Suppressed Expression of Blood Group B Antigen and Blood Group Galactosyltransferase in a Preleukemic Subject

By Akira Yoshida, Takashi Kumazaki, Vibha Davé, Joyce Blank, and Walter H. Dzik

The B antigen activity was severely diminished in a patient’s RBCs at the preleukemic stage prior to chemotherapy or radiotherapy. The amount of H sites of the patient’s RBC membranes was found to be comparable to that of O RBC membranes. The activity of α(1 → 2) fucosyltransferase (H enzyme) was not severely decreased in the patient’s plasma and bone marrow. However, the activity of α(1 → 3) galactosyltransferase (B enzyme), which converts H substance to B substance, was drastically reduced in the patient’s bone marrow. Thus, the diminished B antigen in the patient’s RBCs was caused mainly by the blockage of conversion of the H substance to B substance. It is suggested that the viral oncogene linked to the ABO locus at q34 of chromosome No. 9 would occasionally suppress the expression of blood group A and B enzymes and A and B antigens.

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DEPRESSED EXPRESSION OF BLOOD GROUP B IN LEUKEMIA

30 minutes’ incubation at 25 °C). The patient’s RBCs exhibited high H activity (agglutinability with Ulex europaeus anti-H lectin), which was comparable or slightly lower than control O RBCs.

Quantification of H sites in RBC membranes. RBC membranes, prepared by the method of Dodge, were incubated with UDP-[3H]-GalNAc and the highly purified A1 enzyme, and the amount of GalNAc incorporated into the membranes at saturation were determined, as previously described.

RESULTS

The B antigen activity of the patient’s RBCs was severely diminished and the H antigen activity was conversely elevated. The number of H antigen sites of the patient’s RBCs was 0.74 × 10⁶ per cell. Since the number of H sites of control O RBCs ranged from 0.9 to 1.2 × 10⁶ per cell, the amount of H sites was not substantially decreased in the patient’s RBC membranes.

The H enzyme activity of the patient’s plasma, bone marrow fluid, and bone marrow blood cells was somewhat lower than the average of control samples (Table 1). However, the activity of another leukemic subject with no blood group antigen abnormality was also lower than the average.

Substantial decrease in the B enzyme activity was noticeable in the patient’s plasma and bone marrow fluid (Table 1). The B enzyme activity of the patient’s bone marrow blood cells (membrane bound enzyme) was too low to be detected. The H enzyme activity of the patient’s bone marrow blood cells was 0.006 U/mL, and that of control samples ranged from 0.010 to 0.022 U/mL.

DISCUSSION

Suppressed blood group ABH activity in RBCs and other tissues could result from a decreased activity of glycosyltransferases involved in the synthesis of the blood group substances. Watkins et al reported that plasma H enzyme activity, measured using phenyl-β-D-Gal as an acceptor, was substantially lower in leukemic patients without chemotherapy than in control subjects. By contrast, Khilamani et al reported that plasma α(1→2) Fuc-transferase (corresponding to H enzyme) activity, measured using desialofetuin as an acceptor, and α(1→3) Fuc-transferase, measured using desialodelagactofetuin as an acceptor, were elevated in leukemia and colon carcinomas and returned to the normal level in remission. No rational explanation has been presented for the totally opposite observations, i.e., a diminution of the H enzyme found by one laboratory and an elevation of the H enzyme observed by other laboratories. In a leukemic patient with diminished RBC A antigen, morphological changes were observed, but plasma A enzyme activity was found to be unimpaired. An acquired diminution in the expression of A, H, M, i, and I antigens was observed in a patient with lymphocytic lymphoma. No significant decrease of H and A enzyme activities was detected in the patient’s serum, but marked augmentation of the A and i antigens was observed in the patient’s RBCs by neuraminidase treatment.

Hakomori et al observed a depletion of blood group A and B activities in cancerous tissues, and reported that the activities of A and B enzymes in gastrointestinal epithelium in cancerous tissues were only five to one sixth of those in noncancerous tissues of the same individuals.

Only about 25% of plasma A and B enzymes originate from hematopoietic tissues. In contrast, plasma H enzyme was assumed to be solely derived from bone marrow. This assumption is questionable, since there is no evidence that the expression of the H gene is restricted in hematopoietic tissues. H enzyme activity in bone marrow fluid of the patient (nonsecretor) was found to be equal or often lower than in plasma (Table 1), suggesting that part of the plasma H enzyme was derived from tissues other than bone marrow. In order to define a change of blood group transferases in leukemia and other carcinomas, the enzyme activities of bone marrow and affected tissues should be examined, as was done by Steller and Hakomori.

In the present preleukemic patient with diminished RBC B antigen activity, the amount of H sites in his RBC membranes was near normal, and activity of H enzyme in his plasma and bone marrow was not markedly decreased. On the other hand, the activity of B enzyme was found to be severely diminished in the patient’s bone marrow fluid and bone marrow blood cells. Therefore, the major cause of the diminished B antigen activity in the present case is likely due to the blockage of conversion of the H substance to the B substance, not due to the decrease in synthesis of the H substance.

Based on the observation of independent expression of A- and B-like antigen activities in gastrointestinal carcinoma of AB individuals, Denk et al suggested the possibility of deletion or repression of either A or B gene in the ABO locus in given cancerous tissues. Salmon et al observed the activity of adenylate kinase (AK) in RBCs with diminished A antigen activity, and suggested linkage between the ABO and AK loci.

Recent studies indicated that the human viral oncogene c-abl is located at q34 position of chromosome No. 9. Chromosomal abnormalities, i.e., translocation involving chromosomes No. 9 and 22, were observed in leukemia in a high frequency. The blood group ABO locus is in q34 of chromosome No. 9. It is conceivable that the viral oncogene may occasionally disturb the expression of ABO locus resulting in depletion of blood group A and B activities in RBCs of leukemic patients.

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*Evidence has been presented that the H gene and the Se gene are both structural genes encoding two types of α(1→2) fucosyltransferase in different tissues. Subjects with the Bombay phenotype, who are H-negative in both erythrocytes and secretory tissues, are hh and sse, and subjects with para-Bombay phenotype, who are H-negative in erythrocytes but positive in secretory tissues, are hh and SeSe or Sese. Therefore, the H enzyme should be negative in both Bombay and para-Bombay. The observed absence of the H enzyme in plasma of para-Bombay subjects does not imply that the H enzyme is derived solely from hematopoietic tissues.
Table 1. Blood Groups A, B, and H Enzyme Activities

<table>
<thead>
<tr>
<th>Subject</th>
<th>Blood Type</th>
<th>A Enzyme</th>
<th>B Enzyme</th>
<th>H Enzyme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient (Preleukemia)</td>
<td>B</td>
<td>0.088</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>1 (Leukemia)</td>
<td>B</td>
<td>0.07</td>
<td>0.02</td>
<td>0.018</td>
</tr>
<tr>
<td>2 (idiopathic thrombocytopoetic purpura)</td>
<td>B</td>
<td>0.19</td>
<td>0.16</td>
<td>0.022</td>
</tr>
<tr>
<td>3 (Sideroblastic anemia)</td>
<td>A,B</td>
<td>0.34</td>
<td>0.23</td>
<td>0.03</td>
</tr>
<tr>
<td>4 (bone marrow donor)</td>
<td>A,</td>
<td>0.72</td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>5 (bone marrow donor)</td>
<td>A,</td>
<td>(0.25)</td>
<td></td>
<td>0.024</td>
</tr>
<tr>
<td>6 (bone marrow donor)</td>
<td>A,</td>
<td>(0.13)</td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>Control A,</td>
<td>A,</td>
<td>0.72</td>
<td></td>
<td>0.036</td>
</tr>
<tr>
<td>Control A,</td>
<td>A,</td>
<td>0.44</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>Control B</td>
<td>B</td>
<td>0.26</td>
<td></td>
<td>0.028</td>
</tr>
<tr>
<td>Control B</td>
<td>B</td>
<td>0.22</td>
<td></td>
<td>0.025</td>
</tr>
</tbody>
</table>

The patient’s samples were taken and examined on two occasions. A enzyme activity was assayed at its optimum pH at 6.0 in the case of A, and at its optimum pH at 8.0. B enzyme activity was assayed at pH 7.0. The values are expressed in enzyme units per milliliter of plasma or bone marrow fluid. Subjects No. 4, 5, and 6 are healthy bone marrow donors, and all control subjects are healthy blood donors.

REFERENCES

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