Botulinum Toxin Injections for the Management of Acquired Abducens-Oculomotor Synkinesis Following Abducens Nerve Palsy

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ABSTRACT

Acquired abducens-oculomotor synkinesis results in paradoxical eyelid, pupillary, and/or extra-ocular movements on attempted lateral gaze. To the best of our knowledge, there are only two documented cases of abducens-oculomotor synkinesis of the medial rectus following abducens nerve palsy. The previous cases were managed with muscle recession surgery to produce orthotropia without a decrease in the synkinetic behavior.

We report a case of a 17-year-old male with neurofibromatosis status post sub-occipital craniotomy and resection of pilocytic astrocytoma who developed an acquired abducens-oculomotor synkinesis following an abducens nerve palsy. The patient was managed with botulinum toxin injections into the left medial rectus muscle with promising results.

CASE PRESENTATION

The patient is a 17-year-old male with neurofibromatosis type 1 with remote history of esotropia managed surgically with bilateral medial rectus recession and superior oblique expanders thirteen years earlier. His history was complicated by multiple neurogenic tumors including a stable left optic nerve glioma and a pilocytic astrocytoma of his brainstem developing several years after his strabismus surgery. Best-corrected visual acuity had been 20/20 and stable in each eye. He was treated with chemotherapy for the pilocytic astrocytoma and was in partial remission until 2011, when he was found to have progression of the brainstem lesion on surveillance MRI. Biopsy indicated a recurrence of pilocytic astrocytoma, which was managed by sub-occipital craniotomy in 2012 due to sudden neurologic compromise (Figure 1).

After his surgical resection, he developed left cranial nerve six and seven palsies. He had severe left esotropia of 50 prism diopters (PD) with complete paralysis on abduction. Best-corrected vision of the right eye was 20/20, and the left eye was 20/15. Pupils were equal and reac
tive to light and accommodation bilaterally without an afferent pupillary defect. Vertical extra-ocular motility was fully intact. He also had poor closure of his left lid. Medical management with artificial tears to prevent exposure keratopathy was recommended at that time in hopes that the palsies would resolve.

However, five month later the patient began complaining of worsening left eye movement, diplopia, ataxia and decreased visual acuity (20/80) in the left eye due to severe esotropia (70 PD). Because of his severe esotropia, he was unable to be refracted for spectacles. At this point, 5 units of botulinum toxin were injected into his left medial rectus. Two weeks later, the patient still had significant esotropia (4+), but the nasal conjunctiva was now visible and it was noted that on attempted left gaze the left eye paradoxically adducted without any abnormal pupillary changes (Figure 2).

The patient felt that there was a benefit to the original botulinum injection, so 7.5 units of botulinum toxin was injected into the left medial rectus under anesthesia approximately 2 months...
later. Two weeks after the injection, significant esotropia still existed with motility exam demonstrating left esotropia of 40 PD. Of note the patient reported some improvement of his gait and the diplopia.

The family requested another botulinum injection approximately four months after the previous injection, and 10 units of botulinum toxin were injected into the left medial rectus under anesthesia. Two weeks after the operation, the patient reported considerable improvement of eye movement, visual acuity, and ataxia. For the first time, he felt he was able to ambulate without assistance or a cane. Best-corrected vision was 20/25 in his right eye and 20/50 in his left eye. On exam, it was noted that the esotropia was improved to 25-30 PD with minimal to no improvement in the paradoxical adduction of the left eye.

**DISCUSSION**

Synkinesis is a fascinating condition producing involuntary or paradoxical movements during attempted voluntary action. The most commonly recognized clinical synkineses are of facial nerve origin. An example of facial nerve synkinesis can be seen in crocodile tears syndrome, in which the facial nerve fibers aberrantly regenerate to the salivary instead of lacrimal gland. In regards to ocular synkinesis, the majority are congenital (including Duane retraction syndrome in which the oculomotor nerve innervates the lateral rectus muscle secondary to hypoplastic abducens nucleus and nerve development); however, acquired cases usually occur secondary to nerve trauma. There is much debate as to the mechanism behind synkinesis, yet aberrant nerve regeneration (axonal re-innervation) is the most widely accepted mechanism. Other mechanisms including ephaptic transmission, nuclear hyperexcitability, and central reorganization have been hypothesized.

Abducens-oculomotor synkinesis is the activation of the oculomotor nerve end organs (eyelid, pupil, and/or muscles) upon abducens nerve stimulation, which normally functions in abduction by lateral rectus activation. Thus in abducens-oculomotor synkinesis, an oculomotor end organ will be activated upon attempted abduction leading to eyelid elevation, pupillary constriction, or paradoxical movement. To the best of our knowledge, there have been only two cases of acquired abducens-oculomotor synkinesis following abducens nerve palsy. It appears much more common to have oculomotor-abducens synkinesis following oculomotor palsy.

In our patient, it appeared that his paradoxical adduction of the left eye on attempted left lateral gaze was consistent with abducens to oculomotor synkinesis. His history of intracranial and brainstem manipulation is suggestive of synki
nosis given his lesion was in the caudal pons just medial to the sulcus limitans. In addition, neurosurgical intervention may have interrupted vascular supplies indirectly contributing to the aforementioned neurological deficits. The synkinetic behavior of the medial rectus was not noted initially, but was noticed three months after the abducens palsy, which is consistent with previous cases synkinesis.7

Unfortunately, it is extremely difficult to determine the mechanism behind this specific synkinesis. Obviously, this case involves some component of CNS reorganization given that the lesion is contained entirely within the dorsal pons. It is highly unlikely that a regenerating nerve stump from the abducens nucleus would reconnect only to the oculomotor branch of the left medial rectus. Therefore, in conjunction with Buckley et al., we propose that on attempted left gaze the left paramedian pontine reticular formation (which appeared undamaged in Figure 1) bypasses the damaged abducens nucleus and is diverted up the ipsilateral medial longitudinal fasciculus to the medial rectus sub-nucleus producing left medial rectus activation (Figure 3).6 Nevertheless, it is still entirely possible that other pathologic mechanisms are at play in conjunction to the proposed central reorganization.

The treatment of many acquired synkineses has been experimental at best. Management of facial synkinesis involves either surgery (myectomy or neurolysis), botulinum injections, or facial retraining with biofeedback.8 However, there is a paucity of data regarding the treatment of acquired ocular nerve synkinesis. It appears that muscle resection surgery has been the only successful option for treatment of ocular misalignment.4,5 However, muscle realignment surgery does not alter the synkinetic behavior.

A botulinum toxin trial was attempted to paralyze the aberrant medial rectus because the patient wanted to avoid surgery given his extensive surgical history. Our patient underwent three botulinum toxin injections into the left medial rectus in a six month period. It seemed that there was a dose-weighted response with very little improvement of the esotropia with 5 units, mild improvement with 7.5 units, and moderate improvement with 10 units. However, the aberrant/paradoxical behavior was not affected until 10 units. This may be due to progressive increase of the number of regenerated neurons, newly reconnected neurons of the brainstem, or better needle access to the muscle tissue, given the last two injections were under anesthesia. Similarly, it is plausible that the left abducens nerve was recovering; however, this is unlikely given the patient had the palsy for well over one year. The concern with muscle realignment surgery is negligible synkinetic behavior suppression. Whereas with botulinum injections, other than mild reduction in horizontal gaze range, the harmful effects of botulinum toxin are negligible under the guidance of a trained physician. The advantages to botulinum therapy are multiple. First, this treatment can be tailored to the amount of medial rectus paralysis required to correct the
degree of esotropia, palsy, and synkinetic behavior. Second, it is possible that botulinum toxin inhibits the release of trophic factors and prevents further nerve regeneration and reconnection which would be beneficial if the synkinesis was due to nerve aberrancy. Thirdly, botulinum toxin is effective in managing central lesions as supported by previous research on Duane Syndrome. Therefore, one might consider botulinum toxin as a possible treatment option in synkinesis since it appeared to provide improvement in visual acuity, diplopia, and ataxia for the patient. Whether the botulinum toxin improved the symptoms by alleviating the esotropia or suppressing the synkinesis is difficult to ascertain. We are confident that despite the synkinesis being secondary to central reorganization, botulinum toxin injections can produce clinically acceptable results. The patient had improvement in his esotropia following the injections with a mild improvement in the paradoxical adduction. We propose that though botulinum toxin injections did not completely alleviate the synkinetic behavior of his medial rectus, the use of botulinum toxin pre-operatively can significantly improve quality of life and may have subtle but important biochemical alterations.

**LEARNING POINTS**

1. Acquired abducens-oculomotor synkinesis is a rare complication following abducens nerve palsy.

2. Central reorganization as a pathologic mechanism in ocular synkinesis is less common than aberrant regeneration, but it is an important alternative mechanism to be aware of.

3. Botulinum toxin in the management of acquired abducens-oculomotor synkinesis is a useful adjunct with minimal adverse effects.

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**REFERENCES**


