Jaw-opening oromandibular dystonia secondary to Wilson's Disease treated with botulinum toxin type A

Distonia oromandibular com abertura da boca secundária à doença de Wilson tratada com toxina botulínica tipo A

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ABSTRACT

We have reported a case series of five patients with jaw-opening oromandibular dystonia secondary to Wilson's disease (WD), in which the patients were treated with botulinum toxin type A (BTX-A). In all cases, dystonia score was partially reduced three weeks after injections. The most common side effect was transient mild dysphagia. This preliminary study showed that jaw-opening oromandibular dystonia in WD may be partially responsive to the use of BTX-A.

Key words: Wilson's disease, focal dystonia, oromandibular dystonia.

RESUMO

Relata-se uma série de cinco casos de distonia oromandibular com abertura da boca, secundária à doença de Wilson, em que os pacientes foram tratados com toxina botulínica tipo A. Em todos os casos, a distonia oromandibular com abertura da boca foi parcialmente reduzida três semanas após as injeções. O efeito adverso mais comum foi a disfagia leve e transitória. Este estudo preliminar mostrou melhora parcial da distonia oromandibular com abertura da boca.

Palavras-Chave: doença de Wilson, distonia focal, distonia oromandibular.

Wilson's disease (WD), or hepatolenticular degeneration, is a rare autosomal recessive inherited disease of cupper metabolism, which presents with hepatic, psychiatric, and neurological symptoms[1-6]. The prevalence rate of WD is estimated to be one case per 30,000[1-6]. WD is caused by mutations to the gene coding for ATPase copper transporting beta polypeptide (ATP7B), which is located on chromosome 13, allowing the incorporation of copper into ceruloplasmin and its subsequent excretion into the bile[1,2,5-9]. Neurologic signs include Parkinsonism, dysarthria, tremor, dystonia (particularly craniofacial and oromandibular), and cerebellar abnormalities. The safest and most efficient form of pharmacological therapy remains a matter of debate and includes the use of D-penicillamine and zinc[1-6]. Generally, treatment improves most neurological symptoms and signs to a variable degree. However, dystonic forms, particularly, oromandibular dystonia (OMD), with jaw-opening, are particularly resistant to the treatment[1-6]. The objective of our study was to evaluate the effects of botulinum toxin type A (BTX-A) injections for the treatment of jaw-opening OMD in patients with WD.

CASES

We included five patients (three men and 2 women, mean age 27.2 years-old) with a genetically confirmed diagnosis of WD and neurological involvement. Mean follow-up was 8.6 years-old (Table). All cases presented disabling jaw-opening OMD (three patients had a worsening of OMD after use of d-penicillamine), refractory to other forms of clinical interventions, including anticolinergics (biperiden), baclofen, clonazepam, and tetrabenazine. BTX-A (Botox, Allergan, USA) was injected according to the following protocol: 35 units for each lateral pterygoid muscle (electromyography-guided intra-

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Table. Jaw-opening oromandibular dystonia secondary to Wilson's disease: demographics and botulinum toxin efficacy.

Patient	Age (years)	Gender (M:F)	Follow-up (years)	BFM Scale (Mouth) pre-BTX-A	BFM Scale (Mouth) post-BTX-A	Side effects: dysphagia
1	32	F	12	8	6	Mild
2	30	M	13	8	6	Mild
3	36	M	7	6	4.5	Mild
4	25	F	5	4.5	3	-
5	23	M	6	2	1.5	-
Mean	27.2	3:2	8.6	5.7	4.2	Mild

M: male; F: female; BFM: Burke-Fahn-Marsden; BTX-A: botulinum toxin type A.

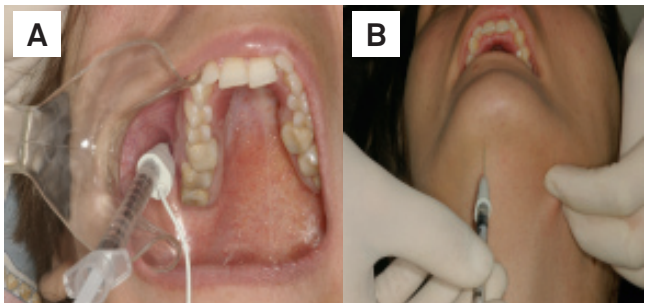

Fig 1. Botulinum toxin injection. (A) lateral pterygoid muscle; (B) submentalis muscle complex.

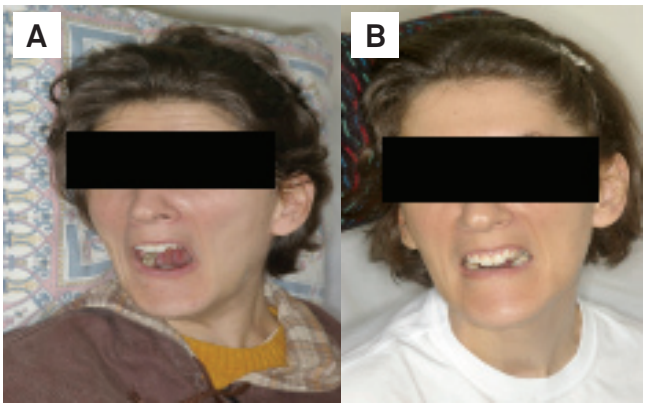

Fig 2. Patient 1 – jaw-opening oromandibular dystonia. (A) pre-botulinum toxin injection; (B) post-botulinum toxin injection.

oral injection); 30 units for the submentalis complex (total amount of BTX-A=100 units), as seen in Fig 1. Patients were assessed at baseline (when injections were performed), after three weeks and three months using the sub-item "Mouth" of the Burke-Fahn-Marsden Scale (BFMS=0–8 points)[10].

The scores for jaw-opening OMD were partially improved after using BTX-A in all cases, ranging from mean value of 5.7 (pre-BTX-A) to 4.2 points (post-BTX-A), as shown in Table and illustrated in Fig 2. Specific informed consent from the patient, for publication of all figures, was obtained. The most common side effect was mild transient dysphagia in three cases.

DISCUSSION

In the classical description of Samuel Kinnier Wilson on the progressive lenticular degeneration, different phenotypes were described, such as the dystonic (including a tremulous form) and Parkinsonian forms[11].

Since then, several additional clinical variants of neurological WD were documented, including the seminal David Marsden's manuscript, which classified WD into three clinical neurological forms: hyperkinetic form, with dystonic syndrome; ataxic form, with postural and intentional tremor associated with cerebellar ataxia; and a Parkinsonian form[3].

In a Brazilian series of 119 patients with WD published by Machado et al., the authors found that 69% of the patients had dystonia[12]. Dystonia in patients with WD is frequently focal, including blepharospasm, cervical dystonia, dystonic dysphonia, lingual dystonia, writer's cramp, and OMD. Segmental and generalized dystonia are less frequent in WD[6,13].

OMD is a rare focal form of dystonia, characterized by repetitive involuntary jaw movements, subdivided in jaw-opening or jaw-closing types. Symptoms may interfere with essential daily living activities, such as feeding, chewing, swallowing, and speaking[14-16]. This form of dystonia is often associated with blepharospasm (defining Meige's syndrome), and cervical dystonia (referred to as cranial-cervical dystonia). Jaw-closing OMD is caused by dystonic spasms of the masseter and temporalis muscles, leading to trismus and bruxism. Jaw-opening OMD is caused by dystonic contractions of lateral pterygoids, anterior belly of the digastric muscle, and submentual muscles[13].

Treatment of WD patients with OMD, particularly jaw-opening OMD, represents a challenging matter, which includes controversial opinions. Additionally, its occurrence has been linked to certain genotypes among the more than 400 mutations already described in the ATP7B gene[1,17-19], and to iatrogenic worsening of neurological manifestations, especially dystonia, in WD patients treated with d-penicillamine[5,6,20-22]. In our small series of WD patients with jaw-opening OMD, 60% had worsening of OMD dystonia after using d-penicillamine.

Pharmacological treatment of OMD includes medications such as anticolinergics (biperiden), tetrabenazine, baclofen and benzodiazepines (clonazepam), but the efficacy

falls below the acceptable one[13]. In general, BTX-A is an effective treatment option in patients with OMD[14]. Jaw-closing OMD is improved by toxin botulinum use in 85% of the patients. Frequently, jaw-opening OMD is less responsive than jaw-closing, and it is more likely to be associated with dysphagia and dysarthria[13-16].

Jaw-opening OMD, involving the injections of lateral pterygoid muscles, requires the use of electromyography, with needle electrodes, using an intraoral approach[16], and the use of BTX-A in the submentalis complex can improve the results[14-16,23]. In our series of Brazilian patients with WD and jaw-opening OMD, the use of BTX-A was performed with the participation of colleagues from the Department of Oral and Maxillofacial Surgery, with the objective of improving our results.

To date, there are no published studies about the use of BTX-A in jaw-opening OMD patients with WD. Our preliminary findings showed that BTX-A is partially effective (mild to moderate efficacy) in improving jaw-opening OMD in patients with WD, and the most common side effect was transient mild dysphagia, which occurred in 60% of our patients.

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