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Case Report

Ocular Anomalies in a Neonate: A Case Report on Right Eye Anophthalmos and Left Eye Microphthalmos

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ABSTRACT

Anophthalmia is characterised by the complete absence of optic structures, while microphthalmia involves underdeveloped eye structures, often accompanied by other defects such as congenital cataracts and coloboma. Both conditions can be unilateral or bilateral and are linked to genetic mutations. Epidemiological studies show a prevalence of 3.0 per 10,000 live births for these anomalies, with maternal factors like advanced age and diabetes being significant risk factors. This case presents a female neonate, born via emergency caesarean section, presented with right eye anophthalmos and left eye microphthalmos. The mother had right eye incomplete cryptophthalmos and left eye microphthalmos, with no family history of congenital disorders or consanguinity. Examination revealed the infant weighed 2.5 kg and had normal neonatal reflexes with normal neurological function. No other external anomalies were found. The left eye was small and malformed with short eyelids, while the right eye orbit was absent. The ophthalmologist confirmed the diagnosis and tobramycin eye ointment was prescribed to prevent bacterial infections. The infant was discharged after receiving thorough parental counselling on the condition's nature, prognosis, potential interventions and the importance of regular follow-ups. In conclusion, this case illustrates the complexity of anophthalmia and microphthalmia, underscoring the need for thorough postnatal examinations and genetic counselling. Accurate diagnosis and personalised management rely on understanding the genetic basis of these conditions. Future research should focus on clarifying genetic pathways to enhance diagnostic and therapeutic approaches.

Keywords: Anophthalmos, Microphthalmos, Coloboma, Congenital Abnormalities, Case report.

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INTRODUCTION

Anophthalmia involves the complete absence of all optic structures, such as the globe, optic nerves, optic foramen and optic chiasm, while microphthalmia is characterised by underdeveloped eye structures. Microphthalmia can affect one or both eyes and often accompanies other eye-related defects, including congenital cataracts, coloboma of the iris and choroid, pupillary obstruction, corneal scarring and ocular muscle imbalance.[1] Epidemiological research has yielded crucial insights into anophthalmia and microphthalmia. According to data from the Texas Birth Defects Registry covering 1999-2009, these conditions collectively affected 3.0 per 10,000 live births, with more than half of cases involving chromosomal abnormalities or syndromes. Factors such as multiple previous foetal deaths and maternal diabetes were linked to higher prevalence rates.[2] Similarly, findings from the California Birth Defects Monitoring Program (1989-1997) indicated a lower prevalence of 0.18 and 0.22 per 10,000 births for anophthalmia and bilateral microphthalmia, respectively, excluding chromosomal anomalies.[3] Advanced maternal age and lower education levels were identified as notable risk factors. These studies significantly advance our understanding of the epidemiology of these conditions and help identify vulnerable maternal populations.[4]

Microphthalmia can occur unilaterally or bilaterally, with variations categorised as colobomatous or non-colobomatous. True anophthalmos is rare, resulting from a failure in optic vesicle development, while consecutive anophthalmos arise from degeneration. Visual acuity varies, often accompanied by hypermetropia and large coloboma may lead to confusion with retinoblastoma. Complications can include glaucoma and retinal detachment. CHARGE (Coloboma, Heart defects, Atresia of the choanae, Retardation of growth and development, Genital abnormalities, Ear abnormalities) syndrome, which encompasses microphthalmia/coloboma and other anomalies, is linked to mutations in the CHD7 gene.[5] Genetic factors, including autosomal recessive and autosomal dominant transmissions,

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contribute significantly to anophthalmia and microphthalmia. The wide phenotypic variability within affected populations, often characterised by high rates of consanguinity, underscores the genetic complexity of these conditions.[6] Recent advancements in clinical molecular testing for genes such as SOX2 and OTX2 represent substantial progress in understanding the genetic underpinnings of anophthalmia and microphthalmia. However, the intricate genetic pathways involved and the variability in clinical presentations necessitate comprehensive genetic evaluations for precise diagnosis and management strategies.[7]

Diagnostic methods encompass eye ultrasound, Visual Evoked Potentials (VEP) and Magnetic Resonance Imaging (MRI) to thoroughly evaluate associated anomalies.[8] Ultrasonography proves to be a convenient, reliable and non-intrusive technique for monitoring the size of the eye and orbit in patients diagnosed with Microphthalmia, Anophthalmia and Coloboma during outpatient visits. While microphthalmic eyes can undergo growth, variations in growth rates among these patients affected unilaterally may lead to increasingly pronounced differences in axial length asymmetry over time.[9] Surgical procedures for anophthalmos and microphthalmos include evisceration and enucleation, which respectively involve removing the eye contents while preserving the sclera or completely excising the eye. Following these procedures, orbital implants are often inserted to maintain socket volume. Socket reconstruction techniques may include socket expansion, mucous membrane grafting and lid lengthening. Ocularists then customise cosmetic prostheses to fit within the socket, restoring facial symmetry. In severe cases, reconstructive surgeries like orbital and craniofacial reconstruction may be necessary to optimise both function and aesthetics.[10]

This case report shows a unique case presentation of a female neonate with combination of right eye anophthalmos and left eye microphthalmos.

CASE DESCRIPTION

A female neonate was admitted to the Neonatal Intensive Care Unit (NICU), appropriate for gestational age, presenting with right eye anophthalmos and left eye microphthalmos (Figure 1). The father's family history was negative for congenital disorders, while the mother had right eye incomplete cryptophthalmos and left eye microphthalmos. There was no consanguinity reported. The pregnancy was normal and the delivery occurred via emergency caesarean section. Antenatal ultrasound did not reveal the ocular abnormalities.

Examination findings revealed the infant weighed 2.5 kg, within normal limits. The baby had normal neonatal reflexes with normal neurologic function and no other external anomalies were found. The left eye was significantly small and anatomically malformed, with short eyelids and a short palpebral fissure. The right eye orbit was absent, with a reduced palpebral fissure. All other organs appeared normal and an abdominal ultrasound confirmed no abnormalities. Haemoglobin and other laboratory values were within normal ranges. Cardiovascular examination indicated normal heart sounds (S1, S2), while respiratory assessment revealed bilateral air entry without additional sounds. Abdominal palpation showed a soft abdomen.

Based upon the examinations, the ophthalmologist confirmed the case as right eye anophthalmos and left eye microphthalmos. As a precautionary measure against bacterial infections, tobramycin eye ointment was prescribed. Following the initial diagnosis and prophylactic therapy, the infant was eventually discharged. Before discharge, comprehensive counselling was provided to the parents including the nature and prognosis of the condition, potential future interventions and available support resources. The parents were also educated on the importance of regular follow-up visits to monitor the child's development and to address any arising complications promptly.

DISCUSSION

Anophthalmia and microphthalmia are rare congenital conditions characterised by the absence or significant underdevelopment of one or both eyes, affecting up to 30 per 100,000 births. Most ocular growth occurs within the first three years of life, predominantly due to posterior segment expansion. These conditions are typically bilateral but can occasionally be unilateral, particularly in cases of isolated microphthalmia. They are significant contributors to childhood blindness.[11,12]

In this case, a female neonate exhibited right eye anophthalmos and left eye microphthalmos. The father's family had no known congenital disorders, whereas the mother had similar ocular anomalies. The presence of similar anomalies in the mother underscores the potential genetic implications and the necessity for genetic testing and counselling. Genetic mutations like c.542delC in SOX2, p.Pro181Argfs*22, p.Glu105X in OTX2 altering stop codons can lead to unusual amino acid sequences, potentially influencing ocular development.[13] Functional insights into gene variants like SOX2 and OTX2 highlight the intricate pathways involved in ocular development. Despite deleterious mutations, the variable expressivity and penetrance of phenotypes underscores the complexity of gene-environment interactions in shaping clinical outcomes.[14] Exome analyses have unveiled novel genetic variants, such as a homozygous stop gain mutation in FOXE3 and AP4M1, linked to isolated anophthalmia. These discoveries emphasise the critical role of genetic research in unravelling the molecular basis of ocular malformations and advancing precision medicine approaches.[15]

Despite a normal pregnancy and emergency caesarean section delivery, the ocular abnormalities were not detected prenatally in this case. Diagnosing anophthalmos and microphthalmos during the prenatal period is particularly challenging, as standard screenings often return normal results.[16] Accurate

Figure 1: This image shows right eye anophthalmos (absence of the right eye) and left eye microphthalmos (undeveloped, smaller left eye). Both conditions are visible, highlighting the significant disparity in eye size and structure.

diagnosis generally depends on postnatal imaging techniques such as ultrasound and MRI, which provide essential insights into ocular structural anomalies and help determine the extent of malformation.[17] Utilising human phenotype ontology to meticulously document each clinical feature beyond just the primary diagnosis allows clinical scientists to apply the most appropriate diagnostic gene panels effectively.[18] Obtaining a molecular diagnosis not only enhances our understanding of the natural history of gene or variant-specific cohorts but also identifies potential therapeutic targets and establishes outcome measures for future treatments.

This neonate had a normal brain and other organs, with only the eyes being malformed. But comorbidities often accompany isolated anophthalmia and microphthalmos, with a notable correlation between unilateral cases and fewer systemic complications, particularly in the presence of a normal contralateral eye.[19] Environmental factors, such as maternal VAD, contribute significantly to foetal development and the prevalence of ocular malformations like anophthalmia. Addressing preventable factors like Vitamin-A Deficiency (VAD) in prenatal care could mitigate the impact on ocular health outcomes, especially in regions with high incidences.[20]

Management of anophthalmia and microphthalmia involves a shared care approach between ophthalmic, paediatric services and a specialist centre. Treatments include socket expanders, prosthetic devices and possibly orbital implants. Long-term management requires regular reviews, monitoring for glaucoma and addressing refractive errors. Early intervention and continuous follow-up are essential for optimising visual and facial development outcomes.[21]

However, lack of genetic testing shows a significant limitation in this report underscoring the need for thorough prenatal screenings and detailed postnatal examinations including genetic testing to identify and manage congenital ocular anomalies effectively.

CONCLUSION

This case highlights the complexity and uncommon nature of ocular anomalies, underscoring the necessity for thorough postnatal examinations and detailed genetic counselling. The hereditary nature of these conditions emphasises the need for advanced genetic testing to identify mutations and understand their impact on eye development. Future research should aim to deepen the understanding of the genetic basis of anophthalmia and microphthalmia, leading to more accurate diagnoses and personalised management strategies. Understanding these genetic pathways can lead to the discovery of potential therapeutic targets, paving the way for the development of gene-based treatments or interventions.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Informed consent was obtained from the patient's legal guardian.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

CHARGE: Coloboma, Heart defects, Atresia of the choanae, Retardation of growth and development, Genital abnormalities, Ear abnormalities; **VEP:** Visual Evoked Potentials; **MRI:** Magnetic Resonance Imaging; **NICU:** Neonatal Intensive Care Unit; **VAD:** Vitamin-A Deficiency.

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