Multiple Simultaneous Intracerebral Hemorrhages

Clinical Features and Outcome

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Background: The simultaneous occurrence of intracerebral hemorrhages in different arterial territories is an uncommon clinical event. Its predisposing factors and pathophysiological mechanisms are not clearly defined.

Objective: To analyze the frequency, risk factors, clinical features, neuroimaging findings, and outcome of multiple simultaneous intracerebral hemorrhages (SIHs).

Patients and Methods: We studied all patients with acute stroke admitted to our hospital from July 18, 1997, through December 18, 1999. Multiple SIHs were defined as the presence of 2 or more intracerebral hemorrhages affecting different arterial territories with identical computed tomographic density profiles. Patients with a history of traumatic brain injury were excluded from this study. Diagnostic investigation included routine blood and urine tests, coagulation studies, a chest radiograph, electrocardiogram, 2-dimensional transthoracic echocardiography, and computed tomography of the head without contrast medium. Disability was assessed using the National Institutes of Health Stroke Scale and Modified Rankin Scale.

Results: Among 142 patients with hemorrhagic stroke, we found 4 (2.8%) with SIHs. All 4 patients had a history of uncontrolled arterial hypertension. We excluded other potential causes of multiple SIHs by using appropriate diagnostic tests. The most common clinical manifestations were headache and weakness. Localization of hematomas was supratentorial, except for one patient who had both infratentorial and supratentorial hemorrhages. The mean National Institutes of Health score on admission was 15 and the Modified Rankin Scale score was higher than 4 at 3 months.

Conclusions: In our study, all patients with multiple SIHs had arterial hypertension and a poor outcome. Additional analytic studies, including new imaging techniques, can help to elucidate the association between arterial hypertension and multiple SIHs, risk factors, and underlying mechanisms of this clinical condition.

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The simultaneous occurrence of intracerebral hemorrhages (ICHs) in different arterial territories is uncommon. The predisposing pathologic factors and underlying mechanisms involved in this clinical condition have not been clearly defined. Historically, multiple simultaneous intracerebral hemorrhages (SIHs) were associated with hematologic disorders, vasculitis, anticoagulant therapy, illicit drug use, cerebral amyloid angiopathy, or were due to multiple infarctions with hemorrhagic transformation.

In 1981, Weisberg described multiple SIHs in 12 patients without finding any identifiable causative factor. Later, Seijo et al reported another 7 cases of multiple SIHs. Three of the 7 cases were associated with hematologic disorders. To our knowledge, these are the 2 largest series describing multiple SIHs. This study analyzes the frequency, risk factors, clinical features, neuroimaging findings, and outcome of multiple SIHs.

RESULTS

Among 507 patients who had a stroke and who were admitted during the study period, 187 (37%) had a hemorrhagic stroke. Forty-five patients (24%) had subarachnoid hemorrhage and 142 (76%) had ICHs. Among those patients with ICHs, we found 4 (2.8%) with SIHs (mean age, 55 years; age range, 40-63 years). All patients with multiple SIHs had a history of arterial hypertension. We excluded other causes of multiple SIHs by appropriate diagnostic testing. Risk factors of patients with a single ICH and multiple SIHs are summarized in...
Table 1

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>No. (%) of Patients With ICH (n = 142)</th>
<th>No. (%) of Patients With SIH (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial hypertension</td>
<td>110 (77)</td>
<td>4 (100)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>34 (24)</td>
<td>0</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>67 (47)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>CAD</td>
<td>27 (19)</td>
<td>0</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>51 (36)</td>
<td>0</td>
</tr>
<tr>
<td>HCL</td>
<td>47 (33)</td>
<td>0</td>
</tr>
</tbody>
</table>

*ICH indicates intracerebral hemorrhages; SIH, multiple simultaneous intracerebral hemorrhages; CAD, coronary artery disease; and HCL, hypercholesterolemia.

Multiple SIHs have been observed in only 2% to 3% of hemorrhagic strokes.1-3 There is no agreement between different authors about the predisposing factors and underlying mechanisms involved. McCormick and Rosenfield4 described 16 patients with multiple ICHs. Nine had leukemia, 3 had other bleeding disorders, 2 had neoplasms, and 2 had vasculitis. Among 600 patients with...
hemorrhagic stroke, Weisberg found 12 (2%) with multiple SIHs. Hemorrhages affected the following areas: the lobe (8 patients), the lobe and putamen (2 patients), thalamus and cerebellum (1 patient), and cerebellum only (1 patient). Only 2 patients had a history of arterial hypertension. No identifiable precipitating factors were found in the other patients. Seijo et al. found 7 patients (2.3%) with multiple SIHs among 297 individuals with ICHs. The location of the bleedings was supratentorial in all cases. Three patients had hematologic disorders and the other 3 had hypertension. Cerebral amyloid angiopathy has also been associated with multiple ICH although it generally occurs in nonhypertensive individuals older than 65 years, sparing the basal ganglia and cerebellum. As defined in the literature, arterial hypertension is the major cause of single intracerebral hematoma. Infrequently, it has been associated with multiple SIHs. In agreement with previous reports from Japan and with other anecdotal cases, all of our patients had a history of uncontrolled arterial hypertension. Only 1 patient with multiple SIHs was being treated with 10 mg/d of oral enalapril prior to admission to our hospital. The remaining 3 patients discontinued antihypertensive treatment in the 3-month period before the hemorrhages occurred. On admission, sodium nitroprusside infusion was used to titrate blood pressure in 2 patients.

In addition, the topographic pattern of the bleeding was similar to the usual location of single hypertensive hematomas. We have not found any other potential cause of ICH such as, hematologic disorders, multiple infarctions with hemorrhagic transformation, vasculitis, or anticoagulant use. Although amyloid angiopathy may also be a differential diagnosis, the localization of the hematomas makes this consideration unlikely. Thus, multiple SIHs in our patients may probably be related to arterial hypertension. The pathophysiological mechanisms of multiple SIHs still remain uncertain. Anatomopathologic studies showed degenerative changes due to hypertension (eg, lipohyalinosis and Charcot-Bouchard aneurysms) in penetrating arteries. These vulnerable wall segments may be directly related to the occurrence of multiple hemorrhages in more than 1 arterial region. Komiyama et al. found simultaneous bleeding from multiple lenticulostriate arteries in a man with hypertension and ICHs by conventional cerebral angiography. Broderick et al. found that some patients with ICHs had an increase in hemorrhage volume. Most of them were persistently hypertensive during the early course of the bleeding. Broderick et al suggested that reactive hypertension might be the cause of continued bleeding. Recently, new techniques with gradient-echo magnetic resonance imaging have shown multiple asymptomatic microhemorrhages in patients with chronic hypertension and ischemic stroke that were not seen on computed tomographic scan. Kwa et al. found that 26% of the patients who had ischemic stroke also had evidence of hemosiderin deposits coexisting with white matter lesions on brain magnetic resonance imaging.

We hypothesize that sustained hypertension during a cerebral hemorrhage could trigger another bleeding owing to acute vascular changes in the penetrating arteries, affecting previously injured intima and media layers.

The confirmation of such consideration may influence the acute management of arterial blood pressure after hemorrhagic stroke.

We understand that our study has several limitations. First, this is a case-series design. These types of studies are useful for hypothesis formulation, but not for testing the presence of a valid statistical association. Another limitation constitutes the lack of a control group. Thus, risk factors or predisposing conditions, even suggestive, may simply be coincidental. Second, the frequency of multiple SIHs in this study could be biased because of the high incidence of ICHs in our population. However, our hospital is not a referral center. We presume that several factors could be involved, such as a poor control of blood pressure, high consumption of alcohol, or ethnicity.

In conclusion, simultaneous intracerebral bleeding may be more common than reported. Further analytic studies, including new imaging techniques, are necessary to determine the association between arterial hypertension and multiple SIHs, the predisposing factors, and underlying pathophysiological mechanisms.

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REFERENCES


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