Depression in Patients with Subacute Myelo-Optico-Neuropathy (SMON)

Tetsuro Konishi¹, Kaori Hayashi¹, Michiyuki Hayashi², Satoshi Ueno³, Souhei Yoshida⁴, Harutoshi Fujimura⁵, Itaru Funakawa⁶ and Misako Kaido⁷

Abstract

Objective We investigated the psychiatric disorders in subacute myelo-optico-neuropathy (SMON) patients by structured interview. The prevalence of major depressive disorder in SMON patients was estimated by structured interview and using Beck’s depression inventory (BDI) questionnaires.

Materials and Methods Psychiatric conditions were evaluated in 26 SMON patients (9 males, 17 females, mean age 70.7 years) living in Kyoto prefecture through a structured interview given by psychiatrists. BDI questionnaires and clinical symptoms of SMON were investigated in 106 patients, ranging from 51 to 91 years in age (mean, 73.5) with SMON patients living in Kinki area. BDI questionnaires were obtained from 92 age-matched aged healthy people, ranging from 57 to 91 years in age (mean, 75.8), living in Kyoto city.

Results Among the psychiatric disorders in SMON patients, the prevalence of major depressive disorder and suicidal ideation significantly increased during the period of clioquinol intake and four patients (15.4%) out of 26 SMON patients still suffer from major depressive disorder. The prevalence of major depressive disorder in SMON patients was estimated at 15.1% (16/106) and this percentage was about seven times as frequent as in the age-matched aged healthy people (2.2%; 2/92). In female SMON patients, the degree of the depressive states was significantly correlated with the severe degree of dysesthesia of the lower extremities, and it was inversely correlated with the duration of SMON disease and the total scores of the Barthel index.

Conclusion This is the first report that shows the prevalence of major depressive disorder in SMON patients at present, which was seven times more frequent than age-matched aged healthy persons.

Key words: clinical study, major depressive disorder, clioquinol, SMON, Beck’s depression inventory, psychiatric disorders, dysesthesia

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Introduction

Subacute myelo-optico-neuropathy (SMON) is a disease caused by clioquinol intoxication, characterized by subacute onset of sensory and motor disturbance in the lower extremities with visual impairment following abdominal symptoms, which mainly occurred during 1950-60’s in Japan (1-3). After the ban of the sale of drugs containing clioquinol in September 1970, a sharp decrease in the number of SMON patients was observed in Japan. It is estimated that the number of SMON patients only slightly exceeded three thousand in 2002, and the mean age of 1,031 SMON patients exceeded 70 years old (mean age±SD, 72.9±9.6) with female predominance (males: females; 1: 2.75) (4). According to the nation-wide survey of 1031 SMON patients by SMON Research Committee, the prevalence of psychological complications was 51.8% and the depressive state was observed in 19.8% of SMON patients (4).

As the prevalence of major depressive disorder in SMON

¹Department of Neurology, Utano National Hospital, Kyoto, ²Department of Neurology, Otsu Municipal Hospital, Otsu, ³Department of Neurology, Nara Medical University, Kashihara, ⁴Department of Neurology, Kansai College of Oriental Medicine, Osaka, ⁵Department of Neurology, Toneyama National Hospital, Toyonaka, ⁶Department of Neurology, Hyogo-chuo National Hospital, Santa and ⁷Department of Neurology, Sakai Municipal Hospital, Sakai

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Correspondence to Dr. Tetsuro Konishi, konishi@unh.hosp.go.jp
patients in Japan has not been studied, we estimated the prevalence of major depressive disorder by structured interview by psychiatrists using Beck’s depression inventory (BDI) questionnaires. We also compared the depressive states of SMON patients with age-matched healthy persons using BDI questionnaires. At the same time, we tried to clarify the factors causing deterioration of the depressive states in SMON patients associated with their clinical symptoms.

### Materials and Methods

Psychiatric conditions were evaluated in 26 SMON patients (9 males, 17 females, mean age 70.7 years) living in Kyoto prefecture through a structured interview given by psychiatrists using BDI questionnaires. BDI questionnaire and clinical symptoms of SMON were investigated in 106 patients (28 males, 78 females), ranging from 51 to 91 years in age (mean, 73.5), living in the Kinki area. Before the entry of this study, we explained to each patient the aim of this study, and promised to keep the results private. Only patients who understood and agreed with the aim of this study were entered. BDI questionnaire was mailed to 300 aged people at random belonging to the golden age club at Ukyo area in Kyoto city, and had reply from 92 old people (41 males, 51 females), ranging from 57 to 91 years in age (mean, 75.8). Thus, the response of the BDI questionnaire was 30.7% (92/300). The clinical symptoms of SMON were evaluated using medical check-up records established by the SMON Research Committee. The degree of the peculiar dysesthesia in SMON patients (2), which includes adherent sensation to sole and sensation of scrubbing, tingling, stabbing or coldness, was classified into four groups; none, mild, moderate and severe. Visual impairments were classified into seven groups; normal, nearly normal, mild, moderate and severely impaired, only perceiving blight sensation and total blind. The gait scores were obtained from condition of gait, which was classified into nine grades as follows: unable to walk, able to move by using a wheelchair, able to walk with aid, walk by holding walls, walk on crutches, walk with a stick, moderately unstable gait, mild unstable gait, normal gait. In each patient, total scores of Barthel index were calculated as the sum of ten questionnaires (total score; 100) (5). Mini-mental state examination (MMSE) was done in all SMON patients and the patients whose scores were less than 23 points were excluded. The study was approved by the ethics committee of Utano National Hospital.

Statistical analysis was made using Spearman’s rank correlation, Wilcoxon’s rank-sum test, or χ² square test. A level of p<0.05 was considered to be statistically significant.

### Results

#### Psychiatric disorders in SMON patients

Structured interview by psychiatrists toward 26 patients with SMON who live in Kyoto area disclosed an increase in the prevalence of major depressive disorder, delirium, suicidal ideation and commitment of suicide during the clioquinol intake period (during in the Table 1). The increase was significant in major depressive disorder and in the suicidal ideation during the clioquinol intake period (6). Four patients (15.4%) out of 26 SMON patients suffered from major depressive disorder at present (present in the Table 1). Significant changes of the prevalence of psychiatric disorders, such as panic disorders, hypochondriasis, conversion disorder, alcohol addict and insomnia, were not observed during the periods of medication of clioquinol and present (6). The suicidal ideation and commitment of suicide during
the clioquinol intake period were observed with the patients, only who were diagnosed as having major depressive disor-
der at the same time.

**Total BDI scores of SMON patients and aged people**

The total scores of BDI questionnaire of these four SMON patients with major depressive disorder in Kyoto prefecture exceeded 25 points, and the score of the other SMON patients without major depressive disorder was under 24 points. It is consistent that 24/25 of the total scores of BDI questionnaire is considered for tentative cut-off point for suffering from major depressive disorder or severe depressive mood in this study. The number of SMON patients with a total BDI score exceeding 25 points was sixteen (15%) out of 106. On the other hand, the score in 2 (2%) out of 92 aged people exceeded 25 points. The difference of these two groups was significant by χ square test (p<0.01).

**Correlation between total BDI scores and clinical characteristics of SMON patients**

In order to clarify factors which might influence the scores of BDI questionnaire, Spearman’s rank correlation were examined among total BDI scores and the scored clinical characteristics of SMON patients analyzed in each gender groups (Table 2). In each gender, the total BDI scores did not correlate with age nor with the MMSE scores. In female SMON patients, the BDI scores were significantly correlated with the severe degree of dysesthesia of the lower extremities and were inversely correlated with the duration of SMON disease and the total scores of the Barthel index. In contrast, the BDI scores of male SMON patients did not show a significant correlation with any clinical characteristics.

**Comparison of the total BDI scores among SMON patients and aged people**

The distribution of BDI scores from 92 aged people living in Kyoto city and 106 SMON patients in Kinki area is shown in Fig. 1. Although the mean age of aged people was 2.3 years older than that of SMON patients, the Wilcoxon’s

Table 2. Spearman’s Rank Correlation Coefficient between Total BDI Scores and Age, Scores of Barthel Index, in Each Gender

<table>
<thead>
<tr>
<th></th>
<th>Males (28)</th>
<th>Females (78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.246</td>
<td>0.034</td>
</tr>
<tr>
<td>MMSE scores</td>
<td>-0.198</td>
<td>-0.128</td>
</tr>
<tr>
<td>Dysesthesia</td>
<td>-0.099</td>
<td>0.292*</td>
</tr>
<tr>
<td>Duration of disease</td>
<td>0.076</td>
<td>-0.270*</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>0.164</td>
<td>0.009</td>
</tr>
<tr>
<td>Gait disturbance</td>
<td>-0.021</td>
<td>-0.216</td>
</tr>
<tr>
<td>Barthel index scores</td>
<td>-0.064</td>
<td>-0.289**</td>
</tr>
</tbody>
</table>

★: p<0.05, ★★: p<0.01

![Figure 1. Distribution histogram of BDI scores of SMON patients and aged people. An arrow indicates cut-off point of 25 score.](image-url)
rank-sum test of BDI scores showed that SMON patients had significantly high scores compared to age-matched aged people (p<0.0001). Using tentative criterion of having major depressive disorder estimated from the high points of BDI scores exceeding 25 (arrow in Fig. 1), two (2.2%) out of 92 aged people and 16 (15.1%) out of 106 SMON patients were suggested to suffer from major depression. The percentage of the patients having estimated major depressive disorder in SMON patients was significantly high compared with those of aged people by χ2 square test (p<0.01). There was no difference in percentage exceed 25 points among male patients [14.8% (4/27)] and female patients [15.2% (12/79)]. The SMON patients were suggested to be suffering from major depressive disorder seven times more frequently compared with the age-matched aged people.

**Discussion**

A nation-wide survey of SMON patients showed more than a half SMON patients were suffering from various kinds of psychological complications, such as depressive mood and hypochondriasis (4). The mean age of these SMON patients was over 70 years old.

Here, we disclosed two significant points. First, the prevalence of major depressive disorder and delirium increased during the cloquinol intake period suggesting that these psychiatric disorders were due to the reactions of acute phase of SMON. Secondly, the prevalence of major depressive disorder in SMON patients at present was about 15% of SMON patients, estimated by two different ways, which percentage of major depressive disorder in SMON patients was seven times more frequent than age-matched aged people. One way of estimation of the prevalence of major depressive disorder among SMON patients was done from structured interview of 26 SMON patients by psychiatrists and four (15.4%) out of 26 patients was diagnosed as having major depressive disorder. The other estimation was obtained using BDI questionnaire from 106 SMON patients, in which 24/25 (12/79) of SMON patients were suggested to be suffering from major depressive disorder which coincided with the results obtained by the structured interview by psychiatrists.

The prevalence of major depressive disorder in aged people was 2.2% (2/92), estimated by the percentage of people, which BDI scores exceeding 25. This estimated prevalence in this study is compatible with other studies of aged people. The six-month prevalence of major depression in three different communities showed 2.2-3.5% with less frequency in aged people over 65 years old (8). The prevalence of major depressive disorder in aged people over 65 years old was reported as 3.7% (9). In Japan, there were two studies on the prevalence of major depressive disorder in elderly people over 65 years old, in which the prevalence was 1.1% (10) and 5.6% (11).

From the correlation study between severity of clinical parameters of SMON patients and BDI scores, the worsening factors for depressive state in female SMON patients closely related with the severity of the degree of dysesthesia of the lower extremities and the degree of disability of ADL. These findings suggest that improvement of the level of ADL and a reduction of dysesthesia of the lower extremities are important factors for the treatment of depressive state in SMON patients. We expect that the alleviation of these factors in the near future by the application of new medications or rehabilitation in SMON patients with a high BDI score will reduce the degree of the depressive mood associated with the reduction of BDI scores.

**Abbreviation:** ADL: activities of daily living

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**References**


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