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Abstract

**Background:** Microphthalmos is an embryonic developmental anomaly that rarely may accompany other congenital ocular disorders.

**Case:** We present a rare complex syndrome in a 13-year-old boy with a chief complaint of progressive blurred vision without any trigger and no familial history of ocular disease. The prominent ophthalmic finding was progressive hyperopia, steep cornea, and short axial length. Slit-lamp examination revealed the optic disk drusen that were demonstrated by echography. Ocular imagings proved foveoschisis and macular fold.

**Conclusion:** Multiple structural anomalies and non-consanguineous marriage of parents suggested a very rare ocular syndrome.

**Keywords:** Amblyopia, Microphthalmos, Optic Disk Drusen, Retinitis Pigmentosa, Retinoschisis of fovea

**Introduction**

Microphthalmos results from arrested ocular development in the embryonic period. It had described in two forms; simple and mixed ophthalmic complications. Axial length in microphthalmos is shorter than two standard deviations of normal eyes. Posterior microphthalmos is a subtype of this disorder with normal anterior segment development. In these cases, unequal development of the sclera and retina with sclera shortage leads to retinal fold, especially in the macular region, and blurred vision (1). There are some reports for simple isolated posterior microphthalmos and complicated posterior microphthalmos accompany by other pathology such as optic disc drusen (1-3). The prevalence of optic disk drusen in children was estimated at 0.4%, but it can be a coexisting finding in 9.2% of patients with retinitis pigmentosa (4). There is some evidence that a combination of posterior microphthalmos and retinitis pigmentosa can be transmitted together as an autosomal recessive trait by a mutation in the Membrane-type Frizzled-related protein (MFRP) gene and crumbs homolog 1 (CRB1).
gene(5). Foveoschisis is a rare finding in posterior microphthalmos (2). A combination of all mentioned pathologies bilaterally is a rare ophthalmic syndrome. Here, we present fundoscopic examination and ophthalmic imaging of a case of complex syndrome of Posterior microphthalmos, with Retinitis pigmentosa, foveoschisis, and optic disk drusen in a 13-year-old boy.

Case report:
A 13-year-old boy with the chief complaint of poor visual acuity had been referred to Nikookari eye ophthalmic clinic. His past medical history was unremarkable. There was no apparent systemic malformation or finding. Developmental stages and mental status were normal. Ophthalmic history was glasses_wearing from 5 years old. Parents, siblings, and the last alive generation were not affected by known ocular and systemic diseases, and their ocular examination was normal. This case was born to a non-consanguineous marriage, and parents were from two apart regions from different cities.

His glasses were +6 diopters sphere, but he complained of blurred vision. It was 20/80, manifest refractive error was +9 diopters sphere with 1.5 diopters cylinder in both eyes, and the cycloplegic refractive error was +11 diopters sphere and 1.5 diopters cylinder. His best-corrected visual acuity was 20/50 in both eyes with +7 diopters spheres. Corneal diameters bilaterally were 11.7mm, both pupil diameters were 3.5mm, anterior chamber depth in the right was 2.9 mm and in left was 3 mm, crystalline lens diameter was in the normal range too (9.3*9.3*4 mm). Ocular alignment with glasses was almost normal. Fundus examination disclosed widely scattered pigmented clumps in the mid-peripheral and peripheral retina. There was neither apparent foveal pit nor macular reflex with macular folds in the papillomacular bundle area (Fig.1_a, b).

The optic disc margin blurred, but retinal vessels were not obscured. There was no hemorrhage. The optic disc was crowded without physiologic cupping.

Keratometry revealed steep corneas with 48.84, 50.22*90 diopters and 48.91, 50.37*90 diopters in the right and left eyes. Goldmann Applanation intraocular pressure was 19 mmHg.
Axial length measurement by IOL master (Karl Zeiss) was 17.12 mm in the right eye and 16.53 mm in the left eye.

There was a hint of papilledema, but we searched for pseudo-papilledema reasons due to the absence of any relevant clinical symptoms such as headache or other neurologic symptoms. Careful echography of the optic disk demonstrated a high-density echo in the optic disk with posterior shadowing compatible with optic disk drusen; the axial length was apparently reduced with the diffusely thickened choroid. (Fig.2). In Spectral Domain Optical Coherence Tomography (SD-OCT) (Heidelberg engineering), we noticed foveoschisis in the middle and outer retinal layers and macular folds. The macular fold was more prominent in vertical scans, retinal thicknesses had increased, and blurred optic disk margin without vessel obscurement was prominent. (Fig.3). full filled Electroretinography revealed photopic, and scotopic b wave reduced in amplitude, implicit time of waves was unremarkable.

We managed blurred vision by a conservative approach of glasses refinement and follow-up. BCVA was 20/50 with +7.00 diopters glasses. The patient was visited four months later; there was no new problem.

Discussion
About our literature review, posterior microphthalmos is an uncommon ophthalmic malformation. This structural abnormality leads to disparity in scleral growth relative to retina and choroid (1). Our clinical examinations of this case revealed the macular fold. Peripheral retinal hypopigmentation and abnormal ERG were compatible with the early stages of retinitis pigmentosa. Still, due to the young age of our patient, characteristic bone spicule clumps were not evident. Fundoscopy and echography confirmed optic disk drusen. There are some reports of simultaneous retinitis pigmentosa, posterior microphthalmos, foveoschisis, and optic disk drusen in both eyes(2, 6, 7). Recent genetic studies show that the MFRP gene has a crucial role in axial length and photoreceptor development (7). There is some evidence that mutations in MRFP can cause photoreceptor dysfunction and a form of retinitis pigmentosa(8). Mutations of the MRFP gene and, more recently, the CRB1 gene were reported in globe-size deformities such as microphthalmos and nanophthalmos. They may be present in a familial form of this
complex syndrome. (6, 7). In all these reports, patients resulted from consanguineous marriage in contrast to our statement that the patient was from a non-consanguineous marriage presented as sporadic form with no other family member involved.

Paun and colleagues described the CRB1 gene mutation of the Turkish family with autosomal recessive inheritance. The presentation was the early onset and severe with retinal atrophy outside of fovea with hyperpigmentation spots and intraretinal macular edema, but drusen were present only in older ones (6). Our case had no hyperpigmentation, but remarkable drusen were present.

Wasmann et al. presented compound heterozygosity for severe MFRP gene mutation in two sisters, three and four years old, with nanophthalmos and macular fold and normal autofluorescence without significant RPE abnormality; they are the youngest in literature due to severe loss of this gene. Adult patients affected by homozygous or compound heterozygous MFRP mutations generally show signs of retinal dystrophy, with ERG disturbances and RPE abnormalities on autofluorescence imaging (7). We recommended a genetic evaluation, but he refused because of cultural unacceptability.

These patients should be followed carefully for additional sequels. They are at high risk of glaucoma development at a young age (2, 9). Crespi J and et al. presented two patients of three affected siblings with this syndrome that developed angle-closure glaucoma in adolescence, which does not seem related to age. One had blinding malignant glaucoma in his left eye. They all had ocular surgery for increased intraocular pressure (2). They had three patients that were older than 40 years. They all had localized foveoschisis, but in older patients, it was more prominent and had macular edema in addition to foveoschisis. (2) In our patient, SD-OCT showed very mild cystic areas are evident in this 13-year-old patient. As in our patient and as described in their patient, it seems that foveoschisis and macular edema is progressive over time. Like patients with retinitis pigmentosa in follow-up, attention should be paid to foveoschisis that might be responsive to dorzolamide eye drop or oral acetazolamide.

**Conclusion:**

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The present case might be the alternative presentation of previous patients with the combined symptoms. Poor visual prognosis due to the high hyperopic refractive amblyopia and other structural anomalies affect treatment. Choroidal effusion and intraocular pressure elevation may worsen visual prognosis.

References


**Figures legend**

Fig. 1

Fig.1_ a: Fundus photography of right eye. b: Fundus photography of left eye. Fundus photography in both eyes showed crowded optic disk with no physiologic cupping. Disc margins are blurred but vessels are not obscured. There is no hemorrhage or exudate. Note absent macular reflex with the macular fold in both eyes and mid-peripheral dystrophic changes.

Fig. 2

Fig.2_ B scan of left (left side of the Fig.2) and right eye (right side of the Fig.2). B scan of both eyes revealed high echo signals in optic disks with posterior shadowing. Axial length was reduced and choroidal thickness was increased.

Fig. 3

Fig.3_ a: SD-OCT of the right eye. b: SD-OCT of the left eye. SD-OCT, In the C scan(right) and B scan (left) illustrated that foveal pit is absent in both eyes with increased macular thickness due to macular folding which is more prominent in vertical scans. Media was clear, Retinoschisis was apparent in the middle and outer retinal layers.
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