Background Factors and Clinical Symptoms of Major Depression With Silent Cerebral Infarction

Tokumi Fujikawa, MD; Shigeto Yamawaki, MD; Yoshikuni Touhouda, MD

Background and Purpose  We previously reported that major depression developing during or after the presenile period is frequently combined with silent cerebral infarction and that these patients have a high risk of stroke. Therefore, we investigated whether the background factors and clinical symptoms of patients with major depression with silent cerebral infarction [SCI(+)] differed from those in patients with major depression without silent cerebral infarction [SCI(−)] before medical treatment.

Methods  Patients with major depression with onset after 50 years of age were classified based on magnetic resonance imaging findings into the SCI(+) (n = 37) or SCI(−) (n = 20) group. The diagnostic criteria for major depression were those of the American Psychiatry Association (DSM-III-R). Patients with stroke or focal neurological symptoms were excluded. The SCI(+) group was subclassified according to whether the infarction area was perforating, cortical, or mixed artery. Family history of affective disorder, risk factors for stroke, and Zung's Self-rated Depression Scale (SDS) score before medical treatment of the group were compared.

A symptomatic or silent cerebral infarction (SCI) is that detected by magnetic resonance imaging (MRI) or other imaging modalities in a patient who demonstrates no localized neurological symptoms or stroke. Patients with SCI, which is classified as a cerebrovascular disorder type III by the National Institute of Neurological Disorders and Stroke, may be at increased risk of subsequent overt stroke, and SCI may represent a prodromal stage before the development of overt stroke.

We previously studied the incidence of SCI detected by MRI in patients with presenile or senile major depression. Our findings suggested that organic depression related to SCI is present in approximately half of those with presenile-onset major depression and the majority of those with senile-onset major depression. Major depression with SCI may be a warning sign of cerebrovascular disease because it is associated with a high risk of subsequent symptomatic ischemic stroke. Therefore, we suspected that the background factors (heredity and risk factors for stroke) and clinical symptoms before medical treatment in patients with major depression with SCI differ from those in patients without SCI.

In this study we classified patients with major depression aged older than 50 years according to MRI findings as those with and without SCI. Differences between these groups in regard to family history of affective disorder, history of hypertension, diabetes mellitus, and hyperlipidemia; and depression scale scores before medical treatment were investigated.

Results  The SCI(+) group had a significantly lower (P < 0.05) frequency of family history of affective disorder but a significantly higher (P < 0.01) frequency of hypertension than did the SCI(−) group. The mean SDS score in the SCI(+) group was significantly higher than that in the SCI(−) group (P < 0.01). The mean SDS score of the mixed artery infarction group was higher than that of the perforating artery infarction group (P < 0.05).

Conclusions  Patients with major depression with silent cerebral infarction present more marked neurological factors and more severe depressive symptoms than do those without silent cerebral infarction. Because these features were more prominent in the patients with mixed artery infarction with broad obstructions, we consider that the area of brain damage caused by cerebral infarction is positively related to the severity of depressive symptoms.

Key Words: cerebral infarction, depression, hypertension, magnetic resonance imaging

References

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were calculated, and Student's t test was used to compare numerical data in the two groups.

Infarct were classified as not having SCI. Periventricular SCI was defined as the presence of four or more small infarcts in the same cerebral hemisphere or one or more large infarcts. Hyperintensity was not assessed.

Infarcts were defined as high-intensity lesions greater than 5 mm on T1-weighted images that coincided with low-intensity lesions on T2-weighted images. To avoid overdiagnosis of SCI, lesions ranging from 5 to 20 mm were defined as small infarcts, and lesions greater than 20 mm were classified as large infarcts. Although these were excluded from analysis because they are difficult to elude from the study. Informed consent was obtained from all subjects according to institutional guidelines.

A total of 57 patients (17 men and 40 women) were studied (mean age, 65.4±7.8 years). Patients with major depression were classified according to MRI findings as 37 patients with SCI [SCI(+) group] and 20 patients without SCI [SCI(−) group]. The SCI(+) patients were subclassified according to infarction area as those with perforating (n=19), cortical (n=6), or mixed (n=12) artery infarction. All patients and family members underwent detailed questioning about family history of affective disorder and, as risk factors for cerebral infarction, the patient's history of hypertension, diabetes mellitus, and hyperlipidemia.

Magnetic Resonance Imaging Findings

Magnetic resonance imaging was performed in 43 patients using a 0.5-T apparatus (Picker Co) at Hiroshima Prefectural Hospital and in 14 patients using a 1.5-T apparatus (General Electric Co) at Hiroshima University School of Medicine. T2-weighted images (repetition time [TR], 2000 milliseconds; echo time [TE], 100 milliseconds) were obtained in the transverse plane parallel to the orbitomeatal line, and T1-weighted images (inversion-recovery; TR, 2000 milliseconds; TE, 100 milliseconds) were obtained as coronal slices at 10-mm intervals.

Infarcts were defined as high-intensity lesions greater than 5 mm on T1-weighted images that coincided with low-intensity lesions on T2-weighted images. To avoid overdiagnosis of SCI, the following diagnostic criteria were adopted: lesions ranging from 5 to 20 mm were defined as small infarcts, and lesions greater than 20 mm were classified as large infarcts. Although detected lesions less than 5 mm may also be small infarcts, these were excluded from analysis because they are difficult to distinguish from état crible.5 Regarding the number of small infarcts that can be interpreted as indicating SCI, Shimada et al8 have reported that the mean number of small infarcts in hypertensive asymptomatic elderly subjects was 2.8±4.6, whereas that in normotensive elderly subjects was 1.1±1.5. Matsubayashi et al9 have studied the relation between small infarcts and cognitive function in normal elderly subjects and reported that four or more small infarcts are associated with the development of cognitive impairment. In the present study SCI was defined as the presence of four or more small infarcts in the same cerebral hemisphere or one or more large infarcts. Patients with fewer than four small infarcts and no large infarct were classified as not having SCI. Perventricular hyperintensity was not assessed.

For statistical analysis, mean±SD values of parametric data were calculated, and Student's t test was used to compare groups. The χ² test was used for comparison of nonparametric numerical data in the two groups.

TABLE 1. Background Factors in Patients With Major Depression With and Without Silent Cerebral Infarction

<table>
<thead>
<tr>
<th>Factor</th>
<th>SCI(−) Group</th>
<th>All Types</th>
<th>Perforating Type</th>
<th>Cortical Type</th>
<th>Mixed Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of affective disorder</td>
<td>7/20 (35.0)</td>
<td>3/37 (8.1)t</td>
<td>2/19 (10.5)</td>
<td>0/6 (0.0)</td>
<td>1/12 (8.3)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1/20 (5.0)</td>
<td>15/37 (40.5)*</td>
<td>7/19 (36.8)</td>
<td>1/6 (16.6)</td>
<td>7/12 (58.3)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1/20 (5.0)</td>
<td>1/37 (2.7)</td>
<td>1/19 (5.3)</td>
<td>0/6 (0.0)</td>
<td>0/12 (0.0)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>3/20 (15.0)</td>
<td>5/37 (13.5)</td>
<td>1/19 (5.3)</td>
<td>0/6 (0.0)</td>
<td>4/12 (33.3)</td>
</tr>
</tbody>
</table>

SCI(−) indicates patients with major depression without silent cerebral infarction (SCI); SCI(+), patients with major depression with SCI. Values in parentheses are percentages.

*P<.01, tP<.05 compared with SCI(−) group.

RESULTS

The mean age of the 2 men and 18 women in the SCI(−) group (61.4±5.8 years) was significantly lower than that of the 15 men and 22 women in the SCI(+) group (67.5±7.8 years) (P<.01).

Comparison of Background Factors in Both Groups

There was a family history of affective disorder in 7 (35.0%) of the 20 SCI(−) patients and in 3 (8.1%) of the 37 SCI(+) patients (P<.05) (Table 1). Hypertension was present in 1 (5.0%) of the SCI(−) patients and in 15 (40.5%) of the SCI(+) patients (P<.01). In the latter group, hypertension was present in 7 (36.8%) of the 19 patients with perforating artery infarction, in 1 (16.6%) of the 6 patients with cortical artery infarction, and in 7 (58.3%) of the 12 patients with mixed artery infarction. There was no difference between groups in the incidence of diabetes mellitus, at 5.0% in the SCI(−) group and 2.7% in the SCI(+) group, or in the incidence of hyperlipidemia, at 15.0% and 13.5%, respectively.

Comparison of Zung's Self-rated Depression Scale Score

The mean SDS score was 52.6±9.1 in the SCI(−) group and 58.8±7.0 in the SCI(+) group (P<.01) (Table 2). In SCI(+) patients the mean score was 56.4±6.3 in those with perforating artery infarction and 62.3±6.2 in those with mixed artery infarction (P<.05).

Discussion

Background Factors in Major Depression With Silent Cerebral Infarction

The risk factors for symptomatic cerebral infarction include hypertension, diabetes mellitus, hyperlipidemia, and atrial fibrillation. Various studies have been conducted to determine whether the risk factors for SCI are the same as those for symptomatic cerebral infarction. A Dutch transient ischemic attack study9 revealed that patients with SCI have a high incidence of advanced age, hypertension, or smoking. Subsequently, in a study of brain screening subjects who had no history of cerebral disease and who were socially active and neuropsychologically normal, Kobayashi et al10 found that a history of hypertension was observed significantly more often in patients with SCI compared with those without SCI.
Houng et al\textsuperscript{10} found that in patients with SCI the rate of complications was significantly higher in those with essential hypertension; they reported a strong causative relation of hypertension to perforating artery infarction. Lechner et al\textsuperscript{11} found that the number of risk factors for cerebral infarction, such as hypertension or diabetes mellitus, was positively associated with the rate of complication after SCI. They also reported that abnormal MRI findings were recognized in all of their patients with three or more simultaneous risk factors.

In the present study of patients with major depression with onset after 50 years of age with and without SCI, hypertension was found to be more frequent in those with SCI, but no difference between the two groups was recognized in the incidence of diabetes mellitus or hyperlipidemia. Thus, we conclude that among patients with major depression, hypertension is more common in those with SCI.

The difference between the two groups in the rate of family history of affective disorder indicates that patients with major depression without SCI frequently have a family history of affective disorder but have fewer risk factors for cerebral infarction. Endogenous factors may be especially important in this group. In contrast, in patients with major depression with SCI, neurological factors may be more important. A subgroup of patients with depression of presenile or senile onset may manifest a sequence of events, ie, hypertension as a risk factor that causes either perforating artery infarction or mixed artery infarction and eventually leads to major depression. Post\textsuperscript{12} and Murphy\textsuperscript{13} described a group of patients with senile depression with poor long-term prognosis. Mendlewicz\textsuperscript{14} reported that as the age at the onset of depression increases, the incidence of hereditary involvement decreases. We therefore suspect that when SCI is present in patients with presenile and senile major depression, the role of neurological factors is increased while that of heredity is decreased, and that such patients have poor long-term prognosis because of cerebrovascular impairment.

**Clinical Symptoms of Major Depression With Silent Cerebral Infarction**

Robinson et al\textsuperscript{15-18} reported that the severity of poststroke depression was significantly increased in patients with left anterior lesions. In a comparative study of poststroke depression and endogenous depression using the Present State Examination (PSE), Lipsey et al\textsuperscript{19} found that the symptomatic profiles of the two types of depression were similar, and there was no difference between the two groups in Hamilton depression scores. However, patients with poststroke depression showed significantly lower PSE scores. In the present study the SDS score of the patients with major depression with SCI was significantly higher than that of those without SCI. In a recent study of the relation between subjective symptoms and MRI findings in 124 normal adults, Kobayashi et al\textsuperscript{20} found that the incidence of SCI and the SDS score in subjects who showed forgetfulness with decreased motivation and concentration were significantly higher than those in subjects who did not. Of our patients with major depression with SCI, those with mixed artery infarction showed significantly higher SDS scores than did those with perforating artery infarction. These results indicate that depression is more severe in patients with mixed artery infarction, and we consider this finding to be due to the larger area of brain damage caused by cerebral infarction.

**Acknowledgments**

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