Alteration of ABH Blood Group Antigens in a Patient with Acute Leukaemia

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ABSTRACT

The loss or weakening of an individual's blood group due to disease is a rare phenomenon, which occurs more with myeloid malignancies. We report here the loss of the A antigen in an 18 year old boy treated for acute lymphoblastic leukaemia with a combination of Cyclophosphomide, Oncovin, Cytosine Arabinoside and predisolone. At first hospital admission he was typed as AB RhD positive but four months later he was typed as B RhD positive.

Introduction

The ABH antigens responsible for the ABO blood group system are complex carbohydrate structures found on glycoproteins and glycolipids and are present on the surface of erythrocytes, endothelial cells, and on most epithelial cells. Alleles of the *ABO* gene code for glycosyltransferases that act on the precursor H antigen resulting in an individual's blood group[1]. Antibodies to these antigens are naturally occurring and they play an important role in transfusion and transplantation medicine. These ABO-specific antibodies were first described by Landsteiner and later studied extensively by other groups [2]. The determination of a patient's ABO antigens (blood group) prior to blood and organ transplantation is a vital part of the daily routine practise in blood bank laboratories. Ignoring the ABO-blood group match between donor and recipient may lead to life-threatening complications, such as haemolytic transfusion reactions and graft rejection in organ transplantation. Since an individual's blood group is inherited, it is expected to last a life time. However, there are disease conditions that may result in the alteration of a patient's blood group. We report here a case in which a patient lost an A antigen in the course of his treatment for Acute Lymphoblastic leukaemia (ALL).

Case Summary

He was an 18 year old year-2 technical college student referred to our unit on account of refractory anaemia and a left sided abdominal swelling of one month duration. These were associated with generalised body weakness,

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gum bleeds and an intermittent high grade fever. Examination at presentation revealed an acutely ill looking young man, who was severely pale, with generalised lymphadenopathy, involving the cervical, axillary and inguinal group of lymph nodes and hepato -splenomegaly of 4cm and 13cm respectively. Haematocrit was 10% and his blood group was found to be AB RhD positive, and was subsequently transfused with four units of blood. Peripheral blood film and bone marrow aspiration cytology were in keeping with ALL L1 FAB classification.

He was commenced on preconditioning therapy with Vincristine and Prednisolone (V+P) and later had Cyclophosphomide, Cytosine Arabinoside, Oncovin and Predisolone (COAP). During therapy, he had neutropenic fever which was treated with antibiotics, and a total of 4 units of fresh whole blood, all of which were AB RhD positive. He was lost to follow up until he represented four months later with a high grade intermittent fever, easy fatigability and a productive cough of 2 weeks duration. He was found to be severely pale with generalised lymphadenopathy and splenomegaly and a pneumonic consolidation in the Chest. His haematocrit was 12% necessitating further blood transfusion; he was then found to be B RhD positive which was confirmed by reverse grouping, and was transfused with four units of same. The patient however died of central nervous system CNS complications thereafter.

Discussion

The first case of alteration of ABO antigen in hematologic malignancy was reported by van Loghem *et al*, who described very weak A antigen expression on the red cells of a patient with acute myeloid leukemia (AML), who had previously shown normal A antigen expression[3]. Since then, loss or diminished expression of red blood cell antigens have been reported in both haematological and solid malignancies and in other types of carcinomas [4-6]. This rare phenomenon which is seen more in haematologic malignancy may appear not to have clinical significance but the loss of expression of blood group antigen have been associated with bad prognosis in patients with non small cell lung cancer[6]. It may also have significant clinical implications in the management of the patient as well as the outcome of therapy[7].

There are two identified mechanisms which may lead to the loss or weakening of these antigens, a direct inactivation of the A and/or B transferase[8] or the inactivation of the H transferase which will in turn result in a decrease in the production of A and/or B substances[8,9]. Both mechanisms have been reported in haematologic malignancies especially in myeloid leukaemias. The mechanism in solid tumor is different from that of haematologic malignancies in that the number of A, B, and H antigens are not altered, so it is believed that the tumors secret large amounts of soluble A and/or B substances which neutralize the typing reagents resulting in an apparent loss of A and B antigens[10]. The genes for the A and B transferases are located on chromosome 9 which is the Philadelphia chromosome, so it has been postulated that in patients with CML who lose their ABH antigens, there is a possible disruption of the gene at the site of the reciprocal translocation, thus preventing the expression of the transferase[7,11]. Though the loss of red cell antigens has been reported in many blood group systems it is more common with the ABO and then the Rhesus blood group systems, this is because these are the two systems mostly typed in transfusion medicine[7].

It is not uncommon for patients to revert back to their original blood group when in remission, though this was not observed in this patient since he succumbed to the illness before going into remission. A peculiarity observed in this patient is the fact that he had a lymphoid malignancy since the loss of red cell antigen occurs more frequently in myeloid malignancies[12]. Loss of ABH antigen in myeloid malignancies is only seen on red cells

as most haemopoetic cells and precursors do not express ABH antigens, it is also believed that the loss of ABO expression in the population of red cells derived from a malignant stem cell is an indication of genetic changes that have occurred in the malignant cells. This may explain why the loss of red cell antigens is commoner in myeloid malignancies since genetic aberrations are not as common in lymphoid malignancies. These changes have also been attributed to the use of chemotherapy in these malignancies[13].

This case highlights the possibility of a loss of any of the red cell antigens in disease conditions, though a rare occurrence, but should not be seen as incompetence on the part of the technical staff. Albeit, all cases should be well investigated to rule out both clerical and laboratory errors.

References

1. Yamamoto F, Clausen H, White T, Marken J and Hakomori S. Molecular genetic basis of the histo-blood group ABO system. Nature. 1990 May 17; 345(6272): 229-233.
2. Stussi G, Huggel K, Lutz HU, Schanz U, Rieben R and Seebach JD. Isotype-specific detection of ABO blood group antibodies using a novel flow cytometric method. Br J Haematol. 2005 Sep;130(6): 954-963.
3. Van Loghem JJ, Jr., Dorfmeier H and Van Der Hart M. Two A antigens with abnormal serologic properties. Vox Sang. 1957 Jan;2(1): 16-24.
4. Limas C, Lange P, Fraley EE and Vessella RL. A, B, H antigens in transitional cell tumors of the urinary bladder: correlation with the clinical course. Cancer. 1979 Dec; 44(6): 2099-2107
5. Winters JL and Howard DS. Red blood cell antigen changes in malignancy: case report and review. Immunohematology. 2001; 17(1): 1-9.
6. Leon-Atance P, Moreno-Mata N, Gonzalez-Aragonese F, Canizares-Carretero MA, Poblet-Martinez E, Genoves-Crespo.M *et al.* Prognostic influence of loss of blood group A antigen expression in pathologic stage 1 non-small-cell lung cancer. Arch Bronconeumol 2012; 48(2): 49-54
7. Winters JL and Howard DS. Red blood cell antigen changes inmalignancy: case report and review. Immunohematology 2001; 17(1): 1-9
8. Van Loghem JJ, Jr., Dorfmeier H and Van Der Hart M. Two A antigens with abnormal serologic properties. Vox Sang. 1957 Jan; 2(1): 16-24.
9. Dobrovic A, O'Keefe D, Sage RE and Batchelder E. Imprinting and loss of ABO antigens in leukemia. Blood. 1993 Sep 1; 82(5): 1684-1685.
10. Treacy M, Geiger J and Goss MF. Substances in serum causing interference with blood group determination. Transfusion 1967; 7: 443-446
11. Reid MC and Bird GW. Associations between human red cell blood group antigens and disease. Transfus Med Rev 1990; 4: 47-55
12. Bianco T, Farmer BJ, Sage RE and Dobrovic A. Loss of red cell A,B, and H antigens in myeloid malignancies. Blood 2001; 97: 3633-3639
13. Starling KA and Fernbach DJ. Changes in strength of A antigens in children with acute leukaemia. Transfusion 1970; 10: 3-5