase assays and the gel card technique but not by the tube method. The IgG antibody with the titer of >32 was not a complement-fixing hemolysin, showed a reduced reactivity with enzyme-treated RBCs, and was detectable through 8 months’ follow-up period. The donor was typed as (Jk(a−)).
CONCLUSION: An unusual naturally occurring anti-Jk(a) detected by solid-phase red-cell adherence but not reacting by tube technique reflected on the sensitivity of the methods used.

Keywords: Alloanti-Jk(a), healthy blood donor, naturally occurring

Introduction

Red cell alloantibody is broadly classified as the red blood cell (RBC)-immune or the non-RBC-immune, the former being produced in response to antigenic stimulus through blood transfusion or pregnancy in the subject who lacks the corresponding antigen. Conversely, the non-RBC immune antibodies are formed in response to environmental agents that have the antigenic similarity to the RBC antigens and hence are called naturally occurring antibodies. While the RBC-immune antibodies are IgG, react at 37°C and clinically significant as to cause hemolytic transfusion reaction (HTR) or hemolytic disease of the fetus and newborn (HDFN). In contrast, the naturally occurring antibodies are IgM, react at lower temperature and innocuous in nature. Antibodies to Kidd blood group are mainly RBC-immune,[1] although a few cases with naturally occurring variety have been documented.[2-4] The autoantibody to Kidd blood groups has also been reported.[5] The present case with naturally occurring IgG alloantibody was found in a nontransfused healthy male. It was detected by the solid-phase automated serology device but not by the manual tube technique on antibody screening test (AST) was unique in nature for investigation.

Materials and Methods

Detection and identification of antibody were carried out by automation

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devices (Immucor, USA) and (Diagast, France) detecting antibody by different serological principles, besides IgG gel-card system (REAGENS Kft, Hungary) and the manual low-ionic-strength solution-indirect antiglobulin test (LISS-IAT) tube method. All the assays were detecting IgG antibodies.

**Results**

**The case**
A 36-year-old male blood donor with early repolarization, a cryptic heart anomaly, was otherwise in good health and used to donate blood on a regular basis without any untoward reaction. The patient was grouped AB, Rh. D positive with a negative AST by manual tube method, although the AST was positive by solid-phase red-cell adherence (SPRCA). Antibody identification test carried out using various automated and manual devices showed anti-Jk(a) specificity [Table 1]. Its activity was reduced from 3+ with untreated RBCs to 1+ with papain-treated RBCs; antibody neither exert complement-mediated hemolysis nor fixed complement on the sensitized RBCs were incubated with fresh serum as source of complement and tested by broad-spectrum antiglobulin reagent. Antibody was IgG in nature as was reacting through the devices meant for the detection of IgG antibodies. Titer value of 1:32 +, observed initially remained the same after the 8 month’s follow-up. The donor was typed as Jk(a−).

**Discussion**

Naturally occurring anti-Jk(a) described by Rumsey et al.[3] was detected only by SPRCA but not by IAT in tube even using potentiators such as LISS or polyethylene glycol or with enzyme-treated RBCs. Kay et al.[5] had tested a large number of RBC-immune anti-Jk(a), of which as many as 26 examples were detected exclusively by SPRCA and not by gel technique, considering the former being more sensitive. The later reports showed the naturally occurring anti-Jk(a) was detected by the gel technique but not by the manual IAT in tube.[3,4] Anti-Jk(a), in our case, was detected by the solid-phase technology, involving diverse principles in antibody detection, and by the gel technology, but did not detect by the tube method in the LISS-antiglobulin phase. This feature may reflect a lesser sensitivity of the tube technique.

The RBCs immune antibodies are developed through transfusion or pregnancy, are IgG in nature, react at 37°C, and may cause HTR or HDFN to incompatible blood transfusion or pregnancy. On the other hand, the non-RBC immune antibodies are stimulated through the factors naturally present in environment, for example, microorganisms, pollen, etc. that share the antigens with humans. Baring from ABO, the naturally occurring antibodies of Lewis, P, MNS systems are clinically innocuous owing to their poor potency and lower thermal amplitude. Antibody to the Kell blood group is usually RBC-immune but occasionally found as naturally occurring in response to microbial exposure.[6,7] Similarly, the antibodies to Kidd blood groups are also RBC-immune, yet a few cases of naturally occurring variety have also been found in association with infections.[2,3,8,9] However, anti-Jk(a) in the present case as well as the one reported by Shastry et al.[10] was found in the healthy male donors without a history of transfusion or infection.

The RBC-immune anti-Jk(a) or anti-Jk(b) is usually short-lived in the absence of continual stimulus and may miss in the pretransfusion compatibility test giving rise to delayed HTR in subsequent transfusion, should the donor happens to have corresponding antigen. Naturally occurring anti-Jk(a) reported by Kim et al.[11] was disappeared in a period of 6 months. However, the antibody in our case was detectable with the same strength even after 8 months presumably due to some unknown stimulus present throughout in his environment.

The RBC-immune anti-Jk(a) and anti-Jk(b) are IgM and/or IgG, fix complement that may lead to hemolysis, detected in the antiglobulin phase at 37°C[10] and give stronger reaction with enzyme-treated RBCs. However, the antibodies in the present case neither bind complement nor it show hemolysis in the test and showed a reduced reactivity with enzyme-treated RBCs. Such a reduce reactivity with the enzyme-treated RBCs was observed in the earlier case as well.[3]

**Table 1: Antibody specificity to Jk(a) antigen as ascertained by automated and manual devices involving different principles of antibody detection**

| Method/device/principle involved          | RBCs tested | Observations                                      |
|------------------------------------------|-------------|--------------------------------------------------|
| SPRCA, capture-R, Neo, Immucor           | 7           | Jk(a+) Jk(a−) Complete match for anti-Jk(a)       |
| SPRCA, Erythemagenetic technology, DIAGAST, France | 8           | Jk(a+) Jk(a−) Complete match for anti-Jk(a)       |
| Gel Card, Column Agglutination Technology, Tulip | 6           | All match for anti-Jk(a) except 2 RBCs in heterozygous state |
| Tube method, manual LISS/IAT             | 20 random   | All negative                                     |

**Notes:** SPRCA=Solid-phase red-cell adherence, LISS=Low-ionic strength solution, IAT=Indirect antiglobulin test, RBCs=Red blood cells

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Conclusion
An unusual IgG anti-Jk(a) detected by the solid-phase assays and gel card technology was failed to react by the conventional tube technique, in spite of having a moderately high titer. This observation may reflect on the sensitivity of the methods used in the detection of such antibody. The case provides the 4th case reported in the literature and the 2nd of its kind from India thus qualifying as the rare entity of naturally occurring antibody.

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Conflicts of interest
There are no conflicts of interest.

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