Case Report

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"Auto-anti-A1" in a healthy young blood donor: A rare cause of ABO discrepancy

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Abstract:

"Auto-anti-A1" has been sparsely discussed in the literature. Only few workers in the past depicted such antibody in transfused and nontransfused patients. The current case is probably the first example of auto-anti-A1 in a healthy young blood donor who was typed as ABO Group "A1B." The cold reacting autoantibody in the donor was serologically characterized in details and was found to be nonhemolytic. ABO discrepancy was resolved and the donor was finally typed as "A1B Negative." Therefore, we concluded that auto-anti-A1 may be a rare cause of ABO discrepancy and its resolution is essential to confirm blood group and subsequent blood transfusion management.

Keywords:

ABO discrepancy, auto-anti-A1, autoantibody, elution, hemolytic anemia

Introduction

Approximately 80% of individuals typing as ABO Group "A" express the A1 antigen on their red cells. Anti-A1 is occasionally found as a naturally occurring IgM alloantibody in 1%–8% of A2 individuals and 22%–35% of A2B individuals.[1,2] These natural alloantibodies react optimally at room temperature or below and are considered clinically insignificant.[1-3] However, development of anti-A1 in individuals carrying A1 antigens on red cells is extremely rare. This antibody designated as "Auto-anti-A1" has been sparsely discussed in the literature. While Rogers *et al*. detected auto-anti-A1 in a nontransfused patient, Castella *et al*. found auto-anti-A1 in a patient with metastatic carcinoma.[4,5] Immune auto-anti-A1 causing hemolytic graft versus host reaction in an A1 recipient following transplantation of "O" Group kidney was discussed by authors in 1987.[6] Most of these workers found cold reacting auto-anti-A1 of IgM type with no clinical significance. However, well-documented cases of autoimmune hemolytic anemia (AIHA) due to auto-anti-A1 have also been published. These autoantibodies have been serologically characterized and found to be IgG alone or a mixture of IgG and IgM.[7-10]

Case Report

Here, we reported a case of anti-A1 in an otherwise young healthy male blood donor carrying A1 antigen on his red blood cells. The gentleman donated blood thrice before elsewhere but could not gather a correct blood group report. Presently, on medical examination the donor was found to be healthy with a hemoglobin value of 13.7 g/dL. Past and present medical and medication history was insignificant. Blood samples of the donor were collected as per the standard operating procedure (SOP).

Blood grouping and antibody screening was performed using the automated solid phase

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technology (NEO Iris, Immucor, USA). On observing a discrepancy in the reverse grouping the blood group of the donor was repeated using conventional tube technique (CTT). A similar discrepancy has been noted with CTT and additional test was performed on both donor red cell [Table 1] and serum [Table 2] specimens. Initial test revealed that the donor is RhD negative but weak D test using human antiglobulin showed a positive result. As the donor Direct antiglobulin test (DAT) was positive therefore the weak D result could not be confirmed. On further investigation the donor ABO Group was typed as A1 using validated commercial anti-A1 reagent (Tulip Diagnostics Pvt. Ltd.), but his serum reacted with both autologous and allogeneic A1 red cells. Heat elution using 6% bovine albumin has been used to dissociate antibodies from the donor red cells.[11] The eluate reacted strongly (≥3+) with five different normal A1 red cells at room temperature and below (4°C>22°C). Anti-A1 in donor serum as well as in eluate did not react with A1 red cells at 37°C. No reactivity was observed on incubation of eluate and donor serum with six different samples of normal "O" Group red cell. Furthermore, IgG auto-anti-A1 activity could be ruled out by treating donor serum with sulfhydryl reagent 0.01 M dithiothreitol (DTT) to abolish the IgM auto-anti-A1 and investigating underlying IgG.[12] Weak D test performed on twice eluted and adequately washed red cells was found to be negative. Antibody screening of the donor revealed no alloantibody in his serum. The confirmed blood group of the donor was "A1B" Negative. Various samples of "A1B" positive and "A1B" negative packed red blood cell (PRBC) were found incompatible with the donor serum. However, no incompatibility was noted with various samples of "A2" "A2B" and "O" red cells [Table 2]. The donor was recalled after 3 weeks for detailed history, repeat investigations and saliva test. Detailed hematological and biochemical investigation ruled out *in vivo* hemolysis in the donor and the presence of non hemolyzing cold reactive "Auto-Anti-A1" was confirmed. Saliva test revealed soluble Group "A" "B" and "H" substances.

Discussion

Discussion on auto-anti-A1 is sparse in the literature. Most cases have been demonstrated in patient population with or without history of blood transfusion.[4-10] The current study may be considered as the first example of auto-anti-A1 in a healthy blood donor. The antibody belonged to IgM immunoglobulin class reactive at colder temperature with no clinical significance. By virtue of the antibody type, its thermal amplitude and clinical significance, the donor demonstrated normal hematological and biochemical values with no obvious *in vivo* hemolysis despite DAT positivity. Auto-anti-A1 has been confirmed by elution of donor red cells and testing the eluate using samples of A1, A2, and O red cells. Szymanski *et al*. reported a fatal case of intravascular hemolysis due to anti-A autoantibody which have been likely to be IgG or a mixture of IgM and IgG.[10] Parker *et al*. observed AIHA in a patient due to anti-A autoantibody and characterized the antibody as purely IgM.[9] Authors in the past also reported IgM auto-anti-A1 antibody apparently formed in the 24 h between the first and second series of blood transfusions. However, these antibodies were reactive at 22°C or below and did not cause overt hemolysis in the patient.[7]

In the present study, investigations repeated on blood specimen on recalling the donor yielded same results. The donor RhD status was confirmed by repeating weak D test on doubly eluted red cells. Titer of auto-anti-A1 in both samples was 2 at both 4°C and 22°C. A saliva inhibition test performed showed that the donor was a secretor carrying "A" substances. Though possibility of *in vivo* neutralization of donor auto-anti-A1 by his "A" substances was initially assumed by the authors, this could not be proven. However, it may be remotely assumed that low titer or concentration of anti-A1 in donor plasma may be the result of some degree of neutralization or inhibition effect. However, donor auto-anti-A1 was inhibitable by known soluble Group "A" specific substance of volunteers. Wright *et al*. in 1980 detected auto-anti-A1 in an elderly man, Group A1

Table 1: Immunohematological investigation on donor red cell specimen

Forward group						Additional test			
Anti-A	Anti-A1	Anti-B	Anti-AB	Anti-H	Anti-D	Weak D	DAT	Elution	Weak D test on eluted RBC
4+	4+	4+	4+	2+	0	2+	2+	Anti-A1 eluted (4°C>22°C)	0

DAT=Direct antiglobulin test, RBC=Red blood cell

Table 2: Immunohematological investigation on donor serum and saliva specimens

Reverse group				Additional test					
A1 cell	A2 cell	B cell	O cell	Antibody screen	Auto control	Titre/thermal amplitude	Crossmatch with A1B (+) and A1B (–) PRBCs (3 units each)	Crossmatch with A2 (–), A2B (–) and O (–) PRBCs (3 units each)	Saliva
2+	0	0	0	0	1+	2/4°C 2/22°C	2+	0	A, B and H substances

PRBC=Packed red blood cell

Le (a + b−). The IgM antibody agglutinated the man's own red cells as well as all random A1 donor cells. The authors observed that over a period of 5 months, the auto-anti-A1 titer was 4 at 22°C however antibody titer on initial sample was not discussed.[7] Previous workers tested gamma-globulin markers Gm (a, x, f) to differentiate autoantibody or alloantibody character of auto-anti-A1 in a patient who acquired hemolytic anemia due to autoantibodies of anti-A1 specificity induced by a Group "O" kidney graft in an A1 recipient as a Graft-versus-Host (GvH) reaction.[6] Castella *et al*. performed detailed characterization of auto-anti-A1 in a nontransfused patient of metastatic adenocarcinoma. The antibody reacted at a wide thermal range and could be inactivated by DTT suggesting its IgM nature. However, no hemolytic anemia was associated in the patient.[5] Rogers *et al*. found anti-A1 in the serum of a patient of blood Group A1 who had never received a blood transfusion. The antibody could be denatured by 2-mercaptoethanol and also could be totally absorbed by red cells from the patient as well as other A1 individuals. The A and H serum transferases of the patient were normal.[4] In the present study, since the donor red cells showed DAT positivity; hence, PRBC unit prepared was discarded as per departmental SOP and the plasma unit was stored for use in patients belonging to "O" or "B" blood groups.

We conclude that although rare but "Auto-anti-A1" may be detected in blood donors or in patients and is an important cause of ABO discrepancy. These autoantibodies need complete serological characterization to resolve the discrepancy and manage blood transfusions.

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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Conflicts of interest

There are no conflicts of interest.

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