Do not forget about Myasthenia Gravis when performing Botulinum Toxin injections

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Keywords: botulinum toxin, myasthenia gravis, ocular myasthenia gravis, cosmetic surgery, cosmetic treatment , side effects

Total words: 771

Total figures: 0

Total talbes: 0

All authors state that the manuscript is original, it has not been published before and it is not currently being considered for publication elsewhere.

All authors contributed equally to the manuscript preparation and revised the final version.

Conflict of interest: none.

Funding: none.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics statement: The patient has given written informed consent to publication of this manuscript.

Dear editor,

Botulinum toxin type A (BTA) is a neurotoxic protein produced by Clostridium botulinum, which causes transient flaccid paralysis by decreasing the presynaptic release of acetylcholine from the nerve terminals at the neuromuscular junction[1]. Nowadays BTA plays a role in the management of various medical conditions, including local dyskinesias and dermatological diseases, such as hyperhidrosis[2] and hidradenitis suppurativa[3,4], moreover it is widely used for cosmetic purposes, especially to decrease wrinkles of the superior third of the face[5]. Local injection of BTA is commonly performed by dermatologists for therapeutic or cosmetic purposes, it has an excellent safety profile and side effects are generally rare, usually related to local or systemic spread of the toxin[2,3,5,6].

We report here a case of a 51 year-old woman who developed right blepharoptosis and binocular horizontal diplopia after BTA injections for cosmetic purposes. Despite those are well known rare side effects of BTA injection[6], the case we describe is unusual because they were the first signs of a latent myasthenia gravis (MG). The patient has been affected with type 1 diabetes since childhood, for which she was in therapy with insulin. She was otherwise in quite good health, there was no history of muscle weakness or diplopia and she had never been treated with BTA injections before. Our patient had received cosmetic injection of BTA (Vistabex®;Allergan) to the glabellar, forehead, and lateral canthal rhytids (total of 38U in one session) two weeks before the symptoms onset. BTA treatment had been performed according to current recommendations with respect to target muscle selection. Except for right blepharoptosis and diplopia, the remainder of neurological and ophthalmological examinations were within normal limits. Blood tests were performed, including thyroid panel and myasthenia gravis panel(acetylcholine-receptor antibodies, muscle-specific-kinase antibodies and anti-low-density lipoprotein receptor-related protein 4 antibodies). They revealed mildly elevated titers of acetylcholine-receptor antibodies, thyrotropin receptor autoantibodies, triiodothyronine and thyroxine; whereas thyroid stimulating hormone was very low-titer. Whole body magnetic resonance did not revealed any abnormalities. A diagnosis of ocular MG associated with Graves' disease was made. The patient was treated with pyridostigmine and methimazole. A complete resolution of symptoms was obtained within 6 months.

We have reported herein a case of ocular MG unmasked by BTA injections for cosmetic purposes.

MG is an autoimmune disease targeting acetylcholine receptors located at the postsynaptic junction causing weakness and fatigability of skeletal muscles. Ocular MG is a subset defined as MG limited to the orbicularis oculis, levator palpebrae superioris, and extraocular muscles[7]. Both MG and BTA act at the neuromuscular junction, and the combination may increase the potency of BTA unmasking a latent MG.

To the best of our knowledge this is the fourth case of latent MG unmasked by BTA injections for cosmetic treatment.

The first case has been described by Glick et al. in 2013. They reported a case of a woman, in treatment with methotrexate for psoriasis, who developed binocular horizontal diplopia as first sign of MG after treatment with BTA. The patient had been already be treated with BTA before, the disease was unmasked when the dose was increased. They hypothesized that the patient's immunosuppression with methotrexate allowed her to tolerate lower doses.[8]

The second case was described by Azita Chegini in 2017: she described a 30-year-old woman presenting with blepharoptosis, diplopia, dysarthria, dysphagia, respiratory distress and muscle weakness after 3 times BTA injections during the previous months. Electromyography and laboratory tests confirmed the diagnosis of MG. Patient's condition was serious, it

required hospitalization in intensive care unit, mechanical ventilation and treatment with plasma exchange, intravenous immunoglobulin, prednisolone and amantadine.[9]

Timmermans et al. reported the third case in 2019: a 43-year-old man with unremarkable medical history started develop bilateral eyelid ptosis, binocular diplopia, dysphagia and generalized weakness six weeks after injection of BTA. Laboratory tests revealed a MG. The patient was treated with pyridostigmine but it took more than 6 months to complete resolve his symptoms.[5]

Other five cases of latent MG unmasked by BTA injections are also described, but in those cases BTA was used with therapeutic purpose for treatment of cervical dystonia, blepharospasm, and oromandibular dyskinesia.[5] All cases reported muscle weakness after BTA injections (diplopia, blepharoptosis, dysphagia, chewing muscles weakness, dyspnea, dysarthria, generalized weakness).[5]

Both, BTA and MG target the same neuromuscular structures, thus BTA can worsen a known MG or unmask a latent MG, and should be avoided in patients affected with MG. Although it is not practicable to perform screening through acetylcholine receptor antibodies or electromyography in all patients undergoing BTA injections, it is important to obtain an accurate medical history and perform a physical examination in all patients to identify possible sign or clinical data of MG. Finally MG should be suspected in all patients developing blepharoptosis, diplopia or other symptoms of muscular weakness after BTA administration.

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