INCREASE IN PLASMA THROMBOMODULIN IN LUPUS ERYTHEMATOSUS WITH ANTIPHOSPHOLIPID ANTIBODIES

To the Editor:

Thrombomodulin (TM), a high-affinity thrombin receptor present on endothelial cell membrane, plays an important role as a natural anticoagulant. It acts as a cofactor of thrombin-catalyzed activation of protein C, and it also inhibits procoagulant functions of thrombin. Soluble TM exists in circulating plasma as heterogeneous fragments. Plasma TM has been found increased in renal dysfunction, disseminated intravascular coagulation, pulmonary thromboembolism, adult respiratory distress syndrome, and acute hepatic failure. It is regarded as a molecular marker reflecting injury of endothelial cells. A close relationship between TM and diabetic microangiopathy has recently been shown. Information concerning TM plasma levels in systemic lupus erythematosus (SLE) is not currently available.

Using a two-site enzyme-linked immunosorbent assay (ELISA) for soluble forms of TM ("Asserachrom Thrombomodulin," Diagnostica Stago, Asnières, France), prepared with two monoclonal antihuman TM antibodies, we investigated plasma TM levels in 40 normal adult blood donors and in 45 SLE patients. The patients were selected to have a normal creatinine level of less than 100 μmol/L because renal impairment per se is known to be associated with an increase in TM. Antiphospholipid antibodies (APL) were assessed by an ELISA according to Harris. We studied IgG and IgM antibodies directed against anionic phospholipids (mixture of cardiolipin/phosphatidylserine/phosphatidylinositol/phosphatidylglycerol/phosphatidic acid) and against phosphatidylethanolamine. The SLE patients were divided into two groups according to the absence (group 1) or presence (group 2) of APL and/or lupus anticoagulant (LA). Twenty SLE patients without APL or LA were included in the group 1. Twenty-five patients were included in group 2: 15 had both APL and LA, 9 had APL without LA, and 1 had an isolated LA. The number of patients suffering from thrombosis and/or recurrent fetal loss is given in Table 1. In agreement with previous study on systemic lupus erythematosus, occurrence of thrombosis and recurrent fetal loss was significantly higher in group 2 (13 of 25) than in group 1 (4 of 20); χ2 = 4.84; P < .03. Mean plasma TM level in normal subjects was 41.2 ± 22.5 ng/mL (mean ± SD). Results of TM level in the two groups of SLE patients and in controls are summarized in Fig 1. TM levels were similar in SLE without APL and/or LA, and in controls. It is of great interest that, among SLE patients, the amount of TM was significantly increased in patients with APL and/or LA, in contrast to those without these antibodies (80.2 ± 50 ng/mL vs 42.5 ± 22.5 ng/mL, P = .0033, t-test).

These results suggest that circulating APL and/or LA can induce an endothelial injury leading to an increased plasma TM level. Because the mechanisms explaining recurrent thrombosis and fetal loss in SLE with APL and/or LA remain a matter of controversy, these findings may indicate a pathogenetic role of antiphospholipid antibodies on vascular endothelium in vivo.

Table 1. Occurrence of Thrombosis and Recurrent Fetal Loss in the Studied Population

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombosis</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Recurrent Fetal Loss</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Both</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>13</td>
</tr>
</tbody>
</table>
ACKNOWLEDGMENT

Supported by INSERM and Grant 86.308.5E from CNAM. M.K. is a fellow from Fondation de la Recherche Médicale.

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REFERENCES


Increase in plasma thrombomodulin in lupus erythematosus with antiphospholipid antibodies [letter]

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