Posterior segment abnormalities in posterior microphthalmos

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ABSTRACT

Purpose: We report a case of posterior microphthalmos with characteristic papillomacular retinal folds, pigmentary retinopathy, and optic disc drusen.

Observations: A 19-year-old female presented with decreased visual acuity and was found to have bilateral posterior microphthalmos with the presence of papillomacular retinal folds, crowded optic nerves with buried disc drusen, and peripheral retinal pigmentary changes. Optical coherence tomography showed presence of retinal folds involving the inner retinal layers and loss of foveal contour.

Conclusions and Importance: Posterior microphthalmos can present with an array of unique clinical findings involving the posterior segment. It is important to recognize these findings as these patients often have decreased visual acuity and are at risk for the development of other posterior complications.

1. Introduction

There is a wide clinical spectrum of small eye phenotypes characterized by an overall reduction in ocular size. Microphthalmos is a developmental ocular disorder defined by an axial length that is at least two standard deviations below the mean within a specific age group. Posterior microphthalmos (PM), a subset of microphthalmos, is characterized by a disproportionately small posterior segment with normal anterior segment dimensions. Because of foreshortening, PM leads to a relative crowding effect of the posterior segment. Evidence of this crowding can be seen on fundus examination by the presence of anomalous discs, papillomacular folds, radial macular folds, absence or reduction of the foveal avascular zone, and pigmentary retinal degeneration. Vision is usually affected in these patients due to high refractive amblyopia coupled with structural macular changes. The authors present a case of PM presenting with papillomacular retinal folds, crowded optic nerves with buried disc drusen, and pigmentary retinopathy.

1.1. Case report

A 19-year-old female with no significant family history of ocular disease was referred for retinal exam with a history of poor vision in both eyes requiring spectacle correction. The patient had high hyperopia with a refraction of +14.5 D sphere of the right eye (OD) and +15.5 D sphere of the left eye (OS). Upon presentation, best corrected visual acuity was 20/60 OD and 20/60 OS. Intraocular pressure was 16 mmHg OD and 17 mmHg OS. The corneal diameters and anterior segments were noted to be normal, with the anterior chambers deep and quiet bilaterally. Anterior chamber depth was measured to be 3.14 mm in the right eye and 2.75 mm in the left eye. Lens thickness was measured as 3.95 mm in the right eye and 4.00 mm in the left eye.

Dilated fundus examination revealed a crowded optic nerve with obscured margins, and a horizontal, elevated papillomacular retinal fold extending to the fovea in both eyes (Fig. 1). There were pigmentary changes scattered in the nasal peripheral retina of both eyes (Fig. 2A and B). With the exception of diffuse speckled staining in the nasal periphery corresponding to the pigmentary changes of both eyes, fluorescein angiography was otherwise unremarkable (Fig. 2C and D). Macular optical coherence tomography (OCT) showed retinal folds in both eyes with loss of normal foveal architecture (Fig. 3). B-scan ultrasonography demonstrated sclerochoroidal thickening and hyperreflective optic nerves with buried disc drusen along with retinal folds (Fig. 4). OCT of the optic nerve showed buried disc drusen (Fig. 5). Genetic testing for microphthalmia was obtained, with the patient found to be heterozygous for a likely pathogenic variant of MFRP (c.1615C>T (p.Arg539Cys)), while also testing heterozygous for a variant of MFRP of uncertain significance (c.546A>G (p.Ile182Met)). Full field electroretinography was not performed.
2. Discussion

Axial hyperopia, which is seen in ocular conditions including PM and nanophthalmos, is characterized by significantly shortened axial lengths. While PM, as seen in this patient, is classically defined as a normal anterior chamber depth and configuration with reduction in size of the posterior segment with associated structural abnormalities, nanophthalmos represents a foreshortening of both the anterior and posterior segments with overall preserved organization of the globe. Although there is debate as to the distinction between PM and nanophthalmos with studies showing that recessive mutations of membrane-type frizzled-related protein (MFRP) and the serine protease PRSS56 can cause both, they may actually represent a spectrum of axial hyperopia rather than two distinct clinical entities. While this patient did test heterozygous for a likely pathogenic variant of MFRP, its overall clinical significance remains inconclusive in conjunction with a heterozygous variant of uncertain significance. Thus, the genetic characteristics of this spectrum of disorders appear to be varied.

The crowding effect that arises in the setting of PM has been reported to lead to certain anatomical changes, including papillomacular folds (typically seen with axial length < 18mm), absence or reduction of the foveal avascular zone, pigmentary retinal degeneration, and crowded optic nerves. The most common findings seen in PM are crowded discs and sclerochoroidal thickening on ultrasonography, while papillomacular folds are seen in up to 72.2% of patients. The poor visual acuity commonly seen in patients with hyperopic folds is the result of a combination of refractive amblyopia and structural macular changes and typically ranges between 20/50 to 20/200, which is consistent with this patient. However, there is at least one reported case of a patient with features typical of PM who achieved normal and age-appropriate development of visual acuity. Compared to the previously reported case, our patient had larger retinal folds and significant contortion of foveal architecture, which may explain the poorer visual acuity.

While the pathogenesis of retinal folds in cases of posterior microphthalmos is controversial, one hypothesis is that there is premature arrest of the deeper, outer layers of the eye (retinal pigment epithelium, choroid, and sclera) via an inhibitory pathway with continued normal growth of the neurosensory retina, leading to redundancy of the inner retinal layers. There is some debate as to whether the papillomacular folds that arise from a densely arranged posterior segment involve only the neurosensory retina, or a combination of the neurosensory retina and the deeper, outer layers. Reports in the existing literature have
supported the former argument that only the inner retinal layers comprise the folds with relative sparing of these deeper layers.\textsuperscript{3,5,10,11} Papillomacular folds may lead to poor development of the fovea, as demonstrated in this patient, due to the inherent presence of inner retinal layers in this region.\textsuperscript{12}

Optic nerve changes that have been reported in highly hyperopic eyes with shortened axial lengths include optic nerve hypoplasia and congested optic discs, due in part to the dense crowding of axons and vessels into a confined, prematurely developed scleral canal.\textsuperscript{5,10} This patient had optic nerve drusen, which thus far has been associated with an autosomal recessive ophthalmic syndrome characterized by posterior microophthalmos, retinitis pigmentosa, foveoschisis, and optic disc drusen caused by a MFRP gene mutation.\textsuperscript{13,14} However, this patient was unusual in that she did not have associated retinitis pigmentosa or foveoschisis. Although pigmentary retinopathy is more commonly seen in nanophthalmos, the presence of retinal pigmentary changes in the nasal periphery as seen in this patient could be an indication of previous uveal effusion.\textsuperscript{3,9} Further complications associated with PM that have been reported in the literature include macular retinoschisis, retinal dialysis, retinal detachment, coloboma, macular hypoplasia, and macular hole.\textsuperscript{3,6,8,15,16}

In conclusion, patients with PM can present with unique clinical findings, one of the most prevalent being papillomacular retinal folds, along with crowded optic nerves and pigmentary retinopathy. Optic disc drusen, although rare, may also be present. While many patients with PM have compromised vision due to refractive amblyopia and abnormal
foveal structure with retinal folds, it is important to monitor these patients for the development of further posterior segment complications.

2.1. Patient consent

Consent to publish this case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

None.

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References

1. Elder MJ. Aetiology of severe visual impairment and blindness in microphthalmos. *Br J Ophthalmol*. 1994;78(5):332–334.
2. Relhan N, Jalali S, Pehre N, et al. High-hyperopia database, part I: clinical characterization including morphometric (biometric) differentiation of posterior microphthalmos from nanophthalmos. *Eur. J. Ophthalmol.* 2016;36(1):120–126.
3. Carricondo PC, Andrade T, Prasov L, et al. Nanophthalmos: a review of the clinical spectrum and genetics. *J. Ophthalmol.* 2018;2018:2735465.
4. Zor KR, Kucuk E, Gunaydin NT, Onder F. Ocular findings in posterior microphthalmos. *Saud. J. Ophthalmol.* 2019;33(1):41–45.
5. Helvacıoğlu F, Kapran Z, Şencan S, et al. Optical coherence tomography of bilateral nanophthalmos with macular folds and high hyperopia. *Case Rep Ophthalmol Med.* 2014;2014:173853.
6. Karlıhanlı B, Maxoumi A, Ebrahimiađ B, et al. Multimodal imaging in posterior microphthalmos. *J. Curr. Ophthalmol.* 2019;31(3):335–338.
7. Novilatay SR, Khan AO, Aldahmesh MA, et al. Biometric and molecular characterization of clinically diagnosed posterior microphthalmos. *Am J. Ophthalmol.* 2013;155(2):361–372 e7.
8. Khairallah M, Messaoud R, Zouali S, et al. Posterior segment changes associated with posterior microphthalmos. *Ophthalmology.* 2002;109(3):569–574.
9. Mihara M, Hayashi A, Gowaši T. Posterior microphthalmos with good visual acuity: a case report. *Am J Ophthalmol Case Rep.* 2019;16:100568.
10. Park SH, Ahn YJ, Shin SY, Lee YC. Clinical features of posterior microphthalmos associated with papillomacular fold and high hyperopia. *Clin Exp. Optom.* 2016;99(6):590–593.
11. Aras C, Özdamar A, Ustundag C, Özkan S. Optical coherence tomographic features of papillomacular fold in posterior microphthalmos. *Retina.* 2005;25(5):665–667.
12. Liu JJ, Chen YY, Zhang X, Zhao PQ. Clinical features of posterior microphthalmic eyes. *Int. J. Ophthalmol.* 2018;11(11):1829–1834.
13. Ayala-Ramirez R, Graue-Wiechers F, Robredo V, et al. A new autosomal recessive syndrome consisting of posterior microphthalmos, retinitis pigmentosa, foveoschisis, and optic disc drusen is caused by a MFRP gene mutation. *Mol. Vis.* 2006;12:1485–1489.
14. Crespi J, Bull JA, Bassaganyas F, et al. A novel mutation confirms MFRP as the gene causing the syndrome of nanophthalmos-retinitis pigmentosa-foveoschisis-optic disk drusen. *Am J. Ophthalmol.* 2008;146(2):323–328.
15. Spitznas M, Gerke E, Bateman JB. Hereditary posterior microphthalmos with papillomacular fold and high hyperopia. *Arch Ophthalmol.* 1983;101(3):413–417.
16. Kim JW, Boes DA, Kinyoun JL. Optical coherence tomography of bilateral posterior microphthalmos with papillomacular fold and novel features of retinoschisis and dialysis. *Am J. Ophthalmol.* 2004;138(3):480–481.