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ORIGINAL ARTICLE

A CASE OF BLOOD GROUP A_2B WITH ANTI A_1 ANTIBODY REACTIVE AT 37°C

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Abstract:
Landsteiner discovered ABO blood group system. It is most important for transfusion medicine. Blood group A has several subtypes and most important are A1 and A2, upon which further groups of A and AB have been classified as A_1, A2 and A_1B, A_2B. Of individuals with A antigen, approximately 20% belong to A2 while rest 80% belong to A1. Anti-A1 Lectin, a cold agglutinin which destroys A_1 cells is clinically significant when they react at 37°C, causing transfusion reactions.

Key words: *ABO blood group, subtypes A_1 and A_2, Anti-A_1 Lectin.*

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Introduction:

ABO blood group was the first blood grouping system discovered by Landsteiner. It includes different genotypes and phenotypes of A, B and O antigens. Two principal subgroup of blood group A are A_1 and A_2. Subgroups of A can result in discrepancy in ABO blood grouping.But haemolytic transfusion reactions are.[11] A_2B individuals can have anti A_1 antibodies which reacts at temperature below 25°C and do not produce problem in transfusion.[11] Reactivity of anti-A_1 at 37 °C can leads to haemolytic transfusion reaction. As ABO discrepancy leads to haemolytic transfusion reaction, hence it is necessary to include anti A_1 lectin in blood grouping Standard Operative Procedure (SOP)

As the patient required immediate transfusion, he was advised to transfuse antigen negative blood ie, transfused with A_2B, B or O group blood unit.

Case report:

A 25 year old female, known chronic kidney disease was admitted in NIKDU,Dhaka with severe anaemia. Her haemoglobin dropped to 4.5 gm/ dl, serum creatinine was 6.2 gm/dl. Urgent blood demand was placed and blood specimen for grouping andcross-match was collected.

Initial forward and reversegrouping result revealedAB and B and Rh typing revealed D positive. And compatibility testwith three units of AB, RhD positive blood at room temperature and at 37°C were incompatible. Compatibility test by Indirect Coombs

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Table-I

Results of blood grouping of patient

Grouping	Forward Grouping					Reverse Grouping			
Test reagents	Anti A	Anti A_1	Anti B	Anti AB	Anti D	A_1 Cells	A_2 Cells	B Cells	O Cells
Test Result	+	-	+	+	+	+	-	-	-

. + agglutination. – no agglutination

Table II

Results of compatibility tests with several blood donor units

Donor Units	Major Compatibility Test		Minor Compatibility Test	
	Saline- RT	ICT-37^{0}C	Saline-RT	ICT-37^{0}C
A_1B RhD+	+	+	N	N
O Rh D+	N	N	+	+
B RhD+	N	N	N	N

ICT- Indirect Coomb's Test. RT- Room temperature, N-Negative/Not agglutinated (compatible)

Test (ICT) at 37°C with anti human globulin (AHG) was also incompatible. The blood group of the patient was repeated with 'washed RBC' by tube method. Both forward and reverse grouping were done and same result noted. Results were confirmed bothmacroscopically and microscopically.As there was no anti A_1 lectin in our centre,the sample sent to referrence laboratory of BSMMU, Dhaka.The blood group of the patient was repeated with 'washed RBC' by tube method. Both forward and reversegrouping were undertaken .For forward grouping anti A_1 lectin was also taken. Blood group reaction was confirmed macroscopically and microscopically (Table:1). For reverse grouping A_1 cells, O cells and A_2 cells were taken. Indirect Coombs test at 37°C revealed agglutination due to patients anti A_1. After evaluating the all redults the blood group of patient was confirmed as A_2B with anti A_1 antibodies and RhD positive.The thermal amplitude of anti-A_1 antibodies was determined by keeping the test tubes at 4°C, 22°C, and 37°C. Next step was the compatibility test for transfusion of safe blood.Patient was asked for family screening, but they failed. Due to non-availability of A_2B group blood unit, compatibility test with two units each of O Rh positive and B Rh positive was undertaken. Blood group O units had minor match problems as expected due to donor anti B, however, both B group blood units were found compatible. A decision to transfuse Bor O units was taken. In total 4, 2 and 2 units of A_1B, O and B Rh positive group blood units respectively were subjected for compatibility test. Result of compatibility test is presented in (Table:2) .B group units had two types of compatibility results due to absence and presence of anti A_2 which was confirmed by using A_1 and A_2 cells.

Table III

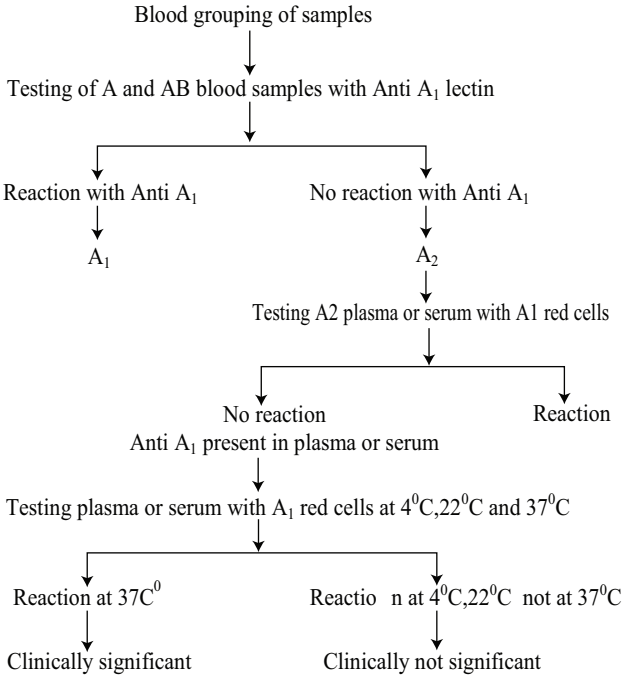
Antigen and antibody of ABO system

Blood Group	Antigen	Antibody
A	A	B
B	B	A
AB	AB	No A or B
O	No A or B	A , B

Table IV

Antigen and antibody of subgroup A_1

Subgroup	Antigen	Antibody
A_1	A_1	Anti B
A_2	A_2	Anti A_1
A_1B	A_1B	None
A_2B	A_2B	AntiA_1



Discussion:

Landsteiner's ABO system of blood groups is most important for transfusion medicine. Major ABO blood group antigens are A, B, AB and O. A_2 and A_2B are rare subtypes of ABO blood group system. Other less prevalent subtypes of A include A_3, A_x, A_{end}, A_y and A_{el}. Differences between A_1 and A_2 are quantitative as well as qualitative. Qualitative difference of A_1 and A_2 lies in their chemical structures. Individuals with A phenotype express A^a, A^b, A^c and A^d determinants while A_2 have only A^a and A^b antigenic determinants. Absence of A^c and A^d is assumed to be a cause of development of anti-A_1 in A_2 and A_2B individuals.[1,2,3] Usually anti-A_1 exist as naturally occurring IgM with a thermal amplitude of less than 25°C. However, cases of anti-A_1 reacting at 37°C have also been reported in the literature.[4,5] Anti-A_1 is important as it is one of the causes of ABO discrepancies, it can develop hemolytic transfusion reaction and its clinical manifestations have also been reported in hemopoietic stem cell and organ transplantation.[6,7] About 0.4% of A2 and 25% of A2B have anti A1 antibodies.[8]

A_1 and A_2 are distinguished by the reactivity of lectin i.e., anti-A_1 which occurs as a cold agglutinin and exclusively agglutinates A_1 cells. About 0.4% A_2 and 25% of A_2B subgroups possess anti-A_1. These antibodies become clinically significant if they react at 37°C destroying A_1 cells. [9]

Approximately, 20% of individuals having A antigen in blood belong to A_2 and thus, forming either A_2 or A_2B subgroups while rest80% belong to A_1, so as to form either A_1 or A_1B subgroups.[10,11] Subgroups of A antigen weaker than A_2 are not frequent. [9]

For blood groups positive for A antigen, i.e., group A and AB, further testing with anti-A_1 lectin was conducted .[12] The individuals were hence, classified under sub-blood groups containing A_1 or A_2.

In a study done on the Muslim population of UP by Hussain R et al., the prevalence of A1 and A1B was 26.52% and 19.34% and A2 and A2B was 2.90% and 1.24% respectively .13 Their study was similar to a study done by Ara G et al., in which prevalence of A1, A1B, A2 and A2B was 24.64%, 20.21% 3.97% and 1.60% respectively .14 A study by Chaitanya Kumar IS et al., concluded that prevalence of A2 and A2B is 0.85% and 1.21% respectively .15 In a study done by Sharma DC et al., in which A2 and A2B were found to be 8% and 8.6% respectively.[16]

One study has reported a case of IgG anti-A_1.[11] Similarly, two other studies have shown hemolytic transfusion reaction due to anti-A_1.[17,18] Development of anti-A_1 antibodies after allogeneic stem cell transplantation and organ transplantation has also been reported.[19]

It has been reported that individuals with A_2B phenotype are more prone to develop anti-A_1 as compared to A_2. This could be explained on the basis of two observations. Firstly, individuals with A_2B have a smaller number of A antigens in comparison to A_2. Secondly, A_2B individuals possess *R101 allele more commonly than A_2 individuals (41% vs 1%) leading to the high frequency of A_2B phenotype.[20]

In our case anti A_1 is reactive at 37°C and transfusion with A_2B blood group unitis ideal but it is not available. Transfusion of O group red cell is also recommended in these recipients. As blood component facility is available at NIKDU, we advised to transfuseO group Red Cell Concentrate units as we anticipated anti B in plasma of O whole blood units leading to haemolytic transfusion reactions considering large volume transfusion requirements. The another choice left is transfusion of B group units. In majority ofB positive cases primary anti A is anti A_1 however primary anti A_2 can be encountered. It is well known that anti-A in B blood group donors generally have primary anti A_1 and occasionally anti A_2 . In management of this case, the importance of blood grouping and AHG phase in compatibility test has been highlighted. [21]

Published cases that have reported clinically significant anti-A_1 antibody are in patients who had undergone cardiac surgery using cold

cardioplegia[22,23]. Cases of anti A_1 reactive at 37°C leading to transfusion reactions are rare .[24,25.]

From a transfusion perspective, individuals with A_2 and A_2B should be transfused with identical blood types. However, due to its rarity especially A_2B, special attention should be given if identical blood type is not available and the patient needs transfusion of Red Cell Concentrate. These individuals can be transfused with O or B group Red Cell Concentrate considering it the next compatible group.

CONCLUSION:

As the prevalence of anti-A_1 in A_2 and A_2B is rare,incorporating them into the ABO grouping system, to rule out the possibility of its wide range of thermal reactivity,can limit these minor but dangerous transfusion incompatibilities. Any discrepancy in these individuals should be resolved before blood/ component transfusion.

Conflict of Interest:

The author stated that there is no conflict of interest in this study

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Ethical consideration:

The study was conducted after approval from the ethical review committee. The confidentiality and anonymity of the study participants were maintained.

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