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Long-Term Follow-up of Strabismus Surgery in Patients With Ocular Myasthenia Gravis

Jason H. Peragallo, MD,

Department of Ophthalmology, Jules Stein Eye Institute, University of California Los Angeles, Los Angeles, CA, USA

Joseph L. Demer, MD, PhD,

Department of Ophthalmology, Jules Stein Eye Institute, University of California Los Angeles, Los Angeles, CA, USA

Federico G. Velez, MD, and

Department of Ophthalmology, Jules Stein Eye Institute, University of California Los Angeles, Los Angeles, CA, USA. Department of Ophthalmology, Olive View – UCLA Medical Center, Sylmar, CA, USA

Stacy L. Pineles, MD

Department of Ophthalmology, Jules Stein Eye Institute, University of California Los Angeles, Los Angeles, CA, USA

Abstract

Purpose—To report the long-term postoperative results of strabismus surgery in patients diagnosed with ocular myasthenia gravis (OMG).

Design—Retrospective observational case series

Methods—The medical records of all patients with OMG who underwent strabismus surgery with at least 6 months of post-operative follow-up were reviewed. Nine patients met the study inclusion criteria. Main outcomes, including ocular alignment, number of surgeries, and sensory status were evaluated.

Results—Of these patients, initially two had horizontal strabismus alone, three had vertical strabismus alone, three had both vertical and horizontal strabismus, and one patient had vertical and torsional strabismus. Length of pre-operative stability was 2.0 ± 2.5 years (range: 0.1–8.0 years). Mean preoperative horizontal and vertical deviations were 40.5 ± 32.5 prism diopters (PD) (range: 0–90 PD) and 25.6 ± 36.7 PD (range: 0–120 PD), respectively. Average length of follow-up after the first surgery was 5.7 ± 4.2 years (range: 0.7–10.6 years). Four patients (44%) underwent two operations. For patients requiring a second operation, time to second operation was 2.3 years (range: 0.4–5.0 years). Six patients (67%) were within 10 PD of orthotropia at distance in primary position at the final visit. Five patients (55%) had single vision after their surgeries.

Conclusions—Strabismus surgery can achieve good long-term binocular alignment in patients with ocular MG.

Keywords

myasthenia gravis; strabismus; adjustable; diplopia; stability

Corresponding Author: Stacy L. Pineles, M.D., 100 Stein Plaza, Los Angeles, CA 90095, Phone: 310-267-1007, Fax: 310-825-0151, pineles@jsei.ucla.edu.

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Myasthenia gravis is an autoimmune disorder in which autoantibodies to the neuromuscular junction result in neuromuscular blockage leading to striated muscle fatigability (1). Myasthenia gravis can be generalized, or may involve only the extraocular muscles, designated as ocular myasthenia gravis (OMG). Establishing the diagnosis of OMG may be difficult as negative serologies do not rule out the disease, and, at times the diagnosis is made on clinical grounds. Intravenous edrophonium and single fiber electromyography are diagnostic studies with the greatest sensitivity.

Involvement of the extraocular muscles may lead to strabismus and diplopia. Strabismus tends to be variable during the active phase of myasthenia gravis (2) and most clinicians agree that strabismus surgery is not indicated during this time. Patients are usually treated with parasympathomimetic and immunosuppressive medications until the disease has stabilized. Some patients may be tapered off their medications, and progress into a phase of remission and decreased disease severity (3). While the clinical course of myasthenia gravis is unpredictable, substantial improvement or spontaneous remission is often seen after the 2nd year of disease (3).

Once ocular alignment in patients with OMG is stable, strabismus surgery may be undertaken (4,5). While previous studies have demonstrated the feasibility of performing both strabismus surgery and botulinum toxin injection for patients with OMG (5–9), long-term outcomes are unclear. The purpose of our study is to provide additional data regarding the role and long-term follow-up of eye muscle surgery in patients with OMG.

Methods

This study was approved by the University of California, Los Angeles Institutional Review Board and conformed to the requirements of the Declaration of Helsinki and the United States Health Insurance Portability and Accountability Act. A retrospective review was performed of the clinical records of all patients in two tertiary care strabismus practices (Arthur L. Rosenbaum, MD, Joseph L. Demer, MD) at the Jules Stein Eye Institute between 1980 and 2011 with the diagnosis of OMG and strabismus. None of the patients in the current study were included in a previous report from this institution (6). Patients who had previously undergone strabismus surgery prior to diagnosis of OMG were excluded.

The following pre- and postoperative characteristics were recorded: age at presentation, age at first surgery, duration of stability of ocular alignment, pre-operative alignment at distance and near in cardinal gaze positions, medications for myasthenia used immediately pre-operatively and in the post-operative period, surgical procedures performed, use of adjustable sutures, initial postoperative deviation achieved following adjustable suture technique, ocular alignment determined at last visit or immediately prior to re-operation, ocular alignment after second surgery, history of thymectomy, presence or absence of acetylcholine receptor antibodies (binding, blocking, and/or modulating), development of generalized myasthenia gravis, and presence of diplopia with or without prisms at final visit. The amount of strabismus surgery was based upon ocular alignment in primary gaze at distance. Surgical information was retrieved from operative reports, including results of forced duction testing, which was performed in every case.

Ocular alignment with spectacle correction was measured in prism diopters (PD) either using cover/uncover and alternate cover testing at distance (3–4 m) in cardinal gaze positions or by Krimsky light reflex testing. Alignment was also assessed in primary position at near (36cm). For the purposes of analysis, the pre-operative ocular deviation was given a positive (+) value and over-corrections were assigned a negative (–) value. For example, if a patient had 25 PD of esotropia pre-operatively, this would be denoted as a

deviation of +25. If that patient had post-operative overcorrection resulting in 10 PD of exotropia, that deviation would be designated as -10. Successful treatment results were defined as freedom from diplopia and alignment within 10 PD of orthotropia in primary position at distance at final visit.

Results

Table 1 summarizes demographic data for nine patients who met inclusion criteria. All were adults with the exception of a single child, aged 9.7 years. The characteristics of each patient's myasthenia gravis are presented in Table 2.

In Table 3 are the individual pre-operative deviations, results of surgery performed, and final ocular deviation at last recorded visit. Adjustable sutures were utilized in all adult cases. Two of eight patients (25%) required adjustment at first surgery, while two of four (50%) required adjustment at second surgery. Of the three patients with unacceptable alignment results (heterotropia >10 PD deviation at the last visit), two had generalized MG, two were over 70 years of age, and all three had evidence of restriction on forced duction testing. Two of three patients who underwent surgery with eye position stable for less than six months, either had unrecognized OMG (patient 9) or profound ocular misalignment (patient 7). Patient 7 had previous bilateral orbital decompression for thyroid eye disease and scleral buckling procedure for retinal detachment in the right eye. No other patient had a diagnosis of co-existent thyroid ophthalmopathy or previous ocular surgery.

Four patients (44%) underwent a second surgery. Time to second surgery was 2.3 ± 2.0 years (range: 0.4–5.0 years). No patients underwent more than two surgeries. For the six patients who initially had, or developed, horizontal deviations, the average preoperative horizontal deviation was 40.5 ± 32.5 PD (range: 0–90 PD) while horizontal deviation at final visit was 12.7 ± 14.9 PD (range: 4–35 PD). Three patients (50%) were within 10 PD of orthotropia horizontally.

All patients initially had, or developed, vertical deviations. Average preoperative vertical deviation was 25.6 ± 36.7 PD (range: 0–120 PD) while final vertical deviation was 7.4 ± 6.4 PD (range: 0–20 PD). Eight patients (89%) were within 10 PD of orthotropia vertically postoperatively.

Regarding sensory status, patient 2 had childhood myasthenia gravis with treated amblyopia and was capable of suppression of one eye. Of the patients ($n = 4$) who continued to have diplopia after surgical intervention, all of them were taking medications for myasthenia gravis post-operatively, two (50%) underwent two surgeries, and all had either positive AChR Abs or edrophonium testing, and three (75%) developed generalized MG after initial presentation of ocular MG.

Two patients had ptosis preoperatively. A total of six patients had ptosis at some point postoperatively, two of which required medication, for MG.

Eight of nine patients (89%) had initial post-operative alignment within 10 PD of orthotropia. At final visit, 5 patients (56%) had a successful result as defined by freedom from diplopia and heterotropia <10PD. Three of these patients underwent a single surgery and 2 required a second surgical procedure. All patients who failed treatment in this study were female and had positive forced ductions.

Of the patients whose AChR Ab status was known, three with positive antibodies failed treatment with strabismus surgery. One of four patients with negative AChR Ab results

failed treatment. Two patients who underwent thymectomy in this study did not have a successful result.

Discussion

Patients with active ocular MG and variable eye position are not considered appropriate candidates for extraocular muscle surgery (6). However, once ocular alignment and disease course stabilize, an appropriate surgical plan may be implemented (4–6,10). Previous reports of patients with OMG undergoing strabismus surgery are summarized in Table 5.

Our study includes the largest number of patients with OMG who underwent strabismus surgery with adjustable suture technique and without botulinum toxin injections. It also has the longest reported average length of follow-up, 5.7 ± 4.2 years, and the highest percentage of patients followed beyond one year (89%). In our series, all patients experienced an improvement in ocular alignment from initial deviation. At final visit, 56% of the patients were within 10 PD of orthotropia. Other reports have shown that the use of adjustable sutures can aid in producing good surgical outcomes (11). In our series, adjustable sutures were utilized in all cases. However, 44% of patients continued to have diplopia after surgery; the remainder either suppressed diplopia (patient 2), or achieved single binocular vision.

We searched for factors affecting the surgical outcome (Table 4). Strabismus surgery was less successful in older patients and those with OMG and thymectomy, positive AchAbs and generalized disease. We did not find a correlation between length of stability of pre-operative ocular alignment and long-term success. Several of our patients with positive forced ductions had a poor outcome. Restriction on forced duction testing could have been due to undiagnosed thyroid eye disease or muscle contracture and atrophy associated with chronic strabismus including myasthenia (12,13).

We acknowledge the limitations of our study. It was retrospective and subject to biases in both patient selection and follow-up. Our sample size was small and establishing the diagnosis of OMG was not standardized but rather based on results of clinical examination, serologic tests and intravenous edrophonium. Single-fiber EMG testing was not utilized in our patients.

Our results suggest that extraocular muscle surgery is a viable option for patients with OMG and stable ocular alignment. However, these patients should be counseled regarding the possibility of multiple surgeries, especially in those with more severe disease, older age, and co-existent restrictive strabismus.

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Table 1

Characteristics of Patients With Ocular Myasthenia Gravis Undergoing Strabismus Surgery

Demographic (Total n=9)	Number (%)
Female	5 (55%)
Age at first surgery	49.9 yrs (range 9.7–74.2)
Length of pre-operative stability of deviation	2.0 yrs (range 0.1–8.0)
Time to second surgery (n=4) ^a	2.3 yrs (range 0.4–5.0)
Initial Horizontal Deviation	40.5 PD (range 0–90)
Initial Vertical Deviation	25.6 PD (range 0–120)
Final Horizontal Deviation	12.7 PD (range –4–35)
Final Vertical Deviation	7.4 PD (range 0–20)
Length of Follow-up	5.7 yrs (range 0.7–10.7)
Thymectomy (n=8) ^b	2 (25%)
AchR Ab (+) or edrophonium (+) (n=8) ^b	6 (75%)

^a n = number of patients who underwent a second surgery^b n = number of patients for whom data was recorded AchR Ab = acetylcholine receptor antibodies

Table 2

Characteristics of Patients with myasthenia gravis undergoing strabismus surgery

Pt	Age at Surgery (years)	Length of Follow-up (years)	Length of Disease Stability (years)	Thymectomy performed	Method of Diagnosis	Pre-op Meds ^a	Post-op Meds	Development of Generalized MG after initial presentation
1	73.9	3.3	0.38	No	Edrophonium (+)	None	Pyridostigmine	No
2	9.7	10.7	1.26	Not recorded	Edrophonium (+)	Pyridostigmine	Pyridostigmine	No
3	55.6	10.6	1.84	No	Edrophonium (+)	None	None	No
4	62.7	3.1	0.58	No	Clinical exam	Prednisone	None	Not recorded
5	22.3	10.3	8.01	Yes	AchRAb +	None	Pyridostigmine	Yes
6	74.2	2.7	3.74	No	Clinical exam	None	None	No
7	72.6	1.5	0.10	No	AchRAb+	Pyridostigmine	Pyridostigmine	Yes
8	39.1	8.1	2.00	Yes	AchRAb+	Pyridostigmine	Pyridostigmine	Yes
9	38.5	0.7	0.16	No	Clinical exam	Pyridostigmine	Pyridostigmine, prednisone	No

^aInclude only the medications the patient was taking immediately pre-operatively

Eye Position and Surgical Outcomes In Patients With Ocular Myasthenia Gravis

Table 3

Pt	Pre-Operative Deviation (PD)	Initial Procedure ^a	Forced Duction Test	Residual Horizontal Deviation (PD) ^b	Residual Vertical Deviation (PD) ^b	Second Pre-Op Horizontal Deviation (PD)	Second Pre-Op Vertical Deviation (PD)	Second Procedure	Second Residual Horizontal Deviation (PD) ^c	Second Residual Vertical Deviation (PD) ^c	Final Horizontal Deviation (PD) ^d	Final Vertical Deviation (PD) ^d
	65 XT	RLRc 8.5, BMRs 7	OD mild restriction to adduction, OU mild restriction to supraduction	0	10	-42.5	0	RMRs 5, RLR advanced from 14 to 8 mm from limbus	0	-3.5	35	10
2	16 LHT	RSRs 4, LJRs 4	(-)	0	0	10	-45	LJRe 4.5, LSRs 4.75	0	0	0	10
3	20 LHT	RSRs 6.5	(-)	0	5						0	4
4	20 XT, 27.5 RHT	LSRs 4.5, BLRc 5.5	(-)	-6	0	-6	10	RSRe 3.5	0	0	0	3
5	28 XT, 25 LHT	LMRs 10, LSRc 8	OS mild restriction to adduction, mod restriction to depression	-10	6						12	10
6	40 ET, 8 RHT	BMRe 5.5 (transp. Inf ½ TW), LJRe 3	(-)	4	0						8	0
7	120 LHT	RJRe 7, LSRc 10	OD mod limit to supraduction, mild limit to infraduction, OS severe limit to infraduction	0	50	0	50	LJR plication 10	0	0	25	20
8	90 XT	BLRc 8, BMRs 6	Limit to adduction OU	0	2	15	25	LJRc 5, BMRs 4	8	10	-4	10
9	14 RHT	LSO Sp 4, LJRe 4	(-)	0	0						0	0

^aProcedures: RLRe = right lateral rectus muscle recession, BMRs = bilateral medial rectus muscle resection, RSRs = right superior rectus muscle resection, LJRc = left inferior rectus muscle resection, LSRs = left superior rectus muscle resection, BLRc = bilateral lateral rectus muscle recession, LMRs = left medial rectus muscle resection, LSRc = left superior rectus muscle recession, BMRe = bilateral medial rectus muscle recession, RJRe = right inferior rectus muscle recession, LJRc = right inferior rectus muscle recession, LSO Sp = left superior oblique muscle spacer, RSRe = right superior rectus muscle recession, Inf transp. ½ TW = inferior transposition one-half tendon width for V-pattern. All procedures are amount of surgery performed prior to adjustment.

^bOn Post-operative Day #1 after initial surgery and after adjustment (if performed)

^cOn Post-operative Day #2 after second surgery if performed, and after adjustment (if performed)

^dOn final recorded visit

Table 4Factors Associated with Surgical Outcome in Patients with Ocular Myasthenia Gravis^a

	Successful (N=5)	Failure (N=4)
Age (mean, median)	48.1 years	52.0
Sex (F)	1/5 (20%)	4/4 (100%)
Thymectomy	0/4	2/4
AchR Ab	0/3	3/4
Generalized MG after initial presentation	0/4	3/4
(+) Forced Ductions	0/5	4/4
Size of Horizontal Deviation	30 PD	45.8 PD
Size of Vertical Deviation	17.1 PD	36.25 PD
Presence of Initial Horizontal Deviation	2/5	3/4
Presence of Initial Vertical Deviation	5/5	2/4
Presence of Initial Horizontal and Vertical Deviation	2/5	1/4

^aTreatment failure defined as continued diplopia or deviation beyond 10 PD of orthotropia

F = female; PD = prism diopter

AchR Ab = acetylcholine receptor antibody positive

Table 5
Summary of previous studies evaluating strabismus surgery in patients with myasthenia gravis

Author, year	N	Surgical procedures	Use of botulinum toxin	Adjustable Sutures	Follow-Up	Definition of Success	Success Rate
Acheson (5), 1991	5	Horizontal muscle faden (n=1), horizontal rectus muscle surgery (n=5), superior oblique tenotomy (n=2)	No	Yes	6 months to 6 years	Not defined	Not defined
Davidson (6), 1993	6	Horizontal rectus muscle surgery (n=6), vertical rectus muscle surgery (n=1), superior oblique tenotomy (n=2)	No	Yes	4 months to 16 years	<10 PD of ocular misalignment	4/6 (67%)
Bentley (7), 2001	9	Horizontal rectus muscle surgery (n=9), vertical rectus muscle surgery (n=1), inferior oblique surgery (n=1)	Yes (n=6)	Yes	6 months to 5 years	Symptom-free	6/9 (67%)
Ohtsuki (8), 1996	4	Horizontal rectus muscle surgery (n=3), vertical rectus muscle surgery (n=3)	No	Yes	8 months to 2.5 years	Single binocular vision	3/4 (75%)
Morris (9), 2004	2	Horizontal rectus muscle surgery (n=1), vertical rectus muscle surgery (n=1)	No	Yes	3 months to 6 months	Not defined	Not defined

N=number of patients