Contralateral Injections of Botulinum A Toxin for the Treatment of Hemifacial Spasm to Achieve Increased Facial Symmetry

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Six patients noted facial asymmetry after botulinum toxin injection for hemifacial spasm. Each patient was injected on the side contralateral to the spasms with 10 to 15 IU over the zygomatic major and minor muscles. Each patient noted improvement in facial symmetry in the resting position and dynamic facial movements. Five of the six patients desired this approach with subsequent injections. This injection method variation proved helpful in the managing of hemifacial weakness created by botulinum A toxin for this condition. (*Plast. Reconstr. Surg.* 90: 972, 1992.)

Botulinum A toxin is effective treatment for hemifacial spasm.[1-7] Hemifacial spasm is a form of facial neuropathy in which there is abnormal excitation at the level of the intracranial portion of the facial nerve.[8] Aberrant impulses reach muscles supplied by one facial nerve and cause synchronous contractions on one side. Additionally, there is often weakness of these facial muscles. Electromyographic analysis has revealed evidence of denervation of the facial muscles on the affected side.[8]

Although botulinum A toxin relieves the involuntary movement associated with hemifacial spasm, patients treated with this therapy often have exaggerated facial weakness on the side injected for weeks to months. Such weakness can lead to substantial facial asymmetry, as noted by flattening of the nasolabial fold, depression of the lateral angle of the mouth, and substantial asymmetry in lip excursions and dental exposure during smiling.

The purpose of this paper is to present a variation of the botulinum A toxin administration technique that mitigates facial asymmetry after toxin injection for hemifacial spasm.

Patients and Methods

Botulinum A toxin was supplied by Oculinum Incorporated. The toxin was constituted in a nonpreservation saline and diluted to a concentration of 2.5 to 5.0 IU/ml. One IU is equal to the LD_{50} for a white mouse.

Patients chosen for this study were those who complained of asymmetry either in dynamic facial movement or in resting facial expression after a previous injection of botulinum A toxin for hemifacial spasm.

Prior to induction into this study, the patients received an informed-consent form stating that the purpose of the study was to evaluate an alternative injection technique that may produce improved symmetry. An explanation was offered that contralateral facial injections would potentially weaken facial movement and tone on the normal side that could camouflage the weakness on the afflicted side.

Each patient complained of at least one of the following:

1. Depression of the lateral angle of the mouth on the side of botulinum injection (Fig. 1).
2. Asymmetry in the position of the vermilion border of the lip or the nasolabial fold during dynamic expression after the injection (Fig. 2).
3. Asymmetry in facial expression, particularly during smiling, causing disfigurement. This complaint was probably the most common, occurring as a result of botulinum toxin–induced facial weakness (Figs. 2 and 4).

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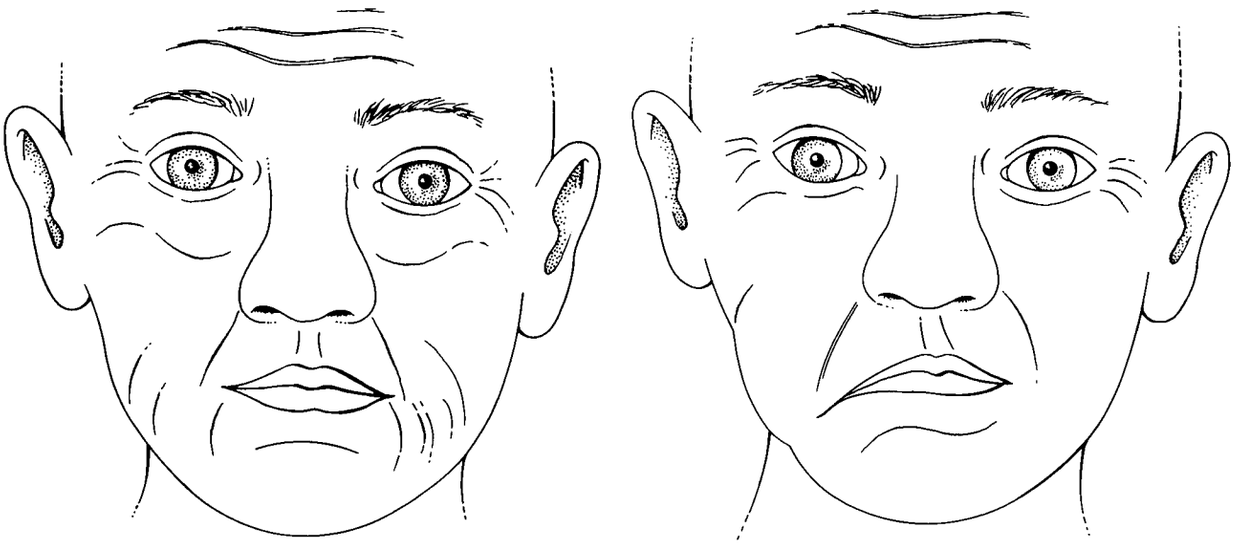

FIG. 1. (*Left*) Facial landmarks in an adynamic state emphasizing the symmetry of the nasolabial fold, vermilion border orientation, chin crease, lateral mouth angle, and degree of lip and tooth exposure. (*Right*) Asymmetry of facial landmarks in patients with facial paralysis in the resting position. Note alterations in the chin crease, nasolabial fold, mouth angle, and vermilion border.

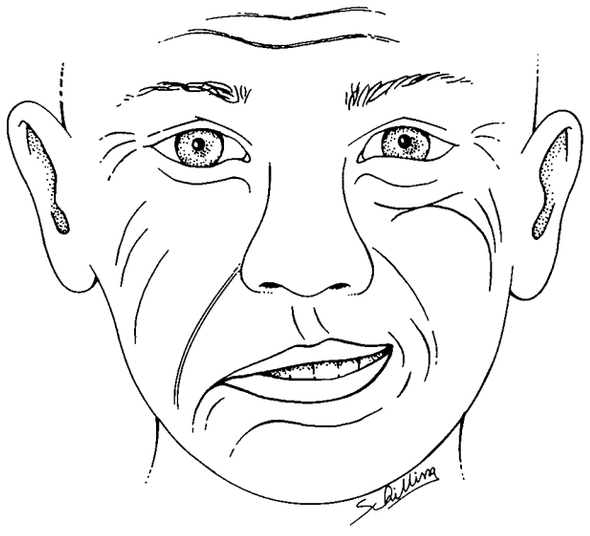

FIG. 2. Asymmetry of facial landmarks during facial expression (smile). The asymmetry in facial landmarks becomes more obvious during facial expression.

Six patients were inducted into this preliminary study. Each received follow-up appointments at 2, 4, and 8 weeks from the time of the injection. Ages ranged between 31 and 76 years. Each patient was asked to judge whether the injections produced an improvement in the degree of asymmetry previously noted. In addition, we observed the degree of asymmetry during the follow-up visits. Patients were asked whether they would prefer contralateral injections during a subsequent injection session. In addition, 35-mm photographs and video photography were used to assess the results.

Since the position of the nasolabial fold, the lateral angle of the mouth, and the elevation of this area of the lower face appeared to be most critical during dynamic facial movements, the zygomaticus major, minor, and occasionally the risorius muscles were targeted as the muscles that would most appropriately be weakened in order to achieve symmetry at rest and during dynamic movements. Three injections were given over the zygomaticus major, minor, and risorius muscles in a triangular configuration, as shown in Figure 3.

The dose range varied between 5 and 15 IU. Injections were given either at the time of treatment of hemifacial spasm or within 2 weeks after the initial treatment if undesirable asymmetry was noted by the patient.

In order to assess adverse effects, patients were asked whether difficulties with speech, smiling, chewing, or lip biting occurred following the contralateral injections.

CASE REPORTS

Case 1

A 71-year-old man with a 17-year history of left hemifacial spasm desired therapy for this condition. He had received a total of eight prior injections of botulinum A toxin ranging from 15 to 25 IU. After six of these injections, he noted substantial weakness on the left side of his mouth. This complication occurred despite lowering the dose of botulinum A toxin to 10 IU on several injection sessions.

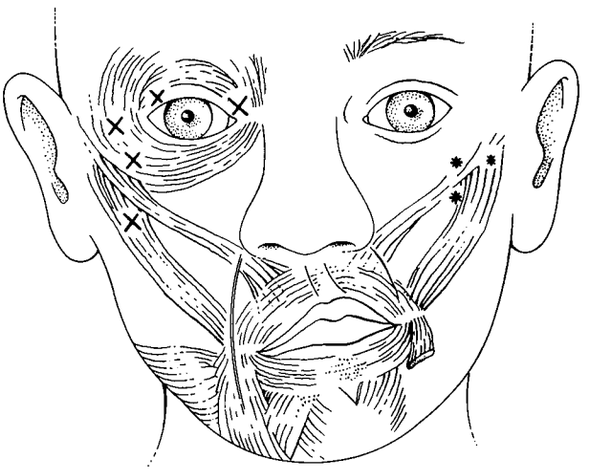

FIG. 3. Drawing demonstrating the support of the nasolabial fold by the zygomatic major and minor muscles. The balance and tone of the facial muscles govern the positions of such vital facial landmarks as the nasolabial fold, angle of the mouth, vermilion border, lip position, and transverse chin crease. The usual injection points for botulinum toxin for the treatment of hemifacial spasm are depicted on the right; however, although spasms are relieved, decreases in facial tone and amplitude of contraction on the right result in asymmetry of facial landmarks that is accentuated during dynamic movements. This asymmetry is diminished by contralateral injections over the zygomatic major and minor muscles, as shown on the left.

In addition to the usual injection points, he received a total of an additional 10 IU over the zygomaticus major and minor muscles on the contralateral side.

He felt his face appeared more even than after prior injections. Objectively, there appeared to be better symmetry in the resting position and during dynamic facial expressions. He desired further injections by this technique.

Case 2

This patient is a 33-year-old woman with left hemifacial spasm. The injections of botulinum A toxin reduced the degree of spasm; however, the patient complained of facial asymmetry, particularly during smiling. She found this to be particularly troublesome, although not as troublesome as the hemifacial spasm. Because of her concern, she was injected on the contralateral side with 15 IU botulinum A toxin over the zygomaticus major and minor muscles.

She felt this approach produced a better facial appearance than prior injections and desired future injections with this technique. Objectively, the facial symmetry appeared improved on follow-up examinations.

Case 3

This 76-year-old man presented with aberrant regeneration of the facial nerve following Bell's palsy. He had received periorbital botulinum A toxin injections that had substantially relieved the synkinetic contraction of the orbicularis muscle during chewing movements. Although there was improvement in involuntary blepharospasm, the patient was troubled by the facial asymmetry the toxin created within the first month after injection.

When he was injected on the contralateral side with 5 IU, he noted some difficulty with active smiling, but he was most pleased with the degree of facial asymmetry achieved.

He desired further injections by this method. Objectively, there appeared to be good symmetry one month after injection.

Case 4

This 53-year-old woman had been treated on four occasions with botulinum A toxin for hemifacial spasm. After each injection, there had been a transient weakness of the muscles on the side that had been injected. The patient received a total of 25 IU at the usual injection points.[1] Following the last injection, she was very displeased with the facial asymmetry produced by these injections despite reduction and elimination of the involuntary movements.

She was injected with an additional 10 IU on the contralateral side 2 weeks later. Over the next 2 weeks, she noted a substantial improvement in the degree of facial symmetry.

Objectively, the examiner noted a depressed smile but improved symmetry. The patient desired further injections by this method.

Case 5

This 71-year-old retired physician had 11 injections of botulinum A toxin for hemifacial spasm that substantially reduced the degree of spasm. Although he was satisfied with the therapy, lowering of the angle of the mouth and flattening of the nasolabial fold with marked asymmetry of movement on each side of the face had been troublesome on several occasions. For this reason, he was given contralateral injections of botulinum A toxin at a dose of 15 IU to the zygomaticus major and minor muscles. He felt that there was depression of "natural facial expression."

When seen in follow-up at weeks 2 and 4, he had noted only modest improvement in the degree of facial symmetry. He was ambivalent as whether the injections should be given on the contralateral side in the future.

Case 6

This patient is a 61-year-old woman with 5-year history of hemifacial spasm. Two weeks after injection of 15 IU into the usual points, asymmetry in the angle of the mouth was noted in resting position (Fig. 4, *left*). Additionally, there were asymmetrical excursions of the upper lip and irregular exposure of the teeth during smiling (Fig. 4, *right*).

The contralateral zygomaticus major and minor muscles were treated with an additional 10 IU botulinum toxin. Two weeks following the contralateral injection, the patient felt that her facial symmetry was better at rest and during active expression. Objectively, there appeared to be an improvement in resting and dynamic facial symmetry (Fig. 5). The patient desired further injections by this method.

COMPLICATIONS

One patient complained that she could not overtly smile for a period of several weeks after the injection, but she found this impairment to be transient.

FIG. 4. *Case 6.* Appearance 2 weeks after botulinum toxin injection demonstrated facial asymmetry.

FIG. 5. *Case 6.* Appearance 2 weeks after contralateral botulinum toxin injection.

No patient described difficulties with chewing, eating, or lip or cheek biting. One patient developed a transient slurring of speech that lasted for 2 weeks.

Objective observation revealed that each patient appeared to have more symmetrical facial characteristics, although the smile pattern changed. Tooth exposure was depressed and nasolabial folds were blunted during smiling. Each patient appeared to have a more symmetrical position of the nasolabial folds and the lateral angle of the mouth during resting position, and there appeared to be a transient depression of movements involved with natural facial expression. Only one patient found this alteration troublesome during routine verbal communication.

DISCUSSION

Botulinum A toxin is a major advance in the treatment of hemifacial spasm. Prior to its application for this condition, effective therapy consisted of posterior craniotomy and microsurgical decompression of the facial nerve from tortuous vessels thought to cause demyelination and damage to the intracranial facial nerve.[9] Although the Jannetta procedure has been effective, the potential risk of surgical intervention may not be

warranted considering the degree of the morbidity caused by this condition.[9]

The major disadvantages of botulinum A toxin for the treatment of hemifacial spasm include (1) the necessity of repeated injections, (2) lagophthalmos created by weakness of eyelid closure with possible exposure keratitis, (3) increased weakness of the muscles of facial expression on the side injected, and (4) ptosis, diplopia, and increased epiphora from diffusion of the toxin into deeper muscles of the orbit from the eyelid injection sites.[10] Variations in the injection method have already been proposed to limit the regional complications. For instance, ptosis is minimized by placing the toxin close to the lash line at the lateral and medial extents of the upper lid, and diplopia can be avoided by not using a medial lower lid injection.[10] The modification of the injection method proposed in this paper addresses directly the issue of facial asymmetry from hemifacial weakness.

The average duration of action of botulinum A toxin for hemifacial spasm is 5.3 months,[1–4] substantially longer than achieved for involuntary movement associated with essential blepharospasm and Meige syndrome (3.1 months). The etiology of hemifacial spasm involves denervation, whereas bilateral facial dyskinesias (Meige syndrome, essential blepharospasm) are due to a central nervous system disorder with no evidence of facial neuropathy. Because of preexisting denervation, injected facial muscles are more sensitive to the weakening effect of the toxin when compared with those in patients with Meige syndrome and essential blepharospasm. Because of this, facial weakness is more pronounced when botulinum injections are used for hemifacial spasm. In fact, the dose requirements are also significantly less than needed to treat Meige syndrome or essential blepharospasm. Facial weakness generally lasts 2 to 10 weeks after injection.

The procedure variation presented in this paper offers a method of reducing the degree of facial asymmetry during dynamic movements and in the resting position. By injecting the toxin into the contralateral zygomaticus major and minor muscles and occasionally the risorius muscle, a relative weakness is produced within these muscles during the same period that the toxin influences the side of the face demonstrating the involuntary movement. Because the contralateral injection effectively weakens the muscles on the normal side, weakness produced by the toxin on the side with the hemifacial spasm is camouflaged by symmetrical changes on the contralateral side. This approach produces a more even smile, as well as a more symmetrical nasolabial fold and vermilion border of the lip. The angle of the mouth at rest and during the movements of facial expression also appears to be more symmetrical, as is the degree of tooth exposure during smiling.

A similar concept of camouflage has been reported by Clark and Berris[12] for a patient who experienced unilateral frontalis muscle paralysis from damage to the temporal branch of the facial nerve following a rhytidectomy procedure. These authors had injected the contralateral frontalis muscle to produce a more symmetrical appearance to the forehead and brow position in this patient.

One potential concern we had in introducing this variation is the treatment of normal muscle with botulinum A toxin and potential long-term effects. It should be noted, however, that there have been no long-term adverse effects with botulinum A toxin for the treatment of essential blepharospasm and Meige disease.[1–7] Muscle biopsies taken from patients after repetitive injections of botulinum A toxin have failed to show any long-term evidence of permanent degeneration, fibrosis, or persistent atrophy. In fact, the toxin injections had been discontinued for a period of 6 to 12 months prior to the time of muscle specimen evaluation, and no evidence of denervation was seen using standard Masson trichrome stains or histochemical analysis with acetylcholinesterase.[11]

A limitation of this study is the lack of a grading system to assess the response to the botulinum toxin injections. Although the objective responses assessed by the physician observer and patient self-assessment are meaningful, grading systems to quantitate clinical results may prove useful in allowing more precise evaluation of results. Additionally, attempts at stereotyping smiling characteristics may prove useful in standardizing the exact muscles to be injected and the dose requirements. For instance, patients demonstrating a preexisting smile and dynamic expression pattern that retracts the central upper lip and exposes dentition may require more weakening in the levator labii superioris, whereas smile patterns not associated with tooth exposure may require more weakening of the zygomaticus major and minor muscles to achieve greater symmetry.

Although most patients with hemifacial spasm

are pleased to rid themselves of the involuntary movement after injection of botulinum A toxin, they can be sensitive to the asymmetry in facial tone and movement after this therapy. It appears that the contralateral injection method can be useful, particularly in those patients with uneven facial appearance several weeks after injection. In addition, it can be useful in those patients who have had this experience and have conveyed this information to their clinician at the time of repeat injection.

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REFERENCES

1. Scott, A. B., Kennedy, R. A., and Stubbs, H. A. Botulinum A toxin injection as a treatment of blepharospasm. *Arch. Ophthalmol.* 103: 347, 1984.
2. Borodic, G. E., and Cozzolino, D. Blepharospasm and its treatment, with emphasis on the use of botulinum toxin. *Plast. Reconstr. Surg.* 83: 546, 1989.
3. Kraft, S. P., and Lang, A. E. Cranial dystonia, blepharospasm, and hemifacial spasm: Clinical features and treatment, including the use of botulinum toxin. *Can. Med. Assoc. J.* 139: 837, 1988.
4. Mauriello, J. A., Jr. Blepharospasm, Meige syndrome, and hemifacial spasm: Treatment with botulinum toxin. *Neurology* 35: 1499, 1985.
5. Brin, M. F., Fahn, S., Moskowitz, C., Friedman, A., Shale, H. M., Green, P. E., Blitzer, A., List, T., Lange, D., and Lovelace, R. E. Localized injections of botulinum toxin for the treatment of focal dystonia and hemifacial spasm. *Adv. Neurol.* 50: 599, 1988.
6. Elston, J. S. Botulinum toxin therapy for involuntary facial movements. *Eye* 2: 12, 1988.
7. Saraux, H. Treatment of blepharospasm and facial hemispasm by injection of botulinum toxin [English Abstract]. *J. Fr. Ophthalmol.* 11: 237, 1988.
8. Nielson, V. K. Electrophysiology of the facial nerve in hemifacial spasm: Ectopic/ephaptic transmission. *Muscle Nerve* 8: 545, 1985.
9. Jannetta, P. J., Abbasy, M., Maroon, J. C., Ramos, F. M., and Albin, M. S. Etiology and definitive microsurgical treatment of hemifacial spasm. *J. Neurosurg.* 47: 321, 1977.
10. Frueh, B. R., Nelson, C. C., Kapustiak, J. F., and Musch, D. C. The effect of omitting botulinum toxin from the lower eyelid in blepharospasm treatment. *Am. J. Ophthalmol.* 106: 45, 1988.
11. Borodic, G. E., and Ferrante, R. Orbicularis Muscle Histology After Repetitive Injections of Botulinum A Toxin. Presented at the Annual Meeting of the American Academy of Ophthalmology, Atlanta, Ga., 1990.
12. Clark, R. P., and Berris, C. E. Botulinum toxin: A treatment for facial asymmetry caused by facial nerve paralysis. *Plast. Reconstr. Surg.* 84: 353, 1989.