Long-Term Results: Botulinum for Sixth Nerve Palsy

ABSTRACT

Eight patients with intracranial malignancies or vascular lesions and sixth nerve palsy were treated with botulinum toxin chemodenervation of the antagonist medial rectus muscle. Primary deviation ranged from 20 to 75 prism diopters (pd) of esotropia. Six were treated acutely (within 3 months of onset) and two, which demonstrated partial recovery of lateral rectus function but with residual esotropia and diplopia, were treated after 6 months. After a mean follow-up of 20.6 months, seven were diplopia-free with excellent rotations. Five had complete resolution of the esotropia and diplopia, with near complete recovery of abduction. One had 6 pd residual esotropia, while another, whose sixth nerve had been resected, required a modified Jensen procedure, resulting in full rotations. The single case of bilateral sixth nerve palsy had a functional improvement but was lost to follow-up. One patient had a vertical strabismus induced with the injection and had a gradual return of the esotropia.

INTRODUCTION

The injection of botulinum toxin into the antagonist medial rectus muscle in cases of lateral rectus muscle palsy and paroxysm has been shown to be effective in relieving secondary contracture. Scott and Kraft were able to prevent secondary contracture of the medial rectus muscle in three of four cases injected within 2 to 8 weeks of the onset of the palsy. Metz was able to avoid surgery in 16 of 20 patients treated for acute lateral rectus palsy.

Although saccadic velocity testing, active force generation, and clinical findings may suggest recovery in some cases, the incidence of spontaneous recovery is not documented in the literature. There is general agreement that isolated sixth nerve palsies associated with diabetes mellitus, hypertension, and atherosclerosis are more likely to resolve than those associated with intracranial vascular or mass lesions. This study was undertaken to determine if botulinum toxin injection could provide prolonged improvement or cure in patients with lateral rectus palsy secondary to intracranial malignancy or structural vascular lesions.

MATERIALS AND METHODS

Eight patients (five males, three females) with lateral rectus palsies were treated. The average age of the patients was 56.3 years (range 47 to 63). The mean follow-up from last injection or following eye surgery in each case was 20.6 months (range 5 to 36). Etiologies of the palsies are listed in Table 1, with additional patient data.

Injections of purified botulinum A toxin were done under audible electromyographic control, as described by Scott. Topical anesthesia was used and 2.5% phenylephrine was instilled to constrict the conjunctival vessels. A unipolar Teflon-coated needle was used to inject the toxin with the patient supine. The needle was passed transconjunctivally approximately 2.5 cm posteriorly. Doses were either 2.5 units or 5.0 units per injection.

Ocular deviations were determined by cover test and prism and alternating cover test with fixation at 20 ft. Lateral rectus duction was graded from –5 (maximal limitation) to 0 (full rotation into field of action) (Table 2). Contraction of the medial rectus was determined by the presence of limitation of abduction of the eye on passive forced duction testing and was graded 0 (no limitation) or + (limitation present).

RESULTS

Nine injections were given; one patient had bilateral injections of the medial rectus muscles for a bilateral palsy. The affected eyes were classified into two groups. Group I (six patients) had no limitation of passive forced duction testing and were injected no later than 12 weeks after onset (mean 8.15, range 3 to 12). Group II (two patients) had

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### TABLE 1
Patient Data

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<tr>
<th>No</th>
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<th>Sex</th>
<th>Etiology</th>
<th>Inj</th>
<th>Unit</th>
<th>Onset to Inj</th>
<th>Initial Dev</th>
<th>Dev Function</th>
<th>Forced Duction</th>
<th>Dev Ten Days</th>
<th>Dev 6 Weeks</th>
<th>Dev Final</th>
<th>LR Function</th>
<th>F/U Months</th>
<th>Comment</th>
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<td>M</td>
<td>Multiple myeloma</td>
<td>R</td>
<td>5U</td>
<td>3 wks</td>
<td>50</td>
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<td>Neg</td>
<td>RXT 5</td>
<td>0</td>
<td>0</td>
<td>24</td>
<td></td>
<td>Transparent ptosis</td>
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<tr>
<td>2</td>
<td>52</td>
<td>F</td>
<td>Meningioma</td>
<td>L</td>
<td>5U</td>
<td>10 wks</td>
<td>50</td>
<td>-5</td>
<td>Neg</td>
<td>LET 14</td>
<td>0 (Jen)</td>
<td>-2</td>
<td>36</td>
<td></td>
<td>Transparent ptosis</td>
</tr>
<tr>
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<td>49</td>
<td>M</td>
<td>Intracranial bleeding</td>
<td>L</td>
<td>5U</td>
<td>10 wks</td>
<td>45</td>
<td>-3</td>
<td>Neg</td>
<td>LET 6</td>
<td>LET 6</td>
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<td>24</td>
<td></td>
<td></td>
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<td>4</td>
<td>62</td>
<td>M</td>
<td>Met Lung CA</td>
<td>L</td>
<td>5U</td>
<td>6 wks</td>
<td>25</td>
<td>-4</td>
<td>Neg</td>
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<td>B</td>
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<td>75</td>
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<td>58</td>
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<td>12 wks</td>
<td>30</td>
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<td></td>
<td>Transparent ptosis</td>
</tr>
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</table>

*Inj = injection, MR = medial rectus, Dev = deviation, pd = prism diopters, LR = lateral rectus, F/U = follow-up, RXT = right exotropia, AVM = arteriovenous malformation*

Group I. Four patients had an exotropia of the injected eye at ten days post injection and were orthotropic at 6 weeks, remain so as of their last visit, and had no limitation of lateral rectus function (full rotation). Two were orthotropic at ten days; of these one had 6 diopters of esotropia at 6 weeks and has remained there. This patient has a residual minimal underaction of the lateral rectus muscle. Patient 2 had 14 pd of esotropia at 6 weeks and eventually required a modified Jensen procedure without medial rectus recession and has good rotations despite having had her sixth nerve resected, according to the neurosurgical operative report, at the time of her tumor resection.

Group II. Patient 7 was initially exotropic, but became orthotropic at 6 weeks and has since remained so. There is no residual limitation of abduction. Patient 8 had an exotropia of 2 pd and a hypertropia of 18 pd at ten days, and had a residual hypertropia of 18 pd at 6 weeks and no horizontal deviation. Her hypertropia lasted over 4 months and her esotropia is gradually returning; it was 20 pd as of most recent visit.

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### TABLE 2
Grading of Lateral Rectus Function (Ductions)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>Normal: can voluntarily rotate eye fully into field of gaze</td>
</tr>
<tr>
<td>-1</td>
<td>Can rotate eye from midline to 75% of full rotation</td>
</tr>
<tr>
<td>-2</td>
<td>Can rotate eye from midline to 50% of full rotation</td>
</tr>
<tr>
<td>-3</td>
<td>Can rotate eye from midline to 25% of full rotation</td>
</tr>
<tr>
<td>-4</td>
<td>Can rotate eye to midline but not into given field</td>
</tr>
<tr>
<td>-5</td>
<td>Cannot rotate eye from opposite field to midline</td>
</tr>
</tbody>
</table>

**Side Effects.** Four patients had transient ptosis and one, patient 8, had a vertical deviation (hypertropia) which precluded fusion.

Seven of eight patients had symptomatic improvement of their diplopia and were generally happy with the treatment, while one became worse.

**DISCUSSION.** All six patients in Group I had an overall improvement in their condition, although one required a modified Jensen
proposition. The excellent abduction obtained in some part is attributable to the botulinum injection preventing secondary contracture of the medial rectus muscle. Although all of the patients may have completely recovered lateral rectus function, the etiologies of their palsies were of the type that frequently do not resolve. Furthermore, resolution of the palsy may have left them with a residual esotropia, as in our two patients in Group II.

If a lateral rectus muscle remains totally paralyzed for a period of time, increasing esotropia may be seen as the medial rectus muscle shortens. A limitation of passive abduction of the eye may be demonstrated and there can be an associated reduction in elasticity (increase in stiffness). The combination of shortening and stiffness constitutes the clinical condition of contracture. Injection of the ipsilateral medial rectus muscle, by allowing the eye to abduct passively, enables a small central area of binocularity to be achieved. If the two paralyzed horizontal muscles regain function at the same rate or over the same time interval, the area of binocular single vision would enlarge.1

Scott and Kraft were able to prevent secondary contracture of the medial rectus muscle in three of four cases injected within 2 to 8 weeks of the onset of the palsy.1 Metz was able to avoid surgery in 16 of 21 patients treated for acute lateral rectus palsy. We are unaware of the etiologies of the palsies in most of these patients, and many may have recovered spontaneously anyway.3 We have previously reported the prevention of secondary contracture in an acutely treated group of patients.6

Some patients go on to recover spontaneously and are left with a residual esotropia, perhaps secondary to a prolonged disruption of fusion. This can be avoided with injection. Recovery rates could be predicted with serial saccades, velocities, or active force generation testing. A double-blind study to document recovery rate by etiology would be helpful.

Of the two patients in Group II, one had an induced vertical strabismus which possibly interferes with a cure for her horizontal strabismus. We feel that patients with esotropia secondary to a lateral rectus palsy may benefit from injection even after the acute period, provided they have good fusional potential, as demonstrated by symptomatic diplopia.

The injection of botulinum toxin into the antagonist medial rectus muscle in cases of lateral rectus muscle palsy and paralytic strabismus has been shown to be effective in relieving secondary contracture.1,3,7 Scott and Kraft postulated that the release of medial rectus shortening and stiffness (contracture) after a few days of denervation implied an internal muscular mechanism of contracture, perhaps sarcomere overlap. Even with repeat injection, however, the contracture often returns and they warned that the toxin itself does not lead to a cure of chronic total lateral rectus palsy.1

Elston and Lee treated five adults with partially recovered lateral rectus palsies after 6 months of observation, and were able to restore binocular sensory and motor functions for periods of up to 21 months. They do not recommend acute treatment, however, and warn that a change of neurologic signs may be obscured following treatment. They suggest that the reversal of diplopia which usually occurs may be very uncomfortable.2 Our patients who were exotropic in the post injection period experienced no increased discomfort.

Induced vertical strabismus is a complication that may very well interfere with spontaneous recovery of a lateral rectus palsy. Fortunately, this is not a frequent occurrence and may resolve in a short period of time. Familiarity with injection technique and adherence to suggested dose schedules will help to avoid this complication.

All of our cases except one had some return of lateral rectus function, which accounts for our successful results. The case that had absent lateral rectus function nevertheless had a successful result following a modified Jensen procedure without recession of the medial rectus muscle. Recently, Fitzsimons et al reported excellent results in the treatment of sixth nerve palsy in adults with combined botulinum toxin chemodenervation and transposition of the vertical rectus muscles.8

We treated a group of patients in which the etiology of the palsy was known and documented and who were poor candidates for spontaneous recovery. Undoubtedly, partial recovery accounted for the good results reported in this study. However, these patients were poor surgical candidates, had a low life expectancy, and were anxious to attempt to have their diplopia resolved or improved. Six months was a relatively long interval of time to be symptomatic for this select group. Since there were no significant side effects and patients were subjectively improved after the diplopia reversal period in which exotropia occurs, our results lead us to recommend botulinum toxin injection for acute and chronic lateral rectus palsy of known etiology.

REFERENCES