Letter to Editor (Editöre Mektup)

A Case of Iatrogenic Botulism with a Toxin of Unknown Formulation

Bilinmeyen Formülasyonlu Toksinle İyatrojenik Botulizm Vakası

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Özet

Amaç: Botulinum toksini estetik ve terapötik pek çok alanda yaygın olarak kullanılan, genel olarak güvenli bir ajandır. Ancak önerilen dozların aşılması veya onaylanmamış/sahte ürünlerin kullanılması iatrojenik botulizme yol açabilmektedir. Bu olguda estetik amaçlı botulinum toksini uygulaması sonrası gelişen iatrojenik botulizm tablosu sunulmaktadır.

Olgu: Daha önce alın ve aksilla bölgelerine botulinum toksini uygulanan, 10 gün sonra ise ayak tabanına hiperhidroz nedeniyle tekrar enjeksiyon yapılan kadın hasta, son uygulamadan 5 gün sonra yaygın halsizlik, üst ekstremite proksimal kaslarında belirgin güçsüzlük, yutma güçlüğü, solunum yavaşlaması ve hafif pitoz yakınmaları ile başvurdu. Nörolojik muayenede bilinci açıktı, kraniyal sinirler sağlamdı; üst ekstremite proksimal kas gücü 4/5 idi. Solunum fonksiyonu stabildi. Klinik izlemde hastanın yutma fonksiyonları düzeldi, oral alımı sağlandı ve destek tedavisi ile taburcu edildi. Olgunun klinik seyri, botulinum toksininin sistemik yayılımı ile uyumlu değerlendirildi.

Sonuç: Bu olgu, standardizasyonu bilinmeyen veya sahte botulinum toksini ürünlerinin ciddi iatrojenik botulizm riskine yol açabileceğini göstermektedir. Estetik uygulamalarda ürün güvenilirliğinin sağlanması, doz ve uygulama protokollerine uyulması ve şüpheli durumlarda erken tanı-klinik yönetimin önem taşıdığı vurgulanmaktadır.

Anahtar Kelimeler: İyatrojenik botulizm, Toksin, Botulinum toksin

Abstract

Objective: Botulinum toxin is widely used for therapeutic and cosmetic purposes and is generally considered safe. However, exceeding recommended doses or using unapproved/counterfeit products may lead to iatrogenic botulism. This report presents a case of iatrogenic botulism following cosmetic botulinum toxin injections.

Case: A female patient received botulinum toxin injections to the forehead and axillae, followed by plantar injections for hyperhidrosis Ten days later, Botox was administered again to the soles of the feet for sweating. Five days after the last procedure, she developed progressive generalized weakness, marked proximal upper-extremity weakness, slowed breathing, mild dysphagia, and ptosis. Neurological examination revealed normal consciousness, intact cranial nerves, and 4/5 proximal upper-extremity strength. Respiratory function remained stable. During clinical follow-up, swallowing improved, oral intake was achieved, and the patient was discharged with supportive treatment. The clinical picture was considered consistent with systemic spread of botulinum toxin.

Conclusion: This case highlights the potential for iatrogenic botulism associated with counterfeit or non-standardized botulinum toxin products. Ensuring the authenticity of the toxin, adhering to recommended dosing protocols, and maintaining strict clinical oversight are essential for safe application. Early recognition and appropriate management of suspected cases are critical to prevent severe complications.

Keywords: Iatrogenic botulism, Toxin, Botulinum toxin

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Dear Editor,

All serotypes block the release of the essential neurotransmitter acetylcholine at the neuromuscular junction, causing muscle paralysis. Weakness caused by botulinum toxin A injection usually lasts for about three months. Botulinum toxins play a very important role, especially in the treatment of strabismus and focal dystonia, hemifacial spasm, various spastic movement disorders, headaches, hypersalivation, and hyperhidrosis. Cosmetological applications include a range of treatments, from correcting lines, wrinkles, and creases on the face, chin, neck, and chest area to dermatological applications such as hyperhidrosis. Botulinum toxin injections are generally well tolerated and have few side effects (1).

We present a case of botulism that was affected by Botox treatment of the forehead and axillae in an external clinic. Ten days later, Botox was administered to the soles of the feet for sweating. According to her statement, she received spinal anesthesia. 5 days after the last Botox treatment, complaints of weakness in the arms and general weakness occurred. About a week after the onset of these complaints, when the patient was at home, her breathing slowed, she had weakness in the proximal muscles, difficulty swallowing, and mild ptosis. The patient, whose complaints had increased over the past 2 days, contacted our emergency department with these complaints. She was taken to the hospital by car. With these complaints, the patient was consulted in the emergency room and admitted to the neurology clinic for further examination and follow-up care.

First examination revealed; no chronic illnesses were present in history. The patient was conscious, oriented, and cooperative. Light reflex was bilaterally positive. Cranial nerves were intact. Motor examination revealed that muscle strength in the proximal bilateral upper extremities was 4/5, distal was 5/5, and muscle strength in the lower extremities was bilateral 5/5. Deep tendon reflexes were normoactive; plantar responses were bilateral flexor. Uvula was in the midline, and there was no edema. The patient could swallow semi-solid liquid food.

The patient, who was admitted to the neurology clinic with the preliminary diagnosis of iatrogenic botulism and whose vitals had stable vitals. Swallowing functions improved, was fed orally, and monitored with spontaneous respiration and planned to be discharged. The patient, who had upper respiratory tract infection symptoms, was discharged with Amoxicillin 1 g / 2x1, mouthwash, and Mestinon 60mg 3x1 treatment. Infection, neurology outpatient clinic control was recommended; in terms of acetylcholine receptor antibody for underlying myasthenia gravis. And imaging will be checked.

Participant was included in the study voluntarily by obtaining their consent via a form.

Doctors who perform cosmetic procedures in their clinics use different types of botulinum toxin. Some doctors also stated; they perform sweating, masseter, and upper face botox at the same time. They also often attend conferences with courses and learn the maximum doses for these different types. At an international conference where botulism cases were discussed, the Ministry of Health's regulation on the subject is shown on screen, and the upper limits for each type of botulinum toxin are discussed. In the presentation, the upper limit for abobotulinum toxin was set at 2500 units of abobotulinum (Dysport) and 1000 units for onabotulinum toxin (Allergan-Botox) in the regulation of the Social Insurance Institution (2-5). In a publication where botulismus cases were collected, it was stated that the consumption should not exceed 500 units in a month (6).

Based on the recommended doses in the FDA botulinum toxin A catalogs, in a review article covering the studies on cases received abobotulinum toxin of unknown formulation, 33 of the 63 individual cases in the review had received doses that were on average 3.2 ± standard deviation (SD) 1.6 times higher than the recommended dose for the specific formulation of botulinum toxin A. For example, nine patients with the specific indication of spasticity all received onabotulinum toxin A at a higher dose than the FDA-recommended dose of 200 units (7,8). In the review, the symptoms those included were generalized weakness in 67.2 % and shortness of breath in 24.5 %. More than half of the cases were treated conservatively (57.1%). In terms of degree of impairment, 20.6% were minimally impaired, 60.3 % had generalized muscle weakness, 7.9 % had respiratory insufficiency requiring support, and 11.1 % had to be admitted to the intensive care unit. The mean time from injection to the onset of symptoms or signs of systemic muscle weakness was 10.9 ± 8.0 days, and the mean duration of symptoms was 3.1 ± 3.0 months (7).

In addition, the patients reported in the recent studies developed a syndrome similar to botulism after intramuscular injections of therapeutic doses of onabotulinum toxin derived from two different batches of the drug. In the first patient, these symptoms occurred after only one dose, while in the second patient, they occurred after five years of regular treatment with the toxin. Clinically detectable weakness was present in the extraocular, bulbar, trunk, and limb muscles, and EMG changes were recorded in all muscles tested. The muscle weakness and EMG changes resolved a few weeks later (8,9).

Given the otherwise excellent safety record of botulinum toxin products, an accidental overdose, possibly due to an unauthorised product or a change in procedure, would be a plausible explanation for the incident described here. This case demonstrates a previously unrecognised potential for large outbreaks of iatrogenic botulism, and there are several lessons to be learned. The systematic error that appears to have led to toxin overdose and subsequent botulism in patients needs to be elucidated so that it can be actively avoided in the future. At the very least, in light of the WHO's 2022 warning about a counterfeit product in Turkey (10). The regulatory mechanisms designed to remove counterfeit toxin products from the market may need to be reviewed. It is an unethical practice for clinics to use counterfeit botox products to make more profit.

We know that some antibiotics enhance the effect of Botox, but it is not really strong enough to have a toxic effect. Its mechanism of action, as with high doses of aminoglycosides, may prevent the release of acetylcholine at the neuromuscular junction and cause a botulism-like clinical condition (11). Previous use of antibiotics has not been reported in our case, but we recommend that doctors take a break of several days after taking antibiotics, depending on the half-life, which reduces the interaction to almost zero.

The Social Security institution revealed Botox toxic doses as 2500 units (5 ampoules) at a time for abobotulinum toxin (Dysport) and 1000 units for onabotulinum toxin (Allergan). In fact, it is emphasized that you do not have to worry about toxicity if you are using an approved product; however, there is a danger with unapproved (counterfeit) products because the number of units is not exactly known. Some of the products are specifically for abobotulinum toxin of unknown formulation, while the toxin dose is zero; in some cases, it is 255 times higher than it should be (12). About toxin poisoning cases, there is the poison control center, calling 114 in Türkiye. There are only 3 provinces in Turkey: Kayseri, Ankara, and Izmir. However, they are sending the antitoxin by ambulance if you are admitted to a hospital with an intensive care unit.

Conflict of interest: The authors declare no conflict of interest.

Informed consent: An informed consent form was taken from the participant.

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