Injection of botulinum toxin A to the upper esophageal sphincter for oropharyngeal dysphagia in two patients with inclusion body myositis

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Inclusion body myositis (IBM) is a progressive degenerative skeletal muscle disease leading to weakening and atrophy of both proximal and distal muscles. Dysphagia is reported in up to 86% of IBM patients. Surgical cricopharyngeal myotomy may be effective for cricopharyngeal dysphagia and there is one published report that botulinum toxin A, injected into the cricopharyngeus muscle using a hypopharyngoscope under general anesthesia, relieved IBM-associated dysphagia. This report presents the first documentation of botulinum toxin A injection into the upper esophageal sphincter using a flexible esophagogastroduodenoscope under conscious sedation, to reduce upper esophageal sphincter pressure and successfully alleviate oropharyngeal dysphagia in two IBM patients.

Key Words: *Botulinum toxin A; Dysphagia; Inclusion body myositis*

Inclusion body myositis (IBM) is the most common acquired muscle disease occurring over the age of 50 years with a prevalence of four to nine per 1,000,000; it affects men twice as frequently as women (1). Dysphagia is a prominent feature of IBM, reported by up to 86% of patients; furthermore, patients with progressive dysphagia have a significantly worse functional class rating and poorer quality of life than patients with non-progressive dysphagia (2).

Cricopharyngeal myotomy (CM) is considered to be the surgical treatment of choice to alleviate dysphagia secondary to cricopharyngeal spasm (3). In five uncontrolled studies (4-8) of patients with IBM, eight patients were reported to show improvement in dysphagia following CM, while one patient showed no improvement (8).

Botulinum toxin A (BTA) injection into the lower esophageal sphincter is effective for the treatment of achalasia (9). The use of BTA to treat oropharyngeal dysphagia is less well studied. Uncontrolled reports indicated that injection of BTA into the upper esophageal sphincter (UES) improves dysphagia in a heterogeneous population of patients with

Injection de toxine botulinique de type A dans le sphincter supérieur de l'œsophage pour de la dysphagie oro-pharyngée chez deux patients atteints de myosite à inclusions

La myosite à inclusions (MI) est une maladie dégénérative et évolutive des muscles squelettiques, qui entraîne l'affaiblissement et l'atrophie des muscles tant proximaux que distaux. La maladie s'accompagne de dysphagie jusque dans 86 % des cas. La myotomie crico-pharyngienne chirurgicale peut s'avérer efficace pour traiter la dysphagie crico-pharyngée, mais la documentation scientifique fait aussi état d'un cas de dysphagie associée à la MI, soulagé par l'injection de toxine botulinique de type A dans le muscle crico-pharyngien, effectuée à l'aide d'un hypopharyngoscope, sous anesthésie générale. Le présent article décrit, pour la première fois, l'injection de toxine botulinique de type A dans le sphincter supérieur de l'œsophage, réalisée à l'aide d'un fibroscope œsophago-gastro-duodénal souple, sous sédation consciente, afin de diminuer la pression du sphincter supérieur de l'œsophage et de soulager efficacement la dysphagie oro-pharyngée chez deux patients atteints de MI.

cricopharyngeal muscle dysfunction (10-12). Only one patient reported in these studies had IBM – an 82-year-old patient whose dysphagia improved for 10 months after BTA injection into the cricopharyngeus muscle under general anesthesia using a hypopharyngoscope (12). We now report the successful treatment of oropharyngeal dysphagia in two IBM patients after BTA injection into the UES using a standard flexible esophagogastroduodenoscope under conscious sedation.

CASE PRESENTATIONS

Two patients with muscle biopsy-confirmed IBM (Table 1) had progressive dysphagia characterized by difficulty swallowing soft food, pooling of saliva, a sensation of food sticking in the back of their throat, choking with deglutition and frequent coughing. Neither had a history of aspiration pneumonia. Patient 1 reported weight loss from 98.2 kg to 79.5 kg over the previous year, whereas patient 2 reported no weight loss. Neither patient reported any medical illnesses, other than IBM, to account for their dysphagia. The dosage of their medications remained stable during the study and there was no

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TABLE 1
Summary of two patients with inclusion body myositis and dysphagia

	Patient 1	Patient 2
Age (years)	74	59
Sex	Male	Male
Duration of dysphagia (years)	4	7
Cricopharyngeal spasm*	No	Yes
UESP (mmHg)		
Pre BTA	32.1	145.0
Post BTA (% reduction)	13.5 (57.9%)	52.0 (64.1%)
Duration of response (months)	8	6.4
Follow-up period (months)	14	32

*Cricopharyngeal muscle spasm and hypertrophy was identified by videofluoroscopy swallowing study. BTA Botulinum toxin A; UESP Upper esophageal sphincter pressure

concurrent use of motility agents. Physical examinations in both patients were unremarkable, other than severe muscle atrophy and weakness affecting the quadriceps and the long finger flexors.

Videofluoroscopy in patient 1 demonstrated leakage with all test meal consistencies (Ultra R 100 to 2000, Therapex, Canada) and accumulation of the contrast material in the valvulae. There was minimal aspiration with the lower consistency contrast (Ultra R 250 and 100, Therapex, Canada) and the contrast was cleared with repeat coughing. Esophageal manometry was performed using a pull through technique with a multilumen, radial port esophageal manometry catheter (Dentsleeve A-E27-LOSS-1, Australia) and a water perfusion system (Nitrogen Gas Model PIP-3, Mui Scientific, Canada). The lower esophageal sphincter pressure (LESP) was measured using the Dentsleeve; whereas, the UES pressure (UESP) was determined by a pull through technique using circumferentially oriented ports. LESP, esophageal body motor profile and the average UESP (32.1 mmHg) were normal (Table 1). This motility study indicated that his dysphagia was due to oropharyngeal muscle incoordination and weakness, leading to an inability to overcome the normal physiological barrier at the UES.

Videofluoroscopy in patient 2 demonstrated cricopharyngeal muscle hypertrophy and spasm, poor contraction of the pharynx and poor coordination between the pharynx and the UES, causing a major impediment to the passage of a bolus. Esophageal manometry showed an elevated UESP of 145 mmHg, but normal LESP and esophageal body motility.

In both patients, esophagogastroduodenoscopy and BTA injection (Botox, Allergan, Canada) were performed under conscious sedation, using intravenous diazepam and meperidine. BTA (100 IU), dissolved in 5 mL of normal saline, was injected into four quadrants of the UES using a 7 Fr, 5 mm disposable varices injector (Wilson Cook Medical GI Endoscopy, LDVI-23, USA).

Patient 1 reported prompt improvement in dysphagia within 3 h of the procedure. Repeat esophageal manometry, 10 days after this BTA injection, demonstrated that the UESP had fallen from 32.1 mmHg to 13.5 mmHg. The first injection resulted in eight months improvement of his dysphagia; when his

swallowing worsened again, he had a second BTA injection which was unsuccessful due to technical difficulties, but a third injection, two weeks later, again produced prompt resolution of his dysphagia without recurrence, to date, at 14 months from the first injection.

Patient 2 reported improvement in dysphagia within 8 h of the first injection. Repeat esophageal manometry after his first BTA injection revealed a normalized UESP (52 mmHg). He had four subsequent BTA injections with satisfactory improvement in symptoms on each occasion; the average duration of response was 6.4 months (range 5 to 8 months). The total follow-up duration from his first injection was 32 months.

No side effects attributable to the BTA injection, including pain, throat discomfort, voice changes, coughing or choking, were reported by either patient.

DISCUSSION

Dysphagia has been reported in up to 86% of IBM patients (2), yet the data on how to treat dysphagia effectively in this patient population are extremely limited. This report is the first documentation of the successful use of BTA injection into the UES, using a flexible endoscope under conscious sedation, to improve dysphagia in two IBM patients. The average duration of response in these two patients was six to eight months.

Medical treatment of IBM is generally unsatisfactory. Immunosuppressive therapy is ineffective although intravenous immunoglobulin (IVIG) infusions may ameliorate dysphagia (13). A randomized, controlled trial of IVIG in 19 IBM patients did not demonstrate any significant benefit in improving limb muscle weakness (14); however, a recent report documented improvement in dysphagia in four IBM patients after treatment with IVIG (13). CM was first performed by Kaplan (15) and several subsequent studies have reported that CM can alleviate dysphagia secondary to cricopharyngeal spasm. However, the response to CM is inconsistent and the selection of appropriate candidates remains problematic (16). Experience with CM for IBM patients is limited to five uncontrolled studies, in which dysphagia improvement was reported for eight of nine patients (4-8).

Oropharyngeal dysphagia improved in five of seven patients after BTA injection into the cricopharyngeal muscle via a rigid hypopharyngoscope under general anesthetic (10) and, in another recent study, dysphagia improved for an average duration of 7.1 months in 12 patients who had UES dysfunction of varied etiology (11). The two IBM patients presented in this report had oropharyngeal dysphagia confirmed by a videofluoroscopy swallowing assessment and by the absence of other esophageal motor abnormalities on esophageal manometry. Patient 2 had an elevated UESP, which decreased from 145 mmHg to 52 mmHg after BTA injection; the improvement in dysphagia was probably due to decreased resistance to bolus transit across the UES. However, patient 1 reported the same degree of dysphagia as patient 2 despite a normal UES motor profile; in this case, oropharyngeal muscle weakness and incoordination impaired bolus transit across a normal UES, and BTA probably produced a reduction in UES pressure to subnormal levels.

This report presents the successful alleviation of oropharyngeal dysphagia in two IBM patients using BTA injection into the UES without unfavorable side effects. The procedure, performed using a flexible endoscope under conscious

sedation, offers a promising, less invasive alternative to surgical CM in this patient population. The efficacy and safety of BTA injection into the UES for the treatment of oropharyngeal dysphagia in patients with IBM should be confirmed in a formal, placebo controlled study.

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