CONCISE REPORT

Plasma Blood Group Glycosyltransferase Activities After Bone Marrow Transplantation

By A. Yoshida, G. M. Schmidt, K. G. Blume, and E. Beutler

Human blood groups (ABO) are known to be determined by the terminal glycosyl residues attached to common carbohydrate chains on the red cell surface. N-acetylgalactosaminyltransferase (A-enzyme) in blood group A persons and galactosyltransferase (B-enzyme) in blood group B persons are responsible for producing A and B substances on the red cell surface, with both enzymes absent in blood group O persons. The plasma transferase (A – and B – ) activity was assayed after the complete replacement of the bone marrow of patients with acute leukemia or aplastic anemia by transplantation bone marrow from donors with ABO blood group differing from the recipient. The patient’s blood type completely changed from the recipient’s type to the donor’s type. However, the A- and B-enzyme activities of the patients changed only slightly after bone marrow transplantation. The results indicate that most of the A- and B-enzymes in the circulatory plasma is not derived from the bone marrow, lymphoid, or macrophage tissue. Other tissues must be the primary source of the enzymes in plasma.

HUMAN ABO blood groups are known to be determined by the terminal glycosyl residues attached to common carbohydrate chains located on the red cell surface. The A substance is produced from a common substrate, the H substance, by the action of an N-acetylgalactosaminyltransferase (A-enzyme), and the B substance by the activity of galactosyltransferase (B-enzyme). The A-enzyme is found in the plasma of blood group A subjects, B-enzyme in those who have blood group B, and neither enzyme in group O individuals. The origin of the plasma enzyme is not clear, since not only red cell precursors but also other tissues contain the A- and B-enzymes.

The complete replacement of the bone marrow, lymphoid, and monocyte-macrophage systems of patients with acute leukemia or aplastic anemia by transplantation bone marrow from donors with ABO blood groups differing from the recipient has provided us with an opportunity to determine the origin of the A- and B-enzymes.

MATERIALS AND METHODS

The transferase activities were assayed by measuring the incorporation of radioactive sugar from nucleotide sugar (i.e., UDP-N-acetylgalactosamine for A-enzyme assay and UDP-galactose for B-enzyme assay) into fucosyllactose, as previously reported. Alternatively, O red cells were incubated with the enzyme and the nucleotide sugar, and the newly produced blood group substance (A or B) was semiquantitatively assayed using anti-A or anti-B agglutinin with serial dilutions. In contrast to usual human plasma, the patients’ plasma examined, particularly from patients UPN-35 and UPN-38, exhibited active hydrolysis of the nucleotide sugars, presumably due to an elevated activity of nucleotide pyrophosphatase and/or plasma phosphatase in the subjects’ plasma. This high background hydrolysis interfered with the first assay method. Therefore, the second method was used for the assay of blood group transferase activity in UPN-35 and UPN-38. UDP-N-acetylgalactosamine was synthesized as previously described. UDP-galactose was purchased from Sigma Chemical, Co. St. Louis, Mo. UDP-N-acetylgalactosamine (galactosamine-1-H3) was purchased from New England Nuclear, and UDP-galactose (galactose-6-H3) was purchased from Amersham Corp. Fucosyllactose was prepared from human milk, as previously described, and further purified by gel filtration with Bio Gel P-2. Agglutinin (anti-A and anti-B) was purchased from Ortho Diagnostics.

The patients’ plasmas were stored at ~65°C until the transferase activity was measured. No significant change of enzyme activity was observed in control plasma during storage.

Patients

Three patients (UPN 18, 29, 38) underwent bone marrow transplantation as a treatment for acute leukemia, and one patient (UPN 35) was suffering from severe aplastic anemia. The three patients with leukemia received high doses of chemotherapy (cyclophosphamide and cytosine arabinoside) and total body irradiation prior to bone marrow transplantation, whereas the patient with aplastic anemia was conditioned for marrow grafting using a high-dose cyclophosphamide regimen. Since three patients (UPN 29, 35, 38) had a major blood group mismatch with their respective donors, total plasma exchange was performed prior to bone marrow infusion. All four patients engrafted the marrow as confirmed by genetic marker analysis, including change in sex chromosomes and bone marrow metaphases. All four patients are alive and hematologically normal without any further therapy 4, 7, 11, and 19 mo after the transplant procedure.

RESULTS AND DISCUSSION

The results of our studies are summarized in Table 1 and Fig. 1. After bone marrow transplantation, the patient’s blood type gradually changed from the original type to the donor’s type, confirming previous observations. The conversion was completed after about 100–120 days. All four patients continue to manifest the blood groups of their bone marrow donors.

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Address reprint requests to A. Yoshida, Ph.D., City of Hope National Medical Center, Duarte, Calif. 91010.
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the activity was expressed as percent of sugar transferred into fucosyllactose under the assay condition.

known to differ widely among individuals with phenotype from 2.8 to 16.8 (mean value 6.44). and B-enzyme activity in 7 plasma samples with phenotype B ranged from 5.0 to 
ranged

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age of mean value of control A, plasma. Hatching is the range of

with blood type 0. The enzyme activity was expressed as percent-

ferase (A-enzyme) activity before and after bone marrow trans-

ferase associated with

Enzyme activity of control A, plasma.

Fig. 1 Blood type and plasma N-acetylgalactosaminyltrans-
ferase (A-enzyme) activity before and after bone marrow transplanta-

(A) Subject UPN 35, originally blood type O, received bone marrow from a subject with blood type A,; (B) subject UPN 19, originally blood type A, received bone marrow from a subject with blood type O. The enzyme activity was expressed as percentage of mean value of control A, plasma. Hatching is the range of enzyme activity of control A, plasma.

In contrast to the erythrocyte antigens, the A- and B-enzyme activities of the patient’s plasma changed only slightly after bone marrow transplantation. UPN 29 and UPN 35 were originally blood type O and received bone marrow from a subject with blood type A,. Weak A-enzyme activity appeared temporarily (in UPN 29) or continuously (in UPN 35) after the treatment. High A-enzyme was continuously observed in plasma from the subject UPN 19, who was originally blood type A, and received bone marrow from a subject with blood type O, as a result the subject blood type completely converted from A, to O (Fig. 1). No measurable B-enzyme activity was detected in plasma from the subject UPN 38, who was originally blood type A, and received B bone marrow, although the subject’s blood type completely converted from A, to B after the treatment.

Transplantation of the hematopoietic tissues of patients with donors who have different ABO blood groups has given us an opportunity to study the origin of the ABO blood-group-determining glycosyltransferases in the plasma. Although, as expected, the red cells produced by the transplanted marrow were exclusively the donor type, very little of the donor sugar transferase appeared in the plasma. Our findings are consistent with the observations made by Schachter et al., who measured the A-enzyme activity in the plasma of a blood chimeral whose A, gene activity appeared to be restricted to bone marrow cells acquired in utero from the subject’s A, twin. In these studies it was estimated that only about one-fifth of A-enzyme in this serum was derived from the bone marrow. Our studies provide additional evidence that most of the circulating plasma activity is not derived from the bone marrow. Moreover, it apparently does not come from the lymphoid or macrophage-monocyte system, since these are also replaced in marrow transplantation. Other tissues, then, must be the primary source of the serum enzymes characteristic of the ABO blood group system.

REFERENCES


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