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Botulinum toxin alleviates dysphagia of patients with inclusion body myositis

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ABSTRACT

Objectives: Oropharyngeal dysphagia is a disabling and undertreated symptom that often occurs in patients with sporadic inclusion body myositis (s-IBM). In this study, we examined the effect of botulinum neurotoxin A (BoNT-A) injections to the cricopharyngeus muscle (CPM) of patients with s-IBM and dysphagia.
Patients, materials and methods: A single-center retrospective study involving 40 biopsy-proven s-IBM-patients treated in the District of Southwest Finland from 2000 to 2013. The incidence of dysphagia, rate of aspirations, rate of aspiration pneumonias and treatment results of dysphagia were analyzed. Patients treated for dysphagia were evaluated before and after surgery by video-fluoroscopy and/or using a questionnaire.
Results: Twenty-five of the 40 s-IBM patients (62.5%) experienced dysphagia. BoNT-A was injected a median of 2 times (range 1–7) in 12 patients with dysphagia. Before the injections 7 patients reported aspiration, none afterwards. The corresponding figures for aspiration pneumonia were 3 and 0. All of these patients had normal swallowing function 12 months (median, range 2–60) after the last injection.
Conclusion: BoNT-A injections to the CPM alleviate the dysphagia of s-IBM patients reversibly and appear to reduce the rate of aspiration effectively.

1. Introduction

Although sporadic inclusion body myositis (s-IBM) is a rare disease, it is the most common inflammatory myopathy in people over 50 years of age [1–2]. s-IBM has a male predominance and a reported overall prevalence of 1–71 per million inhabitants, depending upon the population, with a zenith of 139 per million inhabitants among people over 50 years [1–10]. The cause of s-IBM is unclear and it is refractory to immunosuppressive treatments [11–13].

Dysphagia is common among s-IBM patients: 40–86% of the patients report dysphagia [14–15]. The prevalence of dysphagia at least weekly in the healthy western population is 3% [16]. Presenting symptoms of s-IBM vary, sometimes dysphagia heralds the disease [12]. Dysphagia is probably underreported by the vast majority of s-IBM patients, because often experienced as an embarrassing symptom by the patients [17]. Nevertheless, dysphagia can be reliably diagnosed by asking the patient two simple questions: "Does food get stuck in your throat?" and "Do you have to swallow repeatedly to get rid of food?" [14,17–18]. There is no effective treatment to cure the disease, but there are various ways to alleviate the symptoms.

For decades, our department of otorhinolaryngology (ORL) has used cricopharyngeal myotomy and BoNT-A injections to treat cricopharyngeal dysphagia [19]. BoNT-A was introduced in 1989 by Schneider et al. [20] for patients with spasticity, hypertonia, or delayed relaxation of the upper esophageal sphincter (UES). In our experience, BoNT-A injections to the cricopharyngeus muscle (CPM) alleviate effectively the dysphagia symptoms, especially in s-IBM patients. Since there are only sparse case-studies reported on this treatment [21–25], we have summarized our promising results in this report.

2. Patients, materials and methods

The Ethics Committee of the Hospital District of Southwest Finland approved the study. In order to record all s-IBM patients within the Hospital District of Southwest Finland for evaluation and treatment of dysphagia, s-IBM patients were identified by a computer search of the electronic patient records in the Hospital District of Southwest Finland. The search terms "inclusion body", "IBM" and "inclusion body myositis", as well as the ICD-10 codes M60.8, M60.9 and G72.4 were used and the run was made by the Auria Biobank of the University of Turku, Finland. All patient records of patients treated between January 1, 2000 and December 31, 2013, who came up with these words, parts of these words, or the ICD-10 diagnosis codes were analyzed. The charts of these patients were evaluated for incidence of dysphagia and aspiration as

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well as aspiration pneumonia. The patients treated for dysphagia with BoNT-A injections were analyzed as a subgroup.

IBM diagnosis was always confirmed with a muscle biopsy. The histological biopsy for the diagnosis of IBM was routinely taken from the vastus lateralis muscle (n = 37), and the muscle biopsy findings were compatible with IBM according to the Griggs' or ENMC criteria [26–27]. The histological features for the diagnosis of IBM have been reported earlier [18]. If the vastus lateralis muscle was too atrophic, other muscle, such as anterior tibial or deltoid muscle was used (n = 3).

The s-IBM patients were referred to the ORL department for evaluation of dysphagia. They were examined by videofluoroscopic swallow study (VFSS, n = 10) and by endoscopy (n = 12). The inclusion criteria for BoNT-A-injection were age 18 years or more, biopsy-proven s-IBM, dysphagia, and CPM dysfunction documented by a videofluoroscopic swallow study (VFSS) or a tight CPM verified by rigid endoscopy. The diagnostic criteria of cricopharyngeal muscle dysfunction (CPD) by VFSS vary somewhat in the literature and range from the presence of a horizontal bar at the level of the cricoid cartilage in the posterior aspect of the barium column [28–29] to a cricopharyngeal bar that obstructs ≥50% of the lumen throughout the swallow (which is said to indicate defective opening of the UES) [29–30]. We used the latter as a criterion for CPD by VFSS. For VFSS, the patients were positioned upright for a lateral and anteroposterior view. Thin liquid barium and barium paste were administered three times at each of three volumes—3, 5 and 10 mL—as tolerated by the patient. All studies were recorded digitally for later review by a radiologist and the presence and the level of CPD was recorded.

Information on dysphagia was obtained either from a Deglutition Handicap Index (DHI) questionnaire [31] before and after treatments (filled in by 5/12 patients receiving BoNT-A injections), or from patient interviews during routine out-patient control visits or patient charts, in cases were DHI questionnaires were not available. In addition, each patient receiving the BoNT-A injection, was interviewed by telephone approximately 3 months after each treatment by the same physician who had administered the BoNT-A. If the patient had not returned the DHI questionnaire, the same questions or at least the two most important questions were asked verbally: “Does food get stuck in your throat” and “Do you have to swallow repeatedly in order to get rid of food” [14,17–18]. In addition, the patient was invited to contact the treating physician again when the symptoms of dysphagia returned and the patient had to change the diet from solid to liquid. To avoid unnecessary radiation burden, VFSS studies were repeated postoperatively only if the dysphagia persisted.

2.1. Botulinum toxin A (BoNT-A) injection

BoNT-A was obtained from Botox (onabotulinumtoxin-A, Botox/Vistabel, Allergan Inc., Irvine, CA, USA) as a freeze-dried lyophilized preparation. For clinical use, BoNT-A activity is defined in units, 1 unit representing the estimated median lethal dose for mice. Shortly before use, the 100 IU BoNT-A toxin was dissolved with 2 mL of 0.9% sterile saline solution (without preservative), then drawn into a 1 mL syringe with a dose equivalent to 50 IU/mL. Under general anesthesia and direct laryngoscopic guidance, the bulk of the cricopharyngeal muscle was identified dorsally (Fig. 1). The needle used for the BoNT-A injection is manipulated through a rigid endoscope (usually 300 × 12 × 16 mm in size). To avoid too superficial injection, a length of 20 mm of the tip of the needle was inserted in the cricopharyngeus muscle. If the injection is not intramuscular, BoNT-A may spread too widely, causing diffusion into adjacent pharyngeal musculature. If this happens, hoarseness or swallowing problems may ensue [32]. Botulinum toxin 0.4–0.5 mL, containing an equivalent dose of 20–25 IU of Botox per site, was injected into the left and right lateral sides and sometimes into the dorsomedial part of the muscle at an average total dose of 50 IU (Table 1, Figs. 1–3) [21].

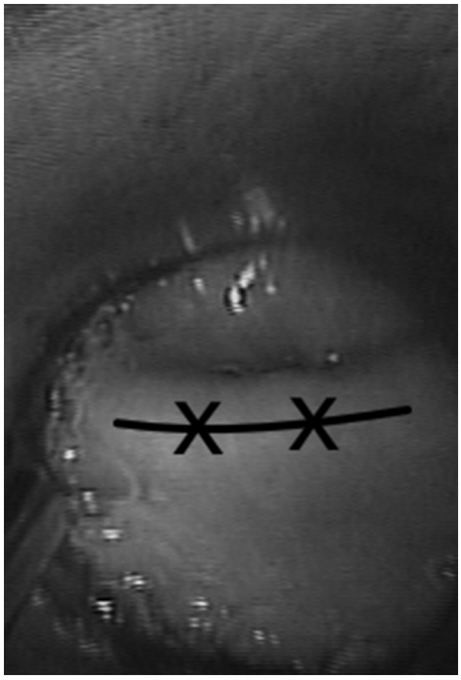

Fig. 1. Tight cricopharyngeus muscle (black curved line) seen through a rigid esophagoscope. The typical points of BoNT-A injection (black crosses) on the cricopharyngeus muscle.

3. Statistical methods

Data are expressed as mean and standard deviation, or median and range. The data was analyzed using the non-parametric Mann–Whitney *U* test because the variables were not normally divided. Values of $p < 0.05$ were considered statistically significant and are reported for the correlations; exact *p* values are reported unless $p < 0.001$. All analyses were conducted in IBM SPSS v. 23.0 software.

Table 1
The effect of botulinum toxin in the treatment of dysphagia in sporadic inclusion body myositis patients. The duration of time in months of the patient satisfaction to the dysphagia treatment was analyzed from the patient charts.

Gender	Age (years)	Aspiration pre	Dose (IU)	Aspiration post	Duration (months)
M	88	yes	50	no	8
F	83	yes	50	no	3
M	82	no	50	no	14
M	84	yes	50	no	8
F	75	no	50	no	6
F	76	yes	50	no	60
M	79	yes*	45	no	12
F	85	yes*	60	no	12
F	76	yes	50	no	12
F	89	no	50	no	14
F	93	no	40	no	2
M	99	yes*	55	no	6
Mean	84		50		14
Median	82		50		12
SD	7		5		15

M = male; F = female; aspiration pre = reported aspiration before Botox injection; yes = patient-reported aspiration; yes* = aspiration pneumonia reported/recorded in medical records; dose (IU) = the amount of botulinum toxin A (Botox, IU) injected to the cricopharyngeus muscle; aspiration post = reported aspiration after Botox injection; duration (months) = the number of months the patient was satisfied with the treatment of dysphagia; SD = standard deviation.