Loss of Blood Group Antigens in Haematolymphoid Malignancy: A Case Series from a Cancer Institute from North East India

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Abstract

Introduction: Altered expression of blood group antigens has been reported to be associated with both solid as well as haematological malignancies. This usually results from genetic mutation leading to incomplete as well as abnormal synthesis of antigens. Transitional loss of RBC antigens especially from ABO system is most commonly found in haematological malignancies causing blood group discrepancies and followed by reversal to its historical blood group during remission. Loss of A, B antigens has also been associated to play a role in lung, bladder and colon cancers. However not much data is available regarding haematological malignancies.

Methods and Methodology: Retrospective review of blood group discrepancy (Forward group) in patients admitted for haematolymphoid malignancy at our institute was done during a period of 3.5 years (13/3/2020 till 12/9/2023). Blood grouping done by Column agglutination test were repeated by conventional tube method. Further confirmation of the group was done by saliva test and adsorption elution test as indicated. The detail history of the patient was collected from the hospital records and analysed.

Results: A total of 7 patients presented with either loss or decrease in antigen expression. Most common diagnosis was Acute Myeloid Leukaemia (AML) with FLT3 mutation and most common antigen affected was A.

Conclusion: Haematolymphoid malignancies has been associated with loss of blood group antigens causing group discrepancy. Blood transfusion is an integral part of the supportive care in these patients. Hence, proper work up of blood group discrepancy cases should be done and recorded so as to prevent delay in blood transfusion.

Keywords: Acute myeloid Leukaemia (AML)- Remission- ABH antigen- Blood group discrepancy

Introduction

The ABO system is the most important of all blood groups in transfusion practice. A, B and H antigens are the small carbohydrate epitopes present in the glycoproteins and glycolipids of erythrocytes, endothelial cells and most epithelial cells [1]. Blood group discrepancy is said to occur when the forward blood group does not match with the results of the reverse blood group. These can be due to conditions related to patient serum (reverse grouping), or with patient’s red cells (forward grouping) or with both serum and cells [2]. Both solid and haematological malignancies have been associated to alter the A, B and H antigen expression leading to discrepancy in the forward group [3, 4]. The loss of blood group antigen was first reported by Van, loghem.et al [5] in the year 1957. The transient loss may be due to inactivation of A/B transferases in chromosome 9 or inactivation of H transferases in chromosome 19 [6, 7]. It may also have a diagnostic and prognostic implications in many cancer patients. They are more commonly seen in haematological malignancy like leukaemia, lymphoma etc [2]. Blood transfusion is an integral part of the supportive care of haematological patients and for that accurate blood group of the patient must be known. We have very limited data regarding such cases from North Eastern population of India. Hence all such rare blood group discrepancies must be solved and properly documented so as to avoid
any delay in blood transfusion and to prevent haemolytic transfusion reactions.

Here we present a case series on the ABO discrepancies due to decrease or loss of expression of blood group antigens in haematolymphoid malignancy.

**Materials and Methods**

Blood centre of our Institute received seven samples from department of medical oncology with decrease in antigen expression in the forward blood group over a period of 3.5 years (13/3/2020 till 12/9/2023). In all seven cases, 5ml of blood sample was collected in an EDTA vial and blood grouping was done using Column agglutination test (CAT) by BIORAD. If any discrepancy was found between forward and reverse grouping, first clerical error is ruled out and then detailed clinical history of the patient is taken from the hospital records. In forward blood group, when there is a loss or decrease expression of antigen by CAT, a repeat blood grouping is done by conventional tube test with monoclonal Anti-A, Anti-B and Anti-D (Tulip diagnostics) after incubation at 4°C for 30 minutes and reverse grouping is done using in-house prepared A, B and O pooled cells. If blood group is still inconclusive, saliva inhibition test is done followed by adsorption and elution studies in few cases. Each time the patient visited the cancer institute, the blood group was repeated by blood centre as all of them were on regular blood transfusion. All the procedures were done following standard technical manuals [8] as outlined in flowchart (Figure 1) and departmental standard operating procedure.

**Results**

**Observations**

A total of 7 cases were reported with loss or decreased antigen expression in forward grouping (Table 1). Loss of expression of antigen was highest with A blood group (5 cases) followed by B group in one case whereas weak expression of antigen was seen in one case. Over all 85.5% (six) cases where Blood group A. On incubation at 4°C for 30 minutes, only single sample i.e. (Case 5) showed increase in the strength of reaction to 1+. Rest all cases still showed no positive reactions. Saliva test could be done in 6 cases out of which 4 were secretors (66.6%). Adsorption elution was done in three cases out of which two cases showing blood group as A and one was inconclusive.

On subsequent follow up, historical blood group started appearing within (1-2) months of starting induction therapy (Table 2). During remission, the forward blood group first showed mixed field reaction by CAT followed by gradual increase in the expression of the corresponding antigens. However complete reversal to historical blood group could be seen in 3 cases and remaining was lost to follow up. Males were affected more than females and the most common diagnosis was AML in 5 cases followed by one case each of Chronic myeloid leukaemia (CML) and T-cell Non-Hodgkin Lymphoma (T-NHL). The most mutation was FLT3 seen in all AML cases. In majority of the cases (six) the discrepancy was found during the course of the treatment and in one case (Case 3) it was present before the treatment started.

**Discussion**

In our case series, blood group A was most commonly affected (85.7%) as seen in multiple case reports [9-11]. Study done by Abegaz SB et al [12] has shown significant decrease in expression of A, B or H antigens between 17% and 37% in leukaemia patients when compared to healthy controls. Majority of our patients presented with AML in 5 cases followed by one case each of Chronic myeloid leukaemia (CML) and T-cell Non-Hodgkin Lymphoma (T-NHL). The most mutation was FLT3 seen in all AML cases. In majority of the cases (six) the discrepancy was found during the course of the treatment and in one case (Case 3) it was present before the treatment started.

![Figure 1. Flowchart Showing Test Sequence for Solving ABO Discrepancy](image)

Table 1. Blood Group Detection by Various Methods

<table>
<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
<th>Case 6</th>
<th>Case 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forward Group</td>
<td>Reverse Group</td>
<td>Saliva test</td>
<td>Adsorption-Elution study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti A</td>
<td>Anti B</td>
<td>Anti D</td>
<td>A Cells</td>
<td>B Cells</td>
<td>O Cells</td>
<td>A, H</td>
</tr>
<tr>
<td>Neg</td>
<td>Neg</td>
<td>4+</td>
<td>Neg</td>
<td>4+</td>
<td>Neg</td>
<td>Not done</td>
</tr>
<tr>
<td>Neg</td>
<td>Neg</td>
<td>4+</td>
<td>Neg</td>
<td>4+</td>
<td>Neg</td>
<td>Not done</td>
</tr>
<tr>
<td>Neg</td>
<td>Neg</td>
<td>4+</td>
<td>Neg</td>
<td>4+</td>
<td>Neg</td>
<td>Not done</td>
</tr>
<tr>
<td>Weak positive</td>
<td>Neg</td>
<td>Neg</td>
<td>4+</td>
<td>None</td>
<td>None</td>
<td>Not done</td>
</tr>
<tr>
<td>Neg</td>
<td>Neg</td>
<td>4+</td>
<td>Neg</td>
<td>3+</td>
<td>Neg</td>
<td>Not done</td>
</tr>
<tr>
<td>Neg</td>
<td>Neg</td>
<td>4+</td>
<td>Neg</td>
<td>3+</td>
<td>Neg</td>
<td>A, H</td>
</tr>
</tbody>
</table>
In conclusion, Haematolymphoid malignancy may show altered expression of blood group antigens. All cases of blood group discrepancy should be properly evaluated and documented. This not only prevents the delay in providing safe blood in case of emergency but also gives us a gist regarding underlying disease condition. Further research and development programme has to be initiated to know the association between loss of antigen expression and cancer biology.

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References

1. Laura. Carbohydrate blood groups. In: Rossi’s principles of transfusion medicine. 5th ed. west sussex: john wiley and sons limited. 2016;159-75.

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Table 2. Patient Characteristics and Follow up

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Gender</th>
<th>Diagnosis</th>
<th>Molecular Study</th>
<th>Drug</th>
<th>Forward Group</th>
<th>Appearance of original group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>36yr</td>
<td>Male</td>
<td>AML</td>
<td>FLT3 mutation</td>
<td>Cytarabine</td>
<td>A +ve</td>
<td>O +ve</td>
</tr>
<tr>
<td>Case 2</td>
<td>36yr</td>
<td>Male</td>
<td>CML</td>
<td>FLT 3 Mutation</td>
<td>Cytarabine</td>
<td>A -ve</td>
<td>O -ve</td>
</tr>
<tr>
<td>Case 3</td>
<td>36yr</td>
<td>Female</td>
<td>AML</td>
<td>Normal cytogenetics</td>
<td>Chemotherapy not started</td>
<td>A +ve</td>
<td>O +ve</td>
</tr>
<tr>
<td>Case 4</td>
<td>36yr</td>
<td>Female</td>
<td>T-NHL Grade IV</td>
<td>CEBPA gene</td>
<td>Decitabine</td>
<td>B +ve</td>
<td>O +ve</td>
</tr>
<tr>
<td>Case 5</td>
<td>36yr</td>
<td>Male</td>
<td>AML</td>
<td>FLT3 mutation</td>
<td>Cytarabine</td>
<td>A +ve</td>
<td>Weak expression of Antigen A</td>
</tr>
<tr>
<td>Case 6</td>
<td>36yr</td>
<td>Female</td>
<td>AML</td>
<td>CD20, CD3&gt;&gt;CD 20</td>
<td>CVP therapy*</td>
<td>A +ve</td>
<td>O +ve</td>
</tr>
<tr>
<td>Case 7</td>
<td>36yr</td>
<td>Male</td>
<td>CML</td>
<td>t (9/22)</td>
<td>Dasatinib</td>
<td>A +ve</td>
<td>O +ve</td>
</tr>
</tbody>
</table>

*CVP (Cyclophosphamide +Vincristine +Prednisolone); AML, Acute Myeloid Leukaemia; CML, Chronic Myeloid Leukaemia; T-NHL, T cell – Non Hodgkin Lymphoma


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