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Paralytic strabismus: the role of botulinum toxin

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SUMMARY Five adults with acute extraocular muscle palsies followed by limited recovery of muscle function were treated with injections of botulinum toxin A to the ipsilateral antagonist of the affected muscle. Three were cases of unilateral sixth nerve palsy, one of bilateral sixth nerve palsy, and one of third nerve palsy. After a period of paralysis, during which the strabismus was overcorrected, the injected muscle recovered and binocular sensory and motor functions were restored and have been maintained for periods of up to 21 months. The treatment is a safe and effective alternative to surgery, particularly in cases in which a general anaesthetic is not advisable.

Adult neurogenic ocular palsies present problems of both diagnosis and management. Despite full neurological investigation the underlying cause may not be established,[1 2] and, even if specific treatment can be instituted, recovery of function may not be complete. Binocularity may not be restored even with a compensatory head posture, or prisms, and despite alternate patching suppression frequently develops. The timing of surgical treatment and the choice of procedure in the individual case are difficult decisions,[3] and the functional result of surgery is unpredictable, particularly after head injury or neurosurgical procedures, when fusional mechanisms may have been disrupted.[4]

In sixth nerve palsy the choice of operation depends on the extent of recovery. If the eye cannot be abducted beyond the midline, a vertical rectus muscle transposition procedure with medial rectus recession will be required.[3 5] Surgery may have to be in two stages, since the anterior ciliary arteries associated with three ipsilateral rectus muscles cannot be simultaneously operated upon in a patient over the age of 20 without risking anterior segment ischaemia.[3] When the affected eye can abduct at least 10° beyond the midline, and saccadic velocity for this is normal, a medical rectus recession and lateral rectus resection should suffice.[3 6] In either case the contralateral medial rectus may have to be recessed and adjustable or posterior fixation sutures used.[7] Surgery in third nerve palsy is less satisfactory.[8] The combination of the size of the exodeviation, the presence of a vertical deviation, and, frequently, acquired oculomotor synkinesis means that normal binocular control cannot be achieved. A satisfactory appearance in the primary position with a small field of binocular single vision will usually require operations on both eyes.[3 8]

Botulinum toxin A (BTXA) causes a flaccid paralysis of skeletal muscle by preventing the release of acetylcholine at the neuromuscular junction.[9] New junctions are formed over six to eight weeks, and the muscle gradually recovers normal activity.[10] In appropriate dosage individual extraocular muscles can be paralysed by direct injection of BTXA under local anaesthetic and the position of the eye within the orbit altered.[11 12] If binocular functions are re-established when the eyes are realigned, as the treated muscle recovers function the incomitant strabismus may not recur.[12] Five adults who would otherwise have been treated surgically for partly recovered neurogenic ocular palsies have therefore had injections of BTXA into the ipsilateral antagonist of the palsied muscle.

Patients, materials, and methods

There were three cases of unilateral sixth nerve palsy, one of bilateral sixth nerve palsy, and one of third nerve palsy (Table 1). The aetiology had been established in all cases and appropriate treatment carried out where indicated. At least six months had been allowed for spontaneous recovery to occur. The patients' general health had been assessed, particularly their suitability for general anaesthetic (Table 1). The visual acuity and visual fields were normal in all cases.

Orthoptic assessment included measurement of the angle of strabismus at near and distance fixation, and the extent of the extraocular movements (Table

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Table 1 *Description and aetiology of paralytic strabismus: five cases*

Patient	*Sex*	*Age*	*Nerve*	*Aetiology*	*General health*	*Fit for general anaesthetic*	*Interval from palsy to treatment*
1	F	19	Right VI	Infectious polyneuritis	Normal	Yes	6 Months
2	F	37	Left III	Trauma	Normal	Yes	5 Years
3	M	45	Bilateral VI	Trauma	Left hemiparesis, bulbar palsy	Yes	9 Months
4	F	73	Right VI	Hypertension	Bronchiectasis, depression	No	3 Years
5	F	18	Right VI	Pontine arteriovenous malformation	Right V and VII nerve palsies, left hemiparesis	No	8 Months

Table 2 *Pretreatment orthoptic assessment*

Patient	*Deviation prism dioptres at 6 m*	*Ocular movements*	*Saccadic velocity*	*Suppression*	*Binocular function*	
					Fusion	*Stereopsis*
1	55 Esotropia	Reduced right abduction	Normal	Intermittent	Yes	Gross
2	65 Exotropia R/L 4	Limited adduction, vertical: acquired oculomotor synkinesis	Slow adduction	Left	Yes	Nil
3	50 Esotropia	Reduced abduction bilateral	Slow abduction	Intermittent	Yes	Gross
4	30 Esotropia	Reduced abduction	Normal	Intermittent	Yes	Gross
5	45 Esotropia	Reduced right abduction	Slow abduction	Intermittent	Yes	Gross

Table 3 *Treatment schedules*

Patient	*Muscle treated*	*Subsequent treatment*	*Period of overcorrection*	*Period to stable result*
1	Right medial rectus	Nil	5 Weeks	8 Weeks
2	Left lateral rectus	Left lateral rectus at 4 weeks	3 Weeks	16 Weeks
3	Left medial rectus	Left medial rectus at 4 weeks Right medial rectus at 10 weeks	3 Weeks	14 Weeks
4	Right medial rectus	Nil	4 Weeks	6 Weeks
5	Right medial rectus	Right medial rectus at 6 weeks	3 Weeks	8 Weeks

Table 4 *Results of treatment*

Patient	*Cover test*	*Binocular function*				*Period of follow-up after stable result achieved*
		Stereopsis in seconds of arc (Titmus stereotest)	*Fusion range (degrees)*		*Area of binocular single vision*	
			Abduction	*Adduction*		
1	Esophoria	40 Seconds	4	10	Normal	21 Months
2	Exophoria	40 Seconds	4	6	30° From fixation	10 Months
3	Esophoria	40 Seconds	4	8	Normal vertical, 30° horizontal	4 Months
4	Esophoria	40 Seconds	4	10	Normal vertical, 30° horizontal	4 Months
5	Esophoria, distance esotropia Controlled by AHP	40 Seconds	2	4	Full in L gaze, 10° R gaze	4 Months

2). The saccadic velocity in the direction of the palsied muscle was judged clinically to be either normal or slow. Fusion and stereopsis were investigated on the synoptophore.

BTXA, $3{\cdot}12\times10^{-4}$ µg, was injected under electromyographic control as previously described[12] into the muscle indicated in Table 3. Clinical assessment and orthoptic measurements were repeated at one, two, and four weeks after treatment, and the injections repeated at the same dosage if necessary to produce

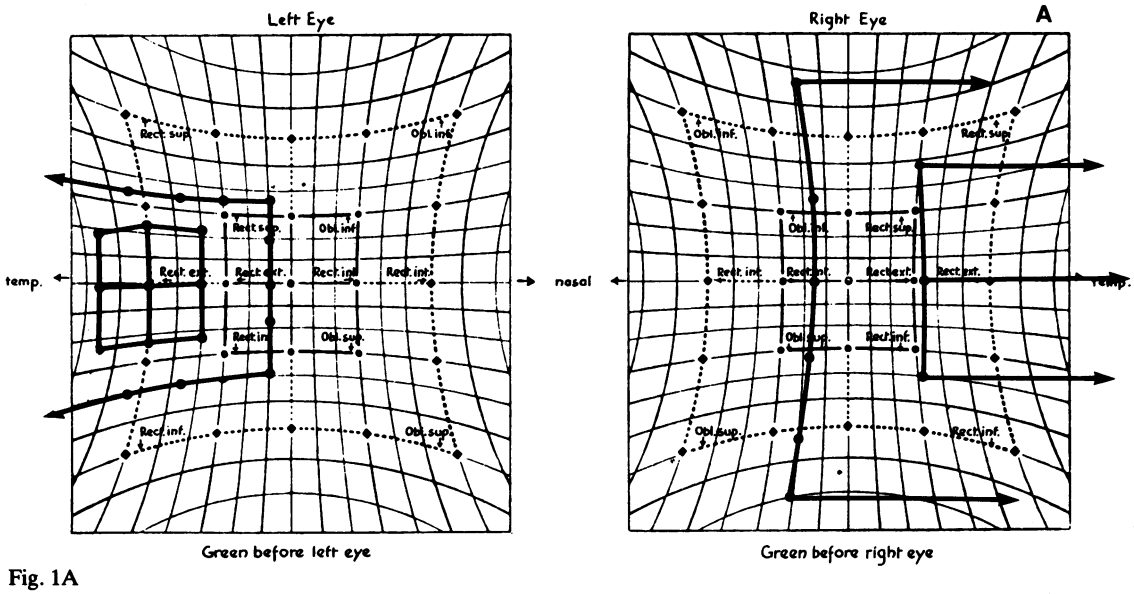

Fig. 1A

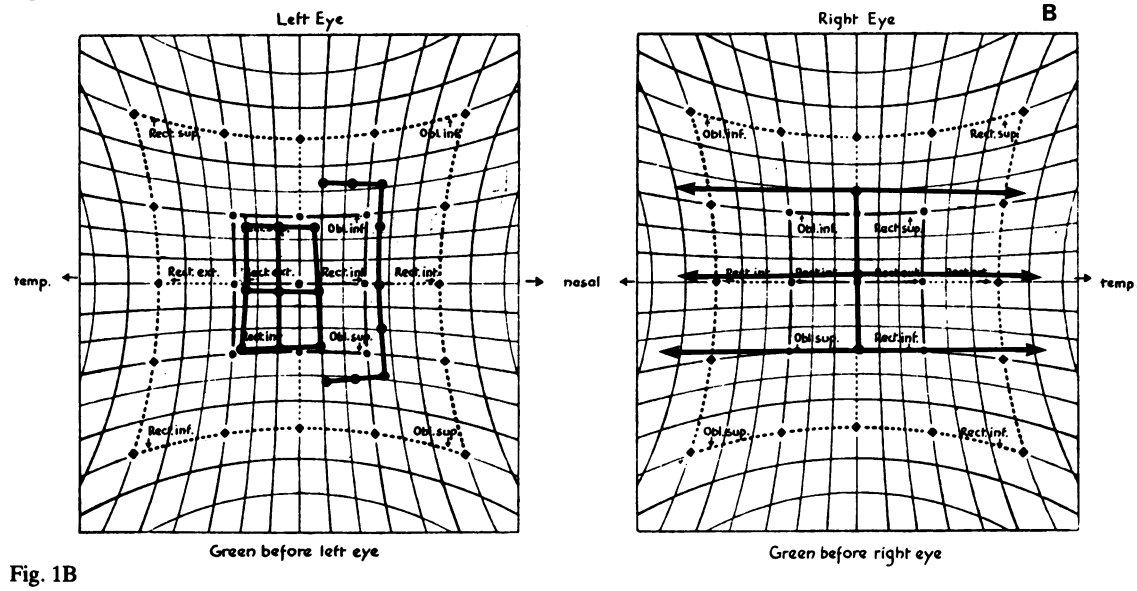

Fig. 1B

Fig. 1 *Hess charts showing the effect of botulinum toxin treatment of the lateral rectus in partly recovered IIIrd nerve palsy.*

an overcorrection of the original strabismus (Table IV). In case 2 pilocarpine drops 0·1% were applied twice a day to the left eye to mediate accommodation in an attempt to re-establish fusion.[8] Follow-up thereafter has been from 4 to 21 months.

Results

There were no local or systemic side effects of the treatment.

The ocular deviation was overcorrected in all cases for a period of between three and five weeks (Table 3), when single vision could be obtained in only one position of gaze. As the treated muscle recovered function, however, the area of binocular single vision (BSV) gradually enlarged. Fig. 1A shows the Hess chart in case 2 before treatment. After the left lateral rectus had been treated, the horizontal muscles on the right eye overacted in both adduction and abduction, but there was a small central area of single

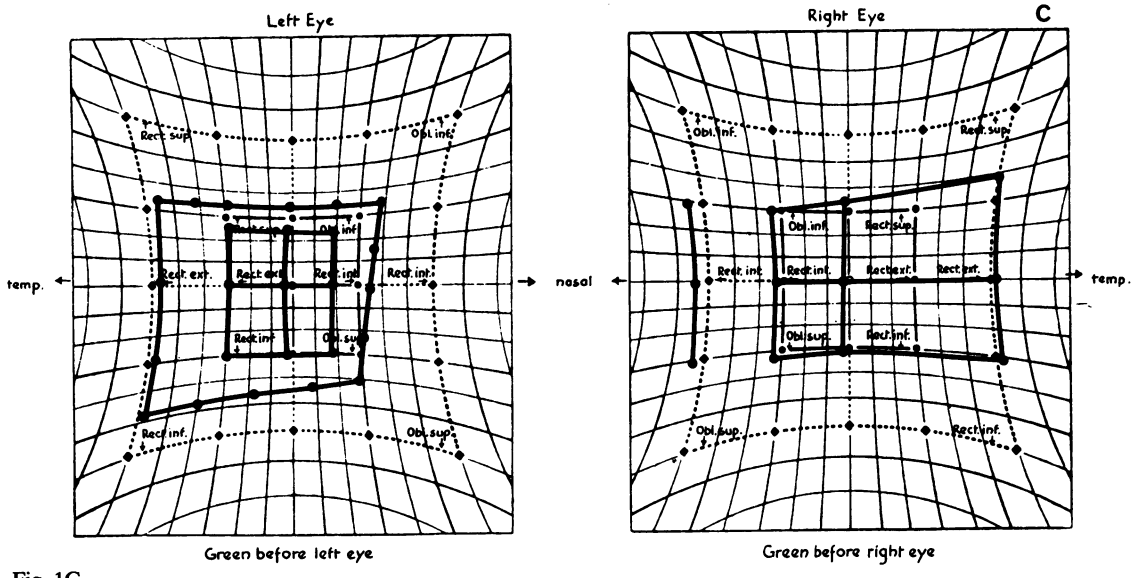

Fig. 1C

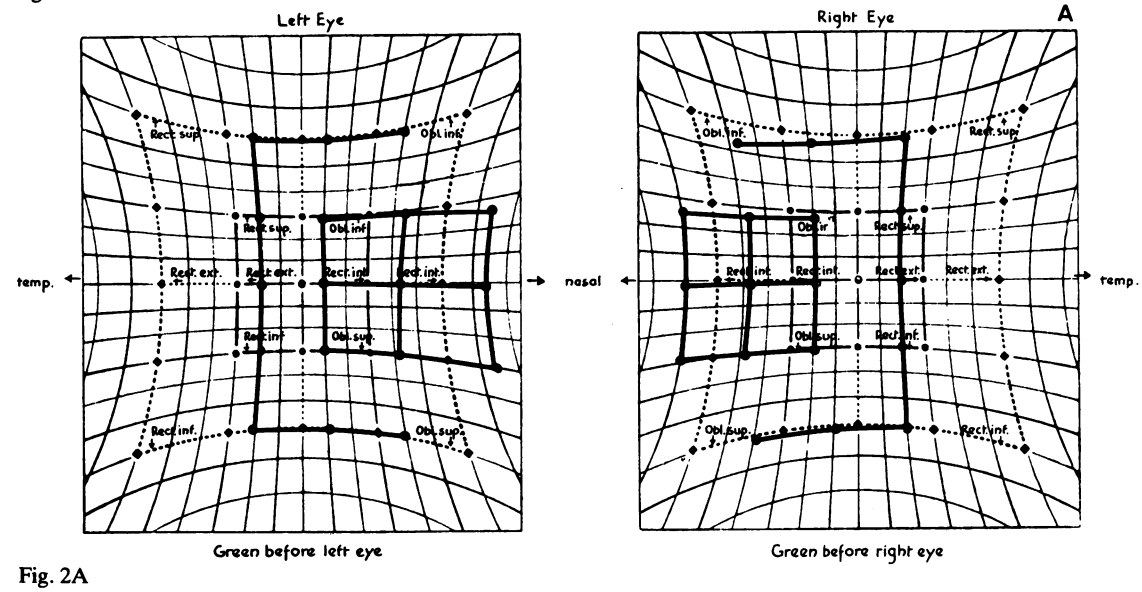

Fig. 2A

vision (Fig. 1B). The area enlarged as the lateral rectus recovered function (Fig. 1C).

Fig. 2A shows the Hess chart in case 3 before treatment. In Fig. 2B, after the left medial rectus had been treated, single vision could be obtained in left gaze, but the patient showed an increasing exotropia as he moved into right gaze. In Fig. 2C the final stable result is shown with minimal bilateral lateral rectus weakness.

Normal stereopsis and fusion were achieved in all patients after between six and 16 weeks; the field of binocular single vision was then normal in cases 1 and 4 but remained limited in cases 2, 3, and 5 because of permanent nuclear or supranuclear abnormalities of eye movement. The functional results have been maintained for periods up to 21 months (Table 4).

Discussion

Conventional treatment of these patients would

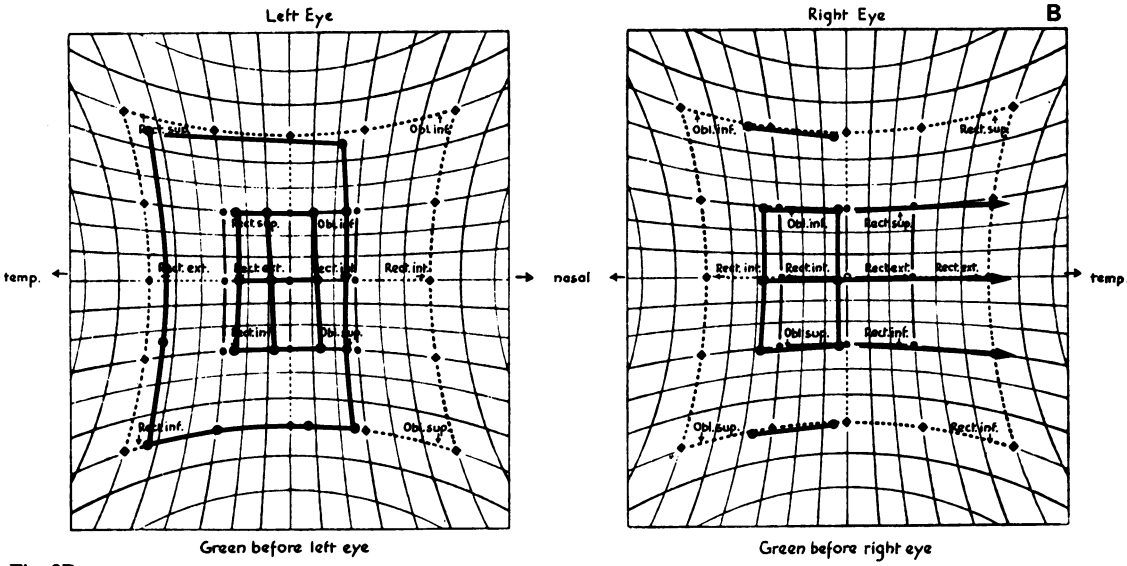

Fig. 2B

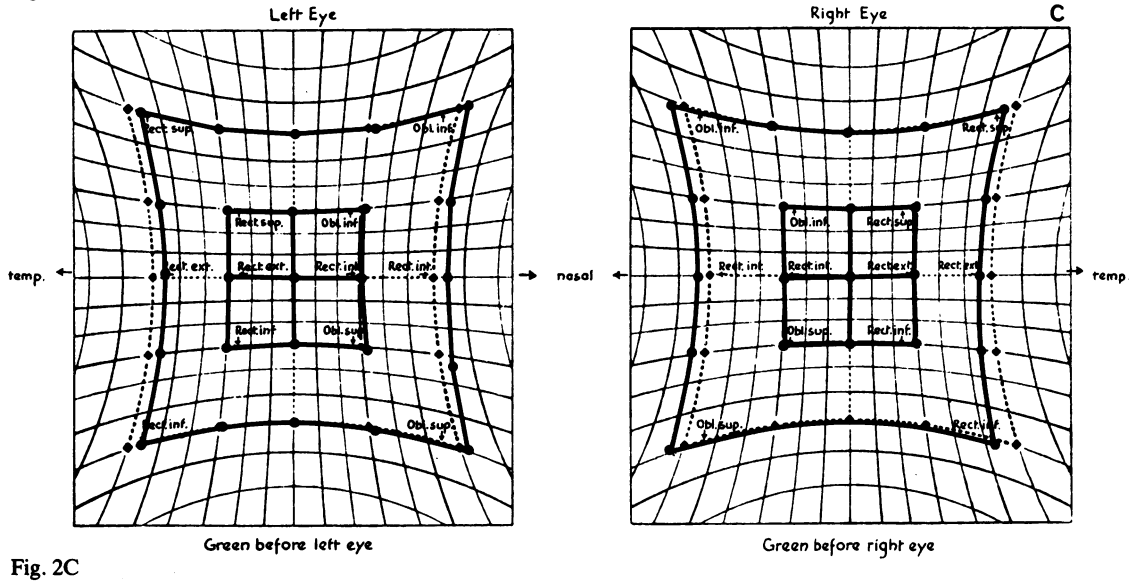

Fig. 2C

Fig. 2 *Hess charts showing the effect of botulinum toxin treatment of the left medial rectus in bilateral VIth nerve palsy.*

require surgery on both eyes for the third and bilateral sixth nerve palsies and, in two of the three cases of unilateral abduction deficit, operation under local anaesthesia. While the benefit of surgery, provided the suppression of the deviating eye was overcome, would be immediate, the potential area of binocular single vision, already limited in cases 2, 3, and 5, would be further compromised by operative reduction of ocular rotations in cases 2 and 3. The patients would be in hospital for three days and need to have local anti-inflammatory treatment for one to two weeks.

In contrast, BTXA treatment of strabismus is an outpatient procedure under local anaesthetic, and, if the muscle to be injected has not been previously operated on, the treatment is easy and painless. There are no systemic side effects,[11 12] and, while there is a theoretical danger of ocular perforation, this has not occurred in over 400 injections by the authors. The eye is padded for two hours,

and thereafter no local treatment is needed.

The period of reversal of the diplopia and horizontal incomitance associated with the newly paralysed muscle was disturbing for all the patients treated. Although there was one position of gaze in which single vision could be obtained, overaction of the contralateral synergist of the injected muscle made this difficult to maintain, and the two images slipped past one another. As the paralysis recovered, the area of binocular single vision gradually increased. In case 2, after five years with suppression of the deviating image and no stereopsis demonstrable, stereo acuity of 40 seconds of arc and a near normal fusion range were achieved, and in general the quality of stereopsis and fusion regained was better than had been expected before treatment. The period of overcorrection when the deviating image is moved well away from the suppression scotoma may explain this finding.

Experience with BTXA treatment of strabismus in patients without binocular functions[12] suggests that the eye tends to drift back to the original position as the paralytic effect of the injection declines. If stereopsis and fusion had not been re-established in these cases therefore, the pretreatment status would have been restored, whereas surgery may have led to intractable diplopia.

BTXA has also been advocated in the management of acute microvascular lateral rectus palsy, when injection of the ipsilateral medial rectus, by allowing the eye to abduct passively, enables a small central area of binocular co-operation to be achieved. It is expected that the two paralysed horizontal muscles would regain function at the same rate, gradually enlarging the area of the binocular single vision. We consider that these benefits to a group of patients with a good prognosis for recovering lateral rectus function are outweighed by disadvantages. A change in neurological signs may be obscured, and the reversal of diplopia on either side of the central binocular area is likely to be very uncomfortable. We are, however, extending the use of BTXA to the treatment of the medial rectus prior to surgery in cases of persistent abduction weakness requiring vertical muscle transposition, with encouraging results.

Conclusion

BTXA treatment of partly recovered adult paralytic strabismus is a simple, safe, cheap, and effective method which avoids the risks of a general anaesthetic. A larger area of binocular single vision may be achieved than by conventional surgery.

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