Short communication

Sudden hearing loss as the initial symptom in Japanese patients with multiple sclerosis and seropositive neuromyelitis optica spectrum disorders

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Abstract

Sudden hearing loss may occur in rare cases of relapsing-remitting multiple sclerosis (RRMS). There have also been reports of idiopathic sudden sensorineural hearing loss (SNHL) in patients with neuromyelitis optica spectrum disorders (NMOSD), but the frequency of such cases is unclear.

We conducted a retrospective analysis of the medical records of 173 consecutive patients with multiple sclerosis (MS) and 101 consecutive patients with NMOSD who tested positive for anti-aquaporin-4 antibodies in addition to 37 consecutive patients with clinically isolated syndromes (CIS) to investigate the frequency and onset timing of SNHL. SNHL was observed in six (3.5%) of the RRMS cases, one (1.0%) of the seropositive NMOSD cases, and three (8.1%) of the CIS cases. SNHL occurred ahead of onset in 4/6 MS patients and in all 3 CIS patients. Patient with NMOSD exhibited SNHL 6 years after the onset of NMOSD. Although SNHL is rare, these results suggest the risk of developing demyelinating lesions in the central nervous system and further conversion to MS in the future.

Key words: Multiple sclerosis
neuromyelitis optica
Clinically isolated syndrome
Sudden sensorineural hearing loss
Sudden deafness
Onset
Initial symptom

1. Methods

A total of 508 patients were examined for diagnosis or treatment with suspected MS or NMO at MS Center, Utano Nat. Hosp. between April 2007 and December 2015. Of these, we retrospectively analyzed the medical records of 173 patients with relapsing-remitting MS (RRMS) that fulfilled the 2010 diagnostic criteria (Polman et al., 2011), 101 consecutive patients with NMOSD who tested positive for anti-aquaporin-4 antibodies in addition to 37 consecutive patients with clinically isolated syndromes (CIS) to investigate the frequency and onset timing of SNHL. SNHL was observed in six (3.5%) of the RRMS cases, one (1.0%) of the seropositive NMOSD cases, and three (8.1%) of the CIS cases. SNHL occurred ahead of onset in 4/6 MS patients and in all 3 CIS patients. Patient with NMOSD exhibited SNHL 6 years after the onset of NMOSD. Although SNHL is rare, these results suggest the risk of developing demyelinating lesions in the central nervous system and further conversion to MS in the future.

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72 years (40.5 ± 15.5 years; 42 years), and the disease duration ranged from 1 to 39 years (11.7 ± 7.7 years; 11 years). The CIS cases included 13 men and 24 women, the age of onset ranged from 19 to 59 years (36.9 ± 9.5 years; 36 years), and the disease duration ranged from 2 months to 13 years (3.8 ± 3.3 years; 3 years). SNHL was treated as a separate episode rather than as a neurological manifestation of RRMS/CIS or NMOSD, and CIS was not diagnosed on the basis of SNHL alone. CIS cases included 25 cases of myelitis, 6 cases of optic neuritis, and 6 cases exhibiting brainstem symptoms such as diplopia and vertigo that were accompanied by MS-compatible findings on brain magnetic resonance imaging (MRI). All CIS cases were negative for anti-AQP4 antibodies and longitudinally extensive transverse myelitis (LETM) (M. Tanaka et al., 2007), which were typical of NMOSD. No cases have converted to MS since their onset (mean 3.8 years), and as of December 2015, all of these patients remained in the CIS group.

2. Results

All patients who experienced SNHL were diagnosed at the department of otolaryngology. SNHL (Table 1) occurred in six of 173 (3.5%) RRMS cases, one of 101 (1.0%) seropositive NMOSD cases, and three of 37 (8.1%) CIS cases. There were no significant differences were noted between MS and NMOSD cases (two-sided p = 0.2664; odds ratio 3.59; 95% confidence interval 0.43–30.28) or between MS/CIS and NMOSD cases (p = 0.1749; odds ratio 4.48, 95% confidence interval 0.56–35.84 by Fisher’s exact test).

SNHL occurred ahead of onset in 6/9 patients with MS/CIS, simultaneously with neurological symptoms in one patient, and after neurological symptoms in only two male patients. SNHL in 9 patients appeared, on average, 1.9 years before the onset of neurological symptoms (median: 3 months ahead of neurological symptoms). The single patient with NMOSD who exhibited SNHL developed the condition 6 years after onset.

In the male patient with RRMS-2, left SNHL appeared 3 months after right SNHL. Although treatment was attempted with steroids and hyperbaric oxygen therapy, only this patient was left with the sequel of right SNHL. Although treatment was attempted with steroids and, hy-

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age of onset (yo)</th>
<th>Duration of illness (years)</th>
<th>Sudden deafness before (minus) or after (plus) the onset of CIS (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMRS-1 F</td>
<td>20</td>
<td>19</td>
<td>0.25</td>
</tr>
<tr>
<td>RRMS-2 M</td>
<td>29</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>RRMS-3 M</td>
<td>28</td>
<td>27</td>
<td>1</td>
</tr>
<tr>
<td>RRMS-4 M</td>
<td>49</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>RRMS-5 M</td>
<td>24</td>
<td>15</td>
<td>0.17</td>
</tr>
<tr>
<td>RRMS-6 M</td>
<td>51</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>CIS-1 F</td>
<td>35</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>CIS-2 M</td>
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<td>8</td>
<td>15</td>
</tr>
<tr>
<td>CIS-3 M</td>
<td>35</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>NMOSD F</td>
<td>26</td>
<td>9</td>
<td>6</td>
</tr>
</tbody>
</table>


3. Discussion

In the literature, SNHL has been reported to occur in 0.4%–4.4% of western patients with MS (Zadro et al., 2008; Hellmann et al., 2011; Leite et al., 2014). Further investigation with a larger sample size is required in the future but our study showed SNHL found in 6/173 (3.5%) RRMS patients and 3/37 (8.1%) CIS patients.

In the present study, it should be noted that the timing for the onset of SNHL was close to that of MS and CIS. Furthermore, in rare cases, SNHL may appear almost simultaneously with other neurological symptoms at times of MS recurrence, suggesting that it is related to MS disease activity. In a report from France (de Seze et al., 2001), in which SNHL was detected in 14 (3.5%) of 400 consecutive MS cases, onset occurred in 12 of these 14 cases when disease activity was high. It often appears before onset (at the time of CIS appearance) in patients with MS, and even if it occurred after onset in some cases, this was usually within 2 years but it occurred 7 and 15 years before onset in 2 of 3 CIS patients without conversion to MS. The fact that SNHL is unlikely to occur as time passes after the MS onset may suggest a broad correlation with MS disease activity.

There have been 15 cases reported in the literature in which SNHL was the only symptom of CIS (Anagnostouli et al., 2012). In a series of cases from Israel (Hellmann et al., 2011), SNHL occurred with MS/CIS in seven cases and within 2 years of CIS onset in 10 of 11 cases. In addition, recent report showed a patient with SNHL 19 years after MS onset (Leite et al., 2014). Although the actual number of reported cases is low, SNHL in patients with NMOSD appears to differ from the SNHL in patients with MS as it does not develop from decreased hearing ability (Birnbaum and Kerr, 2008; Jarius et al., 2013). An older report in the literature indicated that 1% of patients with MS developed SNHL from hearing impairment (Kabana et al., 1973). Our results suggest that it should be noted that some patients who exhibit SNHL, particularly those with good hearing ability prognosis, may exhibit demyelinating lesions of the central nervous system in the future.

Conflict of interest

Dr. Tanaka M. received speaker honoraria from Biogen Idec Japan, Bayer Schering Pharma, Asahi Kasei Medical, Novartis Pharma, and Tanabe Mitsubishi Pharma, and Dr. Tanaka K. has received research support from JSPS KAKENHI Grant Number (23500455, 23249048), Japan, and the Japan Epilepsy Research Foundation and has received speaker honoraria from Biogen Idec, Nihon Seiyaku, Novartis Pharma, Otsuka Pharma, Bayer Schering Pharma, Daichi-Sankyo, and Tanabe Mitsubishi Pharma.

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