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Case report

Tongue strength in patients with subacute myelo-optico-neuropathy

Satoshi Yamashita [a,*], Tatsuya Nakama [b], Mitsuharu Ueda [a], Shoji Honda [a], En Kimura [a,c], Masaaki Konagaya [d], Yukio Ando [a]

[a] Department of Neurology, Graduate School of Medical Sciences, Kumamoto University, 1-1-1 Honjo, Chuo-ku, Kumamoto 860-8556, Japan
[b] Department of Neurology, Minamata City General Hospital and Medical Center, 1-2-1 Tenjincho, Minamata 867-0041, Japan
[c] Department of Clinical Research Support, Translational Medical Center, National Center of Neurology and Psychiatry, 4-1-1 Ogawa-higashi, Kodaira 187-8551, Japan
[d] Department of Neurology, National Hospital Organization Suzuka Hospital, 3-2-1 Kasado, Suzuka, Mie 513-8501, Japan

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ABSTRACT

Subacute myelo-optico-neuropathy (SMON) is a neurodegenerative disease that may be caused by overdose or prolonged oral administration of clioquinol. Recently, dysphagia has attracted attention as a complication of SMON. To investigate lingual control in SMON, we examined patients with SMON using assessments of maximum tongue pressure, compared with dysphagia-related diseases, such as sporadic inclusion body myositis (sIBM) and amyotrophic lateral sclerosis (ALS), and healthy volunteer. The mean maximum tongue pressure (P_{max}) in patients with SMON was 14.7 ± 5.8 kPa, while it was 33.6 ± 4.4 kPa in the controls. In contrast, the mean P_{max} for patients with ALS with or without bulbar involvement was 7.8 ± 2.7 kPa and 34.4 ± 5.7 kPa, respectively, while it was 29.4 ± 8.2 kPa in patients with sIBM. P_{max} values correlated with lower limb weakness in SMON patients. Decreases in P_{max} may be involved in the development of dysphagia in patients with SMON.

1. Introduction

Subacute myelo-optico-neuropathy (SMON) is a neurodegenerative disease characterized by the presence of abdominal symptoms followed by severe myeloneuropathy symptoms, including ascending dysesthesia/paresthesia, loss of sensation, gait impairment with ataxic and spastic paraplegia, autonomic disorders, and visual impairment [1,2]. In the early 1970s, epidemiological studies revealed that SMON is attributable to prolonged oral administration or overdose of clioquinol [3]. In Japan, more than 1400 individuals still have SMON. These patients are affected by further complications as they age (http://www.nanbyou.or.jp/).

Recently, dysphagia has attracted attention as a complication of SMON. One study reported that 30.4% of patients with SMON have difficulties in swallowing, with 13.0% of patients actually having occasional dysphagia [4]. This study suggests that dysphagia in patients with SMON might be related to respiratory dysfunction. Another study reported that 46.2% of patients with SMON complained of difficulty swallowing, and that radiological and endoscopic analyses identified some degree of abnormality in the digestive, oral, or pharyngeal stages [5]. The above study indicates that dysphagia in SMON might be related to aging, since the frequency of dysphagia tends to increase with disease progression. However, the precise mechanism by which it develops remains undetermined.

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease with unknown pathogenesis that can selectively affect both the upper and lower motor neurons. Swallowing and feeding impairments can occur during any stage of the swallowing process due to muscle weakness of the bulbar, respiratory, and limb musculature [6]. Sporadic inclusion body myositis (sIBM) is a progressive inflammatory myopathy with no known cause or definitive treatment. Dysphagia is one of the main clinical features of sIBM. Approximately 10% of patients with sIBM complain of difficulty swallowing at disease onset, with about 40% of patients having dysphagia at the time of diagnosis [7]. Reduced compliance of the sphincter due to inflammatory involvement of the cricopharyngeal muscle is most likely responsible for the swallowing dysfunction [8–13]. A recent non-invasive device that uses an intraoral pressure probe has been used to demonstrate significantly decreased lingual pressure in patients with ALS [14]. However, no studies have evaluated lingual pressure in patients with sIBM thus far.

Our final goal is to discover the mechanism by which dysphagia develops in patients with SMON. However, some patients with

* Corresponding author at: Department of Neurology, Graduate School of Medical Sciences, Kumamoto University, 1-1-1 Honjo, Chuo-ku, Kumamoto 860-8556, Japan.
E-mail address: y-stsh@kumamoto-u.ac.jp (S. Yamashita).

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SMON hesitate to undergo invasive investigations, as they have been negatively affected by clioquinol. Here we aimed to non-invasively investigate whether lingual control is indeed affected in patients with SMON. We also compared lingual control in patients with SMON to those with sIBM and ALS using measurements of tongue pressure.

2. Patients and methods

2.1. Patients

The study was approved by the Ethics Committee of Kumamoto University, Graduate School of Medical Sciences (Rinri No. 938). We prospectively analyzed all 11 patients with SMON who resided in Kumamoto prefecture between September 2014 and August 2015. One patient with SMON was excluded from this study because he had a medical history of lacunar infarction. Twelve consecutive patients with ALS and 12 consecutive patients with sIBM, who were admitted to our hospital at the same time, were also examined. In addition, we enrolled 10 healthy volunteers who were age-matched to the SMON cohort. Diagnoses of SMON, sIBM, and ALS were based on diagnostic guidelines provided by the SMON Research Commission [1], the European Neuromuscular Centre 2013 [15], and the revised El Escorial criteria [16], respectively. The ALS cohort was divided into patients with bulbar involvement and those with non-bulbar involvement based on videofluorographic and/or videoendoscopic evaluations of swallowing. All patients provided informed consent prior to participation.

2.2. Measurement of maximum tongue pressure

To record the maximum tongue pressure, we used the same digital tongue pressure measurement device (TPM-01, JMS Co., Ltd., Hiroshima, Japan) reported previously [17–19]. We instructed patients to compress the balloon of a disposable intraoral pressure probe upward onto their palates for 7 s with maximum voluntary effort of the tongue. The probe was placed between 1 cm and 3.5 cm from the dental zone according to the manufacturer's instructions (Supplemental Fig. 1). Tongue pressures were recorded five times at 1 min intervals without informing the patients of the results of the previous test, and the mean maximum pressure (P_{max}) was recorded.

2.3. Clinical evaluations of SMON symptoms

The annual examination survey conducted by the SMON Research Committee with the support of the Japanese Ministry of Health, Labour and Welfare [20,21] was used to evaluate patients with SMON in the following criteria: visual impairment; dysbasia; muscle weakness, spasticity, and amyotrophy in the lower limbs; superficial sensation (tactile sensation and algesthesia); vibratory sensation; and dysesthesia.

2.4. Statistical Analysis

Data were analyzed using one-way analyses of variance with Bonferroni's multiple comparison tests, or Mann-Whitney tests. Regression analyses were performed using the Pearson correlation test.

3. Results

3.1. Clinical characteristics of patients with SMON

Ten patients (4 men and 6 women) with SMON were included in the study. The clinical characteristics of these patients are summarized in Table 1. Mean age at the time of study was 75.9 ± 8.3 years, with a mean onset age of 29.4 ± 8.2 years. Mean disease duration was 46.2 ± 2.0 years. The most frequently experienced complications were cataracts and hypertension. Visual impairment was observed in 7 patients (70.0%) who could read a newspaper with effort, 2 patients (20.0%) who could read only headlines in a newspaper, and 1 patient (10.0%) who could only discern the number of fingers raised.

3.2. Analysis of maximum tongue pressure

Values of maximum tongue pressure in the participants of the study are summarized in Table 2. Mean maximum tongue pressure (P_{max}) in patients with SMON was 14.7 ± 5.8 kPa, while that in healthy volunteers who were age-matched to the SMON cohort was 33.6 ± 4.4 kPa. In contrast, mean P_{max} for patients with ALS with or without bulbar involvement was 7.8 ± 2.7 kPa and 34.4 ± 5.7 kPa, respectively, while it was 29.4 ± 8.2 kPa for patients with sIBM (Fig. 1A). There was no significant difference in mean age among these groups (Fig. 1B). We next assessed the relationship between P_{max} and age at examination for patients in each group. In the sIBM group, P_{max} had a significant correlation with patient age ($R^2 = 0.526$, $P = 0.008$; Fig. 1C). In both the SMON and ALS groups, older patients tended to have lower values of P_{max} (Fig. 1D and E).

We then evaluated the correlation between P_{max} and clinical findings related to SMON (Table 3). Values of P_{max} significantly correlated with muscle weakness in the lower limbs ($P = 0.038$). P_{max} had no significant correlation with any of the other parameters assessed (Table 3).

4. Discussion

Here we report that decreases in P_{max} may be involved in the development of dysphagia in patients with SMON, as the values for P_{max} had a significant correlation with weakness in the lower limbs. A neuropathological study has analyzed the pathological changes involved in both acute and chronic stages of SMON using data from 14 autopsy cases [22]. In the acute phase, axonal damage is more prominent in the peripheral nerves and spinal tracts. In the chronic phase, demyelination and changes in regenerative capability occur in the peripheral nerves, along with proliferation of Schwann cell nuclei. In addition, some cranial nerve rootlets, particularly those of the vagus nerve, may be disintegrated along with distal portions of peripheral nerves and both sensory and motor tracts of the spinal cord. Interestingly, the bilateral corticospinal tracts were damaged in the middle part of the medulla oblongata, and the vagus nerve rootlets were demyelinated at this same level, suggesting that a dysfunction of the swallowing process is involved in the primary pathogenesis of SMON. We found more severe lower limb weakness in patients with SMON who had dysphagia based on the non-invasive screening methods. This may indicate the involvement of the corticospinal tract in addition to aging as mechanisms underlying swallowing dysfunction. Further research is required to better understand the pathogenesis of dysphagia in SMON.

A digital tongue pressure measurement device was first utilized clinically in 2010. Takeuchi et al. [23] reported that patients with cerebrovascular diseases or neuromuscular disorders had signifi-

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