Anophthalmia and Microphthalmia

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Introduction

Anophthalmia and microphthalmia are characterized by the complete or almost complete lack of the primary optic vesicle, which results in an absent or very small malformed orbital globe.

Definition

Anophthalmia is the complete absence of the orbital globe. Microphthalmia refers to a small, typically malformed orbital globe. These abnormalities can be unilateral or bilateral. The birth prevalence of these two malformations combined is approximately 1 per 10,000 births.[1]

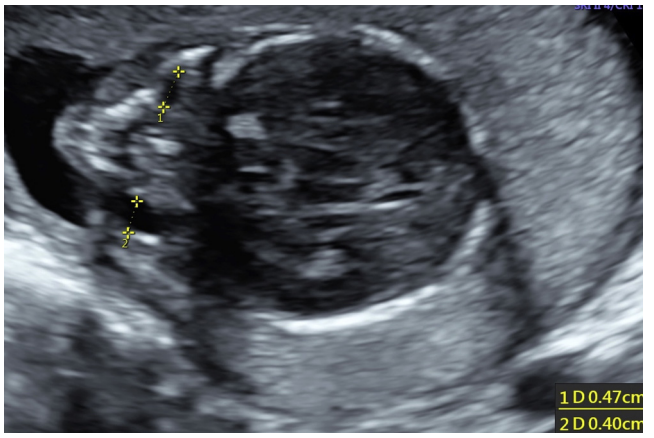
Ultrasound Findings

The fetal orbits typically are detectable by 11–12 weeks of gestation, and the lens is seen as a thin-walled circle within each orbit by 13–14 weeks of gestation.[2] The diagnosis of anophthalmia or microphthalmia is typically a subjective one, although orbital measurements at each gestational age are available.[3] The coronal view of the fetal face is the best way to evaluate the orbits. This view can show the size and shape of the orbits, their positioning on the fetal face, spacing between the two orbits, and associated facial abnormalities. The sagittal view of each orbit is also helpful when the size of the orbit is measured. The lens is seen as a small, thin-walled, circular structure and normally is visible in the anterior aspect of the globe in both the axial and sagittal views. The hyaloid artery is visible traversing the middle of the eye from anterior to posterior usually by 14 weeks of gestation and should disappear by 29 weeks of gestation.[4] Most often, diagnosis of these rare but severe ocular anomalies is made because other fetal anomalies are present and the orbital findings are part of a syndrome. Orbital defects are rarely discovered prenatally as isolated findings (Figure).

Associated Abnormalities

The associated anomalies vary with the fetal syndrome that is involved; therefore, it is crucial to perform a detailed sonographic anatomic evaluation. Triploidy and mosaic trisomies 9 and 13 are among the aneuploidies most likely to feature microphthalmia. Triploidy has early asymmetric fetal growth restriction associated with anomalies of the heart, brain, and face (hypertelorism). Trisomy 13 is associated with midline facial and brain defects, cardiac anomalies, and polydactyly. Trisomy 9 results in early pregnancy loss; survival generally occurs only in mosaic cases. Features of mosaic trisomy 9 include abnormalities of the heart, face, and skull.

FIGURE
Axial view of the fetal head and face



Axial view of the fetal head and face shows the small and asymmetric size of the orbits (*calipers*). This fetus has multiple other anomalies.

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Nonsyndromic conditions that can feature microphthalmia include holoprosencephaly spectrum, congenital viral infections (particularly rubella), and CHARGE association (Coloboma, Heart defects, Atresia choanae [choanal atresia], growth Restriction, Genital anomalies, and Ear anomalies). Other syndromes that are associated with eye anomalies include Aicardi syndrome (female fetus, arachnoid cyst), Fraser syndrome (genitourinary and tracheal anomalies), Fryns syndrome (congenital diaphragmatic hernia), Goldenhar syndrome (ear tags, cleft lip and/or palate, asymmetry of face), Gorlin syndrome (ventriculomegaly), Lenz syndrome (microcephaly), Walker-Warburg syndrome (lissencephaly, ventriculomegaly, cataracts), fetal alcohol syndrome, and others.[5]

Differential Diagnosis

Anomalies of the fetal eye may be bilateral or unilateral and asymmetric. Anophthalmia and microphthalmia refer to the size of the globe and orbit. Congenital cataracts should not be confused with microphthalmia, although both conditions may be present in the same fetus. The orbit may be distorted by masses such as intracranial teratomas (associated with intracranial component), gliomas (usually medial aspect of orbit), or retinoblastomas (rarely seen in utero).

Genetic Evaluation

Diagnostic testing (amniocentesis or chorionic villus sampling) with chromosomal microarray analysis (CMA) should be offered when anophthalmia is detected. If

screening or other ultrasound features are suggestive of a common aneuploidy, it is reasonable initially to perform karyotype analysis or fluorescence in situ hybridization, with reflex to CMA if these test results are normal. Many syndromes are associated with anophthalmia; they can be sporadic, autosomal dominant, autosomal recessive, or X-linked. If there are additional anomalies, consanguinity, or a family history of a specific condition, gene panel testing or exome sequencing may be useful because CMA does not detect single-gene (Mendelian) disorders. If exome sequencing is pursued, appropriate pretest and posttest genetic counseling by a provider who is experienced in the complexities of genomic sequencing is recommended.[6] Maternal infections (rubella), vitamin A deficiency, and teratogenic exposures (thalidomide) have also been associated with anophthalmia; therefore, obtaining a history of maternal exposures and a family history is important. After appropriate counseling, cell-free DNA screening is an option for patients who decline diagnostic evaluation if a common aneuploidy is suspected.

Pregnancy and Delivery Management

A detailed ultrasound examination should be performed and should include comprehensive imaging of the intracranial structures (eg, a neurosonogram) and the fetal heart. A fetal echocardiogram and fetal magnetic resonance imaging to assess for intracranial abnormalities should be considered. Referrals to pediatric ophthalmology, craniofacial clinic, plastic surgery, or other subspecialty services should be based on additional sonographic findings. Pregnancy termination is an option that should be discussed with all patients in whom a fetal anomaly is detected. Shared patient decision-making requires a thorough evaluation and multidisciplinary counseling regarding prognosis. The specific finding of anophthalmia or microphthalmia does not generally affect delivery management, although delivery at a tertiary care center with pediatric genetic, craniofacial, and ophthalmology subspeciality services should be considered as appropriate for the clinical findings.

Prognosis

The prognosis is variable and dependent on the severity, associated anomalies, and underlying genetic cause. Unilateral microphthalmia can have a favorable prognosis other than possible blindness in the affected eye. Mild-to-moderate microphthalmia can be managed with conformers, whereas severe cases may require surgical remodeling. Bilateral microphthalmia is often associated with intellectual disability, and vision is dependent on retinal development. Reported cases of anophthalmia typically represent severe microphthalmia; true primary anophthalmia is rarely compatible with life secondary to associated cerebral anomalies.

Summary

Microphthalmia is a rare abnormality of the eye that generally occurs because of a genetic syndrome, maternal infection, teratogenic exposure, or vitamin deficiency. Diagnostic testing is recommended with CMA and/or molecular genetic testing based on associated anomalies. Prognostic counseling is dependent on the severity of microphthalmia, associated findings, and the underlying diagnosis.

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