CASE REPORT

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Iatrogenic Botulism Following Botulinum Toxin Injection in Palmar Hyperhidrosis: A Case Report

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Abstract

Botulinum toxin (BT) injection is commonly used for the treatment of hyperhidrosis, with palmar hyperhidrosis being a frequent indication. Although generally safe, rare cases of botulism following BT administration have been reported. It is a potentially serious complication of inappropriate administration of high doses with unlicensed product application; therefore, prompt recognition and appropriate management are crucial for satisfying outcomes. We present the case of a 28-year-old woman who presented with progressing clinical condition mimicking myasthenia gravis (MG). Diagnosis was confirmed through clinical examination, laboratory testing, neuroimaging, and electrophysiological findings. The aim of this case report is to highlight the importance of considering iatrogenic botulism in patients presenting with neurological symptoms, particularly weakness, ptosis, dysphagia, and dysarthria, and to underscore the utility of a MG treatment protocol in managing cases of iatrogenic botulism presenting late.

Keywords: Botulism toxin, iatrogenic botulism, muscle weakness, myasthenia gravis, palmar hyperhidrosis

INTRODUCTION

Botulinum toxin type A (BT-A) has grown across various medical fields, particularly neurology and dermatology, for both therapeutic and cosmetic purposes. It is used by a wide range of healthcare providers, including estheticians and specialists. Although generally safe, BT-A can occasionally cause iatrogenic botulism, a potentially life-threatening condition resulting from improper dosage or unlicensed products.[1] This condition can mimic symptoms of myasthenia gravis (MG) and include general weakness, difficulty swallowing, speech disorders, and double vision due to extraocular muscle involvement.[2] The symptoms related to impaired neuromuscular transmission can be observed with both BT-A and antiacetylcholine receptor antibodies.[3]

Here, a case of iatrogenic botulism diagnosed in a patient initially referred to the neurology department with symptoms resembling MG is presented.

CASE PRESENTATION

A 28-year-old woman with no significant medical history presented with weakness in her arms and legs, difficulty swallowing, double vision, and drooping eyelids. Two weeks earlier, she received 200 MU of BT-A (Dysport®) injection into both palms to treat excessive sweating. Neurological examination revealed bilateral ptosis, limited outward gaze on the left side, and peri-orbital muscle weakness. Despite these symptoms, her pupils were isochoric, and her direct and consensual light reflexes were normal. The patient also exhibited slurred speech, weak tongue and masseter muscles, dysphagia, and mild proximal extremity weakness. Laboratory tests and magnetic resonance imaging of the brain and cervical cord were normal. Electroneuromyography (EMG) revealed normal nerve conduction velocities, normal amplitudes of the compound muscle action potential, and no decrement in low-frequency repetitive nerve stimulation at 3 Hz in the facial

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nerves. Single-fiber EMG of the left orbicularis oculi showed impaired neuromuscular transmission with a mean jitter of 133 µs and 60% blocking. Acetylcholine receptor antibodies were negative. Based on these findings, the patient was diagnosed with iatrogenic botulism and treated with oral pyridostigmine (240 mg daily) and supportive therapy. Due to persistent proximal weakness, oral prednisolone was added at a dose of 1 mg/kg/day for 4 weeks. After 2 weeks, ptosis and periorbital muscle strength significantly improved. The patient still had mild nasal speech and weakness in the tongue, masseter, extremities, and neck retroflexion muscles. At the 2-month follow-up, the patient was only on pyridostigmine 120 mg daily, with normal neurological examination. Treatment was tapered and discontinued after 3 months. A written informed consent was obtained from the patient prior to the publication of this report and accompanying images.

DISCUSSION

Botulism is caused by neurotoxins, primarily serotypes A, B, E, and F, which are some of the most potent toxins known to be produced by *Clostridium botulinum*. However, this can also occur in other Clostridium species.[4] Although the lethal dose for humans is not precisely known, experimental animal studies suggest that the lethal dose of purified crystalline BT-A could be around 1 µg/kg in oral intake.[5] Although contaminated food is the most common source of botulism, botulism can also arise from wound colonization or aerosol exposure developed for biological weapon purposes.[6] In recent years, there has been an increase in iatrogenic botulism. Although the primary use of BT-A is therapeutic, treating conditions such as muscle dystonia, spasticity, hyperhidrosis, neurogenic bladder, strabismus, and various pain syndromes, the increase in iatrogenic botulism cases has been linked to the widespread use of high-dose BT-A injections, which are frequently employed for cosmetic applications.[7] Contributing factors include the utilization of unlicensed and inappropriate applications, such as those observed at events termed "botox parties". The circulation of unlicensed products with potentially dangerous contents has also increased due to increased global migration and trade.

Botulism commonly manifests as symmetric descending flaccid paralysis with notable bulbar palsies, frequently involving cranial nerve involvement.[8] Although rare, sensory involvement and even rarer, accompanying pain have been reported.[9] An important feature of iatrogenic botulism is that similar to the toxin's primary effects, its associated adverse effects are typically transient. The diagnosis of iatrogenic botulism hinges on the precise identification of recent BT-A injection history along with clinical manifestations.[10] The differential diagnoses mainly include Guillain-Barre syndrome, MG, stroke, and Eaton-Lambert syndrome.[11] It has been reported in the literature that masked MG can emerge following BT-A injections.[12] Hence, the diagnosis of MG was excluded based on the absence of characteristic clinical fluctuations, minimal abnormalities in EMG findings, and normal antibody levels.

Electrophysiological tests, including assessment of CMAP increment following exercise or high-frequency repetitive nerve stimulation, demonstrate high specificity and sensitivity in the diagnosis of botulism.[13] In contrast, a decremental response after low-frequency repetitive nerve stimulation can be observed, as in our case.[14] In botulism, compound muscle action potential values typically exhibit a decrease, while single-fiber electromyography often reveals increased jitter and blocks, as evidenced in our case.[15] It is noteworthy that exaggerated jitter and blocking were detected in asymptomatic subjects following therapeutic BT-A injections for various conditions. The sensitivity of single-fiber electromyography suggests its utility in detecting subclinical iatrogenic botulism.[16,17]

While awareness of the clinical signs and symptoms of botulism is critical for early diagnosis, there is no need to wait for confirmation of diagnosis via laboratory or electrophysiological tests to provide initial treatment. The rapid administration of antitoxin within the first 48 hours can significantly reduce respiratory complications and mortality.[8-11] Botulinum toxin (BT) is a key component of the treatment, and it neutralizes free circulating toxin by binding concomitant and irreversible.[18] Since supportive treatments have a crucial role in achieving a better response in addition to antitoxin therapy, it cannot reverse settled neurotoxicity. Pyridostigmine, which is commonly used to treat MG, has been investigated for the treatment of botulism, including iatrogenic cases. It works by inhibiting acetylcholinesterase, thus increasing the availability of acetylcholine at the neuromuscular junction. However, in some countries, limited antitoxin availability and high costs have represented critical issues in recent years. Given the critical 48-hour window for administration, emphasis is often placed on the use of pyridostigmine, despite it not being considered a first-line treatment.[19] As the symptoms persisted into the second week, antitoxin administration was not pursued, and treatment commenced with pyridostigmine alongside supportive measures.

Recovery involves axonal sprouting, new motor endplate growth, and protein regeneration, and complete recovery can take months. The recovery reaches a peak after 5-10 weeks in a mouse model.[13] Paralysis can persist for months, depending on factors such as the dosage and

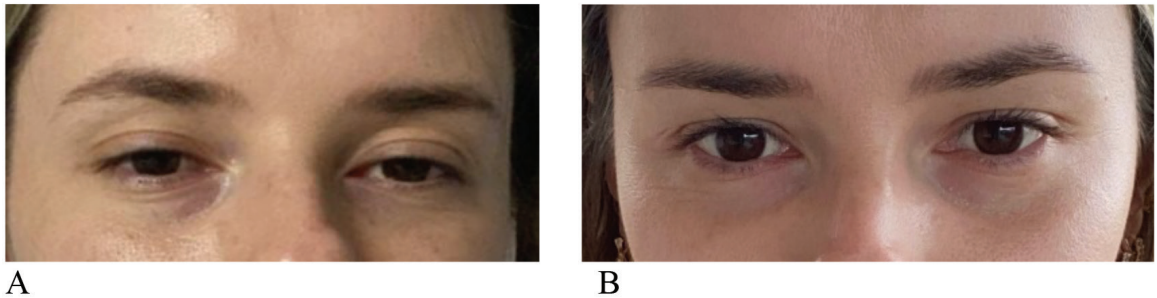

Figure 1. (A) Bilateral ptosis at presentation. (B) Improvement in ptosis at the end of eight weeks follow-up period (a written informed consent was obtained for using her images from the patient).

specific serotype of the toxin. Prolonged muscle paralysis can result in secondary effects, such as neuromuscular junction degeneration and muscle atrophy. Respiratory paralysis can persist for an extended period, sometimes for weeks or even longer. Chronic ventilation may be required in cases of persistent respiratory paralysis. However, prolonged mechanical ventilation poses significant risks of complications and comorbidities, including ventilator-associated pneumonia and other respiratory infections. Furthermore, prolonged ventilation can cause muscle weakness, atrophy, and psychological challenges for the patient.[20] Despite the absence of respiratory symptoms, full recovery was achieved in approximately 3 months.

This case underscores the importance of careful differential diagnosis in botulism, especially in distinguishing botulism from MG, and highlights the necessity of administering botulism-based antibiotherapy (BT-A) under appropriate conditions by experienced professionals.

Physicians and patients must be aware of the risks associated with the illegitimate use of unlicensed BT products. Physicians should ensure that they use only licensed products clinically to minimize potential complications and should include symptoms indicating possible complications clearly in their medical consent forms to protect themselves from medicolegal issues. Entities inappropriately marketing, selling, or using unlicensed BT products should be prosecuted and subjected to full criminal and civil penalties to protect the community from potential future issues.

MAIN POINTS

- With the increasing use of botulinum toxin, clinicians must identify the clinical manifestations of associated complications to facilitate prompt diagnosis and effective management.
- Strict adherence to approved formulations and professional guidelines is essential for safe and effective treatment.
- Iatrogenic botulism and neuromuscular disorders, such as myasthenia gravis can exhibit overlapping clinical presentations. This case underscores the importance of meticulous clinical assessment and the application of precise diagnostic methods to avoid misdiagnosis.

ETHICS

Informed Consent: A written informed consent was obtained from the patient prior to the publication of this report and accompanying images.

Footnotes

DISCLOSURES

Financial Disclosure: The author declared that this study has received no financial support.

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