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## Case Report

# Isolated presentation of congenital microphthalmia on fetal MRI

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## ABSTRACT

A fetal growth scan was performed on a 34-year-old Caucasian woman, G4P3, with a history of gestational diabetes diagnosed at 32 weeks gestation. The examination revealed an absence of normal left globe with an echogenic mass in its expected location with a rim of surrounding hypoechoic fluid. The right orbit and globe were normal, and no other structural anomalies were identified. Prior to this examination, the patient had a normal anatomic survey and fetal echocardiogram at 20 weeks, however due to fetal positioning there was limited visualization of the orbits on initial scan. Fetal MRI was performed at 36 weeks gestation and confirmed near-complete absence of the left globe with asymmetrically smaller size of the left orbit. Normal right orbit and globe were present, and no additional fetal structural abnormalities were observed. **Figure 1** congenital microphthalmia was diagnosed based on the imaging findings, preparing the family and alerting the medical team of appropriate care needed postnatally.

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## Introduction

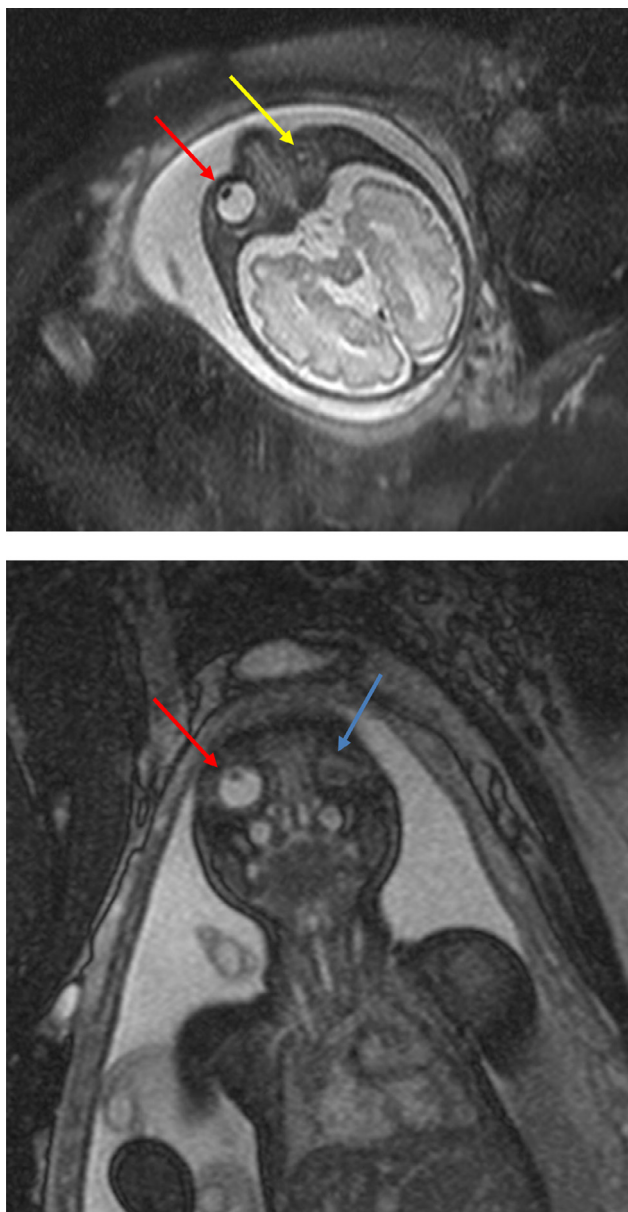
Congenital microphthalmia is the presence of either unilateral or bilateral small eye(s) within the orbit [1]. The incidence of microphthalmia has been estimated at 1.5–19/100,000 births [2–4]. Risk factors for this condition include multiple births, maternal age over 40, infants with low birth weight, parental

consanguinity, and/or early gestational age [1,5]. While it can present independently, it can also be a part of syndromes associated with congenital malformations in other organ systems [6]. Early identification could be crucial for screening for these syndromes, identifying additional malformations, providing emotional support and education for parents, as well as coordinating interdisciplinary care for the infant [7].

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**Fig. 1 – Axial and coronal HASTE images of the fetus, confirming normal right globe and orbital content (red arrow) and asymmetrically smaller left orbit (blue arrow) with focus of T2 hyperintensity, suggesting microphthalmic left globe (yellow arrow). Color version available online.**

## Discussion

Microphthalmia is defined when the mean axial length or diameter of a patient's eye is more than 2 standard deviations below that of age-matched controls [1,8]. The appropriate orbital size for gestational age has been determined by fetal sonography utilizing nomograms that correlate these 2 growth parameters [9,10]. More recently, such growth parameters have been documented utilizing MR imaging [11].

Microphthalmia can be seen on a spectrum of eye malformations known as the Microphthalmia/Anophthalmia/

Coloboma (MAC) Spectrum [6]. Anophthalmia is the absence of the globe in the presence of other ocular structures that normally surround the eye. Coloboma is a segmental defect of the eye that is a result of failure of optic fissure closure [2]. Microphthalmia can then be further subclassified to be termed either simple or complex microphthalmia. In simple microphthalmia the anatomical structure of the eye is normal in spite of its reduced volume [1,12]. By contrast, complex microphthalmia is characterized by a structurally abnormal eye that results in functional impairment. The structural abnormalities of microphthalmia may affect the anterior or posterior segments of the eye. The location of the structural abnormality determines the subsequent functional impairment [1].

Microphthalmia may be unilateral or bilateral and may occur in isolation or in association with multiple congenital anomalies [1,7]. About a half to a third of microphthalmia cases is associated with a syndrome that also affects other body systems [13]. In addition, microphthalmia may have an early or late gestational onset, with the early onset cases more likely to be associated with major structural and chromosomal abnormalities. Both conditions are detectable by fetal sonography as early as the beginning of the second trimester. However, 1 study documents 4 cases in which normal eyes were observed until the third trimester, after which microphthalmia was diagnosed [8].

Embryologically, microphthalmia results from abnormalities in the development of the primary optic vesicle [7]. Both chromosomal and environmental etiologies of microphthalmia have been postulated. Major genes that could be involved include SOX2, OTX2, RAX, FOXE3, BMP4, and PAX6 [6]. However, factors such as maternal vitamin deficiency, pesticide exposure, fever or hyperthermia, and X-ray exposure have been implicated as well [1].

The prenatal diagnosis of microphthalmia can be accomplished using a combination of imaging modalities. As previously mentioned, it is possible to detect this condition utilizing fetal ultrasound by the early second trimester [14]. For pregnancies that have no known risk, a standard fetal ultrasound screening should be performed. If any findings on the ultrasound indicate a MAC spectrum disorder then genetic testing should follow. MRI may be used to supplement ultrasound if concern for microphthalmia is raised on sonographic examination. For pregnancies at increased risk for MAC spectrum more advanced imaging modalities can be used such as transvaginal ultrasound which has been used to examine the eyes as early as 12 weeks although the sensitivity has not been determined. Additionally, 3-dimensional and 4-dimensional ultrasound can be used as a tool to examine ocular malformations [15]. Correlation with cytogenetic studies can be made to determine possible genetic or chromosomal abnormalities. In individuals with severe microphthalmia/anophthalmia, up to 80% can be identified with molecular testing and 20% of individuals on the MAC spectrum [6].

When trying to identify the genetic cause of microphthalmia, a detailed exam should be done that includes family history, physical examination, imaging, and genetic testing. Physical examinations should focus on the ophthalmological, renal, endocrine, cardiac, and neurological systems. Imaging studies that could be done include an ultrasound of the orbit, MRI of the orbit and CNS, renal ultrasound,

and echocardiogram. Any malformations identified should be compared against known syndromes that have similar phenotypes. Management of microphthalmia requires a multidisciplinary approach including an ophthalmologist, pediatrician, and clinical geneticist [6]. Additional tests that are suggested include early assessment of hearing and screening for intranatal infections [16]. It is necessary to ensure proper growth of the orbit with microphthalmia and there are many nonsurgical and surgical methods which aim to help expand the orbit for a painted prosthesis to be used later in life [7]. In microphthalmic eyes that have an axial length of 16 mm or less, the use of expanders is more likely to be necessary to prevent asymmetry [7]. It is important to start this process at an early age because most of the postnatal eye growth is completed by age 3. It is important to consult parents with a family history or MAC spectrum abnormalities concerning their risk in future pregnancies [6].

None of the potential risk factors or genetic causes were identified in the presented patient. This was the fourth pregnancy in the mother with no abnormalities in the 3 pregnancies preceding this one. Although original diagnosis was made with an ultrasound, fetal MRI was helpful in confirming the findings in the orbit and normal evaluation of fetal anatomy, reassuring the mother and the rest of the family in the isolated nature of the finding. The delivery of the fetus was uneventful and prenatal findings were confirmed on postnatal physical examination. An immediate referral was made to a regional center specializing in management of microphthalmia and the anophthalmic socket to initiate further care.

## Conclusion

Microphthalmia can be seen on a spectrum of eye malformations known as the MAC Spectrum, with rare incidence of disease. Although ultrasound can make the initial diagnosis, fetal MRI is helpful in further evaluation and exclusion of additional potential abnormalities which may be seen in association with this entity. In this case report, we present imaging findings of this diagnosis based on fetal MRI in a patient with no known underlying risk factors for this condition.

## Conflict of interest

None.

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