Ophthalmol Ther (2022) 11:1079–1088
https://doi.org/10.1007/s40123-022-00495-x

ORIGINAL RESEARCH

Clinical Characteristics and Surgical Outcomes of Patients with Congenital Fibrosis of the Superior Rectus Muscle

Min Yang · Licheng Fu · Jianhua Yan

Received: January 26, 2022 / Accepted: March 1, 2022 / Published online: March 13, 2022

ABSTRACT

Introduction: Congenital fibrosis of superior rectus muscle (CFSRM) is extremely rare and a difficult condition to manage surgically. The purpose of this report is to summarize the clinical characteristics of patients with CFSRM and analyze the effects of its surgical management.

Methods: Records of nine CFSRM patients were retrospectively reviewed and their clinical features including age, gender, visual acuity, refraction, ocular alignment, ocular motility, surgical method employed and final outcomes were analyzed.

Results: All cases were monocular. There were four cases (44.4%) coexistent with fibrosis of the levator palpebrae muscle and three (33.3%) with fibrosis of the superior oblique muscle. Eight cases (88.9%) presented with hypertropia, and one case showed mild hypotropia. Horizontal deviation was presented in six cases (66.7%). Surgical approaches included either superior rectus recession/tenotomy with or without traction suture; superior rectus recession and inferior rectus resection; or adhesion separation of superior rectus and levator palpebrae muscles. Excellent surgical outcomes were obtained in five cases (55.6%), good in two (22.2%), and poor outcomes were reported for two cases (22.2%). One patient (11.1%) underwent a second surgery.

Conclusion: CFSRM was found to be mainly unilaterally infected, mostly manifesting as hypertropia, and was often associated with fibrosis of the levator palpebrae or superior oblique muscle. Weakening procedures of the superior rectus muscle were the preferred surgical technique. However, success rates were relatively low for CFSRM.

Keywords: Congenital Fibrosis; Extraocular Muscle; Strabismus Surgery; Superior Rectus Muscle; Traction Suture

M. Yang · L. Fu · J. Yan (✉)
Department of Strabismus and Amblyopia, The State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-Sen University, 54 Xianlie Nan Road, Guangzhou 510060, Guangdong, People's Republic of China
e-mail: yanjh2011@126.com

M. Yang
Department of Strabismus and Amblyopia, Tongde Hospital of Zhejiang Province, 234 Gucui Road, Hangzhou 310012, Zhejiang, People's Republic of China

Key Summary Points

Why carry out this study?

There is a severe lack of information regarding the clinical characteristics and surgical management of congenital fibrosis of superior rectus muscle patients. We attempt to achieve a more comprehensive assessment regarding the characteristics and treatments of these patients.

What was learned from the study?

Congenital fibrosis of superior rectus muscle was found to be unilateral, manifested as a hypertropia, and was often associated with fibrosis of the levator palpebrae or superior oblique muscles. Weakening procedures of the superior rectus muscle was the preferred surgical technique, and success rates were relatively low.

INTRODUCTION

Congenital fibrosis of extraocular muscles (CFEOM), a subset of congenital cranial dysinnervation disorders (CCDDs), has an incidence of approximately 1:230,000 [1, 2]. CFEOM is a congenital, non-progressive restrictive strabismus sub-classified as CFEOM1, CFEOM2 or CFEOM3 and may be accompanied by ptosis and aberrant innervation [1]. There have been numerous studies on the clinical features, subclassification, surgical treatments and underlying genetic etiology of CFEOMs [1–13]. Results from previous genetic and neuroimaging studies have established that CFEOM is neurogenic, resulting in fibrotic tissue or atrophy of extraocular muscles due to deficiencies in the innervation of these muscles [4–6]. CFEOM patients mainly showing congenital fibrosis of superior rectus muscle (CFSRM) are particularly rare, and only a few such cases have been described in the literature [3, 9]. Therefore, there is a severe lack of information regarding the clinical characteristics and surgical management of these patients. While surgery represents the treatment of choice for patients with CFSRM, surgical management of this condition can be quite challenging, and the outcomes are often unpredictable, which then necessitates individualized surgical approaches. Common surgical tables used for ordinary strabismus are not suitable for CFSRM because of the extreme degree of abnormalities of involved muscles. Moreover, as a result of the marked restrictions in motility and narrow surgical field, performing each step of muscle surgery becomes problematic. For example, Prakash et al. reported one case of CFSRM requiring three surgeries to obtain a satisfactory cosmetic outcome [3]. Moreover, it can be very difficult to perform strabismus surgery on a frozen superior rectus muscle demonstrating limited motility. As an attempt to achieve a more comprehensive assessment regarding the characteristics and treatments of CFSRM patients, in this report we reviewed the clinical features, imaging findings, surgical methods and surgical results of nine cases of patients with CFSRM that had received orbital imaging examinations and strabismus surgery. To the best of our knowledge, these represent the largest sample of cases with CFSRM that have been analyzed.

METHODS

The medical records of nine patients with CFSRM subjected to surgical correction at the Eye Hospital of the Zhongshan Ophthalmic Center of Sun Yat-sen University, China, from January 2011 to December 2020 were reviewed retrospectively. Only CFEOM patients demonstrating effects mainly involving the superior rectus muscle were included in our study, while those with CFEOM1, CFEOM2 or CFEOM3 presenting with abnormalities in other extraocular muscles were excluded. All patients were seen and treated by one doctor (Yan JH). The following clinical characteristics were obtained from the patients' charts: gender, family history, age at surgery, best corrected visual acuity,

cycloplegic refraction, abnormal head position, orbital imaging, ocular motility and ocular alignment, surgical method employed and surgical outcomes. Limitations of ocular motility in all diagnostic gazes were measured using a 5-point scale (0 to − 4) as described previously [14]. Written informed consent to participate in this study was obtained from all patients. All procedures were performed in accordance with the 1964 Declaration of Helsinki.

Indications for strabismus surgery consisted of either a > 15 PD (prism diopter) hypertropia or obvious abnormal head position. Surgeries were performed under general anesthesia without using suture adjustment. Superior rectus recession was the preferred surgical procedure for this condition. The extent of this surgery is determined by the degree of fibrosis and angle of deviation, when ranging from 3 to 10 mm, while a recession of > 5 to 6 mm is often required for severe cases. The intraoperative forced duction test was also used to determine the amount of recession, and the forced duction test at the end of the surgical procedure was done to assure the releasing of involved muscle. A superior rectus tenotomy or superior rectus recession combined with inferior rectus resection was performed in patients showing a large angle of hypertropia (> 35 PD) and severe restrictive force of the superior rectus muscle. The traction suture was often used for patients with > 35 PD hypertropia and removed at 1 week after surgery. An alignment for vertical strabismus postoperative was considered as excellent with ≤ 10 PD, good with ≤ 20 PD and poor with > 20 PD [12].

RESULTS

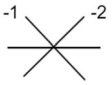
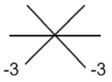
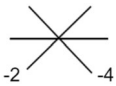
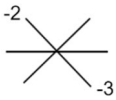
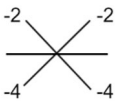
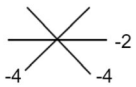
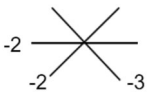
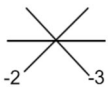
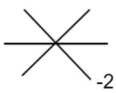
Demographic Data

A summary of the clinical characteristics of the nine CFSRM patients included in this review is contained in Table 1. There were five males and four females, and all cases were sporadic and monocular (four in the right eye and five in the left). The median age at surgery was 10.3 (range = 2.0 to 41.0) years. Eight out of nine cases (88.9%) had hyperopia and astigmatism, while one had myopia. Of the eight patients who had recorded vision, amblyopia was observed in seven (7/8, 87.5%). One patient had undergone a previous strabismus surgery elsewhere. Slit-lamp and fundus examinations were unremarkable in all cases.

Ocular Alignment and Ocular Motility

Vertical strabismus was present in all cases; eight cases (88.9%) showed hypertropia and one (11.1%) showed a mild hypotropia of the affected eye. Six cases (66.7%) presented with horizontal deviation as well, which all presented as exotropia. Varying degrees of restrictions in ocular motility of the affected eye were present in all cases. Slight limitations in elevation were observed in the case with hypotropia. Moderate to severe restrictions in movement of downward gaze were present in seven cases with hypertropia, while restrictions in both elevation and depression movements were observed in another hypertropic case. In addition, horizontal limitations in movement were observed in two cases (22.2%). Levator palpebrae muscle fibrosis was detected in four cases (44.4%), revealed as ptosis in three of these cases and upper lid retraction in the remaining case. Superior oblique muscle fibrosis was observed in three cases (33.3%) with only one of these demonstrating Brown syndrome. One case showed an aberrant innervation of the Marcus-Gunn jaw-winking phenomenon. Two cases had nystagmus, and abnormal head positions were observed in three cases. Orbital magnetic resonance imaging (MRI) and/or computed tomography (CT) examination demonstrated an abnormal thickening of the affected muscle in six cases (66.7%), but no obvious change in the other three cases. As showed in Fig. 1, which included nine diagnostic positions of gaze picture preoperatively and 3 months after surgery, and orbital MRI and CT scans of case 3, the fibrosis present within both the superior rectus and levator palpebrae muscles of the affected left eye was substantially thicker than that observed in the contralateral healthy eye.

Table 1 Clinical features of patients with CFSRM

Case/ age/sex/eye[#]	Amblyopia	Fibrosis muscle[*]	Notable conditions	Deviation preoperative(PD)[$]	Ductions preoperative(0/–4) Adduction abduction
1/4/M/L	Yes	SR, LP	Ptosis	HOT 16, XT 10	
2/3/F/L	Yes	SR	–	HT 35, XT 53	
3/3/M/L	Yes	SR, LP	Upper lid retraction	HT 53, XT 18	
4/6/F/R	Yes	SR, SO	Brown syndrome	HT 18	
5/4/F/R	Yes	SR, LP	Ptosis	HT 58, XT 18	
6/24/M/L	Yes	SR, LP, SO	Ptosis	HT 110,XT 25	
7/41/F/L	Yes	SR	-	HT 30,XT 20	
8/2/M/R	No vision record	SR, SO	Nystagmus	HT 45	
9/6/M/R	No	SR	Marcus-Gunn syndrome, nystagmus	HT 18	

[*] *SR* superior rectus muscle, *IR* inferior rectus muscle, *SO* superior oblique muscle, *LP* levator palpebrae muscle,
[#] *F* female, *M* male, *R* right eye, *L* left eye
[$] *HT* hypertropia, *HOT* hypotropia, *XT* exotropia, *ET* esotropia

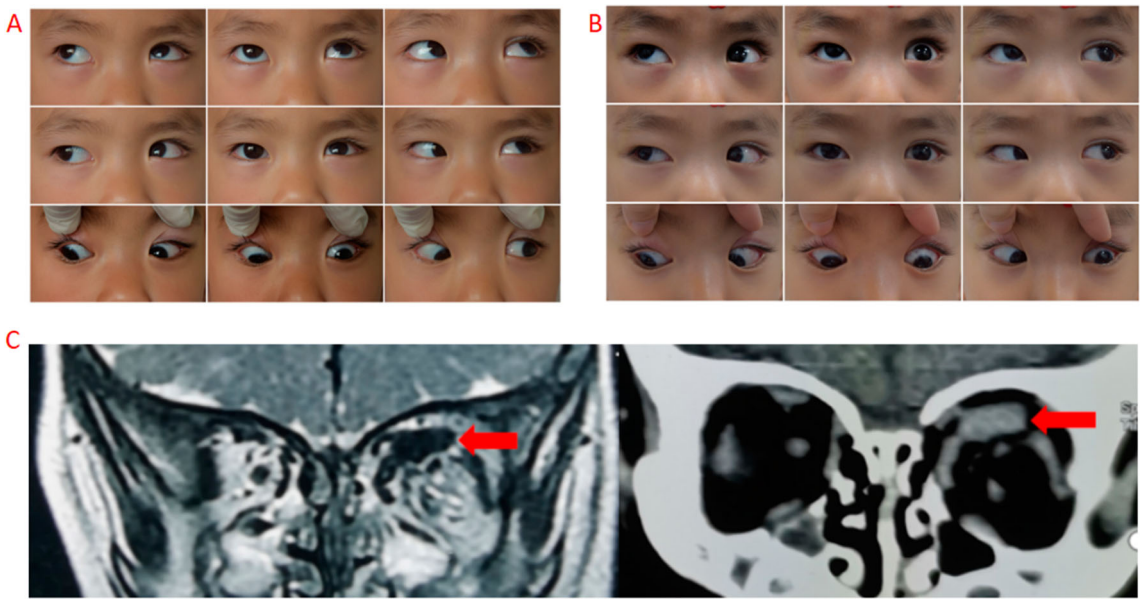


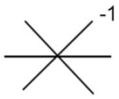
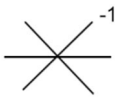
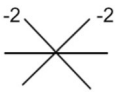
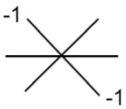
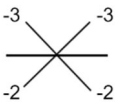
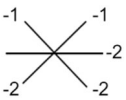
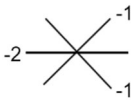
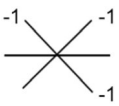
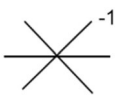
Fig. 1 Case #3: CFSRM combined with levator palpebrae muscle fibrosis within the left eye. A preoperative left hypertropia (53 PD) and exotropia (18 PD) with deficit of down-gaze motility were present (**A**). The hypertropia decreased to 5 PD, and exotropia was corrected with the restrictive movement in downward gaze being entirely corrected at 3 months after a 10-mm recession of the left superior rectus muscle (**B**). Orbital MRI and CT examinations revealed that the superior rectus and levator palpebrae muscles of the left eye were substantially thicker than in the contralateral right eye (red arrow) (**C**)

Surgical Methods and Surgical Outcomes

Results of the forced duction test, as performed under general anesthesia, were positive in all cases (8 in downward gaze, 1 in both downward and upward gazes). All cases received vertical strabismus surgery of the affected eye. The surgical methods and surgical outcomes of all the patients are shown in Table 2. Separation of the adhesion between the superior rectus and levator palpebrae muscles was executed in the patient with mild hypotropia. In this patient there was also fibrosis within the levator palpebrae muscle; although relief of this adhesion decreased his vertical deviation, it was not completely corrected. Of the four hypertropic cases receiving superior rectus recession (extents ranging from 3 to 10 mm), their hypertropias were fully corrected in three cases and decreased in one case. Surgical treatments for the other four hypertropic cases consisted of superior rectus tenotomy, superior rectus recession combined with traction suture, superior rectus recession and inferior rectus resection, and superior rectus tenotomy with traction suture. Of the six cases with exotropia, the exotropic deviation remained unchanged in three cases, decreased to 18 PD in one case (#2) after the first vertical muscle surgery and was corrected after a secondary horizontal muscle surgery, dissipated in one case (#3) after vertical muscle surgery only, and was corrected in one case (#7) following lateral rectus recession (7 mm). Three patients, who had simultaneous fibrosis of the superior oblique muscle (1 with Brown syndrome), received superior oblique rectus tenotomy.

Finally, after a minimum of 3 months follow-up, excellent surgical outcomes were reported for five cases (55.6%), good for 2 (22.2%) and poor for 2 (22.2%). Motility limitations were improved to some extent in all patients, and head positions were improved to varying degrees in the three cases presented as abnormal preoperatively. In case #2, who showed preoperative 35 PD hypertropia and 53 PD exotropia of the left eye, achieved a surgical

Table 2 Surgical methods and outcomes in patients with CFSRM

Case	Surgical method[$]	Deviation postoperative(PD)[$]	Ductions Preoperative(0/−4) Adduction abduction
1	Separate procedure of LR and LP	HOT 12, XT 10	
2	①SRR 6 mm + IRS 5 mm(L) ②SR advance 3 mm (L), LRR 6 mm + MRS 6 mm(R)	HOT 4, XT 5	
3	SRR 10 mm	HT 5	
4	SRR 3 mm + SOT	Orthophoria	
5	SRT	HT 25, XT 18	
6	SRT + SOT + traction suture	HT 35, XT18	
7	SRR 7 mm + LRR 7 mm + traction suture	HT 8, XT 5	
8	SRR10mm + SOT	HT 18	
9	SRR 5 mm	HT 7	

[$] *SRR* superior rectus recession, *IRS* inferior rectus resection, *SOT* superior oblique tenotomy, *SRT* superior rectus tenotomy, *LRR* lateral rectus recession, *MRS* medial rectus resection
[$] *HT* hypertropia, *HOT* hypotropia, *XT* exotropia, *ET* esotropia

outcome of 4 PD hypotropia and 35 PD exotropia of the left eye 4 months after left superior rectus recession (6 mm) and inferior rectus resection (5 mm). However, the vertical deviation increased to 18 PD hypotropia within the left eye 8 months after first surgery, necessitating a second procedure. This surgery was performed at 8 months after the first surgery and involved superior rectus advancement (3 mm, affected eye), along with lateral rectus recession (6 mm) and medial rectus resection (6 mm) in the contralateral healthy eye to correct her exotropia. Finally, a satisfactory outcome was observed when assessed at 6 months follow-up after this second surgery.

DISCUSSION

Among the three types of CFEOM (CFEOM1, CFEOM2, CFEOM3), the clinical presentations of CFEOM3 are the most diverse and can involve unilateral or bilateral impairments within any one of the six extraocular muscles. All cases in this report were presumed CFEOM3. While thinning of affected muscles has been reported in previous studies [7, 8], we found that thickened fibrous muscle was present in 66.7% of our cases. This difference may be attributable to limited assessments regarding imaging features by strabismus surgeons compared with the detailed evaluations from orbital MRI/CT scans as performed by a specialist in orbital diseases in each case of our study.

There is a high frequency of amblyopia in CFEOM patients due to unilateral strabismus and ptosis and high rates of refractive errors. Amblyopia was present in 87.5% (7/8) of our case series. The most frequently observed deviation in our CFSRM cases was hypertropia (88.9%), followed by hypotropia (11.1%). These features were somewhat different from that reported in previous studies, where one case of CFSRM was found with marked hypotropia, severe restrictions in elevation and ptosis in the right eye [3], while another case presented with orthophoric in the primary position along with a marked limitation in depression within the left eye [9]. As superior rectus, superior oblique and levator palpebrae muscles develop together from the upper mesoderm complex and are anatomically related to one another, developmental lesions of superior rectus muscles are often accompanied with abnormalities in these latter two muscles [10]. Levator palpebrae fibrosis was observed in 44.4% of our cases and superior oblique fibrosis in 33.3%, including one case in which both muscles were involved. Prakash et al. [3] and Seyhan et al. [9] also reported single cases where a simultaneous congenital fibrosis of the superior rectus and superior oblique muscles was observed. In addition, an aberrant innervation of the Marcus Gunn jaw winking phenomenon was observed in one of our cases.

When patient showed either a > 15 PD (prism diopter) hypertropia or obvious abnormal head position, we chose a surgery method. However, surgical management of this condition is quite difficult and extremely challenging. Based on our experience, we suggest the following surgical guidelines to increase the potential for a successful outcome. First, we find that superior rectus weakening to release restriction is the preferred surgical method. Second, adequate separation of fibrotic tissue around the involved muscle must be implemented, and a conjunctival closure with sclera bared can be performed. In our case series, the fibrotic tissue to be separated in two cases was so severe and deep in the orbit that the strabismus surgeon was incapable of completing this step, which then required the services of a specialist in orbital diseases to perform this daunting separation involving a deep retractor for exposure. Third, as the horizontal deviation may change after a vertical muscle procedure, horizontal strabismus surgery should be scheduled as a second surgery. Apt and Axelrod stressed that vertical misalignment should be addressed first, followed by horizontal strabismus and then blepharoptosis [13]. Yazdani and Traboulsi also reported that horizontal muscle surgery should be performed when necessary [4]. In our sample, two cases underwent horizontal rectus surgery because of a large angle exotropia. Among two cases combined with exotropia, one obtained an 18 PD exodeviation decrease (case #2, first surgery), while the exodeviation was

corrected in the second case (case #3) after vertical muscle surgery only.

Traction suture can be effective for patients with a large angle of deviation and severe limitations in their ocular motility, particularly when restrictions remain even after weakening of the involved extraocular muscle. This procedure produces the desired 15° to 25° over-correction of the eyeball. Traction suture was used in two cases of our study, and there were significant decreases in the preoperative hyperdeviation at 1 week after surgery following removal of the suture in these two cases. However, in one of these two cases (case #6), which showed an extremely large angle of hypertropia (110 PD), a hypertropic drift occurred during the follow-up period. Although this hypertropia was fully corrected in the primary position within the first 2 weeks after surgery, it recurred to 35 PD when assessed at 4 months follow-up. Previous study demonstrated that traction suture can be as effective as muscle surgery sometimes [11]. Sener et al. also considered traction suture as an effective procedure for patients showing a large angle deviation; surgical effect of traction suture for 3 days and 1 day after surgery was compared, and the former showed a better outcome [12].

Overall, surgical outcomes in our cases were good considering the difficulty and complexity of the correction, with an excellent surgical outcome reported in five cases (55.6%), good in two (22.2%) and poor in two (22.2%) when assessed at a minimum of 3 months follow-up. Although overcorrection in CFEOM patients is rare, one case required a second operation because of an overcorrection that was present after an extended follow-up period. Sener et al. described three CFEOM cases experiencing a horizontal overcorrection, which may be attributable to the possibility of disregarding the exo-drift following inferior rectus recession or an excessive degree of surgical intervention in patients with only mild motility limitations [12]. In general, ocular alignment, ocular motility and abnormal head position in CFSRM cases can be improved, but rarely restored, with varying degrees of strabismus surgery. Accordingly, it is important that both patients and family members be informed as to the expected outcomes from this surgery.

This study has some limitations which should be noted. First, it is a retrospective study, and although it includes the largest sample size available to date, the number of CFSRM cases included remains small. Our findings offer no information on the molecular basis and corresponding genetics of CFSRM. This yet to be elucidated information will be critical in providing some insights into the mechanisms for the abnormal development of the superior rectus muscle and its motor innervation. Finally, the follow-up times reported were somewhat brief. Therefore, larger sample sizes and longer follow-up time periods of assessment will be required to obtain a more precise understanding of CFSRM.

CONCLUSIONS

In summary, the findings of this review reveal that the clinical characteristics of CFSRM can be variable. In general, it is monocular and sporadic with a high incidence of amblyopia. It manifests as a hypertropia with a downward gaze limitation, often associated with fibrosis of the levator palpebrae or superior oblique muscles. A thickened fibrous muscle was found in six of the nine cases reviewed. A weakening of the superior rectus muscle is the preferred surgical approach. For patients with a large angle deviation and marked motility restrictions, a combined inferior rectus resection or traction suture should be performed. While most patients do show improvements with regard to their eye position or ocular motility following surgery, the success rate remains relatively low.

ACKNOWLEDGEMENTS

We appreciate the help of Bingbing Zhu in the process of collecting patient data and all the parents who took part in the study.

Funding. No funding or sponsorship was received for this study or publication of this

article. The journal's Rapid Service Fee was funded by the authors.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author Contributions. All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Min Yang, Licheng Fu and Jianhua Yan. The first draft of the manuscript was written by Min Yang, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Disclosures. Min Yang, Licheng Fu and Jianhua Yan declare that they have no conflict of interest.

Compliance with Ethics Guidelines. Institution approval for this study was obtained from the Research Ethics Board of the Zhongshan Ophthalmic Center of Sun Yat-sen University, China, and all procedures were performed in accordance with the 1964 Declaration of Helsinki. Written informed consent to participate in this study was obtained from all patients.

Data Availability. All data generated or analyzed during this study are included in this published article.

REFERENCES

1. Oystreck DT. Ophthalmoplegia and congenital cranial dysinnervation disorders. J Binocul Vis Ocul Motil. 2018;68:31–3.
2. Reck AC, Manners R, Hatchwell E. Phenotypic heterogeneity may occur in congenital fibrosis of the extraocular muscles. Br J Ophthalmol. 1998;82:676–9.
3. Prakash P, Menon V, Ghosh G. Congenital fibrosis of superior rectus and superior oblique: a case report. Br J Ophthalmol. 1985;69:57–9.
4. Yazdani A, Traboulsi EI. Classification and surgical management of patients with familial and sporadic forms of congenital fibrosis of the extraocular muscles. Ophthalmology. 2004;111:1035–42.
5. Traboulsi EL, Lee BA, Mousawi A, et al. Evidence of genetic heterogeneity in autosomal recessive congenital fibrosis of the extraocular muscles. Am J Ophthalmol. 2000;129:658–62.
6. Demer JL, Clark RA, Engle EC. Magnetic resonance imaging evidence for widespread orbital dysinnervation in congenital fibrosis of extraocular muscles due to mutations in KIF2lA. Invest Ophthalmol Vis Sci. 2005;46:530–9.
7. Okita Y, Kimura A, Okamoto M, et al. Surgical management of pediatric patients with congenital fibrosis of the extraocular muscles. Jpn J Ophthalmol. 2020;64(1):86–92.
8. Kim N, Yang HK, Kim JH, et al. Comparison of clinical and radiological findings between congenital orbital fibrosis and congenital fibrosis of the extraocular muscles. Curr Eye Res. 2018;43:1471–6.
9. Seyhan B, Ozkan H, Cakmak V, Dayanir A. Fibrotic superior oblique and superior rectus muscles with an accessory tissue band. J AAPOS. 2007;11:491–4.
10. Sevel D. A reappraisal of the origin of human extraocular muscles. Ophthalmology. 1981;88:1330–8.

11. Khaier A, Dawson E, Lee J. Traction sutures in the management of long-standing third nerve palsy. Strabismus. 2008;16:77–83.

12. Sener EC, Sekeroglu HT, Ural O, et al. Strabismus surgery in congenital fibrosis of the extraocular muscles: a paradigm. Ophthalmic Genet. 2014;35:208–25.

13. Apt L, Axelrod RN. Generalized fibrosis of the extraocular muscles. Am J Ophthalmo. 1978;85:822–9.

14. Chen MH, Yan JH. Superior rectus recession for hypertropia in thyroid-associated ophthalmopathy. J AAPOS. 2021;25:283.e1-283.e6.