Influence of Liver Dysfunction on Volume of Putaminal Hemorrhage

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We studied the relations of age, sex, hypertension, alcohol consumption, liver dysfunction, and thrombocyte count to the volume of the hematoma in 141 patients with spontaneous putaminal hemorrhage. Hematomas were significantly larger in men, regular alcohol consumers, those with liver dysfunction, and those with low platelet counts. Our findings reflect the fact that almost all of the alcohol consumers were men, most of them had liver disorders, and the volume of hematoma in such patients was relatively large. (Stroke 1988; 19:987-990)

Several authors have pointed out the correlation between spontaneous intracerebral hemorrhage and liver dysfunction.1-3 We have also reported4 that among men with cerebral hemorrhage, many had abnormal liver functions due to excessive alcohol use. As a result, the men had significantly lower platelet counts and serum fibrinogen concentrations, factors that may have contributed to a condition in which hemorrhage is likely to occur.

These considerations led us to hypothesize that patients with liver disorders, specifically those with deficits in the mechanisms of hemostasis, may have hematomas of unusually large size due to the fact that, once bleeding begins, hemostasis does not easily occur. To test this hypothesis, we studied 141 patients with putaminal hemorrhage who came to our clinic over 3 years. We studied these patients with regard to the relations of age, sex, presence of hypertension, alcohol consumption, liver dysfunction, and thrombocytopenia to the volume of the putaminal hemorrhage. Our predictions were confirmed.

Subjects and Methods

Between January 1984 and December 1986, we examined 189 patients with spontaneous putaminal hemorrhage in whom diagnoses of vascular anomaly, such as cerebral aneurysm, arteriovenous malformation, or moyamoya disease, were excluded on the basis of cerebral angiography. There were 141 patients (98 men and 43 women) admitted ≤24 hours after the onset of symptoms and on whom computed tomography (CT scans), platelet counts, and examinations of liver functions (glutamic oxaloacetic transaminase [GOT], glutamic pyruvic transaminase [GPT], gamma-glutamyl transpeptidase [γ-GTP], and γ-globulin fractions) were carried out. The men ranged in age from 30 to 84 (mean ± SD 53.5 ± 11.5) years and the women from 41 to 77 (mean ± SD 59.2 ± 8.0) years.

A history of hypertension was found in 73 men (74%) and 35 women (81%). Histories of liver or gall bladder disorders were found in seven men (three had had acute viral hepatitis, two chronic hepatitis, one liver cirrhosis, and one Weil’s disease) and two women (with cholelithiasis). There were, in addition, three cases of renal failure (one of whom had severe anemia and a prolonged bleeding time), one who had a putaminal hemorrhage while undergoing urokinase therapy for arteriosclerosis obliterans of the femoral artery, and one who had a putaminal hemorrhage while undergoing warfarin therapy following heart surgery.

Alcohol consumption was ≥50 g/day in 58 men (59%) and <50 g/day in 21 (21%); 19 men were nondrinkers (19%). Among the women, however, only one drank ≥50 g/day (2%); seven drank <50 g/day (16%), and the majority (35 women, 81%) were nondrinkers.

Statistical studies were carried out of the correlation between the above factors and the volume of the hematomas calculated from the findings of CT scans. In calculating the volume, hematomas were assumed to be ellipsoid. Volume was obtained from the maximum width (X), length (Y), and height (Z) of the high-density area and was calculated as $\pi/6 \cdot XYZ = \frac{1}{2} XYZ$. The hematoma had penetrated the lateral ventricle in 25 patients, but in all 25 the bleeding there was minor compared with the puta-
TABLE 1. Volume of Hematoma in Relation to Age, Sex, Hypertension, Alcohol Consumption, Liver Disorder, and Thrombocytopenia in 141 Patients With Putaminal Hemorrhage

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of cases</th>
<th>Hematoma volume (ml) Mean±SD</th>
<th>Patients with volume of &gt;60 ml No. % p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 30-59 yr</td>
<td>94</td>
<td>40.76±32.50 NS</td>
<td>19  20.2 NS</td>
</tr>
<tr>
<td>60-84 yr</td>
<td>47</td>
<td>39.89±35.49</td>
<td>8   17.0 NS</td>
</tr>
<tr>
<td>Sex Male</td>
<td>98</td>
<td>44.33±35.20 &lt;0.05</td>
<td>23  23.5 &lt;0.05</td>
</tr>
<tr>
<td>Female</td>
<td>43</td>
<td>31.67±27.28</td>
<td>4   9.3</td>
</tr>
<tr>
<td>Hypertension Yes</td>
<td>108</td>
<td>40.91±34.99 NS</td>
<td>22  20.4 NS</td>
</tr>
<tr>
<td>No, unclear</td>
<td>33</td>
<td>39.03±28.02</td>
<td>5   15.2</td>
</tr>
<tr>
<td>Alcohol consumption ≥50 g/day</td>
<td>59</td>
<td>44.47±34.73 NS</td>
<td>16  27.1 &lt;0.05</td>
</tr>
<tr>
<td>&lt;50 g/day</td>
<td>82</td>
<td>37.59±32.32</td>
<td>11  13.4</td>
</tr>
<tr>
<td>Liver disorder Yes</td>
<td>61</td>
<td>48.41±37.49 &lt;0.02</td>
<td>18  29.5 &lt;0.01</td>
</tr>
<tr>
<td>No</td>
<td>80</td>
<td>34.41±28.70</td>
<td>9   11.3</td>
</tr>
<tr>
<td>Thrombocytopenia Yes</td>
<td>17</td>
<td>64.82±41.44 &lt;0.01</td>
<td>8   47.1 &lt;0.01</td>
</tr>
<tr>
<td>No</td>
<td>124</td>
<td>37.13±30.88</td>
<td>19  15.3</td>
</tr>
</tbody>
</table>

Results

Two methods, mean volume and percentage with volumes of >60 ml, were used for evaluating the volume of the hematomas in relation to the other factors. Significant correlations between mean hematoma volume and sex, liver dysfunction (γ-GTP≥41 IU, GOT≥41 IU, GPT≥36 IU, or γ-globulin≥20%), and thrombocytopenia (<13 x 10⁵/mm³) were found. The percentage of hematomas with volumes of >60 ml was significantly larger in men, consumers of ≥50 g alcohol/day, patients with liver dysfunction, and patients with thrombocytopenia (Table 1). Significant correlation was also found between alcohol consumption and liver dysfunction (p<0.001, Table 2).

The relation between hematoma volume, liver dysfunction, and sex is illustrated in Figure 1. Although 57 of the 98 men (58%) had liver dysfunction, only four of the 43 women (9%) did. Among the 23 men with hematoma volumes of >60 ml, 18 (78%) had liver dysfunction, whereas 39 (52%) of the 75 men with hematoma volumes of ≤60 ml had liver dysfunction (p<0.05). Liver dysfunction was studied separately for γ-GTP, GOT and/or GPT, and γ-globulin fractions (Table 3). Those patients with abnormal γ-GTP, GOT and/or GPT values had significantly larger hematomas, with significance ranging from p<0.01 to p<0.02. A similar trend was seen for γ-globulin, but this relation was not significant. Interestingly, a significantly larger hematoma was found when liver dysfunctions were associated with hypertension (p<0.01). That is, among the 52 patients with both liver dysfunction and hypertension, the mean±SD hematoma volume was 50.13±38.45 ml, whereas among the other 89 patients, the mean±SD volume was 34.82±28.82 ml.

The highest correlation was found between hematoma volume and thrombocytopenia. The mean±SD hematoma volume of the 17 patients with thrombocytopenia was 64.82±41.44 ml, and 12 of these 17 patients were thought to have had thrombocytopenia as a result of liver dysfunction.

A statistical study of bleeding tendencies was not possible because the examination of bleeding tendencies other than thrombocyte counts was incomplete in some patients. Among the 23 men with hematoma volumes of >60 ml, however, 11 had thrombocytopenia, prolonged bleeding times (>5 minutes), prolonged prothrombin times (>15 seconds), a low score on the thrombotest (<50%) and/or hypohemoglobinemia (<11.5 g/dl). Among these 11 men, there were 10 with liver dysfunction. In contrast, among the women, liver dysfunction was not found in any of the four with hematoma volumes of >60 ml. There was, however, one woman who had undergone cardiac surgery for valvular disease and who was still undergoing war-

TABLE 2. Alcohol Consumption and Liver Dysfunction in 141 Patients With Putaminal Hemorrhage

<table>
<thead>
<tr>
<th>Liver dysfunction</th>
<th>Alcohol consumption</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>≥50 g/day</td>
<td>&lt;50 g/day</td>
</tr>
<tr>
<td>Yes</td>
<td>39</td>
<td>10</td>
</tr>
<tr>
<td>No</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
<td>28</td>
</tr>
</tbody>
</table>

χ²=21.36, p<0.001.
*Three patients had a history of liver disease.
farin therapy. She had a prothrombin time of 17.7 seconds and a score of 11% on the thrombotest. There was one other woman with a platelet count of 8 x 10^4/mm^3 and a score of 35% on the thrombotest, again indicating a marked bleeding tendency. In summary, 13 of the 27 patients (48%) with hematoma volumes of >60 ml had abnormal values related to bleeding tendencies, and 10 of these 13 also had liver dysfunction. In contrast, of the 114 patients with hematoma volumes of ≤60 ml, only 12 (11%) showed abnormal values in coagulation parameters.

Discussion
Based on both epidemiologic and pathologic research, there remains no doubt that the major risk factor for spontaneous intracerebral hemorrhage is hypertension. It is also known that intracerebral hemorrhage is 1.4-2.0 times more common in men than women. If hypertension were the only cause of intracerebral hemorrhage, however, its incidence should theoretically be higher among women than men since the incidence of hypertension is almost the same among men and women since there are slightly more adult women than adult men. For this reason, the involvement of other factors must be considered to explain the notably higher incidence of intracerebral hemorrhage in men.

Thrombocytopenia has been documented in alcohol consumers. Recently, several authors have reported that habitual alcohol consumption is a risk factor for stroke. In several studies, however, alcohol consumption was considered important solely as a factor contributing to hypertension and was not discussed in relation to liver dysfunction. Studies of the relation between intracerebral hemorrhage and a bleeding tendency due to liver dysfunction have been reported by McCormick and Rosenfield and Cahill and Ducker. In addition, Boudouresques et al reported an autopsy study in which a significantly higher percentage of patients with intracerebral hemorrhage (16%) had liver cirrhosis compared with a control group. In a previous study, we reported that among patients with intracerebral hemorrhage there were a large number of men with liver disorders due to heavy alcohol consumption, a result of which was a marked decrease in platelet counts and serum fibrinogen concentrations. In our present study as well, we found that patients with liver dysfunction also had significantly larger hematomas. Liver dysfunction appears to be an important risk factor in intracerebral hemorrhage. Moreover, it is likely that, once intracerebral bleeding begins in such patients, the presence of thrombocytopenia, decreased concentrations of coagulation factors, and hyperfibrinolysis—even at a subclinical level—retards hemostasis and, as a result, leads to the formation of large hematomas.

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association in 53 pathological cases. Ann Neurol 1980; 8:204–205

KEY WORDS • alcohol drinking • cerebral hemorrhage • liver diseases • putamen
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