Five Cases of Microphthalmia with Other Ocular Malformations

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We report five cases of complex microphthalmia with other ocular malformations in infants or children, which were evaluated to investigate the relationship between the corneal diameters and total axial length. The size of the globe was measured by using computerized tomographic scans (CT scan), A-scan ultrasonography, or magnetic resonance imaging (MRI). There is a limited range of well-described malformation, including anterior or posterior segment dysgenesis or combined pathology such as corneal opacity, small cornea, iris hypoplasia, lens dislocation, cataract, chorioretinal coloboma, persistent hyperplastic primary vitreous (PHPV), retinal dysplasia, and intraocular tumor. Corneal diameters were correlated significantly with total axial length ($r^2 = 0.88$) and decreased linearly as the total axial length decreased in these cases. However, there was no relationship seen between the total axial length and posterior segment length ($r^2 = -0.06$). The results of this study may aid the clinical ophthalmologist to accurately understand or assess microphthalmia combined with other ocular malformations.

Key words: anterior or posterior dysgenesis, chorioretinal coloboma, microphthalmia, persistent hyperplastic primary vitreous

INTRODUCTION

A microphthalmic eye is assessed when the axial diameter, adjusted for age, is below the 95th centile. Generally, microphthalmia is found in between 1.2 and 1.8 per 10,000 births in white populations. In adults, microphthalmia is identified in eyes with an axial length of less than 18.5 mm, as compared to infants with less than 15 mm. The size of the globe can be measured by ultrasonography, CT scans, or MRI. Additionally, this disorder was usually combined with other ocular abnormalities or systemic abnormalities.

In contrast to the reported western studies concerning the clinical characteristics of microphthalmia involved with other ocular malformations (complex microphthalmia), this condition has not been well characterized in Korea until now. Therefore, we present microphthalmia frequently combined with other ocular malformations such as anterior or posterior segment dysgenesis; small cornea & opacity, lens deformity & cataract, optic disc or chorioretinal coloboma, persistent hyperplastic primary vitreous (PHPV), and analyze the clinical characteristics of complex microphthalmia vis-a-
vis the existing literature. Furthermore, we investigated the relationship between corneal diameters and total axial length, including the posterior segmental length in complex microphthalmias.

CASE REPORTS

Case 1

A 7-day-old male was referred by a local ophthalmological clinic due to anophthalmia, which was a narrow palpebral fissure and deeply set appearance of the eyeball. A MRI of the brain and orbit was performed at this time and, according to the MRI findings, the small left eyeball, as compared to the right eye, had a dysmorphic remnant in the vitreous cavity of the eyeball. The axial length of the lesion eye measured 9.0 mm, although it measured 19.0 mm in the right. There were no way to check the length of anterior chamber, lens length, or vitreous length by MRI due to the deformed small-sized eyeball. We also found that some calcification in the anterior segment of the left eyeball. The diagnosis was a calcification at the anterior segment malformation of the eyeball with microphthalmia in the left eye (Fig. 1A & 1B). There was no history of prematurity, oxygen use, or distinctly ocular or systemic family. As he has a complex microphthalmia without visual potential, we removed the lesion eye at an early age in order to insert a conformer, which may expand the orbit.

Case 2

The second case is a PHPV with microphthalmia in the left eye in a 15 month-old boy (Fig. 2). This patient had a history of normal spontaneous vaginal delivery at postnatal 38 weeks and a 3000 gram birth weight. In particular, he had a systemic anomaly similar to a cleft palate. B-scan ultrasonography showed a solid mass shadow within the intraocular cavity. The axial length of the eyeball, measured 20 mm in the right and 10 mm in the left. Additionally, the posterior segment length from the posterior

Fig. 1. The left globe is significantly small, and only a dysmorphic remnant is observed. The anterior portion of the residual globe shows low signal intensity in both T1 (A) and T2 (B) weighted image, and is thought to be a calcification. Extraocular muscles show a normal appearance.

Fig. 2. The left eyeball is smaller than the right one. A solid mass-like lesion detected with orbital MRI is thought to be PHPV.
Fig. 3. Both eyeballs show a small cornea, and a shallow anterior chamber is observed. Additionally, the eyeball size is relatively small, below 15 mm.

aspect of the lens to the anterior aspect of the retinal surface measured 6mm at the left microphthalmia by A-scan. The white retrorenal processes in the vitreous cavity were revealed as PHPV by MRI. There was no evidence of other ocular findings in the left eyeball. Currently, this patient, with an applied confirmier, is being followed in our eye clinic.

Case 3

A 2-week-old boy presented with microphthalmia in both eyes, small cornea with moderate opacity and a very shallow anterior chamber (Fig. 3). This patient visited our clinic due to leukoria on both eyes since birth. There was no evidence of abnormality in the family or birth history. Both eyes demonstrated a deeply set appearance of the eyeball, with shallow anterior chamber, and moderate degree of corneal opacity. The diameter of the cornea measured approximately 6.0 mm in the right and 8.0 mm in the left. Additionally, the axial length of the eyeball, measured 13 mm in the right eye and 14 mm in the left. The posterior segment length measured approximately 10 mm in the both eyes by A-scan. A confirmier expander application was recommend, but the patient did not follow up in our clinic.

Case 4

This infant was a 10-day-old girl who showed microphthalmia with optic disc and chorioretinal coloboma similar to that seen in morning glory syndrome, as well as lens dislocation (Fig. 4A & 4B). She initially presented with both narrow palpebral fissure and deeply set appearance of the eyeball. There was no history of prematurity or birth trauma, with the exception of C-section delivery. The diameter measured approximately 3.5 mm in both corneas. The total axial and posterior segment length of the eye measured approximately 13.0 mm, 9 mm in the right and 12.0 mm, 9mm in the left. By MRI findings, an elongated ciliary process-like remnant of the hyaloid artery was identified in both vit-
reous cavities. Additionally, the optic disc and chorioretinal coloboma like morning glory disc in both eyes was revealed by the fundus findings. The deformed displaced lens and iris were pulling evidence into the central vitreous cavity. Bilateral PHPV with optic disc and chorioretinal coloboma in microphthalmia was diagnosed.

Case 5

A 4-year-old girl visited our clinic with leukocoria and appearance of a left nanophthalmos. The left eye disclosed a narrow palpebral fissure, deeply set appearance of the eyeball, shallow anterior chamber, and small cornea (about 7.5 mm in diameter). A large yellowish white mass projecting from the retina into the vitreous cavity was present in the posterior pole. The axial length of the eyeball measured 22.3 mm in the right eye and 13.3 mm in the left. Computed tomography of the orbit revealed a distinctly small left eyeball as compared to the right eye and an abnormal soft tissue density surrounding a central calcification in the vitreous cavity of the left eye. The left eye was clinically diagnosed for microphthalmia (Fig 5A). Five months later, left eyeball enlargement occurred. Rapidly growing intraocular mass with multiple calcifications had developed in the left microphthalmia on the CT scan (Fig 5B). Unfortunately, the eyeball was enucleated due to the rapid growth of the intraocular mass (Fig 5C). Microscopically, the tumor cells showed pleomorphic, hyperchromic nuclei with scanty cytoplasm and a poorly differentiated pattern of tumor

Fig. 5. The orbital computed tomography shows that the size of the left eyeball with a high density (calcification) in the vitreous cavity is smaller than that of the right eyeball (A). Five months later. A rapidly growing intraocular mass with multiple calcifications has developed in the left microphthalmos (B). The gross findings of the bi-dissected eyeball shows yellowish mass filling the vitreous cavity, with tumor spreading along the surface of the retina (original size: 25 X 20 X 10 mm) (C).
with some Flexner-Winter-Steiner rosetts. This case was a rare case of retinoblastoma which developed in unilateral microphthalmia.

**DISCUSSION**

According to the classification criteria of microphthalmia, these were classified into “pure”, “colobomatous”, and “complicated” microphthalmia in previous years. The first two classes referred to the ocular morphology; in contrast, the third referred to the presence of systemic anomalies and not to a specific ocular feature. However, a new classification system of microphthalmia is classified them in two parts; phenotype and etiology. The first part, the phenotypic classification, is concerned with the ocular features only, and is divided into two divisions; “total” and “partial” microphthalmia. Total microphthalmia is when both the anterior and posterior segments are foreshortened. Partial microphthalmia means that either the anterior or posterior segment is small or malformed while the other segment is of normal size or larger than normal. According to our results, four cases of microphthalmia were the total microphthalmia and only case 3 belonged to the partial microphthalmia group due to the normal length or size of posterior segment.

The second part, the etiological classification, consists of three classes; genetic, prenatally acquired, and associations. This provides a systemic approach to the possible causes of congenital anomalies such as malformations, disruptions or deformations. Genetic disorders are concerned with deletion and translocation of a gene, such as trisomies 13 and 18, del (18p), del (13q), and del (4p). Prenatally acquired microphthalmia developed from a consequence of maternal ingestion of teratogens like alcohol, thalidomide, and isoretinoic acid or ocular disease such as maternal diabetes and rubella. Microphthalmos and coloboma resulting from associations are concerned with the CHARGE or VATER syndrome. In phenotypic classification, microphthalmia with other ocular malformations of total microphthalmia is common. There are some cases of microphthalmia combined with other ocular malformations, including small cornea, congenital cataract, lens dislocation, iris dysplasia, anterior chamber malformation, coloboma, PHPV, cystic coloboma, intraocular tumor. All our cases belonged to this category (Table 1). Microphthalmia with congenital cataract is known in the sporadic systemic syndrome such as Haller-mann-Streiff syndrome, X linked Nance-Horan syndrome. The chamber angle may be deficiently developed and there may be anterior synechiae. Additionally, there may be defects of the posterior layers of the cornea, for example a cloudy
cornea. Coloboma of the uvea is often present in microphthalmic eyes. They may be of varying size, and minor manifestations in the iris can be seen by transillumination. The colobomatous part may become staphylomatous and occasionally the coloboma forms a cystic lesion in the microphthalmia.\textsuperscript{19,20} Furthermore, the macula and optic nerve are often involved.

Generally, the global size can be measured by ultrasonography, CT scans, or MRI.\textsuperscript{21,22} However, Weiss et al.\textsuperscript{23} reported there was a significant correlation with total axial length — corneal diameter decreased linearly as total axial length decreased, because the corneal diameter is taken as an indicator of globe size. This finding was similar to our result, namely the corneal diameters correlated significantly with total axial length ($r^2 = 0.88$) and decreased linearly as total axial length decreased in our cases. However, there was no relationship between the total axial length and the posterior segment length ($r^2 = -0.06$). Three of the patients in our study had a malformation of the posterior segment, while more than 80% of the eyes in a western report had an anomaly of the posterior segment. This difference suggests that western microphthalmia exists more as a malformation of the posterior segment rather as compared to that of oriental microphthalmia, although a more extended study concerned with complex microphthalmia is needed.

These ocular malformations were caused by the decreased size of the optic cup, abnormally low intraocular pressure (IOP), altered proteoglycans in the vitreous, and abnormal production of growth hormone and paracrine growth factors in the pathogenesis of microphthalmia.\textsuperscript{3,23-27} The optic cup is the supporting framework for ocular development, the constraints imposed by a small optic cup could lead to microphthalmia.\textsuperscript{3} Another factor, the magnitude of IOP, is important because abnormally low IOP prior to birth or during infancy may result in microphthalmia.\textsuperscript{24} In relation to the proteoglycans, which are major constituents of the vitreous and sclera, it is possible that a defect in their metabolism interferes with the growth of the posterior segment, thus causing microphthalmia.\textsuperscript{3,22} Furthermore, the paracrine and endocrine growth factors are recognized to promote ocular growth and development.\textsuperscript{25,27} Overall, the microphthalmia associated with ocular malformation is uniformly due to a decreased growth of the posterior segment, and has multiple causes.

Overall, congenital anophthalmos and microphthalmos are rare conditions that can have associated pathology in the globes and/or systemic anomalies. These anomalies include anterior segment malformation, abnormal lens, persistent hyperplastic primary vitreous, coloboma, or retinal diseases such as ROP, retinal dysplasia and degeneration.\textsuperscript{6-9} Therefore, when a case presents with microphthalmos, we must recognize that a careful ocular examination and regular follow-up is required to detect such accompanying ocular abnormalities and complications.

If complex microphthalmia without visual potential exist, they should be removed at an early age in order to insert a conformer, which may expand the orbit. Orbital expansion has been used in the treatment of microphthalmia for several years. Since the infant eye reaches more than 70% of its adult size at birth and grows most rapidly during the first 12 months after birth, initiating the process during the first year of life has recently come to be seen as an appropriate goal.\textsuperscript{28-30} Considering the degree of tissue growth in infants, expander placement or conformer application should be recommended after postoperative 3 months in order to maintain or support orbital expansion between 20 weeks and 36 weeks.\textsuperscript{30} If microphthalmia exist, early diagnosis and proper treatment, including orbital expansion are required.

**REFERENCES**


