Contralateral Surgery for the Treatment of Third Nerve Palsy with Aberrant Regeneration

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• PURPOSE: To report the results of contralateral recession-resection of the horizontal muscles in oculomotor nerve palsy with aberrant regeneration to correct both the strabismus and the ptosis in one procedure.
• DESIGN: Retrospective case series.
• METHODS: This is an institutional study on patients with oculomotor nerve palsy with aberrant innervation who had contralateral eye muscle surgery in 2 different centers. Patients were included if they have both exotropia and aberrant regeneration with a ptosis that improved on adduction. All patients had contralateral lateral rectus recession and medial rectus resection. Ductions, versions, angle of misalignment, and degree of ptosis were evaluated before surgery and at last follow-up.
• RESULTS: Eleven patients were identified. The mean age at surgery was 15.0 ± 9.2 years. Five patients were male (45%). Trauma was the cause in 8 (72%) cases. The mean angle of exotropia was 42 ± 14 prism diopters. The mean degree of ptosis was 3.9 ± 1.6 mm. The mean lateral rectus recession was 8.2 ± 1.1 mm, and the mean medial rectus muscle resection was 6.7 ± 0.9 mm. The mean follow-up was 6.4 ± 2.5 months. After surgery, none of the patients had residual exotropia > 10 prism diopters. The mean degree of ptosis after surgery was 0.9 ± 0.8 mm. None of the patients required further surgery for ptosis or strabismus.
• CONCLUSION: Contralateral eye muscle in third nerve palsy with aberrant innervation offers the advantage of simultaneous correction of both strabismus and ptosis through a single procedure. (Am J Ophthalmol 2021;222:166–173. © 2020 Elsevier Inc. All rights reserved.)

OCULOMOTOR NERVE PALSY OR THIRD CRANIAL nerve palsy is a challenging condition that usually presents with the involved eye fixed in the down and out position (exotropia and hypotropia) together with upper eyelid ptosis. While recovery of third nerve palsy is common, it is sometimes complicated with misdirection or the so-called aberrant regeneration.[1]

Aberrant regeneration of oculomotor nerve palsy is seen in both congenital cases and in acquired cases caused by brain tumors, aneurysms, or trauma.[2,3] The clinical picture is variable. The most common presentation occurs when fibers from the third nerve that would normally supply the medial rectus muscle now supply the levator palpebrae superioris muscle. The upper eyelid is partially ptotic when the affected eye is in the primary position, elevates when the eye is adducted, and lowers with abduction (inverse Duane sign). Attempted vertical gaze may also elicit several different abnormal responses. Typically, there is poor vertical excursion of the globe, but on attempted downgaze, the upper eyelid retracts (pseudo-Graefe sign).[1,4]

The classic treatment of cases of third nerve palsy with aberrant regeneration usually aims to treat the exodeviation by ipsilateral recess-resect of the horizontal rectus muscles, sometimes with vertical transposition of the rectus muscles to correct the hypotropia, followed by surgical correction of the ptosis in a separate operation.[1,4] In 1980, O'Donnell and associates[5] suggested a new approach to treat cases of aberrant regeneration of the oculomotor nerve using contralateral recess-resect of the horizontal muscles to correct both the strabismus and the ptosis in one surgical procedure. While the technique has gained popularity, little data are available about its results in the published literature. The aim of this study is to report additional experience and improved techniques using this procedure in selected patients with aberrant regeneration of the third cranial nerve.

METHODS

THE STUDY PROTOCOL WAS APPROVED BY CAIRO UNIVERsity Hospital Research Committee and the University of Michigan Institutional Review Board. The study and data collection conformed to all local laws and were compliant with the principles of the Declaration of Helsinki. A retrospective study was performed on patients with oculomotor nerve palsy with aberrant regeneration who had eye muscle surgery in Cairo University Hospital and the Kellogg Eye Center during the period from January 2007 through December 2018. Informed consent for the surgery was

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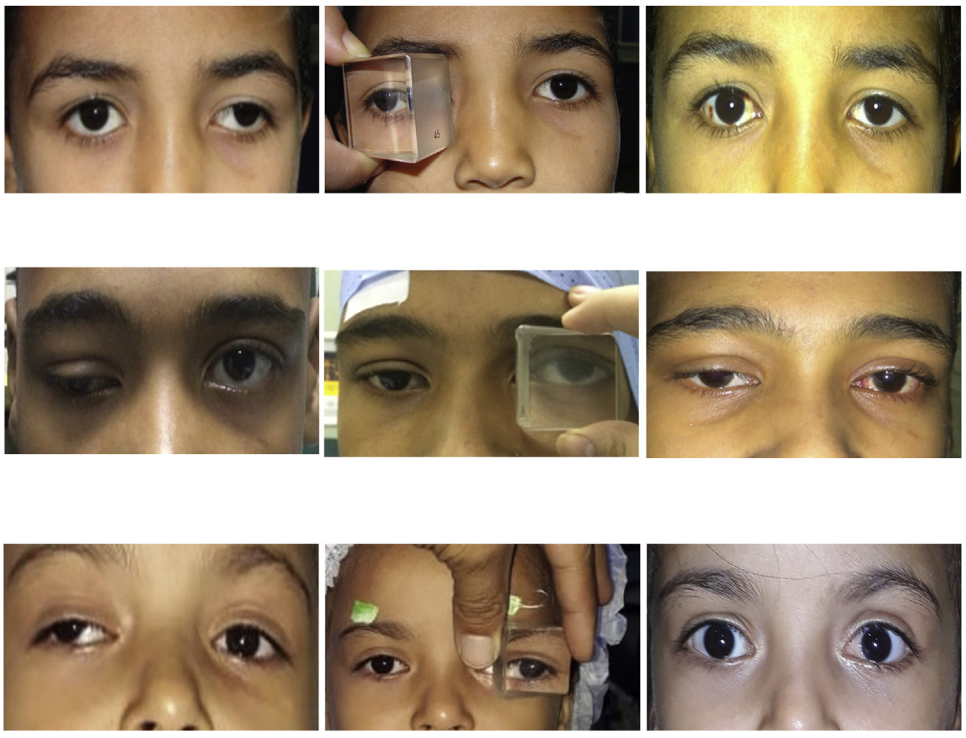


FIGURE 1. Photographs of patient 4 (Top Panels), patient 6 (Middle Panels), and patient 11 (Bottom Panels) showing ptosis of the left upper eyelid in patient 4 and right upper eyelids in patients 6 and 11 (Left), with improvement of the ptosis after placing a base-in prism in front of the sound eye (Middle). Right panels show improvement of ptosis in the same patients after contralateral recession-resection.

obtained from all patients. Patients were included in the study only if they had a minimum follow-up period of 3 months.

A diagnosis of oculomotor nerve palsy was based on the presence of unilateral limited adduction, depression, or elevation in the absence of restrictive lesions. Diagnosis was further confirmed through history taking and neurologic imaging. Patients were included in the study only if they showed evidence of aberrant regeneration of medial rectus to ipsilateral levator with an eyelid ptosis that improves on adduction and worsens on abduction.

Each patient received a complete preoperative ocular examination, which included cycloplegic refraction, assessment of any abnormal head posture, dilated fundus examination, as well as neurologic consultation. The degree of ptosis was calculated as the difference in the marginal reflex distance of both sides in primary gaze.

In addition, all patients had a detailed sensorimotor examination during the initial evaluation and at each follow-up period. The ductions and the versions in all directions of gaze were analyzed. Underaction was graded on a scale of 0 to −4, with 0 representing no limitation and −4 representing no movement into the tested field of gaze. The primary and secondary angles of misalignment were measured in the primary position for both distance and near using the prism and cover test with the prism placed in front of the paretic eye (to measure the primary angle) and in front of the nonparetic eye (to measure the secondary angle). The preoperative and postoperative angles of deviation were calculated for each subject as the angle of misalignment for distance being careful to prevent any anomalous head posture. All deviations were measured with appropriate spectacle correction. In addition, the primary angles of horizontal and vertical misalignment were measured in side gazes as well as in straight up and down gazes. All measurements were done using fully trained ophthalmologists or orthoptists as a part of their routine clinical practice.

All patients had surgery on the contralateral eye. The aim of the surgery was to correct the angle of deviation in the primary position with the head straight and to achieve maximum improvement in the eyelid position. The target angle for contralateral eye surgery was calculated by placing base-in prisms in front of the normal eye and increasing them in power until both the alignment and the ptotic eyelid of the affected eye assumed the best cosmetic appearance (Figure 1). Additional surgery was performed whenever needed on the ipsilateral eye to correct larger angles of deviation.

Surgeries were performed by 4 surgeons using the fornix approach. In all patients, the muscles were exposed and hooked through an inferotemporal fornix approach. For lateral rectus muscle recession, the muscle was secured

with 6-0 polyglactin sutures (Vicryl; Ethicon, Somerville, New Jersey, USA). The muscle was sutured directly to the sclera at the desired amount of recession. For medial rectus resection, the muscle was secured with 6-0 polyglactin sutures just behind the desired the amount of resection. Resection was then performed, and the muscle was then sutured to the sclera at the original insertion. Vertical muscle transposition of the horizontal muscles was done in patients with hyper- or hypotropia to correct any associated vertical deviation.

Data at the last follow-up period were used for statistical analysis. Statistical analysis was performed with SPSS for Windows (SPSS Inc, Chicago, Illinois, USA). Preoperative and postoperative data were analyzed using the *t* test for continuous variables and the Fisher exact test for categorical variables.

RESULTS

ELEVEN PATIENTS WERE IDENTIFIED (TABLE). THE MEAN AGE of patients was 15.0 ± 9.2 years (range 3 to 30 years). Five patients were male (45%). Trauma was the cause of oculomotor nerve palsy in 8 (72%) cases. The mean angle of exotropia was 42 ± 14 prism diopters (PD; range 30-80 PD). The mean degree of ptosis was 3.9 ± 1.6 mm (range 2-7 mm). Hypotropia of the affected eye was present in 3 patients (27%). Only 1 patient had previous surgery on the affected eye (patient 10). This patient had a previous right lateral rectus recession 10 mm and right medial rectus resection 8 mm, with residual exotropia of 15 PD. All other patients did not have previous eye muscle surgeries or eyelid surgeries. All patients showed aberrant elevation of the eyelid on adduction. In addition, 5 patients (45%) also showed aberrant elevation of the eyelid on downgaze (Supplemental Figure 1).

All patients had surgery on the contralateral eye in the form of lateral rectus recession and medial rectus resection. The mean lateral rectus recession was 8.2 ± 1.1 mm (range 7-10 mm). The mean medial rectus muscle resection was 6.7 ± 0.9 mm (range 5.5-8.0 mm). One patient had a large preoperative angle of horizontal misalignment of 80 PD and needed an additional 8-mm lateral rectus recession on the ipsilateral affected eye. In the 3 patients with hypotropia of the affected eye, the contralateral recession-resection was combined with 8 mm downward transposition of both the lateral and medial rectus muscles in 2 patients and with contralateral inferior oblique myectomy in 1 patient.

The mean follow-up was 6.4 ± 2.5 months (range 4-12 months). There was marked improvement of both the exotropia and hypotropia in all patients. The mean angle of horizontal misalignment at the last follow-up was 4 ± 3 PD (range 0-8 PD). None of the patients had residual exotropia >10 PD (Figures 2 and 3; Supplemental Figures 2 through 4). There was no cosmetically noticeable vertical tropia postoperatively in any of the patients in the primary position. None of the patients had limitation of ocular movement of the sound eye. The position of upper eyelid in primary position improved significantly in all cases. The mean degree of ptosis after surgery was 0.9 ± 0.8 mm (range 0-2 mm). None of the patients required further surgery for correction of residual ptosis or strabismus.

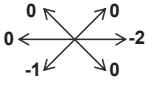
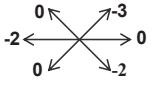
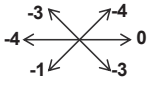
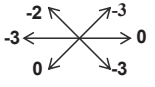
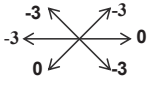
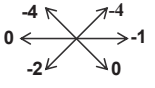
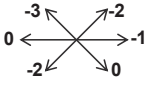
DISCUSSION

THE MECHANISM OF ABERRANT REGENERATION PHENOMENON is thought to be peripheral misdirection of regenerating axons.[2,4] Histologic evidence suggests that this typically occurs when damage results from transection and subsequent disruption of endoneurial integrity.[2,4] A bridging matrix of Schwann cells, fibroblasts, and macrophages is formed that regenerates several neuronal sprouts. These sprouts can then innervate multiple end organs, which leads to cocontraction.[4] Aberrant regeneration is also often seen in cases or congenital third nerve palsy as a developmental anomaly.[5] The most commonly reported signs of aberrant regeneration after third nerve palsy are retraction of the eyelid with improvement of ptosis on attempted adduction or downgaze.[1] Our patients showed both signs of aberrant regeneration.

Surgical treatment of third nerve palsy without aberrant regeneration is usually staged into correction of the eye deviation followed by correction of the ptosis. The presence of aberrant regeneration, however, might influence the surgical decision. Aberrant regeneration usually implies some recovery of the muscle function, which might yield a better surgical outcome. In addition, the improvement of ptosis on attempted adduction and attempted downgaze might allow simultaneous correction of both the ptosis and the strabismus through eye muscle surgery In 1980, O'Donnell and associates[5] reported simultaneous correction of both the blepharoptosis and exotropia in a patient who had third nerve palsy with aberrant regeneration by operating on the fixing contralateral eye. Their rationale was that by making the fixing eye esotropic in primary position postoperatively the innervation to the lateral rectus of the fixing eye as it moves to primary gaze is similar to the preoperative innervation for abduction. Because the involved levator is pathologically innervated by the ipsilateral medial rectus and therefore yoked to the contralateral lateral rectus as a result of aberrant regeneration, the increased innervational flow to the levator of the ptotic lid postoperatively results in elevation of the lid in primary position.

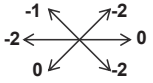
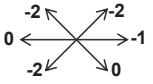
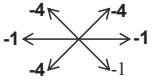
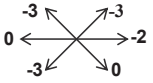
Since then there have been a few case reports in which this technique has been used. Parulekar and Elston[6] suggested a large recession of the lateral rectus muscle and a smaller medial rectus resection on the nonparetic eye. They also suggested combined downward transposition of

TABLE. Details of the Characteristics of the Studied Patients

No.	Age (y)	Sex	Cause	Eye	Duction of the Affected Eye	Horizontal Deviation	Vertical Deviation	Ptosis	Surgery	Follow-Up (Months)	Postoperative Angle	Postoperative Ptosis
1	24	F	Trauma	Right		RXT 45Δ	Hypo 8Δ	2 mm	LLR recession 8.5 mm, LMR resection 6.5 mm, and downward shift 8 mm	4	XT 6Δ	1 mm
2	26	M	Trauma	Left		LXT 40Δ	None	2 mm	RLR recession 8 mm and RMR resection 6 mm	6	XT 4Δ	None
3	13	F	Brain tumor excision	Left		LXT 80Δ	Hypo 10Δ	5 mm	RLR recession 10 mm, RMR resection 7 mm, LLR recession 8 mm, and RIO myectomy	12	Ortho	1.5 mm
4	9	M	Trauma	Left		LXT 35Δ	None	3 mm	RLR recession 10 mm and RMR resection 7 mm	7	XT 6Δ	1 mm
5	30	M	Trauma	Left		LXT 45Δ	None	4 mm	RLR recession 8 mm and RMR resection 8 mm	4	XT 4Δ	1 mm
6	16	M	Trauma	Right		RXT 45Δ	Hypo 10Δ	7 mm	LLR recession 8.5 mm, LMR resection 6.5 mm, and downward shift 8 mm	5	XT 6Δ	2 mm
7	3	M	Trauma	Right		RXT 35Δ	None	4 mm	RLR recession 7 mm and RMR resection 5.5 mm	6	XT 8Δ	None

Continued on next page

TABLE. Details of the Characteristics of the Studied Patients (*Continued*)

No.	Age (y)	Sex	Cause	Eye	Duction of the Affected Eye	Horizontal Deviation	Vertical Deviation	Ptosis	Surgery	Follow-Up (Months)	Postoperative Angle	Postoperative Ptosis
8	21	F	Trauma	Left		LXT 35Δ	None	4 mm	LLR recession 7 mm and LMR resection 5.5 mm	5	Ortho	None
9	3	F	Congenital	Right		RXT 35Δ	None	2	LLR recession 7 mm and LMR resection 5.5 mm	4	XT 6	1 mm
10	11	F	Congenital	Right		RXT 30Δ	None	6	LLR recession 7 mm and LMR resection 5.5 mm	9	Ortho	2 mm
11	9	F	Trauma	Right		RXT 45Δ	None	4	LLR recession 7 mm and LMR resection 5.5 mm	8	XT 8	None

F = female; M = male; hypo = hypotropia; LLR = left lateral rectus; LMR = left medial rectus; LXT = left exotropia; RIO = right inferior oblique; RLR = right lateral rectus; RMR = right medial rectus; RXT = right exotropia; XT = exotropia.

FIGURE 2. Photographs of patient 3 showing left third nerve palsy with left exotropia 80 prism diopters, left hypotropia 10 prism diopters, and left ptosis (Top Panels). There is improvement of the ptosis on attempted adduction. (Bottom Panels) Photographs of the same patient 2 months after right lateral rectus muscle recession 10 mm, right medial rectus muscle resection, left lateral rectus muscle recession, and right inferior oblique myectomy showing improvement of both the exotropia and the ptosis.

the insertions of the medial and lateral recti to correct the vertical deviation. Gottlob and associates[7] managed 2 cases with traumatic third nerve palsy with a similar technique. They also performed superior oblique anterior transposition in the affected eye in all their cases because of the presence of large exotropia. Thanh Naguyen and associates[8] used the same approach in a case of traumatic third nerve palsy with aberrant regeneration by performing the surgery on the unaffected eye, but they used an adjustable technique to optimize the strabismus correction.

In our case series, we report satisfactory outcome through contralateral eye muscle surgery. However, in cases with a severe medial rectus paresis resulting in large exodeviations, it was necessary to do bilateral muscle surgery to be able to satisfactory align the eyes in primary position. Ipsilateral large lateral rectus recession was added to able to correct the full angle of exotropia. O'Donnell and associates[5] recommended avoiding resection of the ipsilateral medial rectus in the presence of aberrant regeneration so as not increase the ptosis.

FIGURE 3. Photographs of patient 11 showing right third nerve palsy with right exotropia 45 prism diopters, and right upper eyelid ptosis (Top Panels). There is improvement of the ptosis on attempted adduction. (Bottom Panels) Photographs of the same patient 2 months after left lateral rectus muscle recession and left medial rectus muscle resection showing improvement of both the exotropia and the ptosis.

The approach offers the advantage of allowing simultaneous correction of both strabismus and ptosis through a single procedure rather than performing an eye muscle surgery to correct the exotropia followed by an eyelid surgery to correct the ptosis. This reduces patient discomfort and expenses by eliminating the need for a second hospitalization. Complications of ptosis surgery, such as overcorrection, entropion, or ectropion, and exposure keratopathy, may be avoided or reduced because the levator muscle is not mechanically shortened. Moreover, if the amount of ptosis correction in primary position is insufficient after the strabismus surgery, then a conventional ptosis surgery can still be performed.[5]

However, this technique is not without disadvantages. Performing surgery on the sound eye might reduce the ductions of the sound eye, especially when large amounts of recession and resection are performed. While we did not measure the single binocular visual field in our patients, one might expect that improvement in the single binocular visual field of the patient might still be limited. The technique will not be suitable in those with a poor eyelid position on attempted adduction. It requires surgery on the uninvolved eye, which might not be acceptable to some patients. In addition, the eyelid retraction on adduction may become more cosmetically displeasing postoperatively.

However, this was not seen in any of our patients. In addition, there is a confounding factor that might have yielded a better outcome in our cases series, which was the simultaneous correction of the hypotropia of the paretic eye. Part of the ptosis might have been a pseudo-ptosis caused by hypotropia, and it might have been improvement—at least partially—with the simultaneous correction of the hypotropia. However, it is noticeable that the results were still satisfactory in those who did not have any simultaneous surgical correction of hypotropia.

Finally, this procedure should be considered as the initial surgical option in appropriate patients. If previous exotropia surgery was performed on the involved eye, there may not be enough residual exotropia correction needed to fully correct the ptosis with this procedure on the contralateral normal eye; this can be assessed preoperatively using a base in prism over the normal eye to be sure the amount exotropia surgery required to correct the ptosis would not overcorrect the residual exotropia. However, patient 10 shows that the procedure can still be effective in such patients if screened with base in prism over the normal eye as described.

While reported by the senior author previously as a case report, to our knowledge this is the largest case series reporting standardized contralateral muscle surgery for the combined correction of blepharoptosis and strabismus in selected cases of third nerve palsy with aberrant regeneration. This case series shows the value of this simple and effective surgical strategy that should be considered as a primary approach in all appropriate patients.

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