

The Surgical Outcome of Strabismus in Patients with General Fibrosis Syndrome

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Background: This study investigates the clinical features of strabismus in patients with general fibrosis syndrome (GFS) and the results of surgery performed on such patients.

Methods: We conducted a retrospective review of patients with GFS who visited our clinic at Chang Gung Memorial Hospital between 1 August 1992 and 31 January 2002. After evaluating the family histories of 9 patients with GFS, patients were given a complete ophthalmic evaluation. Myectomies of the inferior rectus muscle were performed to correct hypotropia and recessions and/or resections of medial rectus and/or lateral rectus were performed to correct esotropia or exotropia, respectively. The post-operative conditions of the survey patients were reviewed for at least 6 months after the completion of the procedures.

Results: Six patients (67%) were identified with inherited autosomal dominance. All patients displayed the characteristic 'chin-up' position, limited extraocular muscle movement and eye abnormalities. High astigmatism (≥ -2.0 diopter) was noted in 9 eyes (50%) and amblyopia was noted in all cases. With regard to vertical eye deviation, 11 eyes (61%) were corrected through myectomy of the inferior rectus muscle to within 5° as measured using a Hirschberg test. Furthermore, three cases (33%) were complicated by lower scleral show.

Conclusion: The presence of GFS complicates the surgical correction of strabismus making procedure results more difficult to predict. Strabismus surgery has been demonstrated to reduce eye deviation in the primary position, thus improving patients' head posture. The resulting improvements to cosmetic appearance and functionality lead us to recommend that strabismus surgery be performed in conjunction with ptosis surgery for GFS patients.

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Key words: general fibrosis syndrome, strabismus, surgical outcome.

Congenital fibrosis of the extraocular muscle was first described by Aebli in 1933.⁽¹⁾ Duane later classified the congenital fibrosis syndrome into five types based on the varying effects the disease had on extraocular muscles. These types were classified as:

(1) general fibrosis syndrome; (2) fibrosis of the inferior rectus muscle; (3) strabismus fixus; (4) vertical retraction syndrome; (5) congenital unilateral fibrosis.⁽²⁾ Brown coined the term general fibrosis syndrome (GFS),⁽³⁾ defining it as a disease character-

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ized by congenital non-progressive bilateral ptosis, restrictive external ophthalmoplegia and eyes usually fixed in a hypotropic position. Affected individuals typically tilt their heads back to compensate for the ptosis and fixed downward globes.

GFS is a dominantly inherited condition^(4,5) but may also occur sporadically.⁽⁶⁻⁸⁾ Families with autosomal-dominant inherency appear to be phenotypically and genetically homogeneous. The gene has been mapped to an 8-cM region of chromosome 12.^(9,10) While the development of restrictive ophthalmoplegia and the hypoplastic and fibrotic changes in the extraocular muscles observed in muscle biopsies have led many to view GFS as a developmental muscle disorder, it remains unproven whether these problems result from primary myopathic or neuropathic processes, or whether they are pathophysiologically related to one another.⁽¹¹⁻¹³⁾ Recent autopsy studies revealed not only abnormal muscle pathologies but nerve abnormalities as well.⁽¹⁴⁾ Observed abnormal innervation in some sufferers of GFS suggests a possible link between GFS and the failure to form normal neuronal connections during early development.⁽¹⁵⁻¹⁷⁾

Myectomy of the affected muscle is used as corrective surgery in patients with ptosis and 'chin-up' position. However, some surgeons advocate an additional recession of the conjunctiva and tendon with or without stay sutures, and resection of the superior rectus muscle was also recommended by a number of surgeons.^(8,11) This study investigates the clinical symptoms of patients suffering from GFS and the outcome of surgery to correct strabismus.

METHODS

We conducted a retrospective review of patients with GFS who visited our clinic at Chang Gung Memorial Hospital between 1 August 1992 and 31 January 2002. Patients who had not undergone strabismus surgery were excluded. Detailed accounts of patients' family histories were taken and an exhaustive ophthalmic evaluation was performed, which included assessments of head position, lid fissure measurements, eye position, ocular motility, cycloplegic refraction and the best corrected visual acuity, as well as slit-lamp and fundus examinations. Each patient's eye position was examined using a Hirschberg test, which involved positioning the

patient's head upright and elevating the ptosised eyelid. Ocular movements, including monocular motility and eye movement in all four primary directions, were recorded.

One surgeon (M.Y.) conducted all strabismus operations included in the survey. Inferior rectus myectomies were performed to correct hypotropia and horizontal rectus muscle recession and/or resection to correct horizontal deviation. A forced duction test was performed prior to surgery under a general anesthesia. Patients were excluded from this study if their post-operative follow-up was less than 6 months.

RESULTS

Nine patients, 3 male and 6 female, were included in this study. Relevant clinical data is summarized in Table 1 below. Post-operative follow-up of patients ranged from 7 months to 3 and 1/2 years (a mean duration of 1.34 years). 6 cases (67%) of surveyed patients had family histories of autosomal-dominant inheritance; others were classified as sporadic. All cases displayed classic GFS symptoms including drooping eyelids, 'chin-up' positions and hypotropia with restricted eye movement. High astigmatism (≥ -2.0 diopter) was noted in 9 eyes (50%). In 8 cases (89%) the astigmatism was greater in the eye with a worse degree of ptosis. Amblyopia was noted in all the survey cases and the best corrected visual acuity was worse in the eye with more ptosis.

Limitation of extraocular muscle movement was noted in all patients and most patients showed convergence jerk on attempted gaze in any direction. Other manifestations of motility were noted including convergence on upward gaze in 3 cases, convergence or divergence on downward gaze in 3 cases, divergence on side gaze in one case and slight downward movement, instead of adduction, in 2 cases.

Forced duction tests performed on both eyes of the survey patients revealed limitation of ocular movement for each direction, especially for the vertical direction. An obvious fibrotic band was noted in one case (case 5). Figure 1 shows the post-operative eye position in the vertical direction for all patients in the survey.

While correction was noted after inferior rectus muscle myectomy procedures, the degree of correc-

Table 1. Patient's Clinical Data

| Patient No. | Gender | FH | High Astigmatism (>= 2.0D) | Amblyopia eye & its BCVA | Surgical treatment of ptosis | Age/last op (yrs) | F/u duration after last op (yrs) |
|-------------|--------|----|--|--------------------------|------------------------------|-------------------|----------------------------------|
| 1 | F | + | - | OS: 0.4 | LR | 5 | 1 |
| 2 | M | - | OS: -4.0X170° | OS: 0.3 | LR | 8.5 | 1 |
| 3 | F | + | OD: -3.5X160° OS: -3.0X180° | X | LR | 3 | 1 |
| 4 | M | + | OD: -2.0X90° | OD: 0.3 OS: 0.5 | FS | 4 | 3.5 |
| 5 | M | - | OS: -2.0X140° | OD: 0.2 OS: 0.2 | 1.FS 2.LR | 16 | 0.6 |
| 6 | F | - | - | OD: 0.2 OS: 0.3 | LR | 14 | 1 |
| 7 | F | + | OD: -3.5X70° OS: -5.0X110° OS: 0.2 | OD: 0.3 FS | 12 | 1.5 | |
| 8 | F | + | OD: -3.0X85° OS: -3.0X80° OS: 0.2 | OD: 0.2 FS | 3 | 1.5 | |
| 9 | F | + | - | OS: 0.2 | FS | 15.5 | 1 |

Abbreviations: F indicates female; M: male; FH: family history; BCVA: best corrected visual acuity; LR: levator resection; FS: frontalis sling; OD: right eye; OS: left eye.

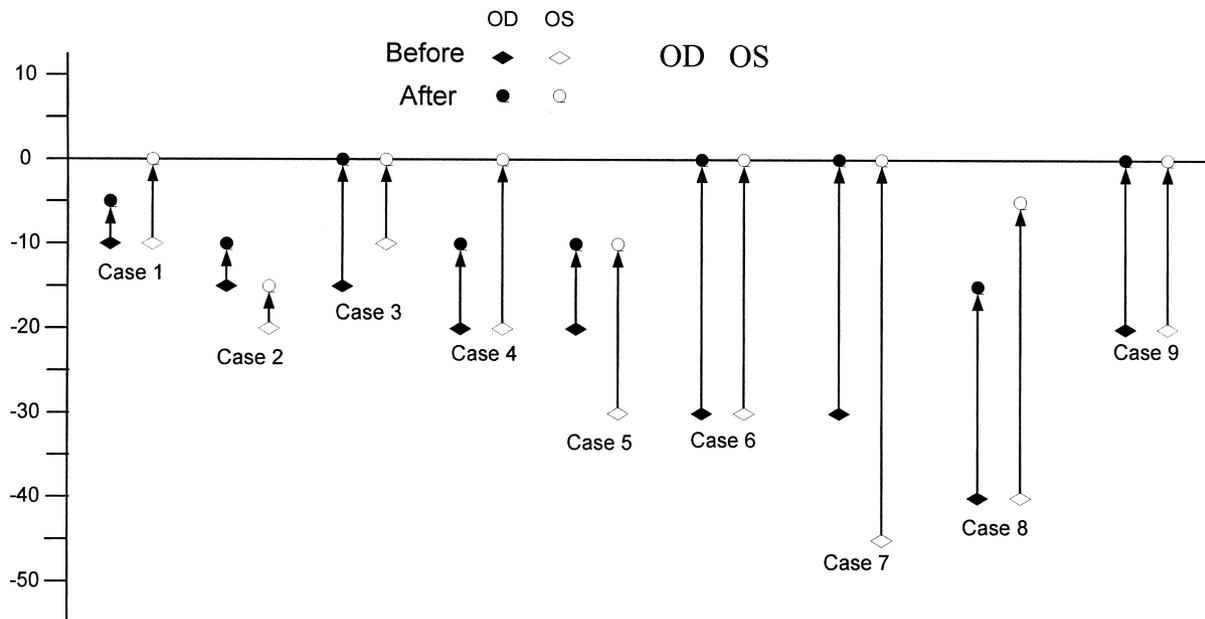


Fig. 1 Comparison of pre-operative and post-operative vertical deviation after myectomy of the inferior rectus muscle.

tion varied even though the procedure was the same. Among the 13 eyes with vertical deviations exceeding 15°, 8 eyes (62%) were corrected to 5° by inferior rectus muscle myectomies. Of the five remaining eyes, with vertical deviations of 15° or less, 4 eyes (80%) were corrected to within 5°. Table 2 shows the post-operative horizontal eye positions. Compared with the surgeon's previous surgical experience, post-operative eye positions in this survey were over-corrected in the 2 esotropia cases and under-corrected in the 3 exotropia cases. No patients had improvements in muscle motility. 3 cases (33%) were complicated by lower scleral show. All survey patients had relatively improved cosmetic appearance and 'chin-up' position. Figure 2 compares the pre-operative and post-operative condition of patient number 8.

DISCUSSION

The occurrence of congenital fibrosis in extraocular muscles is estimated to be 1/230,000.⁽¹⁸⁾ The disease has been found to be related to chromosomes 11q13,⁽⁹⁾ 12⁽¹⁰⁾ and 16q24.2-q24.3,⁽¹⁹⁾ while GFS is related to chromosome 12. GFS is characterized by the replacement of normal extraocular and levator muscle by fibrous tissue.⁽¹²⁾ As mentioned above, recent research has also indicated that nerve abnormalities may also play a role in causing GFS.⁽¹⁴⁾ Images created using computer tomography and

magnetic resonance show atrophy of extraocular muscle and tendinous insertion as well as poorly defined intraconal and extraconal masses that look like scar or inflammatory tissue.^(20,21)

Aberrant innervation is believed to be one possible pathogenesis for GFS.⁽¹⁶⁾ Four patients in this survey displayed unusual eye movement resembling descriptions of neural misdirection. Clinical results included convergence jerk on attempted gaze in any direction, divergence on attempted vertical gaze and a slight downward movement on attempted adduction. Moreover, the palpebral fissure decrease and globe retraction observed during eye adduction attempts by patient number 1 were compatible with the expected characteristics of Duane's syndrome, in which preserved eye movements reflect aberrant innervation. The implication is that such abnormal innervation may be the result either of the GFS or the formation of aberrant neuromuscular connections which preserved muscle fibers while all others were replaced by fibrous tissue.

Refractive error in these patients was significant and variable.⁽²²⁾ Hiatt et al. concluded that refractive error may result from the pull of muscles on the globe. In our observations, refractive error measured with an autorefractor could be highly variable in one individual patient. The variability of refractive error may be also due to differing eye positions while measuring by autorefractor. Checking the refractive

Table 2. Eye Position and Strabismus Surgical Method

| Patient No. | Strabismus surgery | Pre-op eye position | Post-op eye position |
|-------------|--|---|-------------------------|
| 1 | LIR mye + LMRRc 7mm | RHo10°, LHo 10°; ET 30° | RHo 5°, LXT10° |
| 2 | BIR mye | RHo 15°, LHo 20° | RHo10°; LHo15° |
| 3 | 1. BIR mye + RLRRc 7mm 2. LLRRc7mm + LMRRs 5mm | RHo 15°, LHo10° XT 15° | XT10° |
| 4 | BIR mye | RHo 20°, LHo 20° XT 20° | RHo10° RXT5°; LXT10° |
| 5 | BIR mye | RHo20°, LHo 30° | BHo10° |
| 6 | BIR mye + LLRRc 12mm + RLRRc 10mm | RHo30°, LHo30° RXT 15°; LXT 15~30° | XT15° |
| 7 | BIR mye + LMR mye | RHo 30°, LHo 45° ET 15° | RXT10°; LXT5° |
| 8 | BIR mye | RHo 40°, LHo 40° | RHo15°; LHo5° |
| 9 | 1. BIR mye 2. BLRRc 9mm 3. RMRRs 5mm + LMRRs 4mm | 1. BHo 20°; XT 20° 2. XT 20° 3. XT15° | XT10° |

Abbreviations: IR: inferior rectus muscle; MR: medial rectus muscle; LR: lateral rectus muscle; Rc: recession; Rs: resection; mye: myectomy; Ho, hypotropia; ET: esotropia; XT: exotropia; L: left; R: right. The eye position was measured using a Hirschberg test.



Figs. 2 (A) A 3 year-old girl with drooping lids, 'chin-up' position and about a 40° hypotropia as measured using a Hirschberg test (OU). (B) One and half years after surgery, the abnormal eye position was largely corrected. The patient had improved to a 15° hypotropia in the right eye and 5° in the left eye.



error with a retinoscope, allowing patients to fix on a distant target with a habitual position, perhaps could eliminate this error. In our clinical experience, it is relatively difficult to check the refractive error with a retinoscope in a patient with ptosis, squint and who is uncooperative. So retinoscope was not used for every individual.

Patients with GFS exhibit severe bilateral blepharoptosis, bilateral ophthalmoplegia and fixed down eyes. These features force a 'chin-up' position and requires surgery to correct it. Inferior rectus muscle recession or a myectomy are the most common procedures used for correcting hypotropia. For GFS patients, an additional recession of the conjunctiva and tendon with or without stay sutures is advocated. A resection of the superior rectus muscle, as recommended by a number of surgeons, is not an option when the fibrosis and restriction are severe; so this procedure was not performed in this series.

The results of our limited research, focused only on the results of inferior rectus muscle myectomies in GFS patients, indicate that hypotropia can be partially or nearly completely corrected by this single procedure. However, the degree of eye deviation capable of surgical correction did not show much correlation with the pre-operative position of the eye. Pre-operative forced duction tests did not provide the clue either. In terms of inferior rectus complications

after the myectomy, 3 patients in the survey (33%) noted lower lid retraction with scleral show. However, eye position improvements were more apparent in these cases, leaving the 3 patients satisfied with the overall result. No additional lower lid surgery was needed.

In cases of nasal or temporal deviation, recessions and/or resections of the horizontal muscles were performed. Compared with the surgeon's previous surgical experience, the surgery tended to over-correct eyes with esotropia and result in a mild under-correction in eyes with exotropia. These results may indicate that the medial rectus muscle was influenced more severely than the lateral rectus muscle in the eyes with horizontal squint. As, prior to surgery, most patients displayed 'convergence only' movement, some residual exotropia may be acceptable to them.

As found in the research done by Hiatt et al, only limited improvement in muscle motility in the survey patients was noted after surgery.⁽¹¹⁾ Although

less than ideal, the benefits and importance of strabismus correction to GFS patients should not be dismissed. For example, prior to strabismus surgery, patient number 5 had tried a frontalis sling on both eyes. While the sling improved the ptosis it had little corrective effect on head position, as the patient was still required to tilt his head backward and elevate his chin to compensate for his hypotropia. In correcting the hypotropia, strabismus surgery produced a dramatic positive change in head position, resulting in improved cosmetic appearance and general head posture.

It is difficult to predict with accuracy the results of strabismus corrective surgery in patients with GFS. As measured using a Hirschberg test, improvement in hypotropia can be expected to vary from 45° to 5°. The most dramatic positive effects are observed in patients with severe hypotropia, while patients with milder hypotropia have a greater chance of success (defined as within 5° measured using a Hirschberg test). Apart from these rough observations, no other factor was identified in this research series that might shed light on how to predict surgical outcome. Even with so many remaining unknowns, all patients included in the survey achieved final eye positions within 15° as measured using a Hirschberg test, recommending inferior rectus myectomy as an effective surgery for treating strabismus patients with GFS.

REFERENCES

1. Aebli R. Retraction syndrome. *Arch Ophthalmol* 1933;10:602-10.
2. Parks MM, Mitchell PR. Ophthalmoplegic syndromes and trauma. In: Tasman W, Jaeger E, eds. *Duane's Clinical Ophthalmology* Vol. 1 Chap. 20 Revised ed. Philadelphia: Lippincott Williams & Wilkins Co., 1998:9-12.
3. Brown HW. Congenital muscle anomalies. In: Allen JH, ed. *Strabismus Ophthalmic Symposium*. St Louis, Mo: CV Mosby;1950:229-33.
4. Von Noorden GK. Congenital hereditary ptosis with inferior rectus fibrosis. *Arch Ophthalmol* 1970;83:378-80.
5. Apt L, Axelrod RN. General fibrosis of the extraocular muscles. *Am J Ophthalmol* 1978;84:822-9.
6. Harley RD, Rodrigues MM, Crawford JS. Congenital fibrosis of the extraocular muscles. *Am J Ophthalmol* 1978;76:197-226.
7. Leone CR, Weinstein GW. Orbital fibrosis with enophthalmos. *Ophthalmic Surg* 1972;3:71-5.
8. Hiatt RL, Halle AA. General fibrosis syndrome. *Ann Ophthalmol* 1983;15:1103-9.
9. Wang SM, Zwaan J, Mullaney PB, Jabak MH, Al-Awad A, Beggs AH, Engle C. Congenital fibrosis of the extraocular muscles type 2, an inherited exotropic strabismus fixus, maps to distal 11q13. *Am J Hum Genet* 1998;63:517-25.
10. Engle EC, Marondel I, Houtman WA, Vries B, Loewenstein A, Lazar M, Ward DC, Kucherlapati R, Beggs AH. Congenital fibrosis of the extraocular muscles (Autosomal dominant congenital external ophthalmoplegia): genetic homogeneity, linkage refinement, and physical mapping on chromosome 12. *Am J Hum Genet* 1995;57:1086-94.
11. Crawford JS. Congenital fibrosis syndrome. *Can J Ophthalmol* 1970;5:331-6.
12. Harley RD, Rodrigues MM, Crawford JS. Congenital fibrosis of the extraocular muscles. *Trans Am Ophthalmol Soc* 1978;76:197-226.
13. Apt L, Axelrod RN. Generalized fibrosis of the extraocular muscles. *Am J Ophthalmol* 1978;85:822-9.
14. Engle EC, Goumnerov BC, Mckeown CA, Schartz M, Johns DR, Porter JD, Beggs AH. Oculomotor nerve and muscle abnormalities in congenital fibrosis of the extraocular muscles. *Annals of Neurology* 1997;41:314-25.
15. Kishore K, Kumar H. Congenital ocular fibrosis with musculoskeletal abnormality: a new association. *Journal of Pediatric Ophthalmology and Strabismus* 1991;28:283-6.
16. Brodsky MC. Hereditary External ophthalmoplegia, synergistic divergence, jaw winking, and oculocutaneous hypopigmentation: a congenital fibrosis syndrome caused by deficient innervation to extraocular muscles. *Ophthalmology* 1998;105:717-25.
17. Brodsky MC, Dollock SC, Buckley EG. Neural misdirection in congenital ocular fibrosis syndrome: implications and pathogenesis. *Journal of Pediatric Ophthalmology and Strabismus*. 1989;26:159-61.
18. Reck AC, Manners R, Hatchwell E. Phenotypic heterogeneity may occur in congenital fibrosis of the extraocular muscles. *Br J Ophthalmol* 1998;82:676-9.
19. Doberty EJ, Macy ME, Wang SM, Dykeman CP, Melanson MT, Engle EC. CFEOM3: a new extraocular congenital fibrosis syndrome that maps to 16q24.2-q24.3. *Invest Ophthalmol Vis Sci* 1999;40:1687-94.
20. Hertle RW, Katowitz JA, Young TL, Quinn GE, Farber MG. Congenital unilateral fibrosis blepharoptosis and enophthalmos syndrome. *Ophthalmology* 1992;99:347-55.
21. Hupp SL, Williams JP, Curran JE. Computerized tomography in the diagnosis of the congenital fibrosis syndrome. *Journal of Clinical Neuro-Ophthalmology*. 1990;10:135-9.
22. Hiatt RL, Halle AA. General fibrosis syndrome. *Annals of Ophthalmology* 1983;15:1103-9.

先天性纖維化症候群之斜視病人的手術預後

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背景：本研究探討先天性纖維化症候群之斜視病人的臨床特徵及手術預後。

方法：本篇共收集九位先天性纖維化症候群病人，除詳細詢問家族史外並作詳細眼部理學檢查，包括眼位、眼球運動、眼裂測量、屈光檢查、最佳矯正視力檢查等。以下直肌切開術來矯正下斜視，以內、外直肌放鬆或切除術來矯正內、外斜視。術後追蹤六個月以上。

結果：67%病人為體染色體顯性遺傳，50%有高度散光(≥ -2.0 屈光度)，全部病人都有弱視。61%的病人下斜視可矯正於Hirschberg test五度內；至於水平眼位，以一般手術經驗來計算手術量，內斜視者易矯正過量，外斜視者易矯正不足。有33%的眼睛有輕微鞏膜露出的情形。

結論：先天性纖維化症候群之斜視病人的手術預後較一般斜視手術難預測，雖然斜視手術對增進眼球運動幫助不大，但對矯正下斜視並矯正下顎上傾的頭位是很有幫助的。本結果顯示此斜視手術對病人的外觀及功能都有幫助，所以可在上眼皮下垂矯正手術時同時作斜視矯正手術。

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關鍵字：先天性纖維化症候群，斜視，手術預後。

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