CONGENITAL FIBROSIS OF EXTRAOCULAR MUSCLES: A CASE REPORT

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ABSTRACT: -Congenital fibrosis of extraocular muscle (CFEOM) is a rare congenital syndrome characterised by non-progressive unilateral or bilateral restrictive ocular motility with or without ptosis. It results from fibrosis of the extraocular muscle causing restricted ocular motility and optic nuclear dysplasia or hypoplasia. Patient can report with various presentations depending on different phenotypes of disease.

INTRODUCTION: CFEOM is the term used to describe several different inherited strabismus syndromes which manifest as congenital restrictive ophthalmoplegia (restriction of globe movement in one or more fields of gaze), affecting extraocular muscles innervated by the CNIII and/or CNIV. The term Congenital Cranial Dysinnervation Disorders (CCDDs) was coined to refer to the innervation disorders of the extraocular muscles.[1] The various forms of CFEOM are included in the CCDDs.

In this paper we describe the clinical and neuro-radiological findings in a patient with CFEOM who presented to us with a history of congenital watering, restricted ocular motility and ptosis, and review literature with respect to clinical features, genetics and management of this condition.

CASE PRESENTATION

An8-year-old boy visited our department with chief complaint given by informant (father) were unable to move eyeball along with watering in left eye since birth. Sporadic presentation with no similar complaint among siblings. UCVA- (BE) 3/60, on cycloplegic correction- (BE) +5.00sph. BCVA- (BE) +4.00sph (6/60). Chin down position with no signs of ptosis.BE megalocornea 12.5*12.5 mm with intraocular pressure BE 17.3 mmhg. BE pupil were sluggishly reactive to light with BE fundus showed optic disc atrophy with pale

neuroretinal rim, rest fundus within normal limits. On forced duction test it showed restricted ocular motility in all quadrants. further MRI investigation revealed thinning and fibrosis of extraocular muscles.

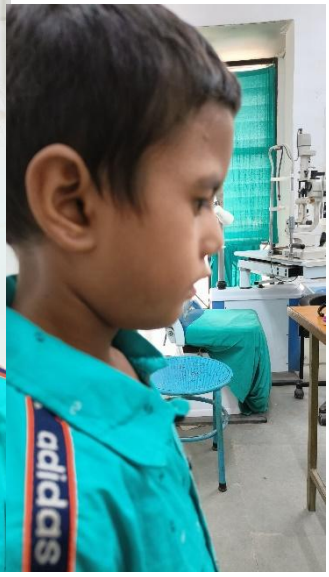

Figure 1.1 **Figure 1.2**

Figure 1.1 showing mask like face with megalocornea

Figure 1.2 showing chin down position.

Abbreviations- UCVA- uncorrected visual acuity, BCVA- best corrected visual acuity, BE- both eyes

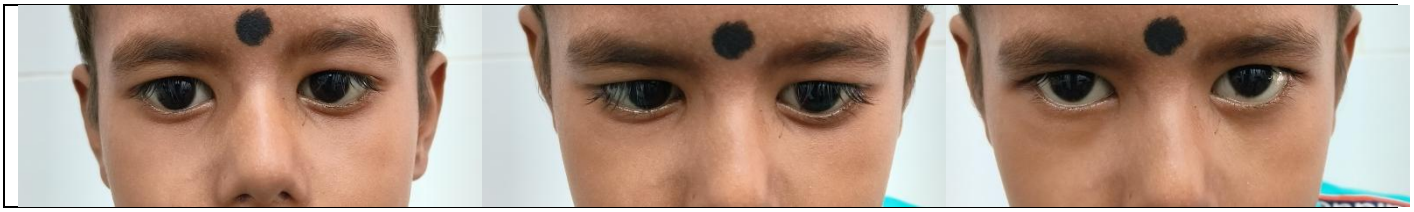

FIGURE 2: showing restricted ocular motility in all quadrants

Upper row- left to right- dextroelevation, elevation, levoelevation

Middle row- left to right- dextroversion, primary position, levoversion

Bottom row- left to right- dextrodepression, depression, levodepression

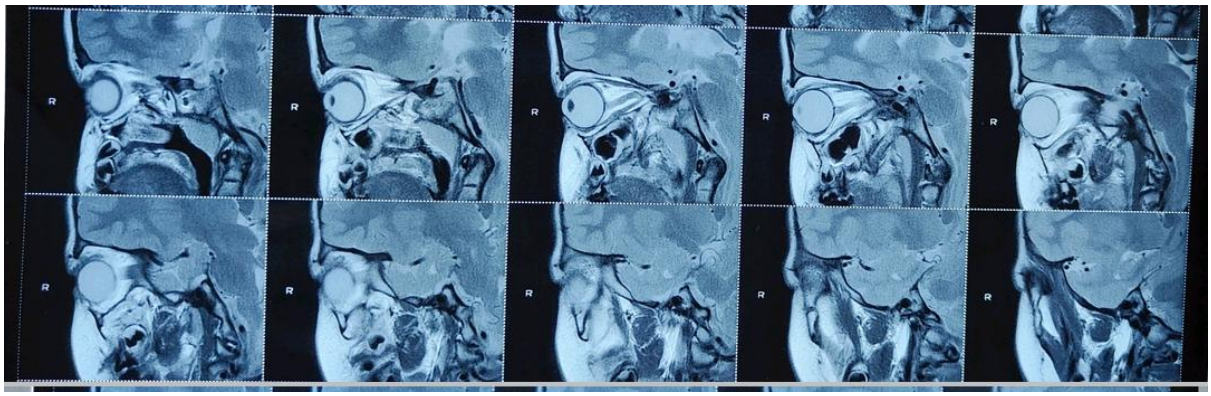

FIGURE 3: Sagittal plane T2-weighted MRI image showing thinned out and ill-defined extraocular muscles with aberrant insertion.

DISCUSSION:

CFEOM is a rare, congenital, and non-progressive disorder with multiple extra ocular muscle restrictions. Its diagnosis and classification are defined by clinical characteristics and genetics. Based on clinical features and genetics, CFEOM can be classified into three types [Table 1]. Bilateral cases of CFEOM might be very asymmetrical. Numerous ocular and systemic associations have been described in patients with CFEOM [Table 2].[6] CFEOM has to be differentiated from other conditions which might mimic it

[Table 3].[6] The diagnosis of CFEOM is made by combining the findings of clinical examination, forced duction test, radiological investigations and genetic analysis. This approach affords the best results in planning management. However, due to the overlap in the clinical features between different CFEOM groups, genetic evaluation is important in confirming the diagnosis.

Table 1

Classification of CFEOM[1–5]

	Type 1	***Type 2***	***Type 3 (A, B, C)***
Orthoptics:	• Bilateral ptosis • Hypotropia • Restricted up gaze, • Horizontal strabismus is common, variable restricted horizontal gaze • In addition, pupils are often small and non-reactive • Positive forced duction	• Bilateral ptosis • Exotropia • Severe restriction of the horizontal and vertical eye movements, variable abduction is present • Miotic, poorly reactive pupils • Positive forced duction	• Some affected individuals do not have classic findings of the disorder. Their eyes may not be infraducted or may elevate above the midline • The eyes may be unilaterally affected • Ptosis may be absent or variable • Positive forced duction
Pathogenesis:	Absence of the superior division of the oculomotor nerve. Abnormalities of the levator palpebrae superior and rectus superior	Absence of the motor neurons in all of the oculomotor and trochlear nuclei with abnormalities of the innervated muscles	Variable developmental anomaly of the oculomotor nerve, (superior branch > inferior branch)
Genetics:			

Type 1	*Type 2*	*Type 3 (A, B, C)*
Locus chromosome 12	Locus – chromosome 11	A: Locus – Chromosome 16
Gene – KIF21A	Gene – PHOX2A (ARIX/11q13)	Gene – TUBB3
Autosomal dominant	Autosomal recessive	B: Locus chromosome 12
Fully penetrant		Gene – KIF21A
Variable expression		C: Locus – Chromosome 13
		Gene – unknown
		Autosomal dominant
		Incomplete penetrance
		Variable expression

Table 2

Ocular and systemic associations[4]

Ocular associations CFEOM

- Refractive errors / amblyopia
- Neural misdirection – MG Phen., synergistic divergence / convergence
- Optic nerve dysplasia or hypoplasia
- Chorioretinal coloboma
- Microphthalmia
- Oculocutaneous albinism
- Marcus Gunn jaw – winking phenomenon

Systemic associations CFEOM

- Other cranial N anomalies – V, VII
- Facial dysmorphism
- Neurodevelopmental defects

Table 3

Differential diagnoses of CFEOM[3]

Neurogenic

- Congenital III nerve palsy
- Partial or complete VI nerve palsy
- Chronic progressive external ophthalmoplegia

Restrictive

- Brown’s syndrome

- Orbital floor fracture
- Thyroid eye disease
- Double elevator palsy
- Möbius' syndrome
- Atypical Duane Syndrome

Myogenic with systemic involvement

- Myasthenia gravis
- Kearns-Sayre Syndrome

CFEOM can be associated with neuro- radiological abnormalities, and neuroimaging has been recommended as part of the evaluation of patients with CFEOM to rule out any intracranial or orbital pathology.[2] Unilateral or bilateral hypoplasia of CN 3 has been demonstrated using high-resolution MRI in many cases of CFEOM.[8] Hypoplasia of CN 3 supports a neuropathic rather than myopathic origin of CFEOM.

CFEOM is not easy to treat. Any refractive error and amblyopia should be corrected. Due to the extreme chin up or chin down posture adopted by some of the patients with CFEOM, eccentric viewing through the corrective lenses is commonly encountered, contributing to a sub optimal refractive correction. This might underlie the reduced visual acuity seen in our patients. Significant changes have been observed in refraction following extraocular muscle surgery secondary to a change in magnitude and direction of the force exerted by the muscles on the globe.[9]

The surgical correction of strabismus and ptosis in CFEOM is challenging. Strabismus surgery is always attempted before ptosis correction. The expectations of strabismus surgery should be realistic and parents and patient should be well informed about these expectations. Very large recessions (12mm) of the affected muscles may be indicated. In CCDDs, resections of extraocular muscles are usually avoided from fear of worsening the enophthalmos.[6] A forced duction test should be done pre-operatively and during the strabismus surgery. With respect to ptosis surgery, due to the absence of Bell's phenomenon and the risk of exposure keratopathy, it is advisable that ptosis is under-corrected. The aim of ptosis correction should be to provide a clear visual axis, partly eliminate the head posture, and prevent deprivation amblyopia.[10]

CONCLUSION:- CFEOM presents with many associated variabilities, as in my patient was diagnosed with CFEOM of type 3 and had bilateral megalocornea 12.5*12.5mm along with optic atrophy with pale optic disc with intraocular pressure in both eyes 17.3mmhg and ocular motility was restricted in

all quadrants. Primary management was done with refractive correction and glaucoma follow-up with surgical intervention planned in near future. Mitochondrial assay is also planned. Constant reporting is needed in cases of CFEOM and added genetic profiling to keep up with the associated variants of CFEOM.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript

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