CASE REPORT

Congenital Fibrosis of the Extraocular Muscles: a Rare Entity

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ABSTRACT

Congenital restriction of ocular movements could be due to various abnormalities. One of the rarest causes is fibrosis of the extraocular muscles. Congenital fibrosis of the extraocular muscles is a congenital non-progressive strabismus syndrome, characterised by diffusely infiltrative orbital lesions with secondary involvement of extraocular muscles, resulting in variable restrictive external ophthalmoplegia due to the cicatricial process. Congenital fibrosis of the extraocular muscles can be unilateral or bilateral and affect any or all of the muscles, and the degree of fibrosis of a muscle can be total or partial. We report on a patient with congenital fibrosis of the extraocular muscles, and review the clinical presentation, magnetic resonance imaging features, and correlation with intraoperative and histopathological findings. A brief literature review is also provided.

Key Words: Fibrosis of extraocular muscles, congenital; Oculomotor nerve

INTRODUCTION

Congenital fibrosis of the extraocular muscles (CFEOM) is a congenital disorder characterised by unilateral or bilateral ptosis, restrictive external ophthalmoplegia with the eyes partially or completely fixed in a downward and strabismic position, and markedly limited and aberrant residual eye movements. Children with this distinct entity can present with variable abnormalities of the eyelids and globes, including eyelid retraction; ptosis or normal eyelid height; and
enophthalmos, exophthalmos, or proptosis.\(^1\) It is generally considered that these clinical abnormalities result from neuromyopathic fibrosis of the extraocular muscles.\(^2\) Biopsy specimens of the affected extraocular muscles from individuals with CFEOM typically contain fibrous tissue or a mixture of myofibres and fibrous tissue.\(^3\) CFEOM is a rare clinical syndrome; the clinical presentation, pathological features, and genetic analysis have been discussed in many articles in recent decades.

Although the ultimate diagnosis relies on histopathological results, the diagnosis of CFEOM could be dispensed earlier in the course of management with the introduction of high-resolution magnetic resonance imaging (MRI) and awareness of its imaging features. We report on a girl with this rare entity, who has been treated jointly by the Department of Ophthalmology and Department of Paediatrics at Queen Mary Hospital, Hong Kong. The clinical features, MRI findings, and their correlation with intraoperative and histopathological findings are reported, and a brief literature review is presented.

CASE REPORT

An 11-month-old girl of full-term normal delivery had right esotropia and ptosis since she was 3 months old (Figure 1). The antenatal and postnatal period was uneventful. There was no positive family history of any motility disorder. On examination, her left eye was within normal limits in all parameters, but her right eye was enophthalmic with upper lid ptosis. Ocular movements of the right eye were found to be restricted in lateral gaze.

MRI showed medial deviation of the right eye. Abnormal ill-defined soft-tissue thickening was located medially in the right orbit, adjacent to the right medial rectus muscle, incorporating the muscle belly (Figure 2). The abnormal soft tissue band remained isointense to other rectus muscles in T1-weighted images, but became slightly hyperintense in T2-weighted images, and demonstrated faint contrast enhancement. No abnormal T2-hyperintensity, swelling, or atrophic change was seen in the extraocular muscles. The cranial nerves were intact, with no atrophic changes or abnormal T2-hyperintensities. Perilesional fat stranding was present. Overall, the features were suggestive of...
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an inflammatory process in the non-active phase, with possible fibrosis, in view of insignificant enhancement. The differential diagnosis included congenital orbital fibrosis.

Incisional biopsies of the right medial rectus muscle and its tendon capsule were performed. The muscle was found to be tight, with an abnormal fibrous band at the postequatorial region. Histopathological examination showed only acellular fibrotic tissue and muscle fibres surrounded by acellular fibrofatty tissue (Figure 3). There was no evidence of malignancy or granuloma. The findings confirmed CFEOM.

DISCUSSION
Normal eye movement depends on the normal motoneuron formation in oculomotor, abducens and trochlear nerves, and the development of extraocular muscles with normal innervation. A number of well-defined syndromes characterised by congenital limitation of eye movements have recently been grouped as the ‘congenital cranial dysinnervation disorders’ (CCDDs), a term used for congenital disorders resulting from aberrant innervation of the ocular and facial musculature. CFEOM, in which there is severe restriction of eye movements and ptosis either from abnormal oculomotor and trochlear nerve development or from abnormalities of extraocular muscle innervation, is uncommon among the CCDDs. Other conditions in the CCDDs involving congenital limitation of eye movements include Duane’s retraction syndrome type I, congenital third nerve palsy, congenital fourth nerve palsy, Möbius syndrome, double elevator palsy, and congenital horizontal gaze palsy. Abnormalities of cranial nerve development have been demonstrated in some of these conditions using MRI and postmortem examination.

CFEOM refers to complex strabismus syndromes characterised by congenital non-progressive ophthalmoplegia with or without ptosis affecting part or all of the oculomotor nucleus and nerve, and its innervated muscles (the superior, medial, and inferior recti, inferior oblique, and levator palpebrae superioris); or the trochlear nucleus and nerve, and its innervated muscle (the superior oblique); or both. CFEOM has been classified by Brown, Harley et al., and Hansen into the following types according to the clinical presentation: general fibrosis syndrome; fibrosis of the inferior rectus with blepharoptosis; strabismus fixus; vertical retraction syndrome; and unilateral fibrosis, blepharoptosis, and enophthalmos syndromes. With more understanding of this condition, CFEOM has been found to run in families and is believed to have a genetic basis (Table). Three distinct phenotypes, CFEOM1 to 3, are recognised. The classic form, CFEOM1, is typified by congenital bilateral blepharoptosis and ophthalmoplegia, with the eyes partially or completely fixed in infaraduction.

In imaging studies, all patients demonstrate an irregular mass or soft-tissue thickening located medially within the orbit, incorporating the medial rectus muscle, as in this patient. The irregular mass and soft-tissue thickening is found to be fibrotic tissue intraoperatively or histopathologically. Differential diagnoses of retrobulbar orbital mass — including pseudotumour, lymphoma, meningioma, neurogenic tumour, and myositis — would usually be considered. Signal intensities in different MRI sequences provide
information about the nature of the lesion. Fibrotic tissue usually demonstrates intermediate or hypointense signal in T1- and T2-weighted images. Hyperintensity in T2-weighted images and contrast enhancement may be observed in the acute inflammatory phase. Intensity of contrast enhancement gradually decreases as the inflammation moves into the chronic phase. Traction or incorporation with adjacent extraocular muscles may occur due to scarring from chronic inflammation. Extraocular muscles may also exhibit variable atrophy and abnormal T1-hyperintensities suggestive of fatty infiltration.

Although CFEOM has traditionally been regarded as a primary eye muscle disease, recent studies suggest that it may be the result of a primary neuropathy with secondary myopathic changes. In affected individuals, MRI sometimes demonstrates atrophy of the levator palpebrae superioris, all extraocular muscles, and small or absent orbital motor nerves. The oculomotor nerve is usually severely hypoplastic, while the abducens and optic nerves are also occasionally hypoplastic. In a study of 19 patients with CFEOM1 due to heterozygous missense mutations of KIF21A, MRI of affected patients who had severe bilateral blepharoptosis, limited supraduction, and variable ophthalmoplegia demonstrated atrophy of the levator palpebrae superioris and superior rectus extraocular muscles, as well as small or absent orbital motor nerves. The oculomotor nerve was the most severely hypoplastic, while the abducens was also affected. In the same study, patients with R954W and R954Q substitutions frequently exhibited A-pattern strabismus, with misinnervation of the lateral rectus muscle by an oculomotor nerve branch. These findings suggest that neuronal disease is primary in CFEOM, with myopathy arising secondary to abnormal innervation from hypoplastic, or even absent, oculomotor and trochlear nuclei and nerves. More insights gained from molecular genetics have also strengthened the hypothesis that CFEOM results from dysinnervation of the extraocular muscles supplied by the oculomotor or trochlear nerves, or both.

Cerebral abnormalities — such as cerebral, cortical, and basal ganglia mal-development — can also be found in patients with CFEOM in MRI studies. Some patients with CFEOM have been reported to have associated central nervous system developmental malformations, including agenesis of the corpus callosum, brainstem atrophy, cerebellar hemisphere atrophy, absence of the cerebral peduncle in the midbrain, colpocephaly, hypoplasia of the cerebellar vermis, expansion of the ventricular system, pachygyria, encephalocoele, and hydranencephaly. Therefore, early high-resolution MRI should be considered at the initial diagnostic evaluation of these patients, particularly when there is developmental delay or other associated neurological deficits.

Apart from orbital and intracranial abnormalities, accompanying ipsilateral facial hypoplasia, orbital wall dysplasia, and decreased orbital volume are sometimes seen on computed tomography and MRI. In addition, patients with CFEOM3A may also have intellectual disability, social disability, facial weakness, or progressive axonal peripheral neuropathy (a form of Charcot-Marie-Tooth disease). Patients with CFEOM3C usually have intellectual disability and facial dysmorphism reminiscent of Albright’s hereditary osteodystrophy-like syndrome. Patients with Tukel syndrome are found to have postaxial oligodactyly or oligosyndactyly of the hands.

Management of patients with CFEOM has always been challenging. In general, children affected have severe limitation of vertical gaze and variable limitation of horizontal gaze. They frequently compensate for the ophthalmoplegia by maintaining abnormal head
positions at rest and by moving their heads rather than their eyes to track objects. Surgery can correct the deviation of the eyes, although it is not possible to restore full movement. It is important to monitor patients with CFEOM to ensure that the cornea receives proper protective lubrication. The ‘lazy’ eye should be treated appropriately to maintain good vision. Recently, horizontal muscle recession, sometimes combined with opposite muscle resection, has demonstrated satisfactory correction of horizontal strabismus in most patients. Ptosis is usually repaired by frontalis sling and levator resection.

CONCLUSION
For most patients, suspicion of CFEOM is first aroused based on ophthalmological findings, and some subtypes depend on identification of associated findings. Bearing in mind the imaging features and pathological association, diagnosis of CFEOM could be made earlier with early high-resolution MRI of the orbit and brain. This approach would significantly aid its management, which is challenging, by recommending appropriate extraocular muscles for biopsy and diagnosing this disease earlier to prevent secondary complications.

REFERENCES