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(CASE REPORT)

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Eyelid ptosis following botulinum toxin injection treated with apraclonidine 0.5% drops

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Abstract

Botulinum toxin injections are among the most commonly performed procedures in aesthetic medicine due to their efficacy in reducing dynamic facial wrinkles. Although generally safe, the most frequent complication following treatment of the glabellar and forehead regions is eyelid ptosis, which typically develops 2–10 days after injection and may persist for 2–4 weeks. Pharmacological management with α-adrenergic agonists represents the mainstay of treatment. Apraclonidine 0.5% ophthalmic solution, a selective α2-adrenergic agonist, stimulates Müller's muscle and produces rapid, temporary eyelid elevation. Topical brimonidine gel has also been reported as an effective alternative, offering a favorable systemic safety profile. Clinical studies, though relatively scarce, support the use of these agents for symptomatic relief of botulinum toxin–induced ptosis.

We report a case of a 39-year-old female who developed unilateral right eyelid ptosis four days after botulinum toxin type A injection for glabellar and forehead lines. Following treatment with apraclonidine 0.5% drops twice daily, the patient demonstrated progressive improvement, with complete resolution of ptosis after six weeks.

Proper injection technique, including placement lateral and medial to the mid-pupillary line and directing the needle away from the midline, remains essential to minimize the risk of ptosis. Overall, α-adrenergic agonists provide a safe, effective, and practical therapeutic option for the temporary management of botulinum toxin–induced eyelid ptosis.

Keywords: Botulinum Toxin; Brimonidine; Eyelid Ptosis

1. Introduction

Botulinum toxin injections are now among the most widely performed procedures in aesthetic medicine because of their proven ability to reduce dynamic wrinkles. Most side effects related to its cosmetic use are uncommon and tend to resolve on their own. The most frequent complication observed after treating the glabellar region is Eyelid ptosis. This condition generally appears between 2 and 10 days after injection, coinciding with the onset of the desired cosmetic effect, and can last for about 2 to 4 weeks [1]. Eyelid ptosis can be managed with α-adrenergic eye drops. These drops stimulate contraction of the upper tarsal muscle, known as Müller's muscle, producing a 1–2 mm elevation of the eyelid, which usually restores a more balanced appearance[2].

A common option is apraclonidine 0.5%, an α2-adrenergic agonist ophthalmic solution. Another selective α2-adrenergic agent, brimonidine eye drops, may also be prescribed as an alternative to apraclonidine for eyelid ptosis [3]. In dermatology, topical brimonidine has also been applied for the treatment of erythematous rosacea because of its strong peripheral vasoconstrictive effect.

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In this report, we describe the management of a patient who developed unilateral eyelid ptosis after receiving botulinum toxin type A (Botox; Allergan) injections for dynamic upper facial lines, successfully treated with 0.5% apraclonidine drop.

2. Case report

A 39-year-old female patient underwent botulinum toxin type A injection for the management of dynamic rhytids involving the glabellar complex and forehead. Four days following the procedure, she came to our hospital with unilateral right ptosis. The patient reported subjective symptoms of ocular fatigue and a sensation of heaviness localized to the periocular region. She was unable to provide details regarding the total dose administered or the precise injection sites. Written informed consent was obtained from the patient for publication of this case and accompanying images

On clinical examination, the right upper eyelid was noted to descend sufficiently to obscure a significant portion of the iris. Elevation of the brow through manual manipulation failed to improve eyelid position, and frontalis muscle function remained intact, suggesting the ptosis was not secondary to brow dysfunction. Objective assessment of eyelid position was performed using standard biometric measurements, including the palpebral fissure height and the marginal reflex distance 1 (MRD1).

The palpebral fissure, defined as the vertical distance between the upper and lower eyelid margins with the eyes in primary gaze, normally ranges between 7 and 12 mm. In this patient, the palpebral fissure measured 6 mm in the right eye compared with 10 mm in the contralateral eye. The MRD1, measured from the upper eyelid margin to the central corneal light reflex, is expected to range between 4.0 and 4.5 mm under physiological conditions. The patient demonstrated an MRD1 of 2 mm in the right eye and 4 mm in the left eye. Based on the patient's clinical symptoms, physical examination findings, and objective biometric measurements, a diagnosis of botulinum toxin–induced right upper eyelid ptosis was established.

The patient applied apraclonidine 0.5% ophthalmic solution. Thirty minutes after the initial instillation, a marked elevation of the upper eyelid was observed. Treatment was continued at a dosage of two drops per day, with regular follow-up consultations. During the follow-up period, a progressive and significant improvement of the ptosis was noted, culminating in complete resolution of ptosis after six weeks of therapy Figure 1

Figure 1: 1st day of consultation (eyelid ptosis after Botulinum toxin injections)

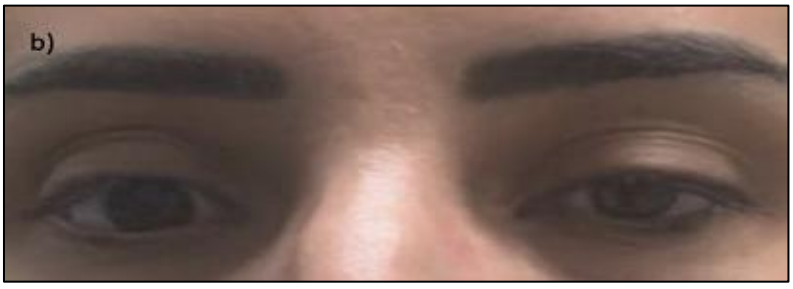

Figure 2 after three weeks of treatment

Figure 3 resolution of eyelid ptosis after six weeks

3. Discussion

The most frequent complication observed after treating the glabellar region with Botulinum toxin injections is ptosis. In the aesthetic field, the physiopathlogy of the eyelid ptosis is generally develops due to unintended diffusion of the toxin into the elevator palpebral superioris muscle, leading to weakness and subsequent drooping of the upper eyelid. It is caused by the diffusion of botulinum toxin across the orbital septum [3]. We know that the elevator palpebral superioris muscle is the principal muscle responsible for elevation and retraction of the upper eyelid. Anatomically, it originates from the lesser wing of the sphenoid bone, superior to the optic foramen, and extends anteriorly before broadening into the levator aponeurosis [1]. The aponeurotic fibers insert into both the skin of the upper eyelid and the superior tarsal plate, thereby facilitating lid elevation. Closely associated with this structure is the superior tarsal muscle (Müller's muscle), a sympathetically innervated smooth muscle that attaches to the levator palpebrae superioris and also inserts on the superior tarsal plate, contributing to additional eyelid elevation [4].

3.1. Epidemiology

A multicenter United States FDA study conducted by Allergan, the incidence of BoNT-A-induced blepharoptosis was estimated to be 5.4% among inexperienced injectors and <1% among experienced injectors [5]. Cavallini et al [6], [7], [8] reviewed 35 articles, with over 8000 patients, concluding the rate of blepharoptosis to be about 2.5%. Incidence appears to have decreased over the years as practitioners become more experienced with BoNT-A administration. To our knowledge, only a few case reports and case series exist detailing this adverse event. Total number of studied patients and blepharoptosis episodes are summarized in Table 1

Table 1 existing literature on cosmetic botulinum toxin-induced blepharoptosis [9][10][11][12][13][14][15][16][17] [18] [19] [20] [21] [22] [23] [24]

Author's Name	Type of research	# of patients in the study
Carruthers et al. 2002	Multicenter, double-blind, randomized, placebo-controlled trial	203 BoNT-A, 61 placebo (5.4% with mild blepharoptosis in BoNT-A group only)
Carruthers et al. 2003	Double-blind, randomized, placebo-controlled trial	202 BoNT-A, 71 placebo (1.0% with blepharoptosis in BoNT-A group only)
Rzany et al. 2006	Multicenter, double-blind, placebo-controlled, randomized trial	146 BoNT-A and 75 placeboes (1.4% with blepharoptosis)
Rzany et al. 2007	Retrospective, cross-sectional patient chart review	945 BoNT-A (0.51% with blepharoptosis)
Monheit et al. 2007	Randomized, double-blind, placebo-controlled trial	279 BoNT-A and 94 placeboes (0.8% with ptosis)
Harii et al. 2008	Double-blind, randomized, placebo-controlled trial	91 BoNT-A, 49 placebo (2.2% with blepharoptosis in BoNT-A group only)
Kawashima et al. 2009	Multicenter, randomized, open-label trial	363 BoNT-A (3.3%–4.4% with blepharoptosis)

Brandt et al. 2009	Randomized, placebo-controlled trial	105 BoNT-A and 53 placebo (3% with ptosis in BoNT-A group only)
Cohen et al. 2009	Open-label phase III trial	1415 BoNT-A(1% with blepharoptosis in fixed group, 2% with blepharoptosis in variable group)
Rubin et al. 2009	Open-label, followed by multicenter, randomized, placebo-controlled, double-blind trial	311 BoNT-A and 155 placebo (3.2% with blepharoptosis in BoNT-A group only)
Kane et al. 2009	Randomized, double-blind, placebo-controlled, phase III trial	544 BoNT-A and 272 placebo (2% with blepharoptosis in BoNT-A group only)
Moy et al. 2009	Open-label phase III trial	1200 BoNT-A (4% with blepharoptosis)
Ascher et al. 2009	Multicenter, randomized, double-blind, placebo-controlled, dose-ranging trial	164 BoNT-A and 54 placebo (0.6% with blepharoptosis in BoNT-A group only)
Wu et al. 2010	Double-blind, randomized, placebo-controlled trial	170 BoNT-A, 57 placebo (0.6% with ptosis in BoNT-A group only)
Karami et al. 2007	Case report	1
Akkaya et al. 2015	Case report	1
Steinsapir et al. 2015	Retrospective case review series	7

3.2. Clinical findings

The ptosis after Botulinum toxin injections typically emerges within 2 to 10 days after injection, and can persist for a duration of 2 to 4 weeks before resolving spontaneously[26]. In some reports, ptosis persisted up to 6-13 weeks. Rarely, very long durations (several months) are documented[25].Occasionally, ptosis is severe enough to partially obstruct vision.

3.3. Management

Pharmacological intervention with α-adrenergic agonists represents the mainstay of management. Apraclonidine hydrochloride, a topical ophthalmic solution, acts primarily as a selective α2-adrenergic receptor agonist with a weaker affinity for α1 receptors and possesses an elimination half-life of approximately eight hours. Clinically, apraclonidine 0.5% is employed as a short-term adjunctive therapy in patients with glaucoma who require further intraocular pressure reduction despite maximal tolerated medical therapy[5]. The 1% formulation, on the other hand, is specifically approved for the prevention and management of acute postoperative elevations in intraocular pressure following laser procedures, such as argon laser trabeculoplasty and argon laser iridotomy.

In addition to its well-documented hypotensive properties, apraclonidine exerts a secondary pharmacological action on the superior tarsal muscle, also known as Müller's muscle. By inducing contraction of this sympathetically innervated smooth muscle, apraclonidine produces a 1–2 mm elevation of the upper eyelid [27]. Although randomized controlled studies are relatively scarce, this distinctive pharmacological effect has been applied in clinical practice to provide symptomatic relief of eyelid ptosis induced by botulinum toxin. Ghadah et al describes the benefit of the brimonidine 0.33% topical gel to treat the eyelid ptosis following botulinum toxin injection [1]. Benkali et al [28]studied the pharmacokinetics and bioavailability of brimonidine following ocular and dermal administration in patients with moderate to severe facial erythema associated with rosacea. They showed that the systemic exposure observed with the higher dose of brimonidine gel (0.5% once daily) was significantly lower than that observed with the ophthalmic solution (0.2%). This makes the systemic safety profile of topical brimonidine better than that of the marketed

ophthalmic solution[28]. Although this study compares systemic absorption, to our knowledge there are no current studies comparing the effects of topical gel versus brimonidine eye drops on eyelid elevation

Subhashie Wijemanne et al described on their study that Apraclonidine effectively improved ptosis in all six patients with BoNT-induced ptosis with no adverse effects [31]

Table 2 Overview of Ophthalmic α-Adrenergic Treatments for Botox-Induced Ptosis

Agent	Mechanism	Onset of Action	Duration	Typical Lid Elevation	Dosage	Safety Notes	Level of Evidence
Apraclonidine 0.5% (eye drops)	α2 agonist (weak α1) → contraction of Müller's muscle	30–60 min	4–6 h	1–2 mm	1 drop 2–3×/day	Ocular allergy, rebound redness	Case reports / series
Oxymetazoline 0.1% (eye drops)	α1 agonist → eyelid elevation + vasoconstriction	15–30 min	up to 8 h	1–2 mm	1 drop/day	Mild dry eye, rebound congestion	Clinical trials (acquired ptosis)
Brimonidine ophthalmic 0.2%	α2 agonist	30–60 min	6–8 h	Variable	1 drop 2–3×/day	Systemic hypotension, allergy	Limited case reports
Brimonidine gel 0.33% (topical dermal)	Topical α2 agonist	1–2 h	Several hours	Case-dependent	1 application/day	Minimal systemic absorption	Case reports

Taken together, these pharmacological properties position apraclonidine as an effective therapeutic option for the temporary management of BoNT-induced eyelid ptosis, while also highlighting its broader applications across ophthalmology and neuro-ophthalmology. Previously, we describe the clinical course and treatment response of a patient who developed unilateral eyelid ptosis after cosmetic injection of botulinum toxin type A.

3.4. Prevention

Risk reduction requires proper injection technique—injecting lateral and medial to the mid-pupillary line and directing the needle away from the midline [29,30].

4. Conclusion

Eyelid ptosis remains the most recognized complication of botulinum toxin injections. α-Adrenergic agonists such as apraclonidine and brimonidine offer effective temporary improvement by stimulating Müller's muscle. Strict adherence to safe injection technique is essential to minimize this complication. Larger studies are still needed to establish comparative efficacy and safety of available agents.

Compliance with ethical standards

Disclosure of conflict of interest

All authors have no conflict of interest to declare.

Statement of ethical approval

This case report was conducted in accordance with ethical guidelines.

Statement of informed consent

The patient provided informed consent for the publication of this case report

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