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Case study

Botulinum toxin A is effective to treat tension-type headache caused by hemifacial spasm

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ABSTRACT

Objective: We examined the relationship between hemifacial spasm (HFS; a form of cranio-cervical dystonia) and chronic primary headache, including tension-type headache (TTH). We also examined whether botulinum toxin A (BoNT/A) therapy for HFS ameliorates concomitant TTH.
Methods: Fifty-one HFS patients receiving BoNT/A therapy were recruited. Patients' characteristics (including age, gender, chronic headache history, exercise habits, stiff neck, cervical spondylolysis history), stress factors, worsening/new onset of headache associated with HFS, and dose of BoNT/A were examined. We diagnosed headache types according to The International Classification of Headache Disorders, 3rd edition, beta. Numerical Rating Scale (NRS) and Headache Impact Test-6 (HIT-6) scores for headache severity were compared between the 6-week baseline before BoNT/A therapy and 6-week follow-up after BoNT/A therapy.
Results: Of 51 patients with HFS, 17 (33.3%) reported worsening or new onset of headache (especially TTH) associated with HFS (Group-S), and 34 were not aware of headache (Group-N). Twelve patients (70.6%) in group-S reported improvement of headache after BoNT/A therapy. NRS (from 7 [5–9] to 0 [0–5], $p < 0.01$) and HIT-6 (from 55 [54–64] to 44 [36–52], $p < 0.001$) scores were significantly improved after BoNT/A therapy. Logistic regression analysis revealed significant interaction between TTH associated with HFS and the presence of stress factors (odds ratio 43.11: 2.95–629.39, $p < 0.001$) and history of chronic headache (odds ratio 28.53: 2.96–275.10, $p < 0.001$).
Conclusions: Primary headache, especially TTH, is associated with HFS. BoNT/A therapy for HFS may also be indirectly effective for treatment of TTH.

1. Introduction

Hemifacial spasm (HFS) is categorized as a form of cranio-cervical dystonia [1,2], and may be caused by vascular compression [2], tumor compression [1], brainstem lesions such as cerebrovascular diseases [3] and demyelinating diseases [4], and secondary factors such as trauma or peripheral facial paralysis [1,5]. However, in some cases of HFS the etiology cannot be established [1]. In these cases, medical treatment (anticonvulsants or GABAergic drugs) and/or intramuscular injection of botulinum toxin A (BoNT/A) are performed to reduce spasms [1]. Though oral medications are generally ineffective [1], BoNT/A therapy can reduce spasms and improve quality of life [1,2]. Unusual involuntary movements can become major stress factors for cranio-cervical dystonia patients [2]. Furthermore, some cases of cranio-cervical dystonia (pharyngeal dystonia, spasmodic torticollis, mandibular dystonia, and lingual dystonia) are associated with secondary headache (headache attributed to cranio-cervical dystonia) due to the abnormal movements or defective posturing of the neck or head arising from muscular hyperactivity [6]. In contrast to other cranio-cervical dystonias, stress factors (via the central pain mechanism [7]) and increasing tenderness of pericranial muscles (via the peripheral pain mechanism [8]) can affect not only the severity of HFS, but also the severity of headache (especially primary headache [7,8]). However, the relationship between headache and HFS is unclear.

Abbreviations: HFS, hemifacial spasm; BoNT/A, botulinum toxin type A; TTH, tension type headache; CH, chronic headache; NRS, Numerical Rating Scale; HIT-6, Headache Impact Test-6.

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Tension-type headache (TTH), which is most frequent form of primary headache [9] in Japan, constitutes about 50% of chronic headache and may adversely affect work and productivity [10,11]. However, there are relatively few reports about TTH compared to migraine, and some cases may be subclinical (associated with other disorders) [11]. Although the coexistence ratio of TTH in patients with HFS is unclear, both stress factors and increasing tenderness of pericranial muscles associated with cranio-cervical dystonia (including HFS) are likely to worsen TTH. Spasmodic torticollis, which is also included in cranio-cervical dystonia, is associated with primary headache, especially migraine and TTH [12].

Recently, BoNT/A therapy has been applied to various movement disorders, such as cranio-cervical dystonia, post-stroke spasticity, and cerebral palsy [13–16]. Trials of BoNT/A therapy for treatment of primary headache have also been performed [17–21]. However, BoNT/A was not effective for TTH [17,18], although it was effective against chronic migraine [19–21]. On the other hand, a beneficial effect on primary headache was reported in cranio-cervical dystonia patients treated with BoNT/A therapy, especially among patients receiving doses higher than 50 U for the treatment of spasmodic torticollis [12]. Hence, we speculated that facial spasm might worsen headache or cause new headache, and we hypothesized that BoNT/A therapy to treat HFS might improve not only facial spasm, but also headache.

To test this idea, we examined the frequency of coexistence of chronic primary headache (CH) and HFS, and the effect on headache of BoNT/A therapy for HFS.

2. Materials and methods

2.1. Study design and ethics considerations

This study was a retrospective study and the subjects were recruited from patients with HFS who had visited at our neurology clinic at Tokai University Hospital for BoNT/A therapy between April 2015 and July 2015 (the period corresponds to one course of BoNT/A therapy). This study was approved by the Tokai University Ethics Committee (No. 16R-062). Informed consent was obtained from all recruited patients. Types of headache were diagnosed according to the criteria of The International Classification of Headache Disorders, 3rd edition (ICHD-III beta) [6].

2.2. Patient population

Fifty-one patients (41 females [80.4%]; mean age ± standard deviation, 64 years ± 14) who met the following inclusion criteria were recruited: received BoNT/A therapy at least once and continuing BoNT/A therapy. We excluded patients with blephalospasm, Meige syndrome, spasmodic torticollis, and medication-overuse headache [22]. Patients who had been treated for headache or microvascular compression before receiving BoNT/A therapy were also excluded from this study.

2.3. Data collection

The following patient data were collected from medical records at our clinic: age, gender, chronic headache (CH) history, exercise habits (defined as previously reported [23]), stiff neck (subjective or objective symptom [muscle tenderness]), history of cervical spondylolysis (diagnosed by an orthopedic surgeon based on clinical symptoms or imaging inspections), stress factors (defined as both "stressful life events" and "minor life events" [24]), worsening of headache in parallel with HFS or new onset of headache accompanied by HFS, and details of BoNT/A treatment for HFS (injection site and total dosage during the investigation period).

2.4. Quantitative evaluation of headache

We used Numerical Rating Scale (NRS) [25] and Headache Impact Test-6 (HIT-6) [26] for quantitative evaluation of headache. We also set two investigation periods: a 6-week baseline period (pre-treatment period) and a 6-week follow-up period after BoNT/A therapy (post-treatment period) according to the previous report [27]. Scores were based on the patients' subjective opinions during the specified periods.

2.5. Primary and secondary outcome

Primary endpoint was worsening or new onset of headache accompanied by HFS. Secondary endpoint was clinical outcome defined in terms of NRS and HIT-6 scores and safety (side effects such as severe facial motor palsy, ptosis, lacrimation, etc.) after BoNT/A therapy.

2.6. Statistical analysis

The chi-square test and *t* test were used for categorical data. For the analysis of the improvement of NRS and HIT-6 score, we used the Wilcoxon signed-rank test. We also used multivariable logistic regression to assess the relative risks of variables for worsening/new onset of headache accompanied by HFS. Statistical analyses were performed using SPSS 23.0 (SPSS, Inc. Chicago, IL, USA). The significance level was set at $P < 0.05$.

3. Results

3.1. Association of HFS with headache

Of the 51 patients with HFS, 17 patients (33.3%) reported worsening or new onset of headache accompanied by HFS (Group-S). Among these 17 patients, 15 had TTH and the other 2 had TTH and migraine (one "migraine without aura" and one "chronic migraine" according to ICHD-III beta). Of these 17 patients, 13 (72.2%) had headache at the ipsilateral side from HFS. The headache type associated with HFS was infrequent episodic TTH or frequent episodic TTH in all cases. The remaining 34 of the 51 patients were not aware of headache, regardless of CH history (Group-N).

3.2. Patients' characteristics

Table 1 summarizes the characteristics of patients and the dose of BoNT/A in each group. Patients were younger in group-S than in group-N (57 ± 17 vs. 68 ± 11, $p < 0.05$). CH history (70.6% vs. 17.6%, $p < 0.001$) was more frequent in group-S than in group-N. Stiff neck (82.4% vs. 52.9%, $p < 0.05$) and stress factors (88.2% vs. 32.4%, $p < 0.001$) were also more frequent in group-S than in group-N. Fig. 1 shows the distribution of patients by CH history and worsening or new onset of TTH. Twelve patients (70.6%) reported worsening of TTH accompanied by HFS among 17 patients with a history of CH. Five patients (14.7%) reported novel onset of TTH accompanied with HFS among 34 patients without a history of CH. There was no significant difference of injection site (0.625–22.5 U of intramuscular injection per muscle) or total dosage of BoNT/A (20.73 ± 13.33 U vs. 17.07 ± 10.68 U) between the two groups.

3.3. Effect of BoNT/A therapy on headache

Twelve patients (70.6%) reported improvement of headache (degree and/or frequency) after BoNT/A therapy in group-S. Fig. 2 showed the transition of headache during the investigation