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CASE SERIES

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

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Abstract

Background and objective: Altered expression of blood group antigens has been reported in association with both solid and hematological malignancies. This alteration usually results from genetic mutations leading to incomplete or abnormal synthesis of antigens. Transitional loss of red blood cell (RBC) antigens, particularly from the ABO system, is most commonly observed in hematological malignancies, causing blood group discrepancies that often reverse to the patient's historical blood group during remission. Loss of A and B antigens has also been associated with lung, bladder, and colon cancers. However, limited data is available regarding hematological malignancies. **Materials and methods:** This retrospective review of blood group discrepancies (forward grouping) was conducted on patients admitted for hematolymphoid malignancies at our institute over a 3.5-year period (March 13, 2020, to September 12, 2023). Blood grouping, initially performed using the column agglutination test, was repeated using the conventional tube method. Further confirmation of the blood group was performed using saliva tests and adsorption-elution tests as indicated. Detailed patient histories were collected from hospital records and analyzed. **Results:** A total of seven patients presented with either loss or decreased expression of blood group antigens. The most common diagnosis was acute myeloid leukemia (AML) with FLT3 mutation, and the most frequently affected antigen was A. **Conclusion:** Hematolymphoid malignancies are associated with loss of blood group antigens, leading to blood group discrepancies. Blood transfusion is a crucial component of supportive care for these patients. Therefore, proper workup of blood group discrepancy cases should be conducted and documented to prevent delays in blood transfusion.

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

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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

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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 a 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 detail 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 (71%) similar to other case reports [11, 13]. We also had one case each of CML and T-NHL. Loss of blood group antigens in CML was also reported by Chenna D et al

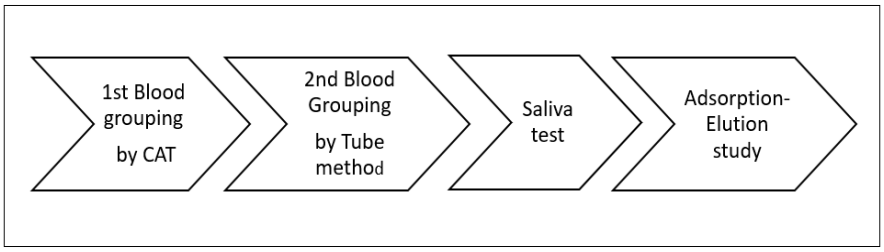

Figure 1. Flowchart Showing Test Sequence for Solving ABO Discrepancy

Table 1. Blood Group Detection by Various Methods

	Forward Group			Reverse Group			Saliva test	Adsorption-Elution study
	Anti A	Anti B	Anti D	A Cells	B Cells	O Cells		
Case 1	Neg	Neg	4+	Neg	4+	Neg	A, H	Not done
Case 2	Neg	Neg	Neg	Neg	4+	Neg	Not done	A antigen present
Case 3	Neg	Neg	4+	Neg	3+	Neg	A, H	Not done
Case 4	Neg	Neg	4+	4+	Neg	Neg	B, H	Not done
Case 5	Weak positive	Neg	Neg	Neg	4+	Neg	None	A antigen present.
Case 6	Neg	Neg	4+	Neg	3+	Neg	None	Not done
Case 7	Neg	Neg	4+	Neg	3+	Neg	A, H	Inconclusive

Table 2. Patient Characteristics and Follow up

	Age	Gender	Diagnosis	Molecular Study	Drug	Forward Group		Appearance of original group
						Before	After	
Case1	28yr	Male	AML	FLT3 mutation	Cytarabine	A +ve	O +ve	60 days
Case 2	8 yr	Male	AML	FLT 3 Mutation	Cytarabine	A -ve	O -ve	37 days
Case 3	36yr	Male	AML	Normal cytogenetics	Chemotherapy not started	A +ve	O +ve	30 days
Case 4	68yr	Female	AML	CEBPA gene	Decitabine	B +ve	O +ve	45 days
Case 5	32yr	Male	AML	FLT3 mutation	Cytarabine	A +ve	Weak expression of Antigen A	42 days
Case 6	56yr	Female	T-NHL Grade IV	CD20, CD3>>CD 20	CVP therapy*	A +ve	O +ve	32 days
Case 7	34yr	Malea	CML	t (9/22)	Dasatinib	A +ve	O +ve	Lost to follow up

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

[11] but no literature could be found related to T-NHL. In one study by Xiros N et al, there was a change in the blood group of a myelodysplastic syndrome patient following blastic transformation to AML [10]. Among the AML patients, most common mutation seen was FLT3 and during induction phase most common drug used was cytarabine. Prakash S et al also reported a similar case of AML on induction therapy with cytarabine but the mutation was in CEBPA genes [9]. Saliva test done to confirm the blood group showed 66.6% as secretors which was very less compared to other Indian studies [14, 15]. It might be due to small sample size of the study or due to disease itself. Historical blood group antigens started appearing between 30 to 60 days after first cycle of induction chemotherapy and complete reversal of blood group could be seen in three cases. During this transition period, initially we observed mixed field reactions in CAT followed by complete reversal of blood group to the original one similar to a case reported by Prakash S et al [9]. In our study, majority of the patients were on chemotherapy (85.7%) and in one patient the chemotherapy was not started. This may be due to loss of antigen expression during the course of disease progression or during chemotherapy and it reappeared during remission period. Multiple causes like inhibitory factor related to antigen-antibody binding or deficiency in transferase synthesis activity or an abnormal distribution or density of antigen sites in the RBC membrane have been linked to decrease in antigen expression [16]. There is paucity of data and research materials related to blood group discrepancy in cancer patients. We could not establish the exact cause of the discrepancy at the molecular level. In this case series, we could however highlight that the loss of blood group antigens was most common in AML patients and blood group A being the most commonly affected group. Hence, we need further molecular and genetic studies to establish the basis for such hypothesis and its implication in disease progression and prognosis.

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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