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CASE REPORT OF AN ATYPICAL PRESENTATION OF CONGENITAL FIBROSIS OF THE EXTRAOCULAR MUSCLES (CFEOM)

Ophthalmology

Dr. Reena Gupta* Professor Regional Institute of Ophthalmology, Pt B D Sharma University of Health Sciences, Rohtak. *Corresponding Author

Dr. Chekitaan Singh Medical Director Ishwar Eye Centre, Rohtak.

Dr. Rohan Madan Resident Regional Institute of Ophthalmology, Pt B D Sharma University of Health Sciences, Rohtak.

ABSTRACT

INTRODUCTION:
CFEOM is a disorder that includes multiple extra ocular muscle restrictions. It is a rare, non –progressive, congenital condition and refers to at least eight genetically defined strabismus syndromes. Commonly presented clinical signs and symptoms in CFEOM includes- congenital non-progressive ophthalmoplegia (inability to move the eyes) with or without ptosis (droopy eyelids) affecting part or all of the oculomotor nucleus and nerve (cranial nerve III) and its innervated muscles. Refractive errors are also common.

CASE REPORT: The patient was the first child of non-consanguineous parents. There was no similar history or any history of ocular motility disorders in family in both paternal and maternal side. There is no prior history of use of glasses, occlusion therapy, surgery or trauma. Typically, binocular vision is absent. The child had difficulty looking at objects in downgaze, up gaze and laterally.
They also observed outward deviation of both eyes which was more for distance. Child had normal weight for age (30 kgs) Head circumference was within normal range (57 cm) There was absence of lid crease in both eyes and chin up head posture was seen for distance. No facial asymmetry was seen. Patient was able to spontaneously alternate fixate in the primary position. Patient had hypertropia of 6 prism diopters in left eye when fixing with right eye and hypertropia was same in upgaze and downgaze. No evidence of globe retraction on ocular movements. Patient had history of ocular deviation since birth which had not changed over the years. Mutations in the KIF21A gene are the primary cause of CFEOM1. Patients typically have convergent-type nystagmus movements with attempted up gaze (synergistic convergence) and an A pattern with divergence of the eyes in downgaze. There was no associated neurologic abnormalities and systemic disorders. The patient was found to have bilateral lagophthalmos, limitation of elevation and depression (vertical gazes). The patient underwent two surgeries. In the first surgery, B/L LR RC (14mm from limbus) and B/L SR RC(11mm)was done.

DISCUSSION: Congenital fibrosis of extraocular muscles is a common condition encountered by pediatric ophthalmologists. If not properly diagnosed, it is often confused with other ocular motility disorders. The treatment of CFEOM must focus on specific pattern of deficit and include management of head position, ocular alignment in primary position and maximizing outcome by preventing ambylopia. Currently no treatment has been developed to restore full functionality and range of motion of the extraocular muscles. Patients presenting with CFEOM1 usually require large bilateral inferior rectus recessions, often enhanced with bilateral superior oblique tenotomies to allow the eyes to come to vertical midline. Patient might also need multiple strabismus surgeries like with our patient. CFEOM is often associated with potential complications like strabismus, decreased binocular vision, ambylopia and facial palsy.

KEYWORDS

congenital fibrosis, CFEOM, CCDD, strabismus, ophthalmoplegia

INTRODUCTION

Congenital cranial dysinnervation disorders (CCDD) is a novel name for a group of neurogenic diseases that do not progress. The fundamental question, first referred to as congenital fibrosis syndrome, was considered to be extraocular muscle maldevelopment. Recent advances in genetics and neuroradiology have determined that the first manifestation of fibrotic muscles is due to a basic lack of innervation from defective, absent, or misdirected cranial nerves.[1]

Congenital fibrosis of the extraocular muscles (CFEOM) is a rare, non-progressive condition that results in restrictive global ophthalmoplegia and congenital ptosis. While CFEOM was classically thought to be a myopathy that resulted in muscle fibrosis, there is recent evidence to suggest that the fibrotic changes are secondary to defective innervations of the muscles during development. It is usually classified into three main types depending upon its clinical features and genetics. The three types to be mentioned are- CFEOM1, CFEOM2, and CFEOM3.[2]

CFEOM usually affects part or all of the oculomotor nucleus and nerve (cranial nerve III) and its innervated muscles (superior, medial, and inferior recti, inferior oblique, and levator palpabrae superioris) and/or the trochlear nucleus and nerve (cranial nerve IV) and its innervated muscle (the superior oblique).[7]

CFEOM type 1, commonly presents with Bilateral ptosis, horizontal strabismus, restricted up gaze and variable restricted horizontal gaze whereas type 2 presents with exotropia and miosis along with bilateral ptosis and severely restricted vertical and horizontal gaze. Type 3 usually has a unilateral presentation with variable or absent ptosis with eyes elevated above the midline.

CFEOM2 is an autosomal recessive disorder of neuronal specification, caused by homozygous mutations in the transcription factor PHOX2A,[3] whereas CFEOM1 and CFEOM3 are autosomal dominant disorders of axon guidance, caused by heterozygous mutations in various genes.

CFEOM1 is a singular eye movement disease with no associated neurological issues.

Patients with CFEOM2 exhibit small, sluggish pupils, as well as eye movement disorders and ptosis. They can also have subnormal visual acuity, which is indicative of retinal dysfunction, but no other neurological problems. Individuals with CFEOM3A may also have intellectual disability, social disability, Kallmann syndrome, facial weakness, and vocal cord paralysis; and/or may develop a progressive sensorimotor axonal polyneuropathy. Individuals with Tukel syndrome also have postaxial oligodactyly or oligosyndactyly of the hands. Those with CFEOM3 with polymicrogyria may also have variety of other neurological abnormalities, including additional cranial nerve defects, intellectual and social disabilities, mild brain malformations, and a progressive peripheral axonal neuropathy.[8]

CASE STUDY

A 10 years old male child reported in the pediatric ophthalmology and strabismus clinic of Regional Institute of Ophthalmology, PGIMS with chief complaints of outward deviation of both eyes since birth and inability to elevate or depress both eyes which had not changed over the years. Few months after birth, parents noticed that the child had difficulty in looking at objects in downgaze, up gaze and medially. They also observed outward deviation of both eyes which was more for distance. There was no significant abnormal head posture observed by

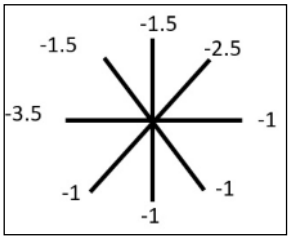
the parents. No similar history or any history of ocular motility disorders was present in the family on both paternal and maternal sides. Patient was the first child of non-consanguineous parents. There was no similar complaint in any siblings. There was no prior history of use of glasses, occlusion therapy, surgery or trauma. There was no history of any intellectual disability, malformation of fingers, facial weakness or vocal cord paralysis, deafness, external ear abnormalities, speech disorder and skeletal abnormalities.

ON EXAMINATION

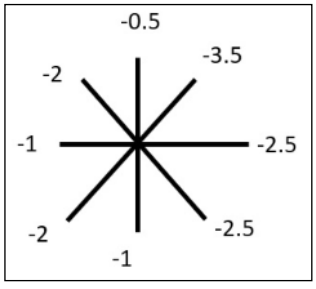
The child had normal weight for age (30 kgs). Head circumference was within normal range (57 cm). There was absence of lid crease in both eyes and chin up head posture was seen for distance along with mild ptosis. There was lagophthalmos (2 mm of both eyes) and lower lid retraction of both eyes (RE- 0.5mm; LE-1 mm), but no proptosis or hypertelorism/ tele canthus. No facial asymmetry was seen. No evidence of broad nasal bridge, high arched palate or low set of ears.

Local examination: The BCVA in the right eye was 6/6 and in the left eye was 6/9. Pupil examination showed two equal symmetrical pupils. There was bilateral limitation of elevation, depression and adduction in all gazes :

Left eye: There is -1.5 limitation in elevation in the left eye which remains same in dextro elevation but increases to around -2.5 on levo elevation. -1 limitation in depression in all gazes and -3.5 limitation in adduction and -1 in abduction.



Right eye: Mild limitation of elevation in right eye which increases to around -2 in dextro elevation and -3.5 in levo elevation. Around -1 limitation in depression which increases to -2 in dextro depression and -2.5 in levo depression. -1 limitation in abduction and -2.5 in adduction.



The limitation was same in both ductions and versions.

Fig 1: Inferior lid retraction both eyes

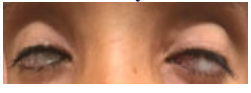


Fig 2: lagophthalmos both eyes

Fig 3: Fixing eye exotropia with hypotropia

V pattern exotropia seen increasing in upgaze. Limitation of movements in lateral gazes and in downgaze, deficit of elevation in adduction in both eyes. On orthoptics evaluation- The patient was able to alternate fixation in the primary position. It was observed that the patient was fixing alternately with fixing eye in downward gaze with hypertropia in non-fixing eye. On fixing with the right eye, the left eye showed moderate angle exotropia and hypertropia. Similarly, when the patient was fixing with the left eye, the right eye showed moderate angle exotropia and hypertropia. When the right eye moved inwards, there was increasing hypertropia of the left eye and vice versa. This ocular alignment varied with the change of fixation and with change in direction of gaze. The exotropia was present both for distance and near in all gazes. On occlusion, abducting nystagmus was present in left eye. There was severe convergence insufficiency. There was no evidence of globe retraction on ocular movements.

On sensory evaluation- Gross stereopsis was present for near which was tested by Titmus fly test, and alternate suppression for distance which was tested by WFDT. The angle of deviation was measured using prism bar cover test (PBCT) in all gazes and using accommodative targets at a distance of 6m and at 33 cm. There was exotropia with alternate hypertropia. The angle was 35 prism diopters of exotropia in primary position, 20 Base In in downgaze and 45 Base In in up gaze indicating a 'V' pattern of 25 prism diopters. Patient had hypertropia of 6 prism diopters in left eye when fixing with right eye and hypertropia was same in up gaze and downgaze.

Anterior segment and posterior segment examination was unremarkable.

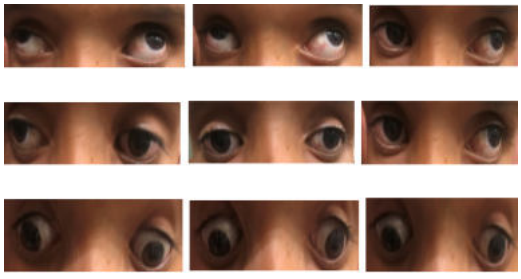


Fig 4: Nine diagnostic positions of gaze showing exotropia with hypertropia left eye when fixing with right eye in hypotropic position.

DISCUSSION:

Congenital fibrosis of extraocular muscles is a common condition encountered by pediatric ophthalmologists in which the child is born with congenital ocular motility abnormalities. It is a term used to describe a group of rare congenital eye movement diseases caused by dysfunction of the oculomotor (CN 3) and trochlear (CN 4) nerves, as well as the muscles they innervate.[9] The present case had history of ocular deviation since birth which had not changed over the years.

A common clinical type of CFEOM is CFEOM type 2. It is an autosomal recessive disorder and is usually presented with clinical signs and symptoms that includes- bilateral ptosis, exotropia, severe restriction of the horizontal and vertical eye movements, variable abduction, miotic and poorly reactive pupils and a positive forced duction test.[11] Therefore, the clinical findings in this patient could be concluded to be a variant of CFEOM 2 as the patient presented with bilateral mild ptosis, bilateral limitation of elevation and depression (vertical gazes) in all gazes and limitation of abduction in both eyes while adduction was preserved. Patient had compensatory chin up for distance which was not very significant for near. In contrast to a typical CFEOM type 2 presentation, pupillary examination was absolutely normal in our patient and he had large exotropia with reversing hypertropia in the primary position with moderately tight forced duction test. There was no associated neurologic abnormalities and systemic disorders.

Moreover, since there is no positive family history, it could be an autosomal recessive presentation, favoring the diagnosis of CFEOM 2. In our patient, CFEOM is not associated with any neurologic abnormalities. It is always a challenge to accurately diagnose such a case as there is always an overlap of presentation in various disorders of CCDD's. The differential diagnosis of CFEOM includes- third nerve palsy, chronic progressive external ophthalmoplegia, isolated congenital ptosis, congenital myasthenic syndrome, Duane syndrome

or horizontal gaze palsy In CFEOM, surgical management is the mainstay of treatment, but it is difficult to obtain an optimal result after one surgery, so the patient needs to be counselled for multiple surgeries. Prior to ptosis correction, strabismus surgery is always attempted. The expectations for strabismus surgery should be reasonable, and both parents and patients should be aware of them.[14] In our case, the plan of surgery was decided after doing intraoperative FDT.

This patient underwent two surgeries. In the first surgery, B/L LR Recession (14mm from limbus) and B/L SR Recession (11mm) was done. Intraoperative FDT showed moderately tight lateral rectus and superior rectus. Intraoperative findings showed fibrous strands in place of muscle fibres, no insertion line was visible, and post-equatorial fibrotic strand was present behind the superior rectus muscle.

Figure 5 – Post operative pictures after 1st surgery

At 4 weeks follow up, residual exotropia of 35 BI was still seen, so second surgery was done after 2 months which consisted of B/L MR Resection (6.5mm) and IR tenotomy in both eyes. Intraoperatively, the FDT was tight in up gaze. Strands of fibrous tissue were seen in place of medial rectus and inferior rectus mainly. Cosmetically, eyes were well aligned (Post op Distance almost ortho, Near 12BI with 5R/L) with restoration of stereopsis of 200 sec of arc.

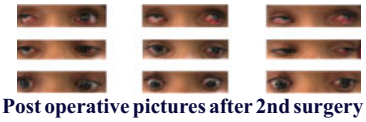


Figure 6 - Post operative pictures after 2nd surgery

Due to the lack of Bell's phenomenon and the possibility of exposure keratopathy, it is recommended that ptosis be under-corrected when it comes to surgery. The goal of ptosis correction should be to create a clear visual axis, partially remove head posture, and avoid amblyopia due to deprivation.14 Since our patient didn't have significant ptosis, the visual axis was clear and it was not of a cosmetic concern for the parents, so, we have not planned a surgical correction for ptosis yet.

FOLLOW UP:

At 4 years follow up:

Patient still had a residual exotropia of 10 BI for distance and 20BI for near which can be explained from the fact that patient had a severe convergence insufficiency as the NPC was 38 cm tested by RAF ruler and he had gross stereopsis which was around 400 seconds of arc by Titmus fly test.

Figure 7 – 9 gaze pictures at 4 year follow up

At 5 years follow up:

Cosmetically the eyes are well aligned, though the residual exotropia is more for near but the patient is satisfied and there is overall improvement in ocular motility and in binocular single field.

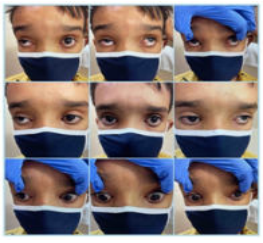


Figure 8 – 9 gaze pictures at 5 year follow up

CONCLUSION:

CFEOM is a congenital, non-progressive disorder characterised by multiple significant extraocular muscle restrictions. It causes constriction of the binocular single visual field and also is of cosmetic concerns for parents as well as the child. Due to variability in its clinical presentation and involvement of almost all extraocular muscles, optimal management is always a challenge for a strabismologist. Surgery is the mainstay of the treatment and the patient has to be counselled for a suboptimal result and the need of multiple surgeries. With recent advancements in genetics and imaging, it is now possible to diagnose and effectively manage CFEOM.

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