Recent trends In Management of Microphthalmia and Related Anomalies

Essay
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Abstract

Microphthalmia is a developmental eye disorders resulting in smallness of one or both eyes with a total axial length at least 2 standard deviations below the mean for that age group. The eye is considered microphthalmic if the total axial length (TAL) is less than 15 mm at birth. The microphthalmic eye has an axial length less than 19.2 mm at 1 year of age. It arises alone or in conjunction with other ocular defects such as coloboma and orbital cyst. It may be also part of more generalized syndromes.

Classification of microphthalmia varies according to anatomical, clinical or etiological aspects with further subdivisions in each type of classification.

Key Words:

Anatomy and embryology of the eye, Classifications of microphthalmia, Management of microphthalmia

List of abbreviations

AC	Anterior Chamber.
TAL	Total Axial Length.
CT	Computerized Tomography.
FFA	Fundus Fluorescein Angiography.
KR	Keratometric Reading.
PHPV	Persistent Hyperplastic Primary Vitreous.
RAM	Relative Anterior Microphthalmos.
ROP	Retinopathy Of Prematurity.
TORCH	Toxoplasma gondii, Rubella virus, Cytomegalovirus (CMV), Herpes simplex virus (HSV).
U/S	Ultrasound.

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Introduction

Microphthalmia has been defined as an eye with an axial length at least 2 standard deviations below the mean for that age group and is also known as a congenital malformation of the globe. Incontrast, the term anophthalmia which means absence of the globe.[1]

The reported incidence of microphthalmia in newborns is 1 in 5300 to 1 in 8300 births [2]. It involves one or both eyes and may occur in isolation with no associated malformation or as a part of multiple congenital malformations for example, the congenital rubella syndrome, the trisomy 13 syndrome…etc.[٢]

The **diagnosis** of microphthalmia is based on clinical examination and imaging studies including: A-scan ultrasonography to measure total axial length; B-scan ultrasonography to evaluate the internal structures of the globe; and CT scan or MRI of the brain and orbits to evaluate the size and internal structures of the globe, the optic nerve and extra ocular muscles, and the brain anatomy .[3]

Evaluation for other malformations, chromosomal analysis, family history, and parental eye examination are mandatory. Genetic counseling may help to establish the underlying cause.[٢]

Different ways of **management** aiming at early diagnosis, cosmetic improvement or rehabilitation are present. Evaluation by oculoplastic surgeons for prosthetic intervention in severe microphthalmia may be essential. **Rehabilitation** includes early intervention and therapy to optimize psychomotor development, life skills, and mobility in children with unilateral or bilateral involvement,

and protection of the healthy eye in children with unilateral involvement. [3]

Re-evaluation of children by a medical geneticist at age four to five years to look for features of a syndrome that may have become more apparent over time is also needed in children with reduced vision in one or both eyes .[3]

Genetic counseling for inherited or denovo chromosome abnormality or a specific associated syndrome is important. [3]

The most recent diagnostic procedure nowadays is **prenatal diagnosis** for pregnant women at increased risk for chromosomal abnormalities. Transvaginal ultrasound examination can detect abnormalities in eyes from 12 week of gestational age; where as three-dimensional and four-dimensional ultrasound examination may be used in some centers to detect complex malformations of the face. [3]

Prenatal and postnatal ocular development

At birth the eye looks nearly the same size as in the adult because the corneal diameter is only 1.7 mm smaller , but its volume increases almost three folds up to maturity and its weight doubles, the average for the full-term newborn eye being, respectively 3.25 cm^3 and 3.40 g. The weight increases nearly 40% by the middle of the second year and nearly 70% by the fifth year. Many changes occur with maturation: normative data are needed for clinical observations during childhood. [4]

Prenatal ocular development

The prenatal development of the eye and brain occurs relatively early in comparison to other systems. Rapid and fluid changes in the eye and brain allow the development of normal vision.[5] by sixth week of gestation the differentiation of the ocular structures of the brain is fairly well developed. So, teratogenic factors occurring within the first trimester commonly result in ocular defect .[4]

In the first three weeks of embryonic development, the two main processes that occur are the differentiation of the cell type into endoderm, mesoderm and ectoderm and the organization of these tissues into a tube like notochord/neural tube structure .[6]

The first sign of the developing eye is seen by day 21 of human gestation while the neural tube is still open, here the optic sulci or optic pit develop as invaginatoin of the inner surface of the anterior neural fold.[4]

Over the next three days the neural tube closes at its caudal and cephalic ends .[4] At day 25, the optic groove is formed in the optic vesicle, which evaginates towards the surface ectoderm, initiating the lens placode. The optic vesicle then begins to invaginate forming a double

layered optic cup lined by the two layers of the neuroectoderm that form the layers of the retina (figure 1). The inner invaginating neuroepithelium that develops later to form the sensory retina and the external pigmented non invaginating epithelium that forms the retinal pigment epithelium. [7]

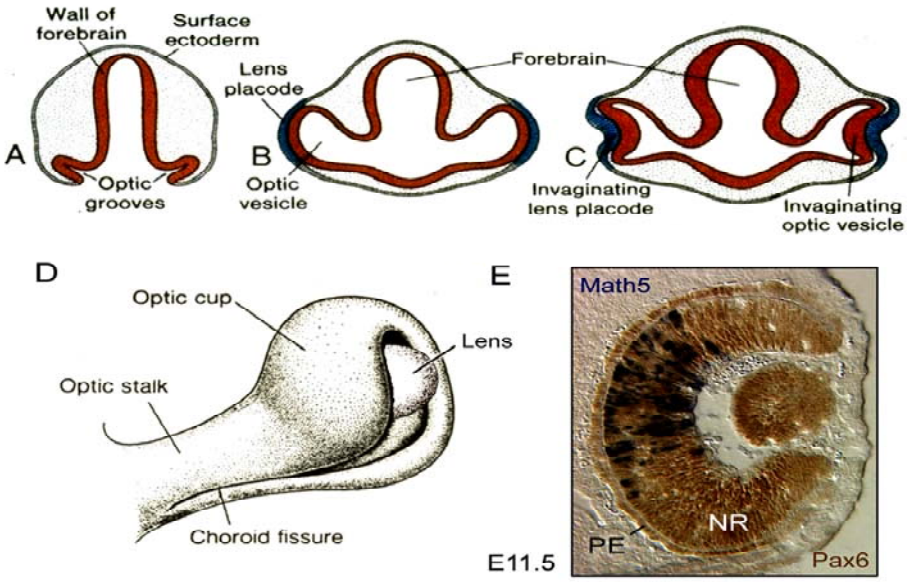

Figure 1: ***Invagination of optic vesicle to form optic cup*** *.a, b, c, and d shows formation of optic groove then vesicle, followed by invagination of vesicle and lens formation e- shows cut section in optic cup.*[8]

The invaginatig optic vesicle cradles the lens placode that develops into lens vesicle, separating from surface ectoderm. As regard the hyaloid artery, it develops from the internal carotid artery and lies within the embryonic fissure and extends to optic vesicle. At 6 weeks intrauterine life, the embryonic fissure closes proximally to distally, **if there is failure of closure, coloboma will result**. At 7 weeks the eye has an optic nerve, two layers of the retina, with starting differentiation of sensory retina and the primary lens vesicle receiving vascular support from the hyaloid artery. The globe is surrounded by mesenchyme and

neural crest cells which differentiate into sclera, choroid, iris, cornea and vitreous between 7 and 15 weeks intrauterine (figure 2) [7].

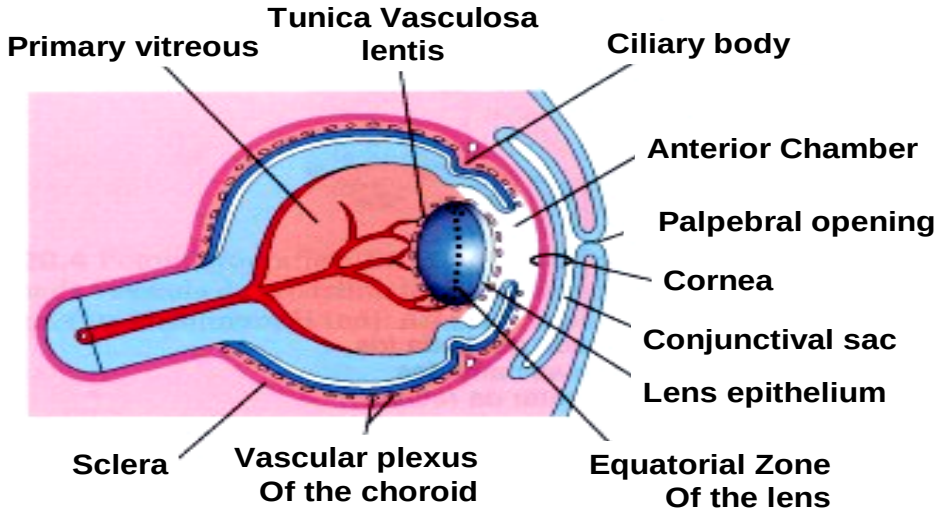

Figure 2*: **Differentiation of the eye between 7th and 15th week of gestation.***[8]

As the eye develops, neural crest mesenchyme surrounds the craniofacial complex which explains the association of ocular anomalies with craniofacial syndromes [7].

So any acute exposure to teratogens during early stages results in an overall deficiency of the neural plate with subsequent reduction in size of optic vesicle. This aberration results in *microphthalmia* which may be associated with a spectrum of secondary malformations [9].

The malformations may arise due to genetic defects that produce anomalies of early embryonic induction or during formation of the optic cup .[10]

Also failure of late closure of optic fissure can result in *microphthalmia* associated with colobomas (*colobomatous microphthalmia*) which may be associated with eye lid cyst (figure 3)[9].

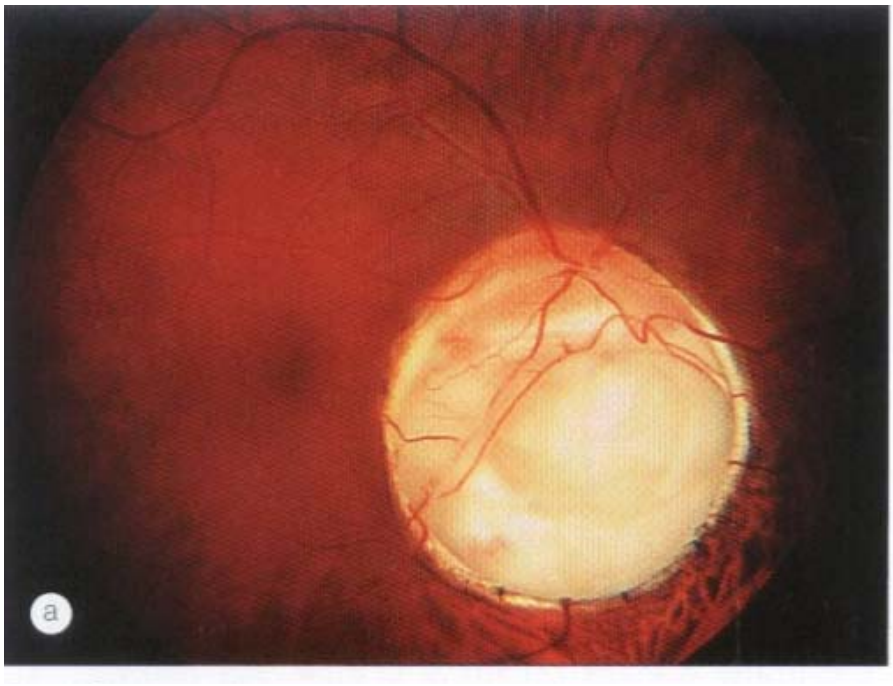

Figure 3: ***Optic disc coloboma as a result of failure of closure of optic fissure.***[11]

The normal development of the lens depends upon apposition between the surface ectoderm and the optic vesicle, following resorption of the intervening mesenchyme. In the absence of this apposition, residual mesenchyme proliferates, with eventual resorption of the developing globe, causing anophthalmia. If the lens has reached a critical size, it is retained within the optic cup and the eye becomes microphthalmic. Vitreous volume is lost, perhaps because it leaks into the orbit through an associated coloboma and/or, more likely, because of its decreased production. Studies of the homozygous microphthalmic mouse have shown that the cause of microphthalmia was failure of secondary vitreous to develop. Although this sequence has been observed primarily in animal models, it is possible that similar events occur in the human [10].

The developmental abnormalities of the eye and brain are frequently concurrent. Severe brain malformation as abnormal closure of the neural tube or severe forebrain midline reduction abnormalities are frequently

accompanied by anopthalmia, *microphthalmia*, anterior chamber cleavage abnormalities, or abnormal ocular placement[7].

Anomalies of the globe formation and development lead to failure of orbital enlargement, making the prosthetic fitting more difficult in children with severe microphthalmos and anophthalmos [7].

Post natal development

The globe size and axial length undergo dramatic changes in the first several years of life. Enlargement continues until 13 years of age but about 50% of the total increase occurs in the first 6 months of life [12].

At birth the anteroposterior diameter of the infant's eye is 70% that of an adult measuring approximately 17 mm.The volume of the infant's eye in contrast is only 50% that of an adult eye [4].

The anterior structures consisting of cornea, lens and the iris are generally more completely developed than the posterior segment of the eye [4]. Growth of the posterior segment accounts for 60% of the prenatal and more than 90% of the postnatal increase in total axial length. As shown below in table 1.