

Dysplasia of extraocular muscles presenting as orbital space-occupying lesions—an extremely rare disorder

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Abstract

• **AIM:** To describe the clinical manifestations, imaging features and surgical treatments in 5 cases of extraocular muscle (EOM) dysplasia presenting as orbital space-occupying lesions (SOL).

• **METHODS:** Records from the 5 cases with EOM dysplasia between 2004 and 2016 were retrospectively reviewed and clinical data were recorded including family history, age at onset, age at surgery, visual acuity, cycloplegic refraction, ocular alignment and motility, stereoacuity, exophthalmos, anterior segment and fundus, orbital computed tomography (CT) or magnetic resonance imaging (MRI) scan, surgical methods and final outcomes.

• **RESULTS:** All 5 cases (1 male, 4 females) were unilateral (3 right, 2 left eyes). The average age was 5.4y (range 4-6y) with no family history. Patients had unilateral strabismus (horizontal and vertical), restricted eye movement, and eyelid changes (abnormal fissures, lagophthalmos, and/or entropion) in the affected eye. None had proptosis; 1 had 2-mm enophthalmos. Orbital CT/MRI showed irregular, ill-defined masses in EOM. Two anterior orbitotomies and 3 strabismus surgeries were performed, and pathology confirmed EOM dysplasia. After surgery, horizontal deviations, which ranged from exotropia (XT) 10 prism diopter (PD) to esotropia (ET) 10 PD (average 6 PD), decreased by an average of 18 PD, while vertical deviations, which ranged from 4 PD to 20 PD (mean 9.8 PD), decreased by an average of 23.2 PD.

• **CONCLUSION:** SOL from EOM dysplasia is non-familial

and typically presenting unilaterally characterized by an irregular, diffusely infiltrating mass within the EOM. EOM involvement causes strabismus, restricted eye movement, eyelid changes, and enophthalmos likely due to cicatricial processes.

• **KEYWORDS:** extraocular muscle; space-occupying lesion; dysplasia; orbit; strabismus

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INTRODUCTION

Extraocular muscle (EOM) dysplasia is a relatively rare condition, which is manifested as strabismus and impaired ocular motility present since birth. It is usually diagnosed as congenital paralytic strabismus. Orbital imaging including magnetic resonance imaging (MRI) and computed tomography (CT) often shows an atrophy of involved EOMs and may be accompanied with cranial nerve III, IV and/or VI agenesis or hypoplasia. In order to achieve normal visual development, surgical correction of the strabismus is required. However, some patients with EOM dysplasia may not show paralytic strabismus, but present with restricted strabismus. In these patients, the forced duction test is positive and the first choice for surgical treatment involves a weakening of the restricted muscles. Orbital imaging of these patients may either show a fibrosis of affected muscles (atrophy), or hypertrophy at the posterior segment of involved muscles. Dysplasia of the EOMs, presenting as an orbital space-occupying lesion (SOL) is extremely rare. The unique clinical features of this disorder were first described by Leone and Weinstein 1972^[1]. Since this original description, only 29 cases have been reported in the literature^[1-15]. Hertle *et al*^[6] referred to this condition as a syndrome involving congenital unilateral fibrosis, blepharoptosis, and/or enophthalmos. Mavrikakis *et al*^[8] considered this condition as a congenital orbital fibrosis. In clinical practice, this disorder may be easily misdiagnosed as orbital tumor lesions. In this paper, we review reports on 5 cases of EOM dysplasia and provide a detailed description

of its clinical manifestations, imaging features, pathological findings, surgical treatment and surgical results.

PARTICIPANTS AND METHODS

Ethical Approval Records from the 5 patients included in this report, who were treated at the Zhongshan Ophthalmic Center Eye Hospital, of Sun Yat-sen University, Guangzhou, China between January 1, 2004 and December 31, 2016 were retrospectively reviewed. Written informed consent to participate in this study was obtained from all patients. Institutional approval for this study was obtained from the Research Ethics Board of the Zhongshan Ophthalmic Center (2021KYPJ184), of Sun Yat-sen University, China, and all procedures were performed in accordance with the Declaration of Helsinki.

Case Selection Criteria 1) Patients showing strabismus and abnormal ocular motility since birth. This presentation remained unaltered throughout their life and was not accompanied with eyelid swelling, photophobia and red eyes. 2) Orbital CT/MRI demonstrated orbital SOL or the EOM dysplasia, along with hypoplasia of other orbital structures were confirmed by pathological examination. These lesions failed to change over the 3-5y period following their initial observation. The following clinical data were recorded from the patients' charts: family history, age at onset, age at surgery, visual acuity, cycloplegic refraction, pre-operative motor alignment at distance and near, stereoacuity at distance and near, exophthalmos, orbital margin palpation, anterior segment and fundus and surgical methods employed. Ocular alignment was assessed with use of cover/uncover and alternate prism cover testing at distance (6 m) in the primary and cardinal gaze positions. Motor alignment at near was assessed at 33 cm with use of spectacle correction. The measurements on the vertical width of eyelid fissures were conducted by a ruler. Stereoacuity at distance was measured by random-dot stereograms and at near by Titmus stereograms. The forced duction test was used to evaluate the restrictive force of each EOM. Each patient underwent an orbital CT or MRI scan. The follow-up time ranged from 6mo to 7y, with an average of 2y.

Surgical Methods 1) In 2 cases, who showed an obvious orbital SOL on CT scan, an anterior orbitotomy with skin incision was performed to explore, release and biopsy the lesion. 2) For the remaining 3 cases, no orbital surgery was performed, rather a strabismus surgery was used to correct the deviation. The surgical protocol for strabismus treatment was as follows: 1) if results of the preoperative forced duction test showed a restrictive factor and the deviation was small, a weakening of the affected muscle was the preferred choice; 2) if the forced duction test was positive and a large deviation was present, then adhesions around the affected muscle were released, the involved muscle was weakened

while antagonistic muscles were strengthened. If results of the pre-operative forced duction test were negative, the surgical methods were selected in accordance with the principles of surgical treatment for paralytic strabismus. That is, if a portion of the affected muscle remained functional, then the affected muscle was strengthened and the antagonist weakened, while non-functional involved muscles were subjected to the Jensen procedure or muscle transposition.

RESULTS

A total of 5 cases (5 eyes) were included in this study. All 5 cases (1 male and 4 females) were unilateral (3 right and 2 left eyes) with an average age of 5.4y (range: 4-6y) and no family history. All cases were referred as complex strabismus by local hospitals and presented with strabismus from birth. No changes in their strabismus were observed following its initial observation. All patients were otherwise healthy and their births were uncomplicated with full term pregnancy. There was no history of ocular trauma, infection, or inflammation throughout their childhood.

Visual Acuity and Refractive Status Among the 5 cases, 4 presented with unilateral amblyopia in the affected eye, and their best corrected visual acuities were fingers counting (FC)/30 cm, 0.02, 0.04 and 0.6. All patients showed varying degrees of hyperopia and astigmatism in both the involved and normal eye after cycloplegic refraction with 1% atropine. The healthy eye showed physiological hyperopia and mild astigmatism. The hyperopia ranged from 0.50 diopter (D) to 1.50 D (average 1.2 D) and the astigmatism from +0.25 to +0.75 D (average +0.40 D). The affected eye displayed a greater degree of hyperopia and astigmatism as compared with that of the healthy eye, with hyperopia ranging from 1.50 to 6.50 D (average 3.70 D) and astigmatism from +0.50 to +2.50 D (average +1.55 D).

Strabismus and Ocular Motility All patients presented with unilateral strabismus and restricted ocular motility. Both horizontal and vertical strabismus was observed within each of the cases (Figures 1-3). Horizontal deviations ranged from 15 prism diopter (PD) of exotropia (XT) to 45 PD of esotropia (ET; average 24 PD), with 3 cases being ET and 2 cases being XT. Vertical deviations ranged from 25 to 45 PD (mean 33 PD), with 4 cases being hypotropia and 1 hypertropia. While 4 cases exhibited both horizontal and vertical motility deficits, the remaining case showed restricted vertical motility only, resulting from a moderate limitation of the right inferior rectus muscle. With regard to horizontal motility, abduction was limited in 3 cases and adduction in 1 case. For vertical motility, elevation of the affected eye was completely restricted in 3 cases and moderately restricted in 1 case. All 5 patients presented with restrictive strabismus, with 1 case showing paralytic strabismus as well, based on the direction

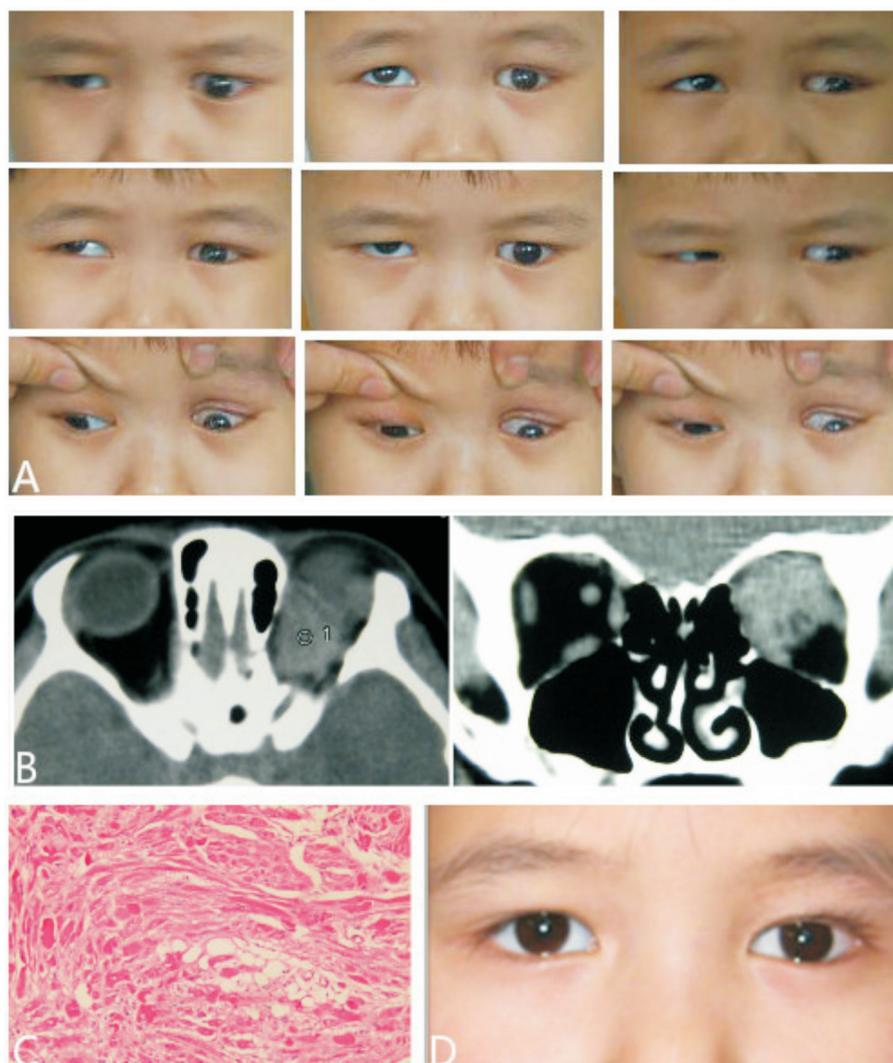


Figure 1 Case 1, a 4 years and 10 months old female with dysplasia of superior rectus, superior oblique and levator muscles of the left eye
 A: Palpebral fissure elevation was 8 mm in the right eye and 10.5 mm in the left eye. Krimsky testing revealed a 15 PD exotropia and 35 PD hypotropia of the left eye. Superior rotation of the left eye was completely restricted and adduction was moderately limited. B: Orbital CT (axial and coronal scans) demonstrated an irregular, 1.6×2.3 cm soft tissue SOL superior to the left eyeball. The superior rectus, superior oblique and levator muscles were incorporated within the mass. C: Histopathological examination of the resected tissue revealed a dense focal fibrosis without inflammation, with obvious evidence of a focal hypoplastic EOM. D: Two years after anterior orbitotomy *via* an eyebrow skin incision, a normal palpebral fissure of the left eye (8 mm) was present and Krimsky testing indicated a 10 PD exotropia and 5 PD hypotropia of the left eye. EOM: Extraocular muscle; SOL: Space-occupying lesion; PD: Prism diopter.

of deviation, ocular motility, forced duction test and orbital imaging findings.

Eyelid Change All 5 cases displayed alterations in eyelids of the affected eye. The palpebral fissure in the affected eye was larger than that of the healthy eye in 4 cases (range: 1mm to 2.5mm; average: 1.63mm), with 1 case showing lagophthalmos (Figures 1, 2). The palpebral fissure in 1 case was 1.5mm smaller than that of the healthy eye (Figure 3). Three cases with both esotropia and hypotropia presented with entropion of the inner lower eyelid.

Degree of Exophthalmos No proptosis was present in any of the 5 cases. On the contrary, 1 case showed a 2-mm enophthalmos. Nor were there any changes in the reading of

exophthalmos after head bowing in all cases.

Orbital Imaging Features Results of orbital CT or MRI scans revealed that orbital soft tissue SOLs were present in all cases. The orbital masses possessed the following characteristics: 1) An irregularly shaped, ill-defined heterogeneous mass located in the path of EOMs (Figure 3). 2) When the mass was incorporated within the superior rectus, superior oblique and levator muscles, it was located above the eyeball (2 cases; Figure 1). 3) When the mass involved the inferior rectus, medial rectus and lateral rectus muscles, it was located below the eyeball (2 cases). 4) When the mass involved all EOMs, it showed an irregular band-like fibrosis that blurred all orbital structures (full orbital fibrosis, 1 case; Figure 2).



Figure 2 Case 2, a 6-year-old female, diagnosed with orbital fibrosis of the right eye (involving all four rectus muscles) A: A large palpebral fissure (9.5 mm in the right eye and 7.5 mm in the left eye), lower eyelid entropion, 45 PD esotropia and 25 PD hypotropia of the right eye were present. Elevation of the right eye was completely restricted and abduction was moderately limited. B: Orbital MRI (axial and coronal scans) revealed an irregular band-like fibrosis that blurred all orbital structures in the right eye and involved the superior, inferior, medial, lateral rectus and superior oblique muscles. PD: Prism diopter.

Table 1 Clinical features and surgical outcomes in patients with dysplasia of EOMs presenting with orbital SOLs

Case	Age (y)	Sex	Eye: involved muscle	Preop. deviation (PD)	Imaging findings	Surgery	Postop. deviation (PD)
1	4.9	Female	Left: SR, SO	RHT 35	A 1.6×2.3 cm soft-tissue mass locates above the eyeball. The SR, SO and levator muscle were incorporated within the mass	Anterior orbitotomy with skin incision	XT10 RHT5
2	6	Female	Right: MR, IR, LR, SR, IO, SO	ET 45 LHT 25	Irregular band-like fibrosis that blurred all orbital structures	Right eye 6-mm recession of MR and 8-mm resection of LR	LHT10
3	6	Female	Right: MR, IR, LR	ET 20 LHT 35	A soft-tissue mass involves the MR, IR and LR	Right eye 5-mm recession of IR, 6-mm recession of MR and SO transposition to the nasal end of SR insertion	ET10 LHT20
4	6	Male	Right: SR	XT20 RHT40	An irregular heterogeneous mass located at the path of SR	Right eye SR recession 7mm, left eye IR recession 5mm and LR recession 12mm	LHT4
5	4	Female	Left: MR	ET20 RHT30	A 1.6×1.5 cm soft-tissue mass locates below the eyeball. The MR and IR were incorporated within the mass	Anterior orbitotomy with skin incision	ET10 RHT10

EOM: Extraocular muscle; SOL: Space-occupying lesion; PD: Prism diopter; XT: Exotropia; ET: Esotropia, RHT: Right eye hypertropia; LHT: Left eye hypertropia; SR: Superior rectus; SO: Superior oblique; MR: Medial rectus; IR: Inferior rectus; LR: Lateral rectus; IO: Inferior oblique.

Surgical Treatment Anterior orbitotomy through a skin incision was performed in case 1 and case 2 to explore, release and biopsy the mass. During the surgical procedure, the orbital mass appeared as poorly-developed orbital tissue, including EOMs, fibrous tissue, blood vessels, fat and cartilage. After partial resection of the tumor, eye position was significantly improved in these 2 cases. In addition, following release of the subcutaneous tissue and levator muscle from scar tissue, the upper eyelid retraction and lagophthalmos were also improved in 1 case. Of the remaining 3 cases, one underwent a 6-mm recession of the right medial rectus and 8-mm resection of

lateral rectus; one received a 5-mm recession of the right inferior rectus, a 6-mm recession of the medial rectus, and transposition of superior oblique muscles to the nasal region of superior rectus insertion; one had a 7-mm recession of the right superior rectus, 5-mm recession of the left inferior rectus and 12-mm recession of the left lateral rectus. After strabismus surgery, eye positions improved significantly in all 3 cases (Table 1).

Pathological Findings The gross appearance and microscopic examination of resected tissue revealed that these tissues demonstrated dense focal fibrosis without inflammation, but

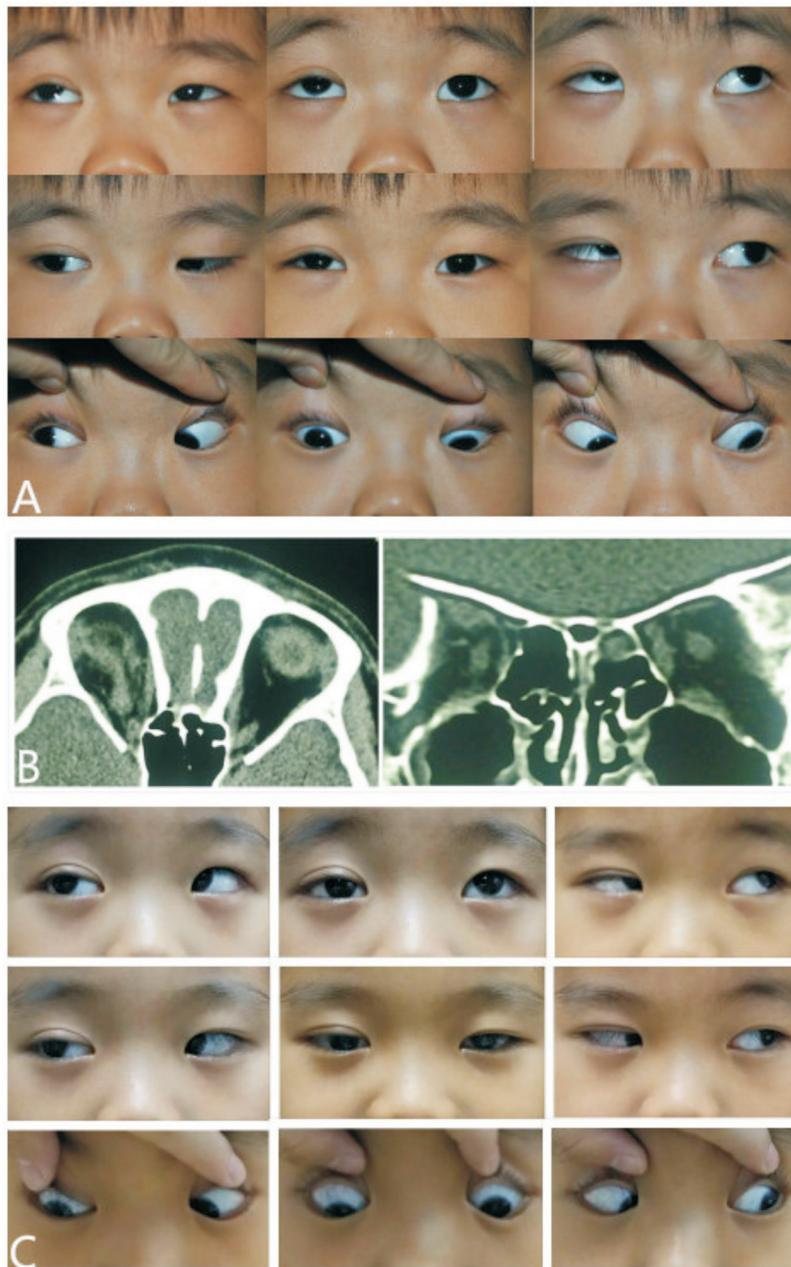


Figure 3 Case 4, a 6-year-old male diagnosed as dysplasia of superior rectus and levator muscles A: Pre-operative nine direction eye position assessment showed an exotropia of 20°-25° and hypertropia of 20°-25° of the right eye, +1 over-action of right superior rectus, +2 over-action of right inferior oblique, and -2 under-action of right inferior rectus muscle. Palpebral fissure in the right eye was 7 mm and 8.5 mm in the left eye. B: Orbital CT (axial and coronal scans) revealed an irregular ill-defined heterogeneous mass located in the path of the superior rectus in the right orbit, affecting the superior rectus and levator muscles. C: Nine months after strabismus surgery, strabismus was no longer present. Ocular motility evaluation showed -2 under-action of superior rectus and -1 under-action of inferior rectus muscles of the right eye.

obvious evidence of a focal hypoplastic EOM in case 1 (Figure 1) and case 5.

Follow-up Results At last follow-up after surgical treatment, horizontal deviations which ranged from XT 10 PD to ET 10 PD (average 6 PD) were decreased by an average of 18 PD, while vertical deviations ranging from 4 to 20 PD (mean 9.8 PD) decreased by an average of 23.2 PD. Although eye position improved significantly, the prognosis for both the amblyopia and binocular vision were quite poor. With the exception of 1 case without amblyopia, the visual acuity showed no

improvement in the other 4 cases, even after refractive correction and ocular covering treatment. No stereopsis was observed in any of the 5 patients.

DISCUSSION

The presence of dysplasia in the EOMs can have a direct impact on the equilibrium of their strength, resulting in the deviation of the eyes^[16-19]. However, when the dysplasia presents itself in the form of soft tissue SOL, it has the potential to generate diagnostic confusion. The exact nature of the pathogenesis of EOM dysplasia showing “tumor like lesions”

remains unclear^[1,3,5-7]. In these cases, physical development of these children is generally good, they show a normal birth history and their mothers were disease-free during pregnancy. Judging from findings of orbital imaging, the development of EOMs, as originating from the mesoderm, can be considered as being divided into two groups. The superior group results in the development of superior rectus, superior oblique and the levator muscle, while the inferior group results in development of the inferior rectus, medial rectus, lateral rectus and inferior oblique muscles. In the patients reviewed within this report, 3 cases were classified as being of the inferior and 2 cases from the superior group.

At least two EOMs were affected in all cases (in 1 case, only the superior rectus muscle was involved, however, the levator palpebrae was affected as well). All patients demonstrated both horizontal and vertical deviations, along with obvious dysfunctions of ocular motility in two directions. The size and location of the eyelids were affected due to fibrosis of EOMs, with 4 cases showing a large palpebral fissure (among them, 1 case with lagophthalmos as well), 1 case with a small palpebral fissure and 3 cases with lower eyelid entropion. These findings are quite different from that observed in patients with another paralytic and restrictive strabismus^[2].

It is precisely because of these changes in the eyelid that prompted us to perform an orbital imaging evaluation. The orbital soft tissue SOL existed in the paths of EOMs. These masses were irregular and located above the eyeball in those cases involving the superior rectus and levator muscles, while in cases involving inferior rectus, medial rectus and lateral rectus muscles, the mass was located below the eyeball. A full orbital fibrosis was observed in a few patients where all EOMs were affected. In spite of the presence of these orbital SOL, as shown in CT or MRI imaging, no proptosis was observed in these cases. This absence of proptosis can be attributable to a lack of any increase in orbital content. In contrast, fibrotic lesions (dysplasia and fibrosis of the EOMs) displace the eyeball posteriorly^[2,8]. One case in our series presented with enophthalmos. However, when bony dysplasia of the affected orbital wall was identified with reduced orbital volume, there was an associated ipsilateral proptosis^[8]. This finding also differs from that of other orbital SOLs. Moreover, the absence of any changes in these clinical findings since birth, with all patients failing to show eyelid swelling, eye pain and red eye, all lead us to the conclusion that other orbital tumors and/or inflammatory diseases may not be involved.

The case 1 and case 5 were diagnosed pre-surgically as orbital SOLs and received anterior orbitotomy to remove a portion of the "tumor" for histopathological examination. During the surgical procedure, we observed that the "mass" was comprised of dysplastic orbital tissues, including hypoplasia

of EOM, fibrous tissue, cartilage and fat. In one case, the lesion was located in the superior portion of the orbit and was involved with the superior rectus, superior oblique and levator muscles. The affected eye could not rotate superiorly and a large palpebral fissure and lagophthalmos were present. After partial resection of the mass, and separation of the adhesion between the mass and upper eyelid, the palpebral fissure resumed a normal appearance and eye position markedly improved. In another case, the lesion located in the inferior portion of the orbit was involved with the inferior rectus and medial rectus muscles, and a large palpebral fissure and lower eyelid entropion were present. After partial resection of the mass, eye position substantially improved and the palpebral fissure returned to a normal size. However, lower eyelid entropion remained, which was corrected after a second surgery for entropion.

As this disease is rare, it is likely that neurofibromatosis, capillary hemangioma and vascular malformations of the orbit will be initially included in the differential diagnosis. In the 4 cases as reported by Mavrikakis *et al*^[8], 2 were thought to be a capillary hemangioma and were treated with corticosteroids. However, the lack of any significant changes or progression in these clinical findings, especially for the enophthalmos (rather than that of the proptosis of the involved eye) would tend to eliminate the possibility that these represent relatively common orbital diseases. It is imperative to accurately differentiate intraoperative tissue specimens from biopsies. In addition, congenital fibrosis of EOM should be differentiated, this entity is mainly associated with abnormal motor innervation without mass-like changes in the EOM path or diffuse infiltrating shadows^[12,20-22].

No anterior orbitotomy was performed in the subsequent 3 cases. One of these cases demonstrated a whole orbital fibrosis including EOM dysplasia with no obvious "mass" on MRI scan. The second case revealed a superior rectus dysplasia and mild involvement of the levator muscle with no indication to remove the "mass". As the third case involved the inferior rectus, medial rectus and lateral rectus muscle and the lesion was located relatively deep in the orbit, it was considered that orbital surgery may aggravate the dysfunction of the dysplastic muscles. Therefore, strabismus surgery was performed in these 3 patients. One patient underwent a 6-mm recession of the right medial rectus and an 8-mm resection of the lateral rectus; one received a 5-mm recession of the right inferior rectus, a 6-mm recession of the medial rectus, and transposition of superior oblique muscles to the nasal region of the superior rectus insertion; the third patient received a 7-mm recession of the right superior rectus, 5-mm recession of the left inferior rectus and 1-2mm recession of the left lateral rectus. After orbital surgery or strabismus surgery, horizontal deviations,

which ranged from XT 10 PD to ET 10 PD (average 6 PD), decreased by an average of 18 PD, while vertical deviations, which ranged from 4 to 20 PD (mean 9.8 PD), decreased by an average of 23.2 PD.

Although surgical outcomes of strabismus corrections were considered satisfactory, the effect of amblyopia treatment was quite poor. Even after receiving refractive correction and cover therapy, their visual acuity did not improve, with only 1 case showing normal visual acuity. In addition, none of these patients achieved binocular vision. These outcomes may be due to the early ocular misalignment, which was present at birth, and/or the delay in treatment for these conditions.

The main limitation of this paper was the small sample size. Moreover, each case showed considerable variations in their clinical features, which diminishes their potential as being representative of severe dysplasia of EOMs. Therefore, a complete understanding of this specific EOM dysplasia disorder requires additional cases reports.

In summary, the major clinical findings of orbital tumor-like lesions of EOM dysplasia are: 1) A stationary lesion present from birth. 2) A complex strabismus, often including both horizontal and vertical deviations, that may be restrictive or paralytic. 3) A frequent appearance of eyelid changes, including large palpebral fissures, lagophthalmos and/or entropion. 4) An absence of proptosis, but a potential for enophthalmos. 5) An irregular, homogeneous, well-defined mass located in the path of EOMs. While complex and not easily corrected, treatment should initially involve removal of the restrictive factors with strabismus surgery. Accordingly, SOLs of EOM dysplasia can be characterized as a non-familial, non-progressive, unilateral clinical entity, involving a diffusely infiltrating irregular mass incorporated within EOMs resulting in strabismus, limited ocular motility, eyelid changes and enophthalmos due to the cicatricial processes.

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