Sir,

Reversible pupillary dilation following botulinum toxin injection to the lateral rectus

Low-dose botulinum toxin (BT) is being widely used in ophthalmology including the management of strabismus,[1] congenital entropion,[2] nystagmus,[3] blepharospasm,[4] and aberrant regeneration of the facial nerve.[5] Previously reported complications following injection to the horizontal recti muscles include ptosis,[6] permanent muscle damage,[7] globe perforation,[8] necrotising fasciitis,[9] and angle closure glaucoma.[10] We report a case of a middle-aged man who developed a reversible pupillary dilation following injection of BT to the lateral rectus (LR) muscle.

Case report

A 69-year-old man was referred to us with a longstanding history of horizontal diplopia following a cerebrovascular accident. The diplopia remained uncontrolled with Fresnel prisms. Examination revealed a 16° right alternating exotropia at 33 cm, increasing to 20° at 6 m. Visual acuity was 6/6 in the right eye (RE) and 6/5 in the left eye (LE). Both pupils were equal sized, reactive, with no relative afferent pupillary defect (RAPD). He was noted to have horizontal hypometric saccades (secondary to his cerebrovascular accident). Rest of the ocular examination was unremarkable.

Following informed consent, 1.25 international units (IU) of BT (Botox®, Botulinum Toxin Type A, Allergan pharmaceuticals, Ireland) was injected to the LR muscle of the RE under electromyographic guidance. A similar dose was repeated a month later. Following this, the ocular deviation was reduced to 4° BI for near and 2° BI at distance and his symptoms resolved. A similar dose (1.25 IU) of BT injection to the LR muscle was repeated twice at quarterly intervals. On review, 3 months later he was noted to have anisocoria (Figure 1). The right pupil measured 6 mm and was fixed, with no direct or consensual response to light and it failed to dilate further in scotopic conditions. There was no RAPD. The left pupil measured 3 mm with brisk direct and consensual light response. There was limitation of the RE in abduction and no diplopia, consistent with a prolonged action of BT. There was no other neurological abnormality. At this stage it was presumed that the dilated right pupil was secondary to effect of BT and a decision was made to withhold further BT injections to the RE. At review, 2 months later, the right pupil returned to its original size and the anisocoria had completely resolved (Figure 2). The RE had become more divergent and there was intermittent diplopia. The patient remains under follow-up.

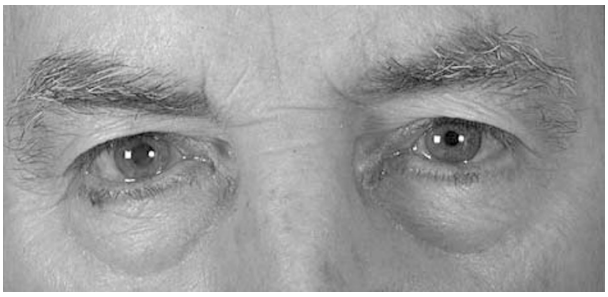

Figure 1 Clinical photograph showing anisocoria. Note the dilated right pupil.

Figure 2 Note the reversal of anisocoria.

Discussion

BT is a protein produced by the anaerobic bacillus *Clostridium botulinum*. It works primarily on peripheral cholinergic synapses where it inhibits the release of the neurotransmitter acetylcholine. The exotoxin possesses two subunits, one of which bind to a membrane receptor and are responsible for cellular specificity. By this means the toxin enters the cell, where the other subunit exerts a toxic effect by inactivating specific enzymes. BT is believed to inactivate actin, a protein involved in exocytosis, by this mechanism.[11] Clinically it produces a transient paresis of the injected muscle by the above mechanism.

Reported complications of BT following horizontal recti muscle injection include ptosis, vertical muscle involvement,[6] permanent extra ocular muscle damage,[7] globe perforation,[8] necrotising fasciitis,[9] and angle closure glaucoma.[10] A Medline and a PubMed search showed no previous clinical reports of reversible pupillary dilation secondary to BT injection to the extraocular muscles. However, retrobulbar injection of BT in rats has been shown to cause mydriasis at a dose of 1.5 ng.[12] In this rat model, the mydriasis resolved in 12 weeks. In our case, the mydriasis resolved by 20 weeks. It is likely that the BT would have affected the ciliary

ganglion, which is located in the intraconal space between the optic nerve and the LR muscle. We speculate that the toxin would have reached the ciliary ganglion by diffusion from the LR muscle, given the proximity of the ciliary ganglion to the LR. Although there was a good audible response with the EMG machine confirming the intramuscular location of the needle, it is possible that the needle could have advanced beyond the muscle into the intraconal space. Alternatively, its action could be at the parasympathetic neuromuscular junctions in the sphincter pupillae of the iris, although this is unlikely as it would require an intraocular injection or an idiosyncratic reaction to the BT. Tonic pupils have also been reported in patients with systemic botulism.[13] There have been no documented cases in the literature of pupillary abnormalities following botulinum toxin injection, although it has been postulated that this may precipitate acute closed angle glaucoma following treatment of blepharospasm.[10] To the best of our knowledge, this is the first documented clinical case of pupillary abnormality following BT injection. Although pupillary changes following BT injection are a rare phenomenon, the treating physician should be aware of this side effect. The pupillary changes are reversible as shown in this case.

References

1 Scott AB, Rosenbaum A, Collins CC. Pharmacologic weakening of extraocular muscles. *Invest Ophthalmol* 1973; **12**: 924–927.
2 Christiansen G, Mohney B, Baratz K, Bradley E. Botulinum toxin for the treatment of congenital entropion. *Am J Ophthalmol* 2004; **138**: 153–155.
3 Ruben S, Lee J, O'Neil D, Dunlop I, Elston JS. The use of botulinum toxin for treatment of acquired nystagmus and oscillopsia. *Ophthalmology* 1994; **101**: 783–787.
4 Frueh B, Felt D, Wojno T, Musch DC. Treatment of blepharospasm with botulinum toxin. A preliminary report. *Arch Ophthalmol* 1984; **102**: 1464–1468.
5 Borodic G, Pearce L, Cheney M, Metson R, Brownstone D, Townsend D *et al*. Botulinum A toxin for treatment of aberrant facial nerve regeneration. *Plast Reconstr Surg* 1993; **91**: 1042–1045.
6 Sener EC, Senac AS. Efficacy and complications of dose increments of botulinum toxin-A in the treatment of horizontal comitant strabismus. *Eye* 2000; **14**: 873–878.
7 Mohan M, Tow S, Fleck BW, Lee JP. Permanent extraocular muscle damage following botulinum toxin injection. *Br J Ophthalmol* 1999; **83**: 1309–1310.
8 Mohan M, Fleck BW. Globe perforation during botulinum toxin injection. *Br J Ophthalmol* 1999; **83**: 503–504.
9 Latimer PR, Hodgkins PR, Vakalis AN, Butler RE, Evans AR, Zaki GA. Necrotising fasciitis as a complication of botulinum toxin injection. *Eye* 1998; **12**: 51–53.
10 Corridan P, Nightingale S, Mashoudi N, Williams AC. Acute angle-closure glaucoma following botulinum toxin injection for blepharospasm. *Br J Ophthalmol* 1990; **74**: 309–310.
11 Rang HP, Dale MM, Ritter JM. *Pharmacology*. Churchill Livingstone, 1996, p 133.
12 Levy Y, Kremer I, Shavit S, Korczyn AD. The pupillary effects of retrobulbar injection of botulinum toxin A (Oculinum) in albino rats. *Invest Ophthalmol Vis Sci* 1991; **32**: 122–125.
13 Monaco S, Freddi N, Francavilla E, Meneghetti F, Fenecia L, Franciosa G *et al*. Transient tonic pupils in botulism type B. *J Neurolog Sci* 1998; **156**: 96–98.

C Hemmerdinger[1,2], S Srinivasan[1,2] and IB Marsh[1]

[1]Department of Ophthalmology, Aintree University Hospitals, Liverpool, UK

[2]St Paul's Eye Unit Royal Liverpool University Hospital, Liverpool, UK

Correspondence: S Srinivasan,
St Paul's Eye Unit,
8Z Link, Royal Liverpool University Hospital,
Prescot Street, Liverpool L7 8XP, UK
Tel.: +44 151 706 2134;
Fax: +44 151 706 5861.
E-mail: sathish@tiscali.co.uk

Eye (2006) **20,** 1478–1479. doi:10.1038/sj.eye.6702366; published online 28 April 2006

Sir,

Bilateral ptosis and gaze palsies following radioactive seed treatment of tectal plate tumours

We report two cases of bilateral ptosis and associated gaze palsies that developed after temporary insertion of ^{125}I radioactive seeds in the treatment of tectal plate lesions. This is the first time that this has been described as a complication of this procedure.

Case 1

A 26-year-old girl was referred with bilateral, symmetrical ptosis and complete downgaze palsy. At the age of 16, she was diagnosed with a low-grade ependymoma in the pineal region and subsequently underwent Gamma knife stereo-radiosurgery, transoccipital transtentorial excision, endoscopic third ventriculostomy, and ventriculo-peritoneal shunt insertion. Histology of the lesion demonstrated a choroid plexus papilloma. In 2003, there was further recurrence