Botulinum induced ptosis for the treatment of neurotrophic keratitis

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ABSTRACT

The main medical indications for botulinum toxin type A injections is to treat certain spasmodic muscle disorders. A 40-year-old Malay lady presented with a right lower motor neurone facial nerve palsy, and associated exposure keratitis and hypopyon, following excision of schwannoma. The keratitis resolved after treatment with lubricants and lateral tarsorraphy. Two months later, she presented with corneal ulcer and hypopyon, which did not respond to topical antibiotics. Complete ptosis was induced in the right eye using Botulinum Toxin type A trans-cutaneous injection to the superior palpebrae superiosis. Following the injection, the ulcer recovered gradually over a period of five weeks. This report illustrates an important role of Botulinum toxin A in the management of refractory exposure keratitis.

Keywords: Botulinum Toxin Type A, corneal ulcer, denervation, keratitis

INTRODUCTION

Botulinum toxin is an exotoxin produced by the ubiquitous bacterium, *Clostridium botulinum,* a spore bearing, anaerobic, gram positive rod. It acts at the neuromuscular junction by inhibiting the release of the neurotransmitter, acetylcholine. Ophthalmic use of botulinum toxin type A was first reported in 1979 by Alan B Scott, who corrected extra-ocular motility disorders in 56 patients by injection of the toxin directly into the targeted extra-ocular muscles to weaken them.[1] This case series showed excellent tolerance to localised injection of botulinum toxin type A into the ocular muscles with no systemic complications. Since then, the use of botulinum toxin has become popular for the temporary management of various ophthalmic conditions. We report a case of refractory exposure keratitis that was successfully managed by botulinum toxin induced protective ptosis.

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CASE REPORT

A 40-year-old Malay lady was referred to the eye clinic, RIPAS hospital with a four day history of redness and pain in the right eye. Three months previously, she had undergone a right sub-occipital craniotomy for excision of an acoustic neuroma and this was complicated by right lower-motor neurone facial

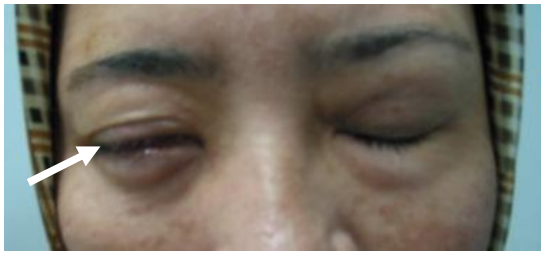

Fig. 1: Right lagophthalmos (arrow) on eye closure at presentation.

nerve palsy and right trigeminal hypoaesthesia postoperatively.

Ocular examination showed right lagophthalmos secondary to the facial nerve palsy. Visual acuity was 6/12 in the right eye and 6/6 in the left eye. The conjunctiva of the right eye was diffusely injected with superficial punctate epithelial defects involving the middle third of the cornea, with associated corneal anaesthesia (Figure 1). The left eye was normal. A diagnosis of right exposure keratopathy, secondary to facial nerve palsy, was made. She was started on Hydroxypropyl methylcellulose (Tears Naturale®, Alcon, USA) eye drops every six hours and liquid paraffin (Lacri-Lube®, Allergan, USA) eye ointment in the right eye every four hours. She was followed up weekly in the eye clinic. Three weeks later, the epithelial defect had increased and her visual acuity deteriorated to 6/24. As she was not responding to conservative management, a lateral tarsorrhaphy was performed. Subsequently, the right keratitis completely recovered in a month period with right vision improvement to 6/10. Treatment with topical lubricants was continued, and the lateral tarsorraphy was kept in view of the persisting facial nerve palsy. However, a month later, she developed another attack of redness and pain in the same eye. Slit-lamp examination showed infected corneal ulcer with hypopyon in the anterior chamber despite the tarsorraphy (Figure 2). She was admitted to the Ophthalmology ward. Scraping was done at the corneal ulcer margins, and samples were sent for gram-staining, and culture. Gram-staining showed a few gram positive cocci and gram negative bacilli. However, culture of the sample showed no growth after 48 hours. She was started on Fortified Gentamicin eye drops (1.3%) and Ceftazidime eye drops (5%) hourly, and Atropine (1%) eye drops twice daily. Meanwhile, the advantage of inducing a protective ptosis by chemodenervation of levator palpebrae superioris was suggested to the patient, to which she agreed. A Hess charting prior to the procedure documented normal extra ocular movements. Subsequently she was given five units of onabotulinumtoxinA (Botox®, Allergan) to the levator palpabrae superioris through a trans-cutaneous approach using a 1-ml syringe with 26 G needle. Two days after the procedure she was noted to have a partial ptosis which progressed to a complete one at the end of one week (Figure 3).

Post injection Hess charting revealed preservation of superior rectus function. Two weeks later, she was discharged from the Ophthalmology ward, and was followed up on a weekly basis in the Ophthalmology clinic. Her keratitis showed gradual improvement, and

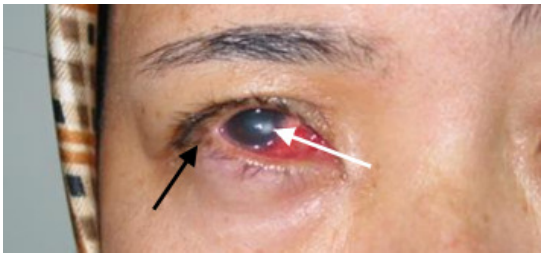

Fig. 2: Infected corneal ulcer (white arrow) in the right eye despite the intact tarsorraphy (black arrow).

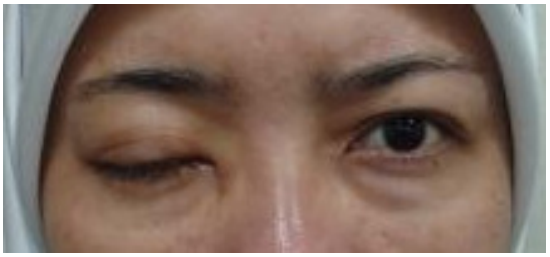

Fig. 3: Complete ptosis of the right upper lid after one week following the injection of five units of botulinum toxin A into the levator palpebrae superioris muscle.

healed completely in a period of five weeks.

DISCUSSION

Botulinum toxin A chemodenervation has greatly evolved in the past few decades. It is used to treat various disorders, including strabismus, hemifacial spasm, blepharospasm, torticollis, spasmodic dysphonia, limb dystoina, hyperhydrosis, achalasia and many other indications. [2] Prior reports document its successful use in ophthalmic conditions like, benign essential blepharospasm, strabismus, upper eye lid retraction, lower eyelid senile entropion, injection into the lacrimal gland in case of primary lacrimal hypersecretion and gustatory epiphora. [3, 4]

To date, there are only limited reports about its use in inducing ptosis as a treatment. [5, 6] Ellis *et al.* assessed the use of botulinum toxin type A injections to the superior palpebrae superioris as an alternative for surgical tarsorraphy in 21 patients. [5] Although five patients developed diplopia following the injections, these spontaneously resolved in all cases. Likewise, Kirkness *et al*. reported superior rectus under-action in 68% of cases treated with botulinum toxin A injections to the lavatory palpebrae superioris, and similarly, all recovered completely in an average of six weeks. [6] In our case, the superior rectus function was normal post injection, and there was no diplopia.

Tarsorrhaphy has been routinely used in the management of exposure keratitis due to lagophthalmos and other indolent corneal ulcers. Its limitations include difficulty in frequent monitoring of corneal pathology and instillation of medications. It can also damage the eyelid margin. Chemodenervation of the levator palpebrae superioris on the other hand is a quick and simple procedure, without causing any permanent effect on the lid. The peak paralytic effect occurs four to seven days after injection and it will last for an average of 8.5 weeks. [6] Transient superior rectus under-action causing hypotropia has been reported to occur in 60-80% of treated patients, which was absent in our patient. [8, 9] The use of botulinum toxin A is contraindicated in patients below 12 years of age. There are no published data suggesting the dose requirement to achieve complete ptosis and doses ranging from 2.5 units up to 20 units have been used.

In our patient, the refractory nature of the keratitis might be due to the neurotrophic and neuroparalytic element, which might be permanent. Ideally botulinum toxin A induced chemotarsorrhaphy should be limited to corneal pathology which is likely to be temporary. As such, we are planning to monitor her closely, while maintaining the tarsorrhaphy.

In conclusion, chemotarsorraphy using Botulinum toxin A is a feasible alternative of treatment in cases of exposure/neurotrophic keratitis not responding to traditional treatment with surgical tarsorraphy.

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