CASE REPORT

Ocular Neuromyotonia Noted after Recent Botulinum Toxin Injection for Sixth Nerve Palsy Following Resection of a Posterior Fossa Skull Base Meningioma

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ABSTRACT

A 56-year-old female complained of diplopia immediately after surgical excision of a recurrent left skull base tuberculum meningioma. She was found to have a left sixth nerve palsy, which was subsequently treated with botulinum toxin injection to the medial rectus muscle. Three months post injection, the patient had partial recovery of the sixth nerve palsy and new-onset ocular neuromyotonia.

Keywords: Botulinum toxin, ocular neuromyotonia, sixth nerve palsy, skull base tumour

Ocular neuromyotonia (ONM) is a rare paroxysmal neuromuscular disorder characterised by involuntary contraction of extraocular muscles. ONM is usually accompanied by episodic diplopia and variable angle strabismus.¹ Reported causes include prior radiation treatment, chronic cranial nerve palsy affecting ocular motility, thyroid-related orbitopathy, compressive lesions, or stroke.^{2,3} There have even been a few reported cases that are idiopathic in origin.³ The precise pathophysiology of the disorder is unknown, but is thought to be related to axonal instability.¹ Hence, membrane-stabilising agents such as carbamazepine and gabapentin have been utilised for treatment.⁴ Currently, sparse literature exists describing the relationship to prior cranial nerve palsies affecting ocular motility or the potential association with botulinum toxin. We present a patient with ONM that developed after botulinum toxin was utilised in the treatment of a sixth nerve palsy that occurred immediately after neurosurgery for resection of a recurrent meningioma with a history of prior radiation therapy.

CASE REPORT

A 56-year-old female presented with diplopia immediately after surgical excision of a recurrent tuberculum meningioma. Fifteen years prior, the patient was diagnosed with a left skull base tuberculum meningioma and underwent a subtotal resection with post-operative radiation therapy.

On presentation, the best-corrected visual acuity was 20/25 in the right eye and 20/20 in the left eye. The intraocular pressure was 19 and 16 mm Hg, respectively. The pupils were equally round and reactive to light, without an afferent pupillary defect in either eye. Ocular motility examination showed a complete abduction deficit of the left eye, with 70 prism dioptres of esotropia in the primary gaze position. The patient was followed for 5 months without any signs of clinical improvement. She tried patching, monocular occlusion, and prisms without successful alleviation of the diplopia. The symptoms were interfering with her ability to perform activities of daily living and thus an intervention was

FIGURE 1 The left esotropia that measured 10 prism dioptres in primary gaze.

FIGURE 2 After prolonged left lateral gaze, the esotropia converted to a left exotropia, measuring 20 prism dioptres, suggestive of ONM.

warranted. She received 7.5 units of botulinum toxin type A to the left medial rectus muscle for treatment of the sixth nerve palsy. Three months post botulinum toxin injection, there was significant improvement of the left sixth nerve palsy. However, she was noted to have a left esotropia (Figure 1) measuring 10 prism dioptres in primary gaze, which converted to a left exotropia (Figure 2) measuring 20 prism dioptres and lasting 30 seconds to 1 minute after sustained left lateral gaze, suggestive of ONM.

DISCUSSION

Ocular neuromyotonia (ONM) is a rare paroxysmal neuromuscular disorder characterised by involuntary contraction of one or more extraocular muscles, resulting in episodic diplopia and strabismus.¹ The episodes of diplopia are usually brief but occur multiple times throughout the day. The periods of diplopia can occur spontaneously or be precipitated by sustained gaze in the direction of action of the affected muscle or following rapid shifts of gaze.¹ ONM typically occurs unilaterally, but in rare cases can occur bilaterally.⁵ Cranial nerve III is most commonly affected (56% of cases), followed by cranial nerve VI (39%) and cranial nerve IV (9%).⁶

The precise mechanism by which ONM occurs is unknown. It is thought to be caused by axonal instability due to demyelination, allowing

spontaneous firing of a single neuron or a group of neurons in a process referred to as ephaptic transmission. In experimental models, spontaneous firing of demyelinated axons was demonstrated in cat dorsal columns⁷ and rat spinal root axons.⁸ This concept of partial demyelination allowing for ephaptic transmission has also been seen in other demyelinating diseases, such as multiple sclerosis, in which it can cause paroxysmal symptoms such as tonic spasms and paresthesias. Radiation, compression, and inflammation may enable ephaptic transmission by damaging the myelin sheath surrounding the ocular motor nerves.⁶

Treatment of ONM involves the use of stabilising agents such as carbamazepine, gabapentin, and phenytoin, with varying success. Several reports indicate that stabilising agents may be successful in resolving or greatly reducing the symptoms of ONM in over 70% of cases. However, some patients stop medication due to side effects, intolerance, or adverse interaction of the stabilising agents with other systemic medications. ONM can resolve spontaneously in rare cases, but generally patients continue using the stabilising agents, if tolerated.⁴

Botulinum toxin was approved by the US Food and Drug Administration for the treatment of strabismus and blepharospasm in 1989, neck problems in 2000, and excessive sweating in 2004. Botulinum toxin paralyzes skeletal muscle by blocking the release of the acetylcholine-containing presynaptic vesicles in

the neuromuscular junction. By blocking vesicle release, the signal causing the muscle to contract is also blocked. Although widely used for cosmetic purposes, botulinum toxin can cause diplopia when injected around the orbit for facial rejuvenation. Diplopia is reported to occur after botulinum toxin injection for facial rejuvenation in 2.1% of patients.⁹ Additionally, botulinum toxin is used for the treatment of strabismus, diplopia, and extraocular muscle palsies, by direct injection into the opposing extraocular muscles,¹⁰ as in our patient. If the botulinum toxin diffuses away from the intended muscle, it can affect other extraocular muscles and possibly potentiate ONM.¹⁰ It is also possible that injection of the botulinum toxin expedited the clinical detection of the ONM rather than potentiating the actual onset. There are currently no published studies or case reports discussing the potential role of botulinum toxin in causing ONM when injected in extraocular muscles.

Radiation therapy for parasellar and sellar tumours also has a well-established side effect profile. Sixth nerve palsies are common and known to occur months to years after radiation therapy. The development of ONM following radiation is rare, but has been reported in approximately 27 cases. However, there are no reports of ONM following a partially recovered sixth nerve palsy after radiation as seen in our patient.

Our patient demonstrates the importance of evaluation for atypical gaze-evoked strabismus with partial or complete recovery of cranial nerve palsies. Determining the effect of sustained lateral gaze on ocular alignment in the primary gaze position is essential in patients with cranial base tumours. Although transient diplopia and acute strabismus are commonly seen with tumour recurrence, they may in fact be ONM, which is generally not amenable to surgical treatment. Future studies

should evaluate the potential role of botulinum toxin, radiation, and surgery in development of sequential ONM.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Note: Figures 1 and 2 of this article are available in colour online at <http://informahealthcare.com/oph>.

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