

Botulinum toxin A and trihexyphenidyl in treatment of meige syndrome: two case reports.

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Abstract

Meige Syndrome or Segmental Craniocervical Dystonia Syndrome is a rare variant of dystonia. It is clinically accompanied by dystonia in facial, masseter, and trapezius muscles together with symmetrical blepharospasm. Even though drugs such as anticholinergic, antidopaminergic, benzodiazepines, and tetrabenazine are used with botulinum toxin in its therapy, success of therapy is low and side effects are a lot when they are used alone. In this study, we reported two cases with Meige syndrome, that were a 60-year-old male patient and a 50-year-old female patient who had ongoing dystonia complaints even though they had previously received other therapies and then were successfully treated with a combined therapy of trihexyphenidyl, which is an anticholinergic, and Btx without any side effect. This rare clinical picture is mostly supposed to have a psychogenic origin. Also, it is mainly confused with entity tardive dystonia in differential diagnosis. Clinicians should be careful in order not to miss out diagnosis of Meige Syndrome or establish misdiagnosis like psychogenic movement disorders in differential diagnosis. It also should be kept in mind that chance of success for treatment of Meige Syndrome increases with combined medical therapies such as Trihexyphenidyl and Btx.

Keywords: Botulinum toxin A, Trihexyphenidyl, Treatment, Meige syndrome.

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Introduction

Meige Syndrome or Segmental Craniocervical Dystonia Syndrome is classified between Focal and segmental dystonia. It is clinically accompanied by dystonia in facial, masseter, and trapezius muscles together with symmetrical blepharospasm [1]. Meige Syndrome frequently starts in the 5th or 6th decades and is observed 3 times more in women than men [2]. Furthermore anxiety as a clinical entity that exacerbate motor symptoms in Meige syndrome [2]. Despite not having a clear pathogenesis, the pathology is thought to exist in upper brainstem and basal ganglions and idiopathic dopamine receptor supersensitivity is emphasized [3]. Even though drugs such as anticholinergic, antidopaminergic, benzodiazepines, and tetrabenazine are used in its therapy, success of therapy is low and side effects are a lot [4]. Botulinum toxin (Btx) is used for many dystonic movement disorders. Besides, its efficacy on treatment of Meige Syndrome is limited in many cases [1]. In this study, we represented two cases with Meige Syndrome who were successfully treated with a combined therapy of trihexyphenidyl, which is an anticholinergic, and Btx and without any side effect.

Method

Case 1

A 60-year-old male patient applied to our clinic with the complaint of blepharospasm and contraction in chin and neck for three months. It was stated that his complaints constantly continued throughout the day and increased in the moments of excitement and anxiety but disappeared in sleep. Biperiden 2 mg/day was recommended to the patient who was previously diagnosed with blepharospasm in another center. The patient could not use the drug due to its side effects. The patient was thought to have meige syndrome firstly because he had not only blepharospasm but also oromandibular dystonia. Laboratory examinations carried out towards etiology, Brain CT and MRI examinations were normal. 40 IU Botulinum toxin A was injected to bilateral orbicularis oculi and corrugator supercillii muscles because of blepharospasm and 50 IU Botulinum toxin A was injected to pterygoideus lateralis and digastricus muscles on both sides due to oromandibular jaw-opening dystonia. It was observed in the control that blepharospasm disappeared however oromandibular dystonia decreased but continued. Trihexyphenidyl 2 mg/ day was

started to be administered to the patient. Symptoms of Meige Syndrome were not observed in the patient in the follow-up. The patient observed with complete remission was followed up for 6 months as once every three months with Btx injection and trihexyphenidyl without any side effect.

Case 2

A 50-year-old female patient applied to our clinic with complaint of blepharospasm and jaw contradiction lasting for 1 year. She indicated that her complaints increased in stressful times. Sertraline 100 mg/day and clonazepam 2 mg/day were administered to her in another clinic by considering that current movement disorder was psychogenic but the patient did not benefit from this therapy. An increase was not observed in her complaints after the drugs patient took were discontinued gradually. Laboratory examinations on serum towards etiology, Brain CT and MRI examinations were normal. After trihexyphenidyl 4 mg/day was administered to the patient who was thought to have Meige Syndrome, a partial recovery was observed in blepharospasm but no change was observed in oromandibular dystonia. 30 IU Botulinum toxin A was injected to orbicularis oculi muscles because of blepharospasm and 50 IU Botulinum toxin A was injected to pterygoideus lateralis muscles due to oromandibular jaw-opening dystonia. It was seen in the control that blepharospasm disappeared; however, oromandibular dystonia decreased but continued. There upon, dystonia symptoms of the patient completely disappeared after trihexyphenidyl 8 mg/day was administered in controls. The patient has been followed up with Btx injections and trihexyphenidyl administered once every 3 months.

Discussion

We represented two cases with meige syndrome for whom complete remission was obtained with the combined therapy of Btx and trihexyphenidyl. Meige Syndrome is a rare variant of dystonia. It may take months-years for symptoms to settle or it may not progress more than a certain stage. It is typical for complaints to increase with stress, physical activity, and bright light [2]. Especially anxiety and other neurotic disorders may exacerbate motor fluctuations of dystonia syndromes like Meige Syndrome.

It can be supposed that this rarely seen clinical picture is mostly psychogenic. Also, it is mainly confused with entity tardive dystonia in differential diagnosis. It is not possible to make clinical distinction for most cases and history of neuroleptic use is considered the only criterion [5]. Tardive dystonia can also arise from increasing of plasma concentrations of antipsychotics due to combined drug use [6]. It was stated in a case report that dystonia recovered after sertraline was discontinued following craniocervical dystonia case appearing after use of antipsychotic (aripiprazole) and antidepressant (sertraline) and this was associated with increasing of aripiprazole's plasma level depending on inhibition of cytochrome p450 system by sertraline (6). Both of our cases did not use antipsychotic. In addition, while case 1 did not have a psychiatric symptom, case 2 had depressive

symptoms but the fact that dystonia did not recover after antidepressant and benzodiazepine were discontinued and a response was received from medication administered made the diagnosis of Meige Syndrome definitive.

Trihexyphenidyl, which is an anticholinergic agent, block outs acetylcholine in central muscarinic receptors. It is the only one anticholinergic agent that its efficiency was proven for all dystonia types in young patients [7]. Botulinum toxin which is produced by *Clostridium botulinum* bacteria shows action by blocking out release of acetylcholine from cholinergic synapses. Success of therapy for cervical dystonia, blepharospasm, and some other dystonia is high. In addition, its efficacy is limited in oromandibular dystonia due to its difficult administration technique and side effects causing dose increase [7]. In these case series, it was indicated that the combined therapy of trihexyphenidyl and Btx can be much more effective in treatment of meige syndrome when they were used alone. Efficiency of trihexyphenidyl is low in meige syndrome. However, it is considered to increase efficacy of Btx and cause extension of the activity time when it was used with Btx therapy [1]. In our cases, while success of therapy was low with only trihexyphenidyl treatment, success of therapy was very high when the combined therapy of Btx and trihexyphenidyl was administered.

In a study published in Japan, the combined therapy of aripiprazole, trihexyphenidyl, and Btx was administered to 3 cases with meige syndrome. While complete success of therapy was achieved in 2 of the cases, almost complete recovery was observed in 1 case [1]. Because complete remission was provided in our cases with the combined therapy of trihexyphenidyl and Btx, no additional drug was required. Deep Brain Stimulation (DBS) is efficiently used in recent years for treatment of Meige syndrome and has increased the chance of success. In cases for whom the response was not received from medical treatment, Globus pallidus internus (GPI) neurostimulation is applied [4]. DBS was not required in our cases because complete success of therapy was achieved with medical treatments in craniocervical dystonia syndrome.

Consequently, clinicians should be careful in order not to miss out diagnosis of rarely seen Meige syndrome or establish misdiagnosis like psychogenic movement disorders in differential diagnosis. It also should be kept in mind that chance of success for treatment of Meige syndrome increases with combined medical therapies such as Trihexyphenidyl and Btx.

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