Case Report

# A intermediate ($A_{int}$) subgroup with warm anti-$A_1$ antibody: A case report

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## ABSTRACT

A intermediate ($A_{int}$) subtypes exhibit characteristics intermediate between $A_1$ and $A_2$. Plasma from $A_{int}$ individuals contains different enzyme, UDP-GalNAc: fucosylgalactoside-a-3-N-acetylgalactosaminyl transferase, which is different from the enzyme in $A_1$ and $A_2$ plasma. We encountered the case of a 54-year-old female (having pneumonia and chronic kidney disease) for pre-transfusion testing. On routine grouping, we encountered group discrepancies. On testing, anti-A gave 4+, anti-B-0, anti-$A_1$ lectin-2+, anti-H lectin, and anti-AB antisera gave 4+ reactions. Reverse grouping gave 4+ with B cells, 2+ at room temperature with A cells, and 4+ and 1+ at 37°C and 4°C. Saliva inhibition studies showed A and H substances. It was typed as an $A_{int}$ group with warm anti-$A_1$ antibody. It's the 1st time ever we encountered $A_{int}$ case with a warm type anti-$A_1$ antibody. Here, O group packed red cells are the suitable blood units to transfuse.

**Keywords:** A subgroup, $A_{int}$, Anti-$A_1$, Red cell antibody, Warm antibody

$A_1$ and $A_2$ are the major subgroups of A. This differentiation is based on the reactivity of $A_{1\ cells}$ and not $A_{2\ cells}$ with anti-$A_1$ lectin. $A_{2\ cells}$ show increased reactivity with anti-H lectin [1].

We report the case of a 54-years-old female having a rare A intermediate ($A_{int}$) subgroup having warm type anti-$A_1$ antibody which is the first such case encountered by us. Warm anti-$A_1$ antibody reactive at 37°C may cause hemolysis if transfused with $A_1$ red cells.

## CASE REPORT

A 54-year-old female sample was sent for pre-transfusion testing at our department. She was having pneumonia for the past 2 months and chronic kidney disease for the past 20 months approximately. As per the patient's husband, she had her last red cells transfusion nearly 4 months back without any adverse event in some outside private hospital (ABO group of the last red cells transfused unknown). She had no history of any red cell alloantibody identified previously and she was typed as "A positive."

On routine grouping, her blood group came out to be "A positive" with anti-$A_1$ antibody reacting at room temperature which got enhanced at 37°C. No such case has ever been reported in this region (central India) and at our institute previously. Typing this case as group "A" (as was done previously at some private institute) and transfusing with a simple $A_1$ group could lead to a hemolytic transfusion reaction.

All tests were done with the conventional test tube method. Test sample first underwent forward and reverse blood grouping [2]. Blood grouping was done at three temperatures (room temperature, 4°C and 37°C) due to discrepancy and was followed by saliva testing [2]. All the antisera were from the BioRad company and were as per the quality standards (known $A_2$ red cells were unavailable). $D_1$ and $D_2$ in the forward grouping were IgM anti-D antisera from different lots of the same company. For saliva testing, only controls with saline tubes were put as saliva from known secretor, non-secretor, and anti-Lewis antisera which were unavailable. Plasma enzyme determination and molecular testing facilities were unavailable.

On further testing, anti-$A_1$ lectin gave 2+ reaction, anti-H lectin and anti-AB antisera gave 4+ reactions. Reverse grouping had clear cut 4+ reactivity with B cells, while reactivity with A cells varied with temperatures (Table 1) [2]. Table 2 [1] shows the reactivity patterns of $A_1$ and $A_2$ subtypes of A (Tables 1 and 2 show the comparison of reaction between the test sample and that of $A_1$ and $A_2$ to establish intermediate antigen strength). Saliva inhibition studies demonstrated the presence of A and H substances as the reactivity of the test saliva on inhibition test showed nil reaction with test tubes containing anti-A antisera and anti-H lectin, while test tube with anti-B antisera showed 1+ reaction showing absence of B antigen in saliva. Saline controls were negative (Table 3) [3]. It was typed as an $A_{int}$ group with warm type anti-$A_1$ antibody. Fig. 1a shows the reactivity of red cells

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**Table 1: Forward and reverse grouping [2]**

| Anti-A | Anti-B | Anti-H | Anti-$A_1$ | Anti-AB | Anti-$D_1$ and $D_2$ | $A_c$ | $B_c$ | $O_c$ | Autocontrol | |
|---|---|---|---|---|---|---|---|---|---|---|
| 4+ | 0 | 4+ | 2+ | 4+ | 4+ | 2+ | 4+ | 0 | 0 | RT |
| 4+ | 0 | 4+ | 2+ | 4+ | 4+ | 4+ | 4+ | 0 | 0 | 37°C |
| 4+ | 0 | 4+ | 2+ | 4+ | 4+ | 1+ | 4+ | 0 | 0 | 4°C |

RT: Room temperature, $A_c$: Pooled A cells, $B_c$: Pooled B cells, $O_c$: Pooled O cells

**Table 2: Normal red cell and serum reactions with $A_1$ and $A_2$ cells [1]**

| Red cell reactions with anti-sera and lectins | | | | | Serum reactions with reagent red cells | | | |
|---|---|---|---|---|---|---|---|---|
| Red cell phenotype | Anti-A | Anti-B | Anti-A, B | Anti-H | $A_1$ cells | B cells | O cells | Saliva (secretors) |
| $A_1$ | 4+ | 0 | 4+ | 0 | 0 | 4+ | 0 | A, H |
| $A_2$ | 4+ | 0 | 4+ | 2+ | 0/2+ | 4+ | 0 | A, H |

**Table 3: Inhibition testing result on saliva testing [3]**

| | Inhibition test with test sample saliva | | | Saline controls | | |
|---|---|---|---|---|---|---|
| | Test tube with saliva+Anti-A+A cells | Test tube with saliva+Anti-B+B cells | Test tube with saliva+Anti-H+O cells | Test tube with normal saline+Anti-A+A cells | Test tube with normal saline+Anti-B+B cells | Test tube with normal saline+Anti-H+O cells |
| Reactivity with unknown (test sample) test tubes | 0 | 1+ | 0 | 1+ | 1+ | 1+ |

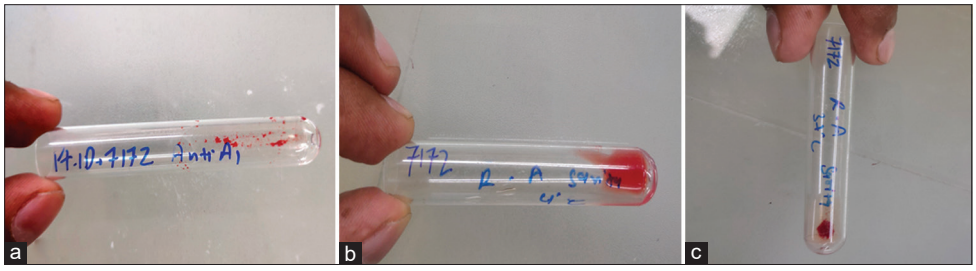


**Figure 1: Test sample with (a) anti-$A_1$ lectin; test sample reverse with Ac at (b) 4°C; (c) 37°C**

with anti-$A_1$ lectin and Fig. 1b and c show reverse A cells at 4°C and 37°C (titer of warm anti-$A_1$ antibody could not be performed as patient succumbed to illness 2 days after we received blood and saliva sample).

## DISCUSSION

Landsteiner and Levine first recognized an additional subtype of A, that is, $A_{int}$. It is considered a heterogeneous subgroup which is more common in Black people than in White people. In India, the incidence of Aint was reported to be 2% [3]. Plasma from $A_{int}$ individuals contains glycosyltransferase enzyme different from $A_1$ and $A_2$ which is UDP-GalNAc: 2'-fucosylgalactoside-a-3-N-acetylgalactosaminyl transferase. This $A_{int}$ enzyme shows a strong affinity to UDP-GalNAc and low affinity to 2'-fucosyllactose, which is a soluble analog of H substance [4].

Three different enzymes were detected when $A_1$, $A_2$, and $A_{int}$-type plasma were examined for glycosyltransferases [5]. It is possible to differentiate the A subtypes by examining the kinetic characteristics of α-N-acetylgalactosaminyltransferases in the plasma of various A subtypes. Mutations in ABO alleles result in differences in the specificity and activity of glycosyltransferase enzymes [6]. $A_2$ organs can be transplanted to O recipient [1], so the distinction of $A_{int}$ group is very important as no clear-cut guidelines are available for $A_{int}$ group organ transplantation and $A_{int}$ group is underreported in our country and especially in the region of Central India. The prevalence values of $A_1$, $A_2$, and weak subgroups in South India were reported to be 98.4%, 1.85%, and 0.01%, respectively [7]. The importance of subtyping A blood group and identification of $A_{int}$ has been discussed in a case report in South India [8]. A subgroups like $A_2$ or others may have anti-$A_1$ antibody reactive at 37°C and should receive either O group or same group packed red cells but not $A_1$ red cells [1]. Yoshida *et al*. showed in a study that an individual can be even $A_{int}$ B group and plasma enzyme determination is better than routine serological methods in determination of $A_1$, $A_2$, or $A_{int}$ subtypes [9,10].

## CONCLUSION

We have previously encountered $A_{int}$ case in this region but it's the 1st time ever we encountered an $A_{int}$ case with a warm-type anti-$A_1$ antibody. Here, O group packed red cells are the suitable blood units to transfuse. It's recommended to always test any

anti-$A_1$ antibody encountered in various temperatures so that any hemolytic transfusion reaction could be prevented.

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