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Iatrogenic botulism after botulinum meurotoxin exposure: A contemporary case series with clinical and electrophysiological insights

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Abstract

Backgorund & Objective: Iatrogenic botulism is a rare but potentially serious complication of botulinum neurotoxin (BoNT) use, increasingly recognized in association with cosmetic and therapeutic applications. This study aimed to describe the clinical characteristics, diagnostic challenges, electrophysiological findings, management strategies, and outcomes of patients with iatrogenic botulism. *Methods:* We retrospectively analyzed ten patients diagnosed with iatrogenic botulism who were evaluated and followed at a tertiary neurology center between 2019 and 2025. Demographic characteristics, indications for BoNT administration, time to symptom onset, initial clinical manifestations, electrophysiological findings, treatments, and clinical outcomes were systematically reviewed. *Results:* The cohort consisted predominantly of female patients, with therapeutic and cosmetic indications—most commonly migraine prophylaxis and facial aesthetic procedures—being the leading causes of BoNT exposure. Initial symptoms included cranial nerve involvement such as ptosis, diplopia, dysarthria, and dysphagia, frequently accompanied by generalized weakness, blurred vision, nausea, and vomiting. Electrophysiological studies revealed presynaptic neuromuscular junction dysfunction, characterized by low-frequency decremental responses and high-frequency or post-exercise incremental responses on repetitive nerve stimulation, as well as increased jitter on single-fiber electromyography. Treatment strategies included botulinum antitoxin administration and adjunctive pyridostigmine therapy, along with supportive care. Clinical outcomes were favorable in all patients, with gradual and complete neurological recovery observed over days to weeks.
Conclusion: This case series highlights the evolving clinical spectrum of iatrogenic botulism and emphasizes the importance of early clinical recognition, appropriate electrophysiological evaluation, and timely management. Increased awareness and stricter regulation of BoNT use are essential to prevent this potentially avoidable complication.

Keywords: Iatrogenic botulism, botulinum neurotoxin, electrophysiology, antitoxin, pyridostigmine

INTRODUCTION

Botulinum neurotoxin (BoNT) has become an integral component of contemporary neurological, rehabilitative, and cosmetic practice because of its capacity to induce targeted and reversible chemodenervation. Clinicians routinely employ BoNT for a wide spectrum of indications, including movement disorders, pain syndromes, hyperhidrosis, and aesthetic procedures. Over the past decade, the global use of BoNT—particularly for cosmetic purposes—has expanded markedly, driven by increasing demand and broader access to injection services across both medical and non-medical settings.[1,2] This rapid expansion has raised growing concerns regarding dosing practices, practitioner training, and overall patient safety. Iatrogenic botulism refers to systemic BoNT toxicity occurring as an unintended consequence of therapeutic or cosmetic administration of BoNT. The diagnosis is primarily clinical and is based on the temporal association between toxin exposure and the development of characteristic symptoms such as cranial nerve palsies, descending weakness, and autonomic dysfunction, supported by electrophysiological evidence of presynaptic neuromuscular junction dysfunction.[1,2]

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Parallel to the increasing use of BoNT, the number of reported cases of iatrogenic botulism has also increased. Systemic dissemination of BoNT following injection may produce a clinical syndrome indistinguishable from other forms of botulism, characterized by cranial nerve involvement, descending flaccid paralysis, and, in severe cases, respiratory compromise.[1-3] Recent surveillance reports indicate that cosmetic procedures account for a substantial proportion of iatrogenic cases, frequently associated with excessive dosing, use of unlicensed or counterfeit toxin preparations, or administration by inadequately trained individuals.[2,4] These observations underscore the emerging significance of iatrogenic botulism as a preventable patient safety and public health concern.

Despite growing awareness, the diagnosis of iatrogenic botulism remains challenging due to its rarity and clinical overlap with other neuromuscular junction disorders, including myasthenia gravis and acute neuropathies.[5,6] Moreover, BoNT exposure may unmask subclinical neuromuscular vulnerabilities, further complicating the diagnostic process. Laboratory confirmation of BoNT remains the diagnostic gold standard; however, available assays are limited in sensitivity and accessibility, making clinical recognition paramount.[7]

Between 2019 and 2025, patients with suspected iatrogenic botulism were evaluated and followed at our neurology center. Given these challenges, well-characterized case series are critical for enhancing clinical recognition, guiding diagnostic strategies, and informing therapeutic decision-making. The present series aims to describe the clinical features, diagnostic pathways, management strategies, and outcomes of patients with iatrogenic botulism following BoNT exposure. By doing so, we aim to contribute to the evolving evidence base on this preventable condition and provide practical insights for clinicians and public health authorities.

METHODS

Study design and setting

This study was designed as a retrospective case series based on routine clinical practice. We reviewed consecutive patients diagnosed with iatrogenic botulism who were evaluated and managed at a tertiary referral neurology center between January 2019 and December 2025.

Participants

Patients were eligible for inclusion if they had a documented history of BoNT exposure for cosmetic or therapeutic purposes and subsequently developed clinical features consistent with systemic BoNT toxicity. Diagnosis was established based on the temporal relationship between BoNT administration and symptom onset, characteristic clinical findings, and supportive electrophysiological evidence when available. In the present study, the diagnosis of iatrogenic botulism was established based on three criteria: (1) Documented exposure to BoNT; (2) Compatible clinical manifestations such as cranial neuropathies and descending weakness, and (3) Supportive electrophysiological findings and exclusion of alternative diagnoses.

Data collection

Clinical and demographic data were obtained through a retrospective review of medical records. Collected variables included age, sex, indication for BoNT injection, estimated dose when available, injection site, time from injection to symptom onset, initial neurological manifestations, electrophysiological findings, treatment modalities, need for respiratory support, and clinical outcomes. Information regarding the administered BoNT dose and prior exposure to BoNT was recorded whenever available. In cases where injections were performed outside medical institutions, the exact dose could not be reliably obtained. All data were anonymized prior to analysis.

Electrophysiological assessment

Electrophysiological evaluations were performed using standard techniques. Repetitive nerve stimulation (RNS) was conducted at low frequencies (2–3 Hz) and high frequencies (20–60 Hz), as well as following brief exercise, to assess neuromuscular junction transmission. Single-fiber electromyography (SFEMG) was performed in selected cases when clinically indicated. Electrophysiological findings were interpreted by experienced neurophysiologists and were considered supportive of iatrogenic botulism when they demonstrated features of presynaptic neuromuscular junction dysfunction, such as post-exercise or high-frequency facilitation and increased jitter.

Treatment and follow-up

Management strategies, including administration of botulinum antitoxin, acetylcholinesterase inhibitors, and supportive care, were determined by the treating clinicians based on clinical severity and progression. Patients were monitored during hospitalization and followed until clinical recovery. Follow-up data were obtained from outpatient visits or telephone interviews when necessary.

Ethical considerations

This retrospective case series was conducted using anonymized clinical data obtained from routine medical care. In accordance with national regulations and institutional policies, formal ethics committee approval was not required. The study was conducted in compliance with the Declaration of Helsinki. Written informed consent for participation and publication of clinical details was obtained from all patients.

THE CASES

Patient 1

A 42-year-old woman underwent cosmetic injection of BoNT type A to the glabellar and lateral canthal rhytids. Within 24 hours, she developed bilateral ptosis, binocular diplopia, and mild dysphagia. The patient presented to the emergency room with these complaints. The patient was admitted to the neurology ward with a preliminary diagnosis of iatrogenic botulism, and Electromyography (EMG) was planned. On the second day of hospitalization, the patient developed rapidly progressing respiratory distress. Other etiologies that could cause respiratory distress were ruled out. Electrodiagnostic studies were limited by the very early stage of symptom onset. Repeated nerve stimulation, electromyography, and nerve conduction studies were within normal limits. She was monitored in the hospital and treated with botulinum antitoxin (BAT) and intravenous immunoglobulin. The exact dose of BoNT administered during the cosmetic procedure was not available in the medical records as the procedure had been performed at an external cosmetic center. The patient did not require endotracheal intubation or mechanical ventilation. Intravenous immunoglobulin was administered at a total dose of 2 g/kg divided over five days. She received symptomatic therapy, leading to full recovery over a week. Early antitoxin administration and intensive monitoring prevented progression to severe neurological symptoms, emphasizing the value of timely intervention.

Patient 2

A 55-year-old man received BoNT injections for the treatment of cervical dystonia. For the treatment of cervical dystonia, the patient received a second injection of AbobotulinumtoxinA at a dose of 150 International Unit (IU) per affected muscle. Two days post-injection, he presented with dysarthria, generalized weakness, and mild respiratory compromise. EMG confirmed neuromuscular junction involvement. On physical examination, the patient's vital parameters were stable and within normal ranges. Neurological assessment revealed; hypophonic and slowed speech, reduced muscle strength graded as 3/5 in head flexion, arm abduction, shoulder elevation, and lower limb movements, while deep tendon reflexes were preserved. Electrodiagnostic studies revealed:normal compound muscle action potentials (CMAP) in the right and left tibial and fibular nerves, and also normal sensory nerve action potential (SNAP) amplitudes in the lower extremities (right sural and right superficial fibular nerves). High Frequency- Repetitive Nerve Stimulation (HF-RNS) (30-40-60 Hz) (HF-RNS, from the right ulnar nerve to the abductor digiti minimi, from the median nerve to the abductor pollicis brevis, from the radial nerve to the anconeus, and from the fibular nerve to the tibialis anterior) showed an amplitude increase of at least 15% in several muscles; the maximum value was 60%; all increases showed a progressive pattern. During contraction, motor unit action potentials (MUAPs) were polyphasic, high-amplitude, and the contraction was reduced. Following the diagnosis of iatrogenic botulism, the patient was treated with a single vial of heptavalent BAT. Within 48 hours after administration, a marked improvement in dysarthria and speech clarity was noted, along with resolution of muscle weakness. On follow-up examination, muscle strength was assessed as full (5/5).

Patient 3

A 42-year-old woman presented to the neurology outpatient clinic 17 days after the onset of

diplopia, blurred vision, and impaired facial gestures and expressions. These symptoms developed on the fourth day following a cosmetic procedure involving BoNT injections to the forehead, periorbital, and perioral regions at a cosmetic center.

On neurological examination, bilateral ptosis was observed, with no other focal neurological deficits. HF-RNS EMG demonstrated a significant incremental response (50–60%) at high-frequency stimulation (40 Hz) as well as with double stimulation, findings consistent with a presynaptic neuromuscular transmission disorder.

Given the gradual spontaneous improvement of symptoms over time and the relatively low estimated dose of BoNT (approximately 50 IU), botulinum antitoxin therapy was not administered. During follow-up, the patient showed continuous clinical recovery, and all neurological symptoms had completely resolved by day 30.

This case is presented as an example of iatrogenic botulism with spontaneous resolution.

Patient 4

A 38-year-old man, who had received 50 IU of AbobotulinumtoxinA in each axilla for hyperhidrosis, was admitted to the hospital 7 days later with complaints of arm weakness and limitation of abduction and adduction; neurological examination revealed neck flexion, extension, and bilateral upper extremity muscle strength of 4-/5, and he single-breath count of 28.

In an EMG study performed 10 days after injection, normal CMAP and SNAP amplitudes and nerve conduction velocities were found in the right and left median, ulnar, and axillary nerves;In repetitive stimulation starting at low frequency and increasing to high frequency (from the right ulnar nerve to the abductor digiti minimi, from the median nerve to the abductor pollicis brevis, and from the axillary nerve to the deltoid) increased amplitudes were detected.Post-exercise CMAP increase (tested in eight muscles) was observed. Rest-state needle examination revealed mild myokymia and fibrillation in the deltoid muscle, one of the two upper extremity muscles tested. During contraction, MUAPs were sometimes polyphasic, high-amplitude, and decreased in contraction. Supportive care resulted in gradual symptom resolution over ten days.

Patient 5

A 60-year-old man received BoNT injections for post-stroke spasticity involving the upper and lower limb flexor muscles; a total of 450 IU of OnabotulinumtoxinA was administered as the first dose. Within 48 hours of treatment, he developed dysphonia, proximal muscle weakness, and mild respiratory difficulty. He was initially misdiagnosed with acute neuropathy.

Electrophysiological evaluation demonstrated marked incremental responses (50–60%) on HF-RNS (40 Hz) and after brief exercise, findings indicative of a presynaptic neuromuscular transmission disorder. There was no significant decrement on LF-RNS, and sensory nerve conduction studies were normal. Additionally, motor nerve conduction velocities, distal latencies, and F-wave responses were preserved, with no evidence of conduction block or temporal dispersion. These findings argued against acute inflammatory demyelinating polyneuropathy or axonal polyneuropathy, in which abnormalities of nerve conduction parameters and F-wave responses are typically observed.

Taken together, the electrophysiological pattern was inconsistent with postsynaptic disorders such as myasthenia gravis, which characteristically demonstrate low-frequency decrement, as well as with acute polyneuropathy, and instead supported the diagnosis of systemic BoNT –induced presynaptic neuromuscular transmission failure.

Given the clinical and electrophysiological suspicion of systemic BoNT toxicity, heptavalent BAT was administered intravenously as a single standard dose during the early phase of symptom progression, in line with current recommendations emphasizing early administration to neutralize circulating toxin before irreversible synaptic binding occurs. The patient was closely monitored in the intensive care unit for potential respiratory compromise. Following antitoxin therapy, neurological symptoms gradually improved, and the patient achieved full recovery over a four-week period. This case underscores the importance of recognizing systemic BoNT toxicity and initiating timely antitoxin therapy, even after therapeutic doses.

Patient 6

A 50-year-old woman underwent BoNT injections for the treatment of axillary hyperhidrosis, with additional injections into the masseter muscles

for bruxism. The day following the procedure, she developed mild facial weakness, ptosis, and generalized limb fatigue, without evidence of respiratory compromise.

Electrophysiological studies revealed subtle incremental responses on HF-RNS, consistent with mild presynaptic neuromuscular transmission involvement. There was no decrement on LF-RNS, and routine motor and sensory nerve conduction studies were normal, excluding a postsynaptic disorder such as myasthenia gravis and acute polyneuropathy.

Given the mild and non-progressive nature of symptoms, the patient was managed conservatively with close outpatient follow-up and supportive care, without administration of BAT. Symptoms gradually resolved, and the patient achieved complete recovery within two weeks. This case illustrates that even localized BoNT injections for hyperhidrosis and bruxism can rarely result in systemic manifestations, underscoring the importance of clinical vigilance following treatment.

Patient 7

A 47-year-old man received BoNT injections for the treatment of chronic migraine. Three days after the procedure, he developed generalized muscle weakness, blurred vision, and dysphagia. He was hospitalized for close neurological and respiratory monitoring.

Electrophysiological studies demonstrated a presynaptic neuromuscular transmission defect, characterized by significant incremental responses on HF-RNS up to 60 Hz and after brief exercise, with no decrement on LF-RNS. Motor and sensory nerve conduction studies were otherwise normal, with preserved conduction velocities and F-wave responses. These findings supported a diagnosis of systemic BoNT–induced presynaptic dysfunction rather than a postsynaptic disorder such as myasthenia gravis or an acute polyneuropathy.

In accordance with current recommendations emphasizing early neutralization of circulating toxin, heptavalent BAT was administered intravenously as a single standard dose. Despite stabilization of symptoms following antitoxin therapy, residual neuromuscular transmission impairment persisted. Therefore, oral pyridostigmine was initiated as adjunctive symptomatic treatment, aiming to enhance acetylcholine availability at the neuromuscular junction. Following combined therapy, the patient showed progressive clinical improvement and achieved complete recovery within three weeks.

This case highlights the preventable nature of iatrogenic botulism, the importance of early electrophysiological evaluation to guide management, and the potential role of acetylcholinesterase inhibitors as supportive therapy after antitoxin administration.

Patient 8

A 33-year-old woman presented to the emergency room of a different hospital with complaints of newly developed shortness of breath and chest discomfort. Her medical records indicated progressive fatigue and weakness in both her upper and lower extremities for the past five days, and blurred vision that had started the day before. Neurological examination revealed hypophonia and slowed speech; muscle strength testing showed weakness in 3/5 of head flexion, shoulder abduction, and proximal movement of both upper and lower extremities; deep tendon reflexes were preserved.

Based on the initial clinical presentation, a neurology team from a different neurology clinic considered a preliminary diagnosis of myasthenia gravis and initiated pyridostigmine treatment on the patient. The patient, who showed no significant clinical improvement despite treatment, was referred to our clinic after an increase in swallowing difficulties, double vision, bilateral eyelid drooping, and shortness of breath was detected within 24 hours, and was admitted to the intensive care unit for close monitoring.

A more detailed medical history revealed that the patient had undergone a gastric BoNT type A injection procedure approximately four days before the onset of visual symptoms. It was learned that a total of two vials (total dose ~1000 units) of BoNT were administered during the procedure. The patient underwent the procedure twice. In light of this information and the evolving neurological findings, a diagnosis of iatrogenic botulism was considered. Accordingly, the patient was treated with a single vial (10–22 mL) of heptavalent BAT.

Clinical improvement became evident within 12–24 hours following antitoxin administration. Diplopia and dysphagia regressed, speech quality improved, and both ptosis and generalized muscle weakness resolved. Muscle strength returned to full power (5/5) in all tested muscle groups. The

patient's oxygen requirement diminished within 24 hours, and neither noninvasive nor invasive ventilatory support was required. She was discharged two days after receiving antitoxin therapy.

Single-fiber electromyography (SFEMG), performed two days after antitoxin administration and three days after initiation of pyridostigmine, demonstrated findings consistent with neuromuscular junction transmission impairment at the motor end plate level. At an eighth-week follow-up conducted via telephone, the patient reported complete resolution of all symptoms, confirming full clinical recovery.

Patient 9

A 49-year-old female patient presented to the neurology outpatient clinic with complaints of progressive dysphagia and dysarthria that had started approximately 7 days earlier. According to the medical history obtained from the patient and her relatives, she had received bilateral masseter muscle injections of a "BoNT six-peptide lyophilized powder" at a non-medical institution approximately one week prior to admission; the exact dose was unknown. Pain at the injection site developed the day after the procedure.

Several days later, she experienced the sudden onset of bilateral ptosis, dysphagia, dysarthria, and generalized myalgia. As her symptoms gradually began to improve, she presented late to the neurology outpatient clinic rather than the emergency department.

On neurological examination, vital signs were within normal limits. Cranial nerve examination revealed bilateral ptosis (right palpebral fissure 3 mm, left 4 mm), with normal pupillary light reflexes and full extraocular movements in all directions. Mild dysarthria was noted. Motor examination showed proximal muscle strength of grade 4/5 and distal strength of grade 4-/5 in all extremities. Sensory examination and deep tendon reflexes were normal.

Electrophysiological evaluation, including repetitive nerve stimulation, revealed no pathological findings. Laboratory and imaging studies were unremarkable.

Based on the temporal relationship between BoNT exposure, the characteristic pattern of bulbar and proximal muscle weakness, and the exclusion of alternative diagnoses, a clinical diagnosis of iatrogenic botulism was considered. As the patient's symptoms were already improving at presentation, no specific antitoxin treatment was administered. During follow-up, spontaneous and complete clinical recovery was observed. Spontaneous complete recovery was observed approximately two weeks later.

Patient 10

A 38-year-old woman was referred to our hospital in Çorum from an external center with a preliminary diagnosis of suspected infectious botulism, despite the absence of fever. She presented with several days of bilateral ptosis, blurred vision, nausea, vomiting, dysphagia, dysarthria, and generalized fatigue. Her medical history revealed that she had received BoNT injections for migraine prophylaxis approximately ten days before symptom onset; the procedure was performed outside a medical institution, and the administered dose was unknown.

At the outside hospital, although no fever or clear signs of systemic infection were present, the combination of gastrointestinal complaints and progressive bulbar symptoms raised concern for an infectious neurological process, and botulism was considered in the differential diagnosis. However, due to diagnostic uncertainty, the patient was referred to our center for definitive evaluation and management.

The patient was admitted to the Neurology Department in Çorum. On neurological examination, bilateral ptosis and mild dysarthria were observed. Pupillary light reflexes were preserved, and extraocular movements were full. Motor examination demonstrated predominantly proximal muscle weakness, while sensory examination and deep tendon reflexes were normal.

Electrophysiological studies were performed to evaluate neuromuscular transmission. LF-RNS (2–3 Hz) demonstrated a reduced CMAP amplitude, while HF-RNS (20–50 Hz) and post-exercise facilitation revealed a significant incremental response exceeding 50%, findings that are characteristic of presynaptic neuromuscular junction disorders such as botulism, as described in the literature. These electrophysiological features reflect impaired acetylcholine release from the presynaptic terminal and are considered supportive of the diagnosis.

Based on the characteristic clinical presentation, exposure history, and confirmatory EMG findings, a diagnosis of iatrogenic botulism

was established. The patient was treated with botulinum antitoxin, followed by oral pyridostigmine for symptomatic management. She showed progressive clinical improvement, and complete resolution of neurological symptoms occurred within 14 days of symptom onset, with no residual deficits on follow-up.

Written informed consent was obtained from all patients for publication of their clinical details and any accompanying images. The study was conducted in accordance with the principles of the Declaration of Helsinki. A summary of all cases is presented in Table 1.

DISCUSSION

In this case series, patients diagnosed with iatrogenic botulism exhibited clinical features consistent with systemic BoNT exposure, including prominent cranial nerve involvement and generalized muscle weakness. Across our cohort, cranial nerve involvement—including ptosis, diplopia, dysphagia, and dysarthria—emerged as an early and dominant feature, frequently preceding the development of generalized or proximal limb weakness. The preservation of deep tendon reflexes in several patients further supported a presynaptic neuromuscular junction disorder rather than a primary neuropathic process. These findings are consistent with contemporary literature showing that the clinical phenotype of iatrogenic botulism closely resembles that of foodborne and wound-associated botulism, regardless of the route of toxin exposure.[1,8] The temporal relationship between BoNT administration and symptom onset observed in our cases further supports a causal association.

Recent studies published between 2021 and 2025 have increasingly highlighted cosmetic BoNT injections as the predominant source of iatrogenic botulism. Surveillance data and outbreak investigations from Europe, the United Kingdom, and Asia indicate that excessive dosing, use of unlicensed or counterfeit toxin preparations, and administration by non-medical practitioners are the principal contributors to systemic toxicity.[4,9,10] In our series, cosmetic and medical indications—including glabellar, periorbital, masseter, and migraine-related injections—accounted for a substantial proportion of cases. Therapeutic indications such as cervical dystonia, post-stroke spasticity, hyperhidrosis, chronic migraine, and gastric BoNT-A injections were also represented, underscoring that systemic toxicity may occur even after approved medical uses when high doses or susceptible patient factors are present. Our findings align with these observations and reinforce the notion that iatrogenic botulism is largely preventable through regulatory enforcement and standardized clinical practice.

Diagnostic delay remains a significant challenge in the management of iatrogenic botulism. In our case series, several patients were initially misdiagnosed with neuromuscular junction disorders such as myasthenia gravis or acute neuropathies, reflecting a well-documented diagnostic pitfall in the literature.[5,6] One patient was initially treated for presumed myasthenia gravis with pyridostigmine before clinical deterioration prompted reassessment, while another was initially considered to have an acute neuropathy. These cases illustrate how overlapping clinical features—such as fluctuating weakness, bulbar involvement, and preserved reflexes—can obscure the diagnosis. This overlap is particularly problematic given that BoNT exposure may unmask subclinical neuromuscular disorders, further complicating the diagnostic process.[11] Although laboratory confirmation of BoNT remains the diagnostic gold standard, recent reviews emphasize the limited sensitivity and accessibility of available assays, underscoring the continued reliance on clinical judgment.[7]

Electrophysiological assessment provided critical diagnostic support by revealing marked facilitation on high-frequency repetitive nerve stimulation and post-exercise testing, while sensory nerve conduction studies remained intact. This combination of findings is characteristic of impaired presynaptic acetylcholine release and helped distinguish iatrogenic botulism from postsynaptic disorders such as myasthenia gravis. In selected cases, single-fiber electromyography demonstrated increased jitter and blocking, confirming neuromuscular junction involvement even after partial clinical improvement. Notably, early or mild presentations occasionally showed normal routine EMG and nerve conduction studies, emphasizing that normal electrophysiological findings do not exclude iatrogenic botulism in the acute phase. These observations are in line with existing literature highlighting both the diagnostic value and limitations of electrophysiological studies in botulism.[7]

Early administration of BAT remains the cornerstone of treatment. While randomized

Table 1: Summary of iatrogenic botulism cases

Case	Age/ Sex	Indication for BoNT	Dose of BoNT (IU)	Previous BoNT Exposure	Time to Symptom Onset	Major Clinical Findings	Electrophysiology	Treatment	Respiratory Support	Outcome
1	42/F	Cosmetic (glabellar & lateral canthal rhytids)	Unknown	No previous documented exposure	<24h	Bilateral ptosis, diplopia, mild dysphagia	Early EMG/NCS normal	BAT + IVIG	Monitored; no intubation	Full recovery in 1 week
2	55/M	Cervical dystonia	BoNT type A (150 IU per muscle)	Yes	2 days	Dysarthria, generalized weakness, mild respiratory compromise	HF-RNS: amplitude increase 15–60%, polyphasic MUAPs	Single vial BAT	Monitored; stable vitals	Full recovery in 48h
3	42/F	Cosmetic (forehead, periorbital, perioral)	~50 IU	No previous documented exposure	4 days	Diplopia, blurred vision, impaired facial expressions	HF-RNS: 50–60% increment	Conservative	None	Complete recovery by day 30
4	38/M	Hyperhidrosis	BoNT type A (50 IU per axilla)	No previous documented exposure	7 days	Weakness in arms, limited abduction/ adduction, neck flexion 4-/5	HF-RNS: amplitude increase; mild myokymia	Supportive care	None	Full recovery over 10 days
5	60/M	Post-stroke spasticity	450 IU	No previous documented exposure	2 days	Dysphonia, proximal weakness, mild respiratory difficulty	HF-RNS: 50–60% increment, normal LF-RNS	Single vial BAT	ICU monitoring	Full recovery over 4 weeks
6	50/F	Axillary hyperhidrosis + masseter (bruxism)	Unknown	No previous documented exposure	1 day	Mild facial weakness, ptosis, limb fatigue	HF-RNS: subtle increment	Conservative, supportive care	None	Full recovery in 2 weeks
7	47/M	Chronic migraine	Unknown	No previous documented exposure	3 days	Generalized weakness, blurred vision, dysphagia	HF-RNS: up to 60% increment, no LF-RNS decrement	BAT + oral pyridostigmine	ICU monitoring	Full recovery in 3 weeks
8	33/F	Gastric BoNT injection	~1000 IU	Yes	4 days	Weakness, blurred vision, dysphagia, ptosis, chest discomfort	SFEMG: neuromuscular junction impairment	Single vial BAT + pyridostigmine	None	Full recovery in 8 weeks
9	49/F	Masseter injection (non-medical institution)	Unknown	No previous documented exposure	~1 week	Dysphagia, dysarthria, bilateral ptosis, myalgia	RNS normal	Conservative, no BAT	None	Complete recovery in 2 weeks
10	38/F	Migraine prophylaxis	Unknown	No previous documented exposure	10 days	Bilateral ptosis, dysarthria, proximal weakness, fatigue	LF-RNS decrement; HF-RNS >50% increment	BAT + pyridostigmine	Monitored	Complete recovery in 14 days

Abbreviations; BoNT, Botulinum toxin; BAT, Botulinum antitoxin; IVIG, Intravenous immunoglobulin; EMG/NCS, Electromyography / Nerve conduction study; HF-RNS, High-frequency repetitive nerve stimulation; LF-RNS, Low-frequency repetitive nerve stimulation; MUAPs, Motor unit action potentials; SFEMG, Single-fiber electromyography; IU, International Unit; ICU, Intensive Care Unit; F, Female; M, Male

controlled trials specific to iatrogenic botulism are lacking, contemporary case series and observational studies suggest that antitoxin administration during the progressive phase of neurological impairment may halt further deterioration and reduce the duration of mechanical ventilation.[12,13] Patients who received botulinum antitoxin during the active progression of symptoms demonstrated earlier neurological stabilization and more rapid functional recovery, whereas those managed conservatively after symptom plateau experienced slower but complete improvement. These observations support current recommendations emphasizing early antitoxin administration to neutralize circulating toxin before irreversible synaptic binding occurs. Supportive care, including close respiratory monitoring and intensive care support when indicated, was essential for recovery, consistent with recent reports emphasizing the prolonged neuromuscular recovery associated with BoNT–mediated synaptic blockade.[14]

Adjunctive treatment with acetylcholinesterase inhibitors was used in selected patients. Pyridostigmine was initially administered during diagnostic uncertainty or after antitoxin therapy in patients with residual neuromuscular transmission impairment. Although it did not reverse acute progressive symptoms, it appeared to provide partial symptomatic benefit during recovery, supporting its role as adjunctive rather than definitive therapy.

From a public health and preventive perspective, recent World Health Organization and Centers for Disease Control and Prevention guidance underscores the importance of surveillance systems, practitioner accreditation, and patient education to mitigate the risk of iatrogenic botulism.[10,15] Our case series reinforces these recommendations by demonstrating preventable morbidity associated with unregulated administration, high cumulative doses, and delayed recognition of systemic toxicity. Several studies have advocated for stricter regulation of cosmetic BoNT use, particularly in non-medical settings, and for improved reporting of adverse events to national surveillance systems.[16]

Despite increasing recognition, significant gaps remain in the understanding of iatrogenic botulism. Most published data from 2021 to 2025 consist of case reports, small case series, and outbreak investigations, limiting the ability to define incidence rates, dose–response relationships, and predictors of disease severity.[13,17] The heterogeneity observed in our cohort with respect to indication, dose, electrophysiological findings, and recovery time further underscores the need for standardized reporting and multicenter data collection. Additionally, the mechanisms underlying systemic toxin dissemination following localized injection remain incompletely understood and may involve patient-specific factors such as underlying neuromuscular vulnerability or altered toxin pharmacokinetics.[18]

Several limitations of this case series should be acknowledged. The retrospective nature and limited sample size restrict generalizability, and incomplete laboratory confirmation may introduce diagnostic uncertainty. However, the strength of this study lies in the detailed clinical and electrophysiological characterization of cases and the use of contemporary literature for contextual interpretation. By contributing systematically documented cases, this series helps bridge existing knowledge gaps and supports ongoing efforts to improve clinical recognition, management, and prevention of iatrogenic botulism.

İn conclusion, this contemporary case series highlights iatrogenic botulism as a rare but clinically significant complication of BoNT exposure, arising from both cosmetic and therapeutic applications. Our findings demonstrate that systemic BoNT toxicity can occur even after procedures generally perceived as low risk, and may closely mimic other neuromuscular junction disorders, frequently leading to diagnostic delay or misdiagnosis. Prominent cranial nerve involvement, proximal muscle weakness, and fluctuating bulbar symptoms should raise clinical suspicion, particularly when there is a temporal association with recent BoNT administration.

Electrophysiological evaluation plays a pivotal role in supporting the diagnosis, with characteristic presynaptic patterns—including preserved nerve conduction studies, absence of low-frequency decrement, and significant facilitation on high-frequency repetitive nerve stimulation or post-exercise testing—providing valuable diagnostic clues. Early recognition of these features is essential to differentiate iatrogenic botulism from conditions such as myasthenia gravis or acute neuropathies and to guide appropriate management.

Timely administration of BAT during the progressive phase of symptoms was associated

with clinical stabilization and favorable outcomes in our series, while adjunctive therapies such as pyridostigmine may offer symptomatic benefit in selected patients. Importantly, delayed presentation or spontaneous improvement does not exclude the diagnosis and should not preclude careful neurological assessment.

From a preventive perspective, this series underscores the need for stricter regulation of BoNT use, particularly in non-medical settings, improved clinician awareness, and enhanced reporting of adverse events. Increased vigilance, early electrophysiological assessment, and prompt therapeutic intervention remain central to reducing morbidity associated with this preventable condition.

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