

An Unexpected Result of Increased Cosmetic Anxiety: Botulinum Toxin Side Effect

İD Gözde Yılmaz Dursun¹, İD Hatice Nur Karakartal¹, İD Rukiye Aytekin Akdağ¹, İD Necmi Baykan¹, İD Ömer Salt¹

¹Department of Emergency Medicine, Kayseri City Hospital, Kayseri, Türkiye

Abstract

Botulinum toxin inhibits acetylcholine release at the neuromuscular junction, thereby reducing muscle contraction. Although it was initially used therapeutically to treat strabismus, its clinical role has expanded rapidly over the years and its range of use has expanded to include the treatment of various musculoskeletal, neurological disorders and dermatologic and cosmetic areas. A previously healthy 34-year-old woman presented to the emergency department with complaints of diplopia, slurred speech and generalized muscle weakness that started about 4 hours ago. The patient's medical history is negative for any surgical interventions. It was learned that the patient had her 4th botox procedure 6 days ago for wrinkles on the glabella, nasal tip and around the eyes. Following a 12-day inpatient stay, the patient was discharged to outpatient care as their symptoms improved. Treatment of side effects of botulinum toxin primarily involves administration of botulinum antidote, close neurologic and respiratory monitoring and supportive care. This case report presents a unique instance of systemic manifestations following facial botulinum toxin administration, diverging from the predominantly reported localized adverse effects in existing literature, thereby highlighting a potentially underrecognized spectrum of clinical presentations.

Keywords: Botulinum, deglutition disorders, diplopia

Introduction

The bacterium *Clostridium botulinum* produces botulinum neurotoxin (BoNT), the world's most powerful poison. BoNT blocks acetylcholine release at nerve terminals. This interrupts the communication from the nerve to the muscle fiber and reduces muscle contraction. Since its Food and Drug Administration (FDA) approval in 1989, BoNT has been used in many different areas beyond the conditions for which it was initially approved, such as facial movement disorders and strabismus (1). The most frequently reported adverse effects are local effects such as erythema, edema, bruising and are self-limiting. Serious side effects such as muscle weakness and allergic reactions may also be observed but are very rare. The incidence of complications increases in a dose-dependent manner. Complications are approximately 33 times more likely to occur in therapeutic cases compared to cosmetic cases (2). Reasons for side effects include the use of elevated doses of toxin than recommended or the use of unlicensed products (3). Treatment of botulinum toxin side effects primarily includes administration of botulinum antidote, close neurologic and respiratory monitoring and supportive care. Individuals suspected of having botulism should be hospitalized in the Intensive Care Unit (ICU) for close monitoring of their vital signs and rapid assessment

of their need for antitoxin treatment. The most important step of treatment is antitoxin administration and the earlier it is administered, the better the clinical response (2). As an anticholinesterase agent, pyridostigmine prolongs the action of acetylcholine by inhibiting acetylcholinesterase at synaptic sites, thus improving muscle strength in conditions characterized by impaired neuromuscular transmission (4). A retrospective review of patients experiencing significant adverse events, including dysphagia and dyspnea, after head and neck botulinum toxin injections demonstrated that pyridostigmine was well-tolerated and resulted in notable symptom improvement, indicating its potential in modulating more widespread effects (5). The purpose of this case report is to emphasize side effects of botulinum toxin, the use of which is increasing especially in the cosmetic field today, and its systemic effects and treatment process besides its local effects in the application area.

Case Report

A previously healthy 34-year-old woman presented to the emergency department with complaints of diplopia, slurred speech and generalized muscle weakness that started about 4 hours ago. The patient's medical history is negative for any surgical interventions. During the medical history taking,

Corresponding Author: Gözde Yılmaz Dursun

e-mail: beau_gozde@hotmail.com

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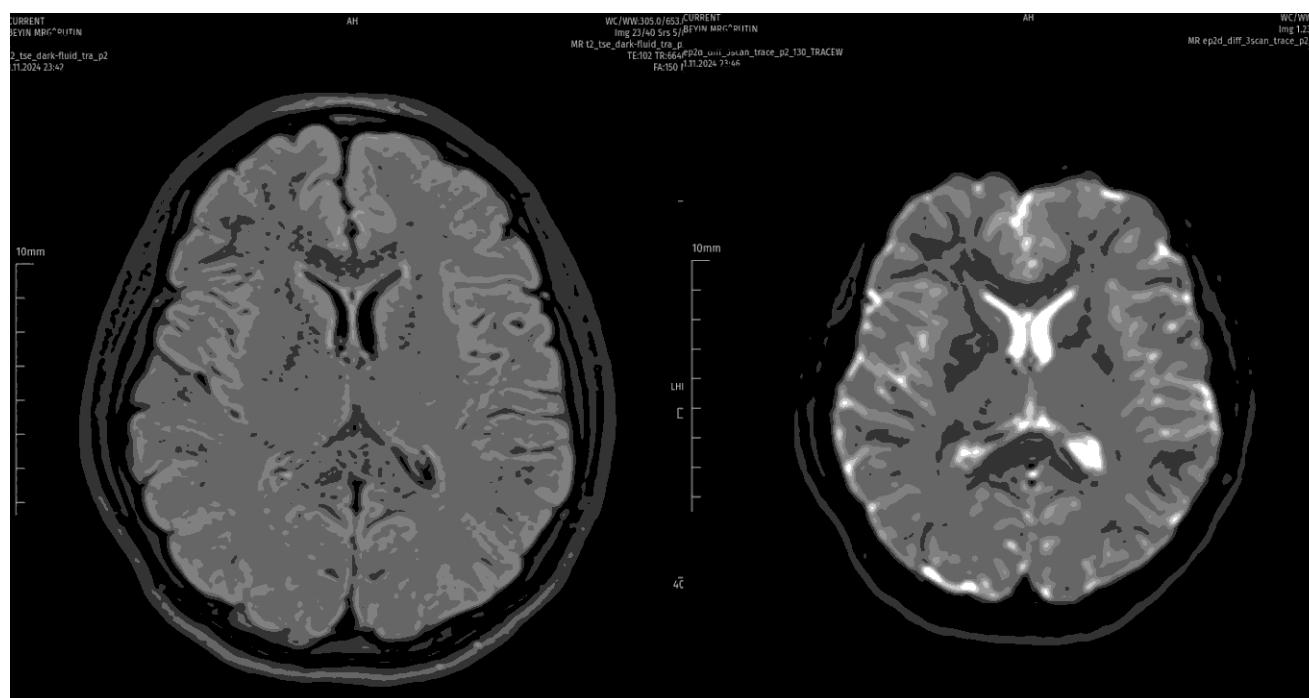


Figure 1. No pathological findings in patient's MRI

it was learned that she underwent botox procedure 6 days ago for wrinkles on glabella, tip of the nose and around the eyes. It was stated that this was the patient's fourth botox procedure. The patient's blood pressure was 117/76 mmHg, pulse rate: 96/min, saturation: 99%, temperature: 36.6 oC. No pathologic findings were detected on electrocardiogram (ECG). To comprehensively evaluate the patient's atypical presentation of systemic neurological symptoms following botulinum toxin administration, and to rigorously exclude alternative etiologies encompassing autoimmune neuromuscular disorders such as Myasthenia Gravis and inflammatory polyradiculopathies like Guillain-Barré syndrome, as well as acute cerebrovascular events including ischemic or hemorrhagic stroke, a thorough neuroimaging workup, including computed tomography (CT) and/or magnetic resonance imaging (MRI) (Figure-1) of the central nervous system, was promptly undertaken. Cranial imaging and blood tests were ordered to exclude a differential diagnosis; no pathology was found in these tests. The patient was consulted to a neurologist with a prediagnosis of BoNT side effect. Botulinum antidote was administered. Symptomatic supportive treatment was started. The patient was transferred to the ICU. 4*60 mg pyridostigmine was added to the intensive care unit treatment. On the second day of intensive care unit follow-up, dysphagia developed with progression in speech disorder. The patient's nutritional support continued with nasogastric tube. The intensive care period continued for 5 days and swallowing function improved. After the swallowing function improved, ward follow-up was initiated. After the patient's dysphagia and

diplopia were completely resolved and his speech disorder improved to a great extent, he was discharged after 7 days of ward follow-up and was discharged to outpatient care.

Discussion

The occurrence of pronounced systemic bulbar symptoms, specifically progressive dysphagia and diplopia, after routine facial botulinum toxin administration, as presented in this previously healthy 34-year-old woman, represents a rare observation in contrast to the prevailing literature focused on localized effects. The subsequent positive response to pyridostigmine therapy suggests a crucial role for cholinergic modulation in managing these less common systemic manifestations.

While local adverse events following cosmetic botulinum toxin administrations are commonly reported, systemic adverse events are considered rare. However, a recent systematic review (6) indicates the potential for systemic symptoms such as fatigue and muscle weakness. In rare instances, distant spread of the toxin has been associated with severe systemic effects, including dysphagia (7). This case report presents a novel instance of an unusual systemic reaction within the existing literature.

BoNT is a neurotoxic protein; it causes flaccid paralysis by inhibiting the release of acetylcholine neurotransmitter from axon terminals. Botulinum inhibits the exocytosis of acetylcholine (ACH) in the cholinergic nerve endings of motor nerves, preventing it from binding to the membrane

where the neurotransmitter can be released in the vesicle where acetylcholine is stored. BoNT exerts this effect through endopeptidase activity against SNARE (Soluble N-ethylmaleimide-sensitive factor Attachment protein REceptor) proteins (the protein required for ACH vesicle binding to the presynaptic membrane). The presence of acetylcholine stores in the synaptic cleft acts as a buffer that delays the effects of neurotoxins and therefore toxicity may take 24-48 hours to occur. In our case, toxicity symptoms appeared on the 6th day. The paralytic effect of neurotoxin continues until the axonal regeneration process required for the repair of damage to the neuromuscular junction is completed, and this period is generally estimated to be between 2-6 months (8, 9). In the case we presented, recovery was observed in a period of approximately 2 weeks from the onset of toxicity findings. This was probably because we started antidote treatment early after the toxicity findings were observed. Although it was initially used therapeutically to treat strabismus, its clinical role has expanded rapidly over the years and its range of use has expanded to include the treatment of various head, neck, gastrointestinal, urogenital, musculoskeletal, neurologic disorders and dermatologic and cosmetic areas (2). In the present case, it was detected that BoNT was used for cosmetic purposes rather than therapeutic purposes. According to the literature, our case is an example of the less expected side effects of Botox in cosmetic use compared to its therapeutic use. Botulinum toxin administration has demonstrated a favorable safety profile and high patient satisfaction rates. Pain, edema, erythema, ecchymosis and short-term hyperesthesia may be observed after botulinum toxin injection. These are general local side effects that may also occur after other drug injections (2). The most common complication of botulinum toxin administered to the glabella region is ptosis of the upper eyelid (blepharoptosis). The most prevalent side effects of BoNT injections in the lateral periorbital region are diplopia, transient strabismus, ectropion, lagophthalmus and xerophthalmia (2). The same side effects were observed in our case in accordance with the literature. Hoarseness, dysphagia and neck weakness may occur after BoNT injection. Dysphagia, xerostomia, neck weakness and dysarthria may occur as a result of high doses of botulinum toxin or its administration into deeper muscles. In a study, it was reported that dysphagia and odynophagia occurred in a significant proportion of patients with cervical dystonia who received BoNT injection (10). These side effects are more common in elderly patients. The reason is that higher doses of toxin are required in elderly patients and the toxin diffuses easily into the deeper muscles of the neck because of the decreased soft tissue in the neck. These complications take at least 3-4 weeks to heal and are very rare (10). In our case, these side effects were observed in a young patient and healed in a time compatible with the literature data.

Conclusion

This case report presents a unique instance of systemic manifestations following facial botulinum toxin administration, diverging from the predominantly reported localized adverse effects in existing literature, thereby highlighting a potentially underrecognized spectrum of clinical presentations.

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Declaration of Helsinki

This study was conducted in accordance with the principles outlined in the World Medical Association's (WMA) Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects.

Written informed consent to publish this case report (including all clinical information and any related images) was obtained from the patient.