CASE STUDY

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A Treatment Approach in Congenital Fibrosis of Extraocular Muscles

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ABSTRACT

Background: Congenital fibrosis of extraocular muscles (CFEOM) is a group of genetically defined eye-moving disorders. The syndrome is clinically characterized by congenital non-progressive ophthalmoplegia caused by dysinervation of the cranial nerves with or without ptosis. As a main sign of a CFEOM, extraocular muscles get shrunken and fibrotic, which makes surgery more technically demanding and the result more unpredictable, which makes the treatment challenging and highly customized. Our paper presents variations of the clinical picture and treatment cases of CFEOM1. **Objective:** To outline the importance of the clinical examination with the exact measurement of deviations for the patients with ocular fibrosis and passive duction test under general anesthesia, establishing them as the main criteria for treatment. **Methods**: We treated seven patients (14 eyes) with CFEOM1. The decision of the treatment was based on the measurement of the eye position in the primary position (PP), the severity of compensatory head position (CHP), restriction of motility, and passive motility test performed before surgery in general anesthesia. In 3 cases, patients were treated conservatively with the treatment of refractive error and amblyopia. However, in 4 patients, CHP and position of the eyes in PP were not acceptable, motility was severely impaired, and patients underwent surgery. The first surgery was performed on eye muscles: recession of inferior rectus muscle (IRM), anteposition, and resection of superior rectus muscle (SRM). As a second step procedure, ptosis surgery was performed. When the muscle was too tight, and it wasn't possible to have a satisfying result with conventional surgery, we used a tissue expander to improve the position and motility of the affected eyes. **Results:** In all operated cases, CHP has significantly improved and the position of the eyes in PP. **Conclusion:** Exact eye and head position measurements and a passive motility test during general anesthesia should guide the surgery. In the case when conventional surgery is not possible, implantation of a bovine pericard is a safe and effective method.

Keywords: Congenital fibrosis of extraocular muscles, ophthalmoplegia, incomitant strabismus, ptosis

1. BACKGROUND

Congenital fibrosis of the extraocular muscles is a group of genetically defined eye movement disorders comprising at least seven inherited strabismus syndromes (CFEOM1A, CFEOM1B, CFEOM2, CFEOM3A, CFEOM3B, CFEOM3C, Tukel syndrome, and CFEOM3 with polymicrogyria) (1, 2). Congenital Fibrosis of Extra Ocular Muscles 1 (CFEOM1) is the most common form in the group, affecting 1 in 230 000 people. Inheritance is usually in autosomal dominant manner (Figure 1). De novo mutation and the disease resulting from germline mosaicism of one of the parents are also possible, and the affected individual may have unaffected parents (3). The disorder is affecting some or all of the oculomotor nuclei and nerve itself, as well as the trochlear nucleus and its innervated muscle (4). Diagnosis is made by a thorough clinical examination with special attention to the presence of other systemic malformations. Molecular and genetic testing is available to identify mutations and confirm the diagnosis (5, 6). The syndrome is clinically characterized by congenital non-progressive ophthalmoplegia with or without ptosis, bilateral but usually asymetric. Although the disorder is primarily neurological, extraocular muscles are changed in their structure with fibrous tissue, or mixture of myofibres and fibrous tissue which results in stiffness and impaired motility (7). Defective eye motility in this disorders is

GROUPS	Type of treatment	Patients	strabismus			ptosis				BCVA		PERFORMED SURGERY	POSTOP.FINDINGS			
			CHP	Eyes in PP	Motility	MRD I (mm)		LF (mm)					CHP	Eyes in PP	MRD I (mm)	
						RE	LE	RE	LE	RE	LE				RE	LE
GROUP 1.	Conservative treatment	Patient 1 Girl, 4 years	Chin up 5°	5° below midline	No elevation Good depression Good horizontal	2	2	4	4	0.6	0.6	None				
		Patient 2 Boy, 3 years	Chin up 2°	midline	Restricted elevation RE restricted horizontal Good depression	2	4	4	4	0,4	0,4	None				
		Patient 3 Girl, 4 years	Chin up 5°	3° bellow midline	No elevation Restricted horizontal Good depression	2	3	5	5	0,6	0,6	None				
GROUP 2.	2 A) Conventional Surgical treatment	Patient 4 Boy 3 years	Chin up 20°	10° below midline	No elevation both eyes	2	2	5	4	0,3	0,3	*MRI recession (-4 RE/-5LE)*	2° chin up		*2*	*2*
		Patient 5 Girl , 9 years	Chin up 25°	15° below midline Left tilt 5°	No elevation Limited Depression Abberant eye movements Good Horizontal	1	0	6	0	0.8	0.8	*MRI recession* (-4 RE, -5 LE) *MRS anteposition* (+4 RE/LE) *Frontalis suspension*	< 5° chin up	2° below midline	*1.5*	*1*
		Patient 6 Girl, 3 years	Chin up 20°	10° below midline	No elevation Aberant eye movement Restricted horizontal Restricted depression	3	4	6	6	0,4	0,4	MRI recession (-7 RE/-6LE)	5° chin up		3	4
	2 B) Surgical treatment with tissue expander	Patient 7 Boy, 4 years	Chin up 40°	25° below midline	No Elevation No Depression Restricted horizontal	2	2	4	4	0,4	0.3	*MRI recession* (-7 RE, -6 LE) *Anteposition of MRI* (+2mm) *with Tutopatch implant* (+6 RE, +8 LE)	5° chin up	2° below midline	*2*	*2*

Table 1. Clinical characteristics, surgeries performed and results in 7 patients (14 eyes) of CFEOM1 VA-visual acuity,SA-stereoacuity, CHP – Compensatory head posture, PP – primary position of gaze, MRD 1- margin reflex distance I, LF- levator function, BCVA- best corrected visual acuity, RE right eye, LE left eye, IRM – inferior rectus muscle,

a result of both: inadequate innervation as well as stiffness. Muscles can have abberant place of insertion to the globe, usually the superior recti, that can be found far behind their physiological insertion. Affected individuals have incommitant form of strabismus, often with fixed position in primary gaze that can be esotropic or exotropic, but most usually with their eyes fixed in an infraducted position sometimes positioned well below horizontal midline, up to 20°-30°. They typically have severe limitation of vertical gaze (usually up gaze) and variable limitation of horizontal gaze which they compensate by maintaining compensatory head positions (

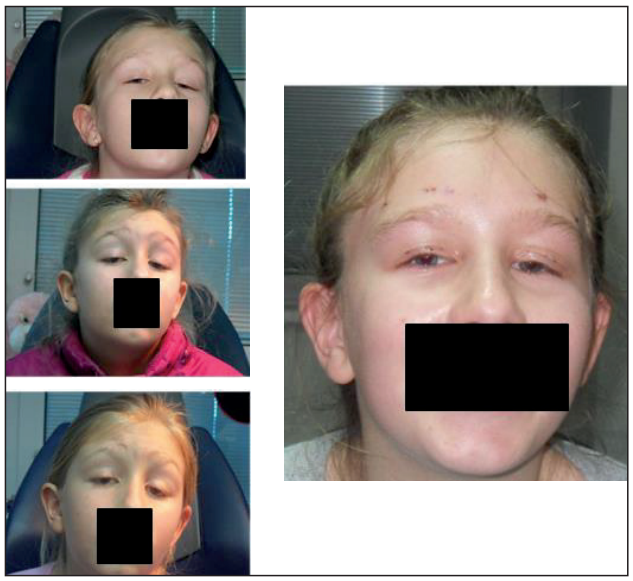

Figure 1. Compensatory Head Posture of the patient No5 before surgeries, after the first and second eye muscle surgery and after the final ptosis surgery.

CHP) and by moving their heads rather than their eyes to track objects. Dysinervation motility patterns and aberrant eye movements can be visible as well as the A or V pattern (8, 9). Refractive errors, amblyopia, impaired binocular vision and corneal exposure are common as well. Conservative approach is based on treating amblyopia and refractive errors with glasses, contact lenses and patching. When needed, surgeries are performed as early as the second year of life with the main surgical goal of improving unacceptable abnormal head position. After improving eye misalignment ptosis surgery should be performed (10).

2. OBJECTIVE

To outline the importance of the clinical examination with the exact measurement of deviations for the patients with ocular fibrosis as well as passive duction test under general anesthesia establishing them as the main criteria for treatment. In the cases of surgical treatment when conventional surgery is not possible, we recommend implantation of Bovine pericard implants.

3. PATIENTS AND METHODS

A retrospective review of 7 patients (14 eyes) diagnosed in our clinic with Congenital Fibrosis of Extra Ocular Muscles 1 on clinical characteristics of the strabismus, family history and lack of system features. All of them had undergone standardized ophthalmic and orthoptic evaluation, and four were operated on by the same surgeon. Each parent/patient has signed the written consent that the photos of the patients can be used for scientific purposes. The follow-up was three years.

Seven patients, aged 3 to 9 at the time of presentation, were referred to our clinic because of complex incommitant strabismus, present from birth. All of them had a compensatory head position (CHP)–chin up, infraducted eyes in primary gaze, defective vertical movements, mostly unaffected horizontal eye movements, negative

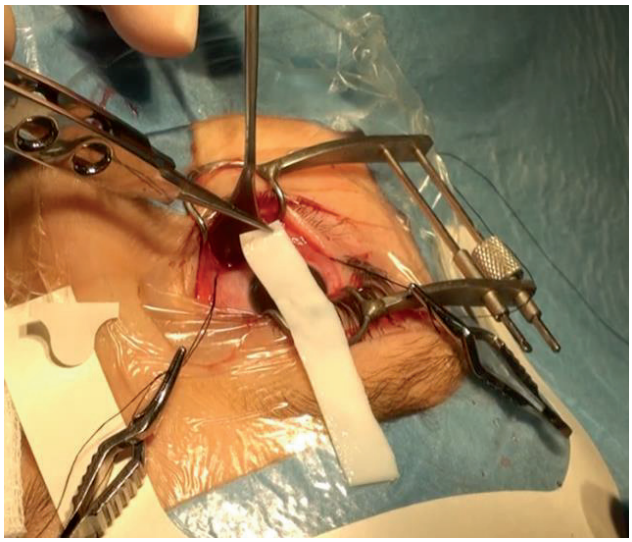

Figure 2. Elongation of the muscle by implantation of Tutopatch

Bells phenomenon and a variant degree of congenital complex ptosis.

Imaging was not performed, while the most important and guiding criteria for the type and amount of surgeries performed on our patients were clinical picture and muscle restriction during the passive motility test.

Management of these patients was different and customized, according to their CHP, degree of infraduction of the eyes in primary position (PP), motility of the eyeball and the severity of ptosis

Compensatory head position referres to the angle the head forms with the body on the horizontal, vertical and anteroposterior axis and was measured using orthopedic goniometry and expressed in degrees. The deviation of the eyes in the primary position was assessed by measuring the angle between the horizontal midline and the corneal light reflex of the deviating eye. At the beginning of the surgery, a forced duction test was performed under general anesthesia by holding the eye globe with two toothed forceps at the limbus and pulling the eye in the direction opposite of the field of function of the tested muscle in order to measure the mechanical restriction of the globe movement. The amount of restriction is graded from l to IV. The amount of ptosis was measured with Marginal Reflex Distance 1 (MRD1) and Levator Function (LF). Bell's phenomenon was tried and not present in all patients.

The main clinical characteristics and performed surgical procedures of cases are summarized in Table 1.

Patients are divided into two groups. Group l was formed of 3 patients whose head position "chin up" was less than 5° and whose motility of the eyes was satisfying in PP, so they did not require surgery. All patients in this group had impaired elevation but good depression and good horizontal movement. 1 child, patient No 2, had restricted abduction of the RE to 20° which did not impair the primary position. All of the patients in this group had an amount of ptosis that was two or more mm over the central reflex which did not require surgery. However, they were treated with refractive correction as well as amblyopia treatment.

Group ll was formed of 4 patients that required surgical treatment. In three cases conventional surgery was performed and, in a patient, No 7 conventional surgery was combined with tissue expander implantation. The CHP "chin up" severity was measured from 10° to 40° in all four patients (20°,15°,20°,40°). Depression of all the patients in group II was restricted. Patients No 4 and 6 had restriction gr II, No 5 had gr III, and patient No7 had severe restriction of elevation graded as an IV stage with severe impairment of other eye movements. Horizontal movements were restricted in 2 patients. Patient No 6 had restricted abduction grade II and No7 had abduction restricted on both eyes gr I. Patient No 5 had good horizontal motility but aberrant eye movements when attempting vertical movement: on attempted elevation eyes converge and diverge on an attempt to depress. All the patients in this group had eyes fixed below midline in PP (10°, 15°,10°,25°

4. RESULTS

In all operated patients first surgery was on the eye muscles. Prior to the first surgery under general anesthesia, a passive motility test was performed. A forced duction test was performed by holding the eye globe with two-toothed forceps at the limbus and pulling the eye up to test the restriction of the inferior rectus muscle. Inspection revealed all the patients had fibrotic and thick Inferior Rectus Muscle (IRM). The superior rectus muscle (SRM) was examined and was fibrotic and hypoplastic in cases 4, 6 and 7. Patient No 5 had severely hypoplastic SRM (half of the normal size) with insertion 10 mm behind the limbus.

Since all of the patients had severely restricted elevation as a first surgery in all cases, a recession of the IRM was performed. The amount of the surgery was calculated according to the passive motility test. In patient No 4 IRM recession of 4mm on RE and 5 mm on LE was performed, and Patient No 6 underwent 7mm on the RE and 6mm on the LE of IRM resection. In Patient No 5, the first surgery recession of 4 mm RE and 5 LE was made, which improved her fixation in downgaze to 10° under the midline with her chin up 15° when upper eyelids were held open. In the second surgery both superior recti muscles were found hypoplastic, half of the normal size located 10 mm behind the limbus and a second surgery of SRM anteposition 4mm on both eyes was performed.

The result of the second surgery was primary eye position significantly improved with both eyes positioned slightly under the midline with possible 2°of up gaze and 5-10° of down gaze with some A pattern still visible.

The third surgery was the ptosis surgery of frontalis suspension with 2.0 mersilen suture.

The amount of surgery was conservative, taking into consideration the negative Bell's phenomenon. The result is significantly improved AHP with residual chin-up position less than 5°. A pattern was later corrected with 5 PD BT on both sides.

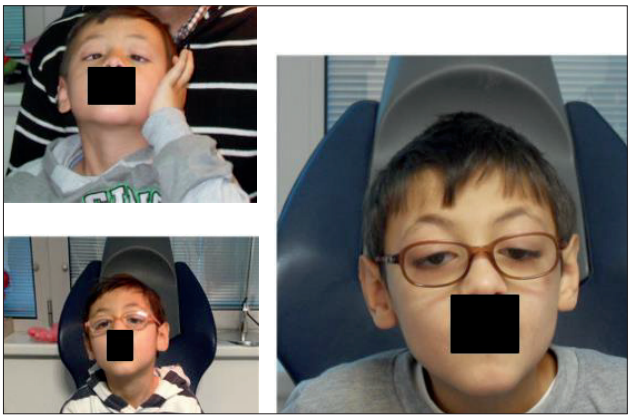

Figure 3: Compensatory Head Posture of the patient No7 before surgeries, after the first and second eye muscles surgeries.

Patient No7 was a four-year-old boy with a family history of a father and grandfather with Congenital Fibrosis of Extraocular Muscles 1 characteristic (Figure 1).

The patient had compensatory head posture-chin up for 40˚, with eyes fixed in downgaze 25° bellow midline, no elevation and depression, restricted horizontal movements and Bell's phenomenon negative. Ptosis was on both eyes with poor LF: 4/4 and compensatory frontalis action visible.

On first eye muscle surgery, a passive motility test revealed completely restricted elevation with severe restricted depression on both sides of stage lV. Horizontal movements were also restricted with abduction only to 20° with the tendency of incyclotorsion. Both inferior recti muscles were found fibrotic and thick with contracture during the surgery. The first surgery was listed in Table 1 Recession of both IRM 7mm of RE and 6 mm on the LE.

After the first surgery, his fixation in downgaze improved to 15° under the midline with CHP chin up for 20 ˚.

During the second surgery passive motility test still showed restricted elevation on both eyes with restriction grade II, so we antepositioned both inferior recti muscles for 2mm and elongated them with Tutopatch pericardium patch graft 6mm on the RE, and 8 mm LE (Tutiplast, TUTOGEN Medical GmbH, Neunkirchen

LE 2 mm of anteposition of superior recti with 8 mm Tutopatch implant.

The result of the last surgery was primary eye position significantly improved with both eyes positioned slightly under the midline with of 2°of up gaze and 5° of chin up.

5. DISCUSSION

Although the genetic basis of Congenital Fibrosis of Extraocular Muscles 1 has been intensively under research recently and it has provided some information for further understanding of brain development, the treatment of the disease has not substantially changed. Treatment is conservative and surgical when needed and has to be highly individualized. Conservative treatment aims to prevent and treat amblyopia. The main goals of surgical treatment when dealing with patients are: releasing the patient from an unacceptable head po-

sition, improving the alignment of the eyes in the primary position of gaze, and performing ptosis surgery when it is responsible for Compensatory Head Position. The best results are achieved very early (e.g. 1-2 years old). With early surgery head position is earlier improved, secondary complications are avoided, better eye motility in children is achieved and orthopedic consequences of compensatory head posture are avoided, as well as social problems (1). Early surgery is also indicated because of the quality of the muscles alone: with time the fibrous tissue in muscles gets shrunken and thicker, making the surgery more technically demanding and unpredictable. Deterioration of motility happens with time, in the form of pseudoprogression, resulting from interference of the globe growth and further fibrotic thickening of the muscles (3). When some of the Congenital Fibrosis of Extraocular Muscles disorder is suspected, the child should be addressed to a pediatric ophthalmologist as soon as possible. In the cases when early treatment is not possible, later treatment can also give satisfying results, as seen in our cases. If no amblyopia is present, the most important goal is successfully treating Compensatory Head Position. Because muscles are highly fibrotic and not regularly innervated, often with asymmetric muscle actions, results of the surgery are less predictable and special care for dosage should be taken forced duction test is obligatory to define the amount of the restriction produced by the affected muscles because it gives the most relevant information for planning of the surgery. It is recommended to do recessions instead of resections, with the first surgery done on the most fibrotic muscle. If the fibrosis is extremely strong with no possible passive motility muscle elongation can be performed by implantation of Tutopatch. The benefits of elongation with this tissue expander The additional advantage of this method is the replacement of the implant with surrounding biological tissue which enables the expander to act as a physiological tendon and enhances the action and motility of the operated tissue. Ptosis surgery, as the last step when needed, is usually done with frontalis suspension since the function of the levator muscle is usually poor, and asymmetry between two eyes is often present. Therefore levator resections are usually not recommended. The ptosis surgery aims to position MRD1 from 1 to 2 mm because of the negative Bells phenomenon and the risk of exposure keratopathy.

6. CONCLUSION

In the light of unpredicted surgical results in cases with CFEOM, we encourage exact measurement of muscle motility together with the position of the eyes and head in the primary position and measurement of passive motility in general anesthesia rather than imaging as a guide for the type and amount of the surgery. Muscle elongation with tissue expanders implantation such as bovine pericard (Tutopatch) is a safe and effective method for elongation of the extraocular muscles in cases where muscle tissue is too fibrotic for conventional surgery. The additional advantage of this method is the replacement of the implant with surrounding tissue which enables the expander to act as a physiological tendon and enhances the action and motility of the operated tissue.

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