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Multimodal imaging in non-syndromic microphthalmia: a case series

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Abstract

Microphthalmia is a rare congenital or developmental anomaly in which the globe is abnormally small. Between one-third and one-half of affected individuals have microphthalmia as part of a syndrome that affects other organs and tissues in the body. These forms are described as syndromic. When microphthalmia occurs by itself, it is described as nonsyndromic or isolated. We aimed to describe the clinical and paraclinical features of nonsyndromic microphthalmia through three cases. The first patient was an 8-year-old female child who presented with bilateral refractive accommodative esotropia due to hypermetropia. She was diagnosed with bilateral posterior microphthalmia qualified as non-syndromic and simple. Eyeglasses prescription has been upgraded and a 6-month clinical monitoring has been undertaken. The second case was about a 16-year-old female patient who had a bilateral amblyopia due to a non-syndromic microphthalmia. She presented with unilateral high intra-ocular pressure. Anterior Segment OCT showed unilateral narrow angle with iridotrabecular contact in the right eye. Microphtalmia has been qualified as complex in the right eye and simple in the left eye. The patient has been put under IOP-lowering topical medication for the OD and peripheral YAG laser iridotomy has been performed. IOP reduction was noticed within five days. The third case was a 7-year-old male child with bilateral non-syndromic complex nanophthalmia. Ophthalmic examination revealed bilateral microcornea and OCT of the macula showed bilateral retinal folds with apical surface corrugations. Optical correction and active surveillance were adopted. Non-syndromic microphthalmia is a rare and potentially blinding disease. We highlighted the interest of ocular ultrasound, especially in young hypermetropic children completed by an examination in OCT. Non-invasive, objective and repeatable, OCT seems to be of great interest in both the diagnosis and the monitoring of microphthalmia.

Introduction

The process of eye formation is controlled by a network of genes, and any disruption of these morphogenetic events by genetic or environmental influences can potentially result in growth and structural defects [1]. Microphthalmia is a rare congenital or developmental anomaly in which the globe is abnormally small. Although the diagnosis may be clear by observation, this can be clinically defined by an axial length of the eye < 21mm in adults and < 14mm in newborns. Microphthalmia, reported in up to 11% of blind children, is among the most severe developmental eye abnormalities and is frequently responsible for severe visual impairment [2]. The pathophysiological mechanisms responsible for this entity remain poorly understood. Between one-third and one-half of affected individuals have microphthalmia as part of a syndrome that affects other organs and tissues in the body. These forms of the condition are described as syndromic. When microphthalmia occurs by itself, it is described as non-syndromic or isolated. In addition, microphthalmia can be classified as simple or complex. Simple microphthalmia refers to an eye with reduced size, but which is anatomically intact. In contrast, when microphthalmia is associated with abnormalities of the anterior or the posterior segment, it is defined as complex. When microphthalmia is combined with an optic fissure closure defect, it is referred to as colobomatous microphthalmia [3]. We aimed to describe the clinical features and the paraclinical aspects of non-syndromic microphthalmia through a retrospective, descriptive case series study.

Methods

We conducted a retrospective, descriptive study including three patients with isolated microphthalmia. All three patients underwent complete ophthalmological examination, A-scan ultrasound biometry, B-scan ultrasonography and Optical Coherence Tomography. MRI examination has not been performed.

Results

Case 1: an 8-year-old female child presented to our Department of Ophthalmology for bilateral visual decline. The child has been wearing prescription eyeglasses as optical correction of hypermetropia since the age of 18 months. Medical history taking did not note any environmental factors that might affect early development, such as nutrition shortage during pregnancy, radiation, infections (rubella) or exposure to teratogens. Best corrected visual acuity (BCVA) was 20/50 in the right eye (OD) and 20/40 in the left eye (OS). Refractive errors were +12.50 and +11.75 Diopters (D), OD and OS respectively. Both eyes (OU) were amblyopic. Orthoptic screening examination revealed bilateral refractive accommodative esotropia. Axial length (AL) was measured using ocular ultrasound in A-mode, indicating 18.52mm (OD) and 18.1 mm (OS) (Figure 1). Slit-lamp examination displayed a normal corneal diameter and an anterior chamber and a lens of normal dimensions in both eyes. Intraocular pressure (IOP) was 14 mmHg OU. Fundus examination was unremarkable. Anterior segment OCT as well as macular OCT did not show any disruption. General medical examination did not reveal any extra-ophthalmic abnormality. The diagnosis of bilateral posterior microphthalmia has been made. We qualified the disease as non-syndromic and simple (pure). Eyeglasses prescription has been upgraded and a 6-month clinical monitoring has been undertaken.

Case 2: a 16-year-old female child presented to our institution seeking a refractive procedure. The patient had a history of visual and learning difficulties and had no systemic illness at presentation. The patient denied previous ocular surgery or a family history of visual dysfunction. On ocular examination, BCVA in the right eye (OD) was 20/63 with a subjective cycloplegic refraction of +14.75 - 0.75 x 150° and 20/50 in the left eye (OS) with a subjective cycloplegic refraction of +13.50 - 0.50 x 30°. The interpupillary distance was 62 mm. IOP was 24 mmHg in the OD and 16 mmHg in the OS. Slit lamp examination showed shallow anterior chamber and mild cataract in the OD, yet no abnormalities in the OS. White-to-white corneal measurements were 12.6mm OD and 12.8 mm OS as measured with the slit lamp. The corneal thickness measurements were 518 µm OD and 511µm OS. The biometric measurements of the anterior chamber depth revealed 2.45 mm OD and 3.01mm OS. Indirect ophthalmoscopy was remarkable for crowded optic discs. Bilaterally, retinal tissue and retinal blood vessels appeared to be normal. Anterior Segment OCT showed unilateral narrow angle with iridotrabecular contact in the OD (Figure 2). Macular OCT did not reveal any retinal disruption. We diagnosed non-syndromic microphthalmia in both eyes (OU), qualified as complex in the OD and simple in the OS. The patient has been put under IOP-lowering topical medication for the OD and peripheral YAG laser iridotomy has been performed. IOP reduction was noticed within five days and remained stable at 14mmHg (OD) during one-year follow-up. In regards to the OS, IOP remained normal ranging from 14 to 16mmHg and we did not notice any angle narrowing.

Case 3: we report the case of a 7-year-old male brought by his parents to our Department due to serious scholar issues. History taking revealed that the child has been earlier under optical correction. However, he had not been wearing eyeglasses since the age of five. Born from a consanguineous marriage, pregnancy and childbirth had proceeded normally while no notion of trauma or inflammation of the eye was noted in his history. BCVA was 20/200 in the OD with +23.50 D, and 20/100 in the OS with +22.50 D. The patient was orthophoric and had normal oculomotricity. Slit lamp examination showed bilaterally a microcornea, an anterior chamber of normal depth and a clear vitreous. The corneal diameter was 9.2mm in both eyes. Examination of the fundus revealed bilaterally a small crowded optic disc with a small excavation and a thick raised retinal fold in papillomacular location. The retinal vessels were normal. On A-mode ocular ultrasound, the axial length was 14mm in the OD and 14.20mm in the OS. The depth of the anterior chamber was 2.80mm

OU and the thickness of the lens was normal. B-mode ultrasound showed sclera-choroidal thickening. The OCT B-scan of the macula showed bilateral retinal folds consisted only of partial neural retina with apical surface corrugations. We noted the disappearance of foveolar depression secondary to the dome-shaped thickening of the foveolar retina. The hyperreflectivity of the complex pigment epithelium - Bruch membrane - choriocapillary was normal. No choroidal fold was highlighted. OCT C-scan allowed to locate the retinal fold with more accuracy (Figure 3). On the basis of clinical examination and paraclinical investigation, we diagnosed a bilateral non-syndromic complex nanophthalmia. The family investigation and the clinical examination was unremarkable. As to manage this case, optical correction and active surveillance were adopted.

Discussion

Microphthalmia is a rare bilateral hereditary condition characterized by reduced eye volume. It is defined by an eye with a total axial length less than two standard deviations from normal for the same age group [4]. Microphthalmia is the most common birth defect in the eye. It can be isolated as part of a simple or pure microphthalmia [5,6], but most often it is associated with other ocular disorders such as an iris or chorioretinal coloboma, a congenital cataract or corneal anomalies. In contrast of syndromic microphthalmia diagnosed in the context of mental retardation or cranial deformities, non-syndromic microphthalmia don´t affect other organs and tissues [7,8]. The term “nanophthalmia” is commonly used to describe microphthalmia associated with shortening of both anterior and posterior segments. This phenotypic abnomality involves a microcornea (Case 3), a thick sclera and a relatively normal-sized lens located inside a small eye, which leads to an increase in the volume ratio lens/eye and to a tendency to spontaneous or postoperative uveic effusion [9-12]. A rare type of microphthalmia that disproportionately affects only the posterior segment of the eye and gives a normal outward appearance has been described as "posterior microphthalmia" [13]. This anomaly is characterized by a normal anterior segment, with therefore a normal corneal diameter, an anterior chamber and a lens of normal dimensions. The size incongruity affects only the posterior segment which is shortened (Case 1) [11,14]. This pathology is rare and usually isolated, not associated with other eye syndromes or malformations [10,13]. The existence of strong hyperopia (often greater than 10 diopters) is characteristic of this condition. Visual acuity is usually reduced, often with deep amblyopia [10,15,16]. The existence of a raised papillo-macular fold of variable size and orientation is pathognomonic of posterior microphthalmia.

Whether congenital or acquired, other lesions of the posterior segment can be observed, such as retinitis pigmentosa, albescent punctate retinopathy, retinal and chorio-retinal folds, crowded disc and uveal effusion. Microphthalmia is often associated with chronic angle-closure glaucoma caused by normal growth of the lens in an eye that is initially too small (Case 2) [17,18]. The closing of the angle can be secondary to anatomical anomalies but also to uveal effusion which can lead to an anterior displacement of the iris and the ciliary body, and a secondary development of anterior peripheral synechiae [19]. A multicenter study conducted in the USA, Sweden and Tunisia has demonstrated a link between posterior microphthalmia and angle-closure glaucoma through a genetic mutation involving the serine protease (PRSS56) [20]. Ocular ultrasound in A-mode and B-mode is of a crucial importance since it establishes and confirms the diagnosis by assessing measurements of the anterior and posterior segments. While the anterior segment is normal in posterior microphthalmia, the axial length is reduced and the shortened posterior segment is associated with sclerochoroid thickening [8,9,20]. The papillo-macular retinal fold is not apparent on fluorescein angiography, which shows the absence of dye leakage and no abnormalities of the retinal pigment epithelium [10].

Multimodal imaging in microphthalmia includes OCT. It provides objective and precise data. On B-scan, we can evaluate the importance of the retinal fold and the increase in the thickness of the overlying retina (Case 3). Moreover, radial lines acquisition enables an accurate analysis of retinal fold position relative to the central fovea [8,21]. Cystic spaces within the retinal tissue can be noticed [22]. Futhermore, OCT allows to distinguish between retinal folds and chorioretinal folds [8,13]. Coronal sections (C-scans) have the advantage of specifying the location, the extent, the shape, the orientation and the structure of the papillo-macular fold. C-scans allow to study the vitreo-retinal junction and to locate small lesions not detected on scans B. OCT is noninvasive, fast, not expensive and can be repeated during the follow-up of posterior microphthalmia. In regards of the pathogenesis of posterior microphthalmia associated with a papillomacular retinal fold, Boynton *et al*. hypothesized that growth cease of the posterior outer layers of the eye, including the pigment epithelium and choroid, is responsible for a short posterior segment [8]. As the neurosensory retina has continued to grow, there is a formation of a fold located usually in the papillomacular region [10,11,14]. The management of microphthalmia appears to be challenging. Therapy aims to maximise existing vision and enhance cosmetic appearances rather than improve sight. Genetic counselling and antenatal diagnosis are highly recommended.

Conclusion

Non-syndromic microphthalmia is a rare and potentially blinding disease. We highlighted the interest of ocular ultrasound, especially in young hypermetropic children with normal-looking eyes in order to diagnose the anomaly as soon as possible. The ultrasound should be completed by an examination in optical coherence tomography. Non-invasive, objective and repeatable, OCT seems to be of great interest in both the diagnosis and the monitoring of non-syndromic microphthalmia.

What is known about this topic

- *Non-syndromic microphthalmia is a rare and potentially blinding disease. Among the most severe developmental eye abnormalities, it is frequently responsible for severe visual impairment;*
- *Ocular ultrasound has a high interest in the diagnosis of microphtalmia;*
- *The management of non-syndromic microphtalmia is particularly challenging and the prognosis is variable.*

What this study adds

- *Non-invasive, objective and repeatable, Optical Coherence Tomography (OCT) seems to be of great interest in both the diagnosis and the monitoring of non-syndromic microphthalmia;*
- *OCT is beneficial in the analysis of both anterior (cornea, angle) and posterior (macula) segments.*

Competing interests

The authors declare no competing interests.

Authors' contributions

All the authors have read and agreed to the final manuscript.

Figures

Figure 1: (A) scan ultrasound biometry showing an axial length of 18.52mm; (B) scan showing the ultrasound aspect of a microphtalmic eye

Figure 2: anterior segment optical coherence tomography (optovue RTVue XR 100 avanti) showing a narrow angle with iridotrabecular contact

Figure 3: optical coherence tomography (optovue RTVue XR 100 Avanti) of the macula showing a

retinal fold consisted only of partial neural retina with apical surface corrugations

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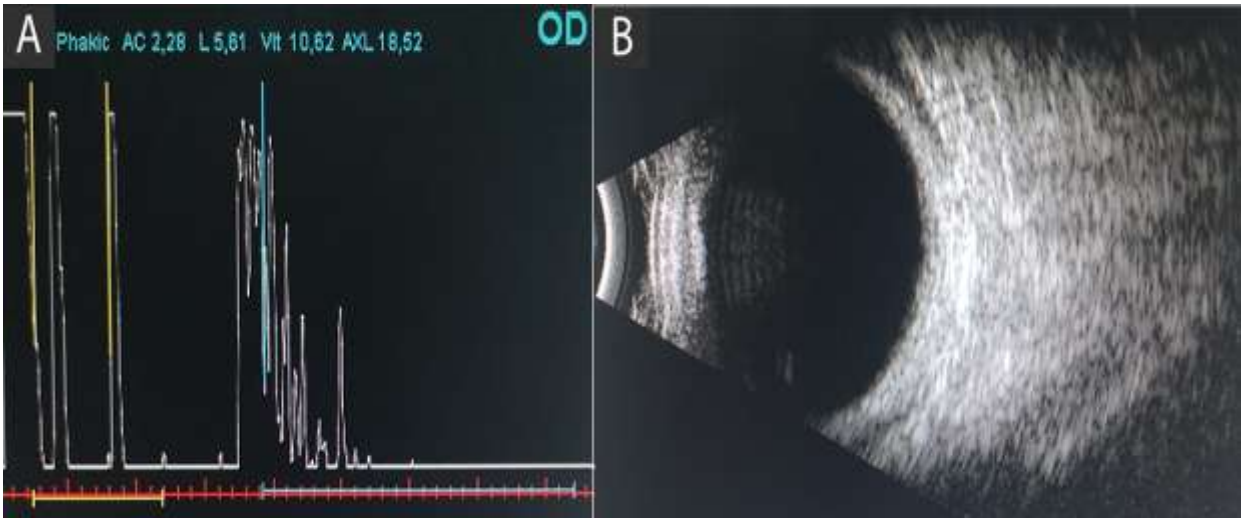

Figure 1: (A) scan ultrasound biometry showing an axial length of 18.52 mm; (B) scan showing the ultrasound aspect of a microphtalmic eye

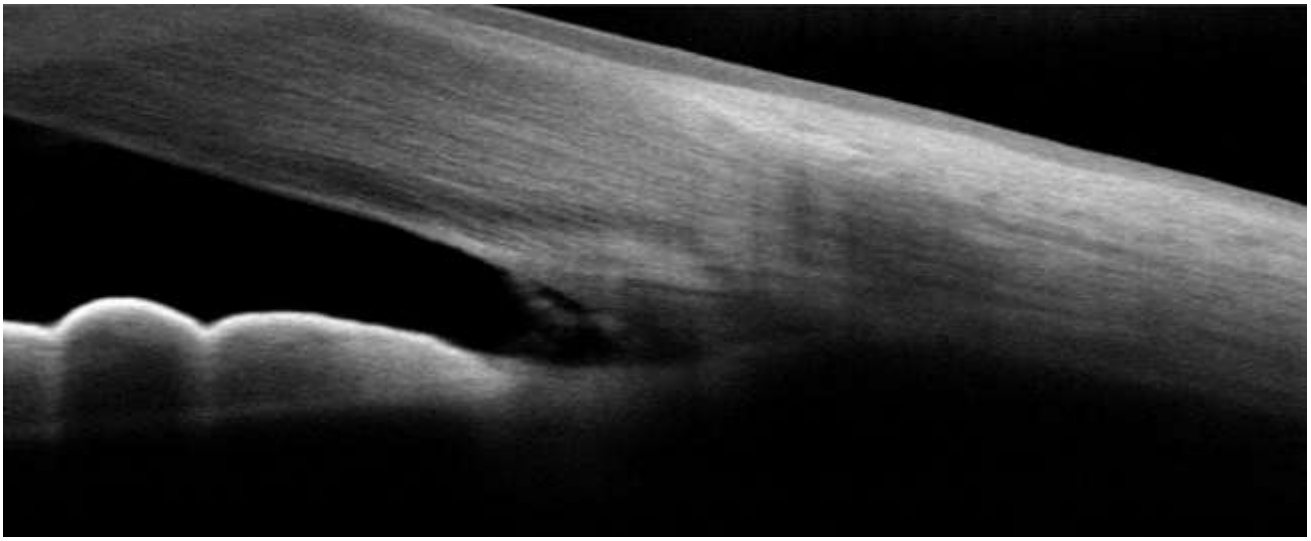

Figure 2: anterior segment optical coherence tomography (optovue RTVue XR 100 avanti) showing a narrow angle with iridotrabecular contact

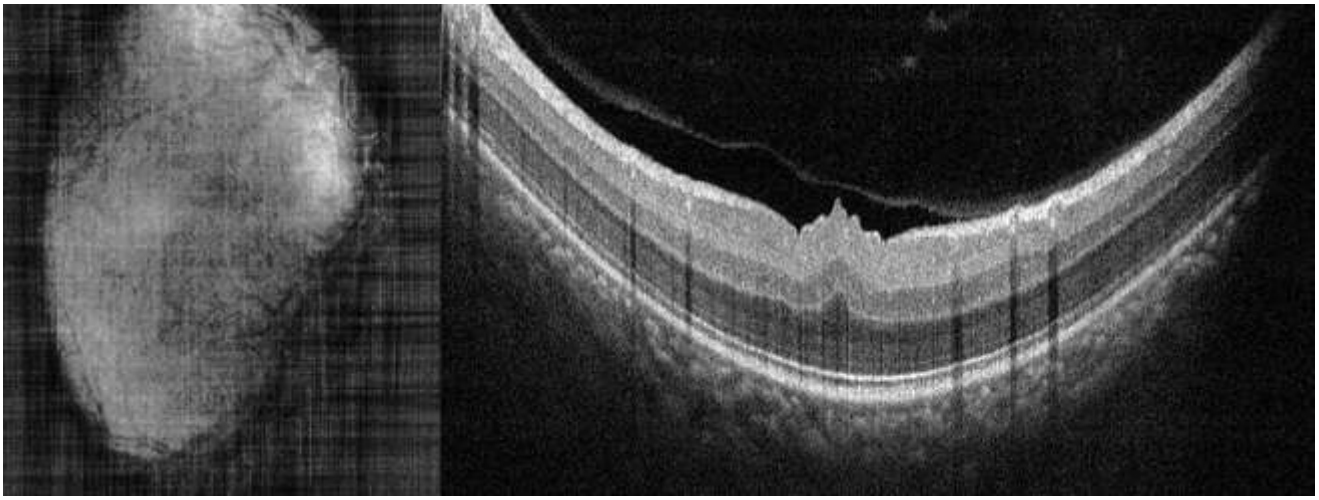

Figure 3: optical coherence tomography (Optovue RTVue XR 100 Avanti) of the macula showing a retinal fold consisted only of partial neural retina with apical surface corrugations