International Medical Case Reports Journal

Dovepress
Taylor & Francis Group

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CASE REPORT

Cyclopia Syndrome with Neck Presentation: A Case of Alobar Holoprosencephaly and Prenatal Diagnostic Challenges

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Abstract: Alobar holoprosencephaly is the most severe and common subtype of holoprosencephaly (HPE), a developmental defect that arises during the embryonic period due to heterogeneous factors. This condition is characterized by incomplete development and separation of the forebrain, often accompanied by facial deformities, especially in severe cases. Most severe cases result in stillbirth or neonatal death shortly after delivery. We report a case of a 28-year-old multiparous woman who presented with preterm labor and preterm premature rupture of membranes (PPROM). Ultrasound imaging revealed fetal malformations consistent with alobar HPE, including cyclopia syndrome. The patient delivered a stillborn infant vaginally in an unusual neck presentation. We discuss the etiology of HPE, including potential contributing factors such as toxoplasmosis in our case, along with diagnostic and management considerations. Additionally, we highlight the special presented part of the infant during vaginal delivery and its possible reasons. Early prenatal diagnosis of cyclopia syndrome is crucial, as it significantly impacts family counseling regarding pregnancy continuation. It also underscores the need for additional genetic and serological viral tests to investigate potential underlying causes.

Keywords: alobar holoprosencephaly, cyclopia, facial malformations, toxoplasmosis, special presented part, vaginal delivery, case report

Introduction

Cyclopia is a rare congenital anomaly with a global prevalence of 1 in 100,000 live births.[1] As the most severe form of facial malformation associated with holoprosencephaly (HPE), it typically results in miscarriage, stillbirth, or neonatal death.[2] The condition is characterized by distinctive craniofacial dysmorphisms, including a single eye located within a midline orbital cavity and a proboscis - a trunk-like structure with a single nostril positioned superior to the orbit - indicating complete or near-total nasal agenesis. These facial features are often accompanied by concurrent extracranial congenital anomalies.[3] Various factors are implicated in causing cyclopia, including viral or parasitic infections (eg, toxoplasmosis).[4] This case report adheres to SCARE criteria.[5]

Despite advancements in prenatal imaging, early and accurate diagnosis of severe fetal anomalies, such as cyclopia syndrome, remains challenging, particularly in resource-limited settings where access to advanced diagnostic tools like high-resolution ultrasound, MRI, and serological tests is limited. This report underscores the diagnostic and management difficulties in severe HPE presenting as cyclopia, including an atypical delivery outcome.

Case Presentation

A 28-year-old multipara woman (G5P2L2A2) presented to our hospital at the 30th week of gestation, complaining of cramps, back pain, and fluid leakage from the vagina that had started 8 hours prior. Her blood pressure was 110/70 mmHg, and the heart rate was 80 beats per minute. Vaginal examination revealed a 2 cm dilation and 80% effacement of the cervix, with ruptured membranes and the shoulder being the presenting part. There was not no degree of kinship between her and her husband. She denied taking any medication in pregnancy except for supplements and vitamins. She

Received: 8 April 2025
Accepted: 16 July 2025
Published: 18 July 2025

mentioned first-time contact with a cat in the first trimester of gestation, but could not recall the exact date. She had a history of two miscarriages: one at the 5th week of gestation and the second at the 8th week, both treated by dilatation and curettage (D&C). She had no significant medical or family history and denied alcohol and tobacco use.

Laboratory tests revealed normal hemoglobin and platelet count (Hb: 12.2 g/dl, platelets count: 234×10^3/ul), white blood cell count: 21×10^9/L (granulocytes: 91%, lymphocytes 6.6%), blood glucose level: 97 mg /dL, urea: 10 mg /dL, creatinine: 0.9 mg/dL, SGPT: 19 units per liter of blood serum, prothrombin time (PT): 13s, and partial thromboplastin time: 27.5s.

Ultrasound revealed a singleton live fetus in an oblique lie with a very large fundal placenta, enlarged brain lateral ventricles, intracranial calcifications, fusion of thalami, absence of the septum pellucidum, agenesis of corpus callosum, and fetal bowel dilatation. Fetal spine did not reveal any abnormality.

After 6 hours, the cervix was 4 cm dilated, but we noticed that the presented part had changed. A soft structure was palpated, but we did not know what it was by exact. The fetus remained in an oblique lie, with the head in the left lower abdominal quadrant confirmed by abdominal examination and ultrasound.

Two hours later, a stillborn female was delivered. The posterior aspect of the neck and the shoulder was the presenting part (Figure 1). On gross examination: a 2000 g female with a single, midline, fused eye in a single orbit below a proboscis (Figure 2).

There was no cleft lip or cleft palate, but the neck and shoulder were edematous with scaly skin (Figure 3). The abdomen was swollen, and each hand had 6 fingers. The placenta weighed 500 g with a diameter of 20 cm and a thin umbilical cord (Figure 4). The patient was discharged from the hospital 1 day later.

Discussion

During embryonic life, the brain develops from the enlarged cranial part of the neural tube. By the end of the fourth week, this enlarged cephalic part exhibits three distinct dilatations called primary brain vesicles: the prosencephalon

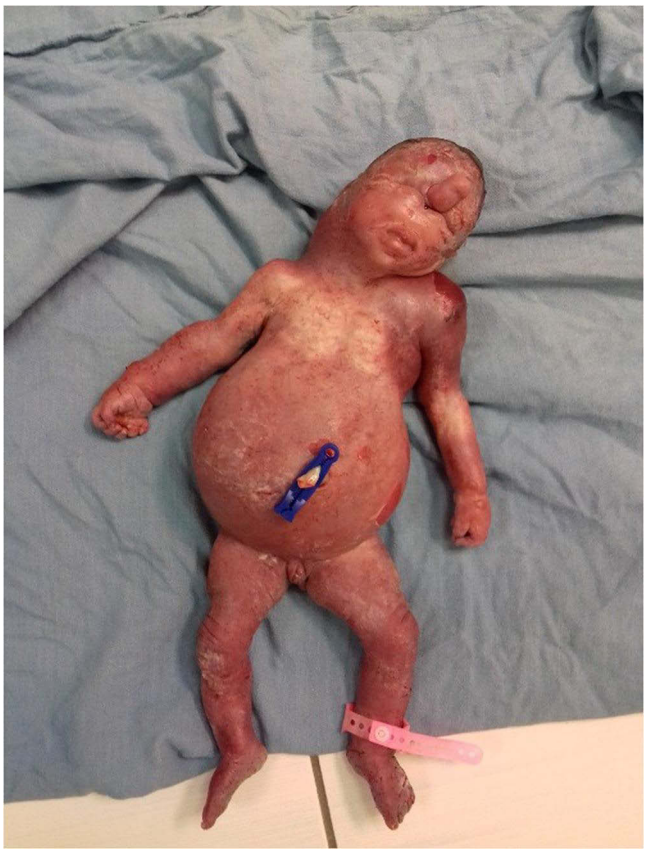

Figure 1 The delivered stillborn female.

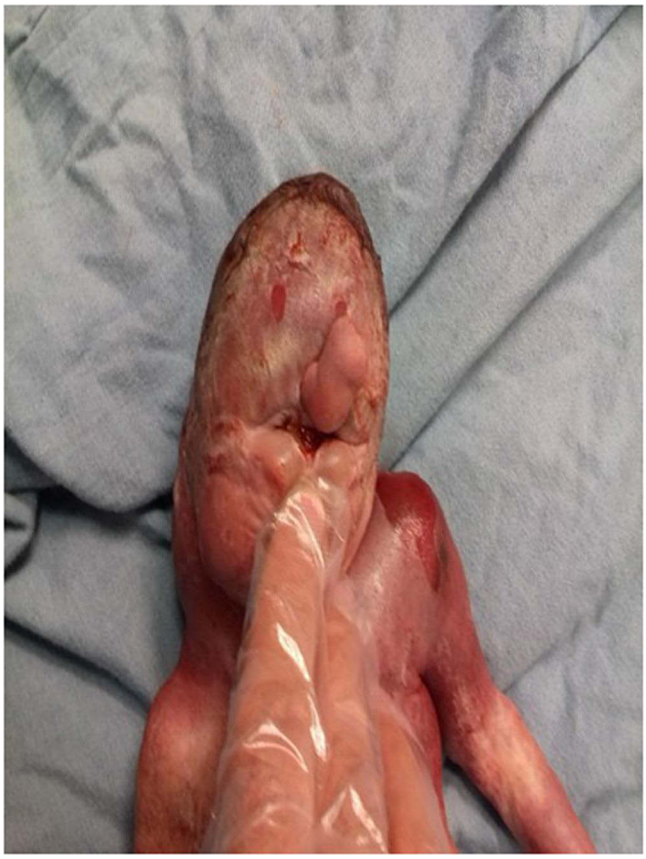

Figure 2 A single, midline, fused eye in a single orbit below a proboscis.

(forebrain), mesencephalon (midbrain), and rhombencephalon (hindbrain). Their cavities form the ventricular system of adult brain. The prosencephalon gives a rostral telencephalon and caudal diencephalon (interbrain). The telencephalon develops lateral diverticula by evagination, which enlarge, overgrow, and cover the caudal diencephalon to form the cerebral hemispheres.[6] Therefore, incomplete cleavage of the forebrain between the 18th and the 28th days of gestation results in holoprosencephaly, the most common forebrain malformation in humans.[7]

Holoprosencephaly is categorized into four subtypes based on the degree of cerebral hemisphere separation. The most severe and common subtype is alobar holoprosencephaly, where the forebrain completely fails to divide into two hemispheres, as seen in our case. Less severe subtypes include: semilobar holoprosencephaly, characterized by partial separation of the forebrain, and lobar holoprosencephaly (the least severe form), where there are two distinct ventricles but with cerebral continuity across the frontal cortex. Middle interhemispheric variant (MIHF) is another milder subtype in which posterior frontal and parietal lobes fails to separate.[7,8]

The degree of facial dysmorphism correlates with the cerebral anomalies. Mild forms of HPE may present with microcephaly, microphthalmia, ocular hypotelorism, midfacial hypoplasia, and cleft lip. Severe forms are associated with more severe midline facial defects, such as a primitive nasal structure (proboscis), cyclopia (a single midline eye), and midfacial clefting. In our case, the condition matched the alobar subtype, presenting with cyclopia and a proboscis but without midfacial clefting, accompanied by extracranial malformation such as fetal bowel dilatation, placentomegaly, and polydactyly.[9]

The etiology of HPE is very heterogeneous and unclear, involving both genetic and environmental factors such as maternal diabetes, ethanol, salicylates, antiepileptic medications, retinoic acid.[4] Familial occurrences of holoprosencephaly suggest genetics reasons; approximately 18–25% of live births with HPE have monogenic syndrome, and 24–45% have chromosomal anomalies, most commonly numerical anomalies in chromosomes 13, 18, and 21. Therefore,

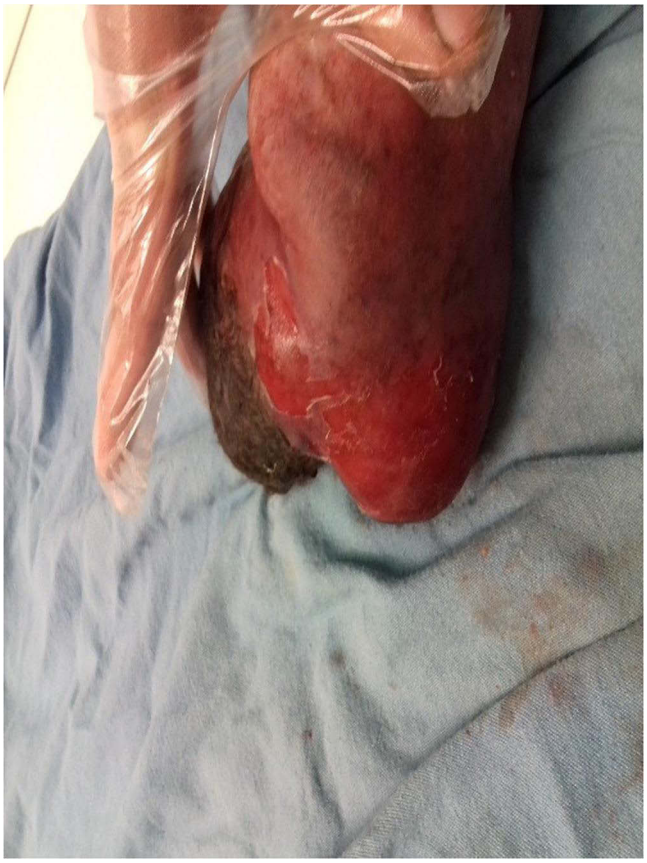

Figure 3 The presented part which is the edematous neck and shoulder with scaly skin.

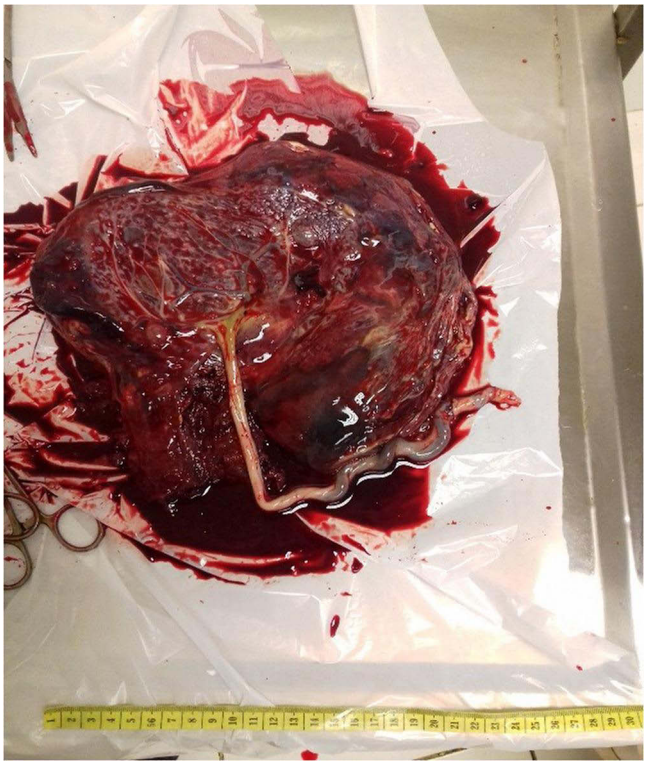

Figure 4 A 20 cm diameter placenta.

cytogenetic and molecular testing is recommended to determine the specific genetic causes of holoprosencephaly in each case if possible.[10]

In our case, toxoplasma gondii was the suspected pathogen in causing holoprosencephaly, supported by the patient's history of first-time contact with a cat early in pregnancy and the presence of signs associated with congenital toxoplasmosis (cerebral ventricular dilatation, intracranial nodules, placentomegaly, and hyperechogenic bowel). Unfortunately, no serological tests were done to confirm toxoplasmosis.

Prenatal diagnosis of holoprosencephaly can be reliably made using ultrasound in the first and second trimesters, although diagnosing less severe subtypes in early pregnancy is more challenging. Associated facial malformation such as cyclopia, cebocephaly, ethmocephaly, or cleft lip, can also be detected via ultrasound. Mild forms of HPE may not be diagnosed until much later or may go unnoticed.[11,12] High-resolution MRI scans in the third trimester can provide better characterization of subtle malformations identified on prenatal ultrasound.[6] Additionally, 3D/4D sonography can rapidly and precisely evaluate facial malformations associated with HPE.[13]

Alobar HPE is the most severe and lethal form of HPE, typically associated with major facial (eg, cyclopia, as seen in our case) and extra facial abnormalities such as polydactyly, renal dysplasia, and omphalocele. These severe cases have a poor prognosis, with most resulting in stillbirth or death shortly after birth.[1,13] The survival rate correlates with the severity of brain malformation.[4] Facial abnormalities come with severe brain malformation, which can help predict severe cases through sonographic identification of facial dysmorphism.[13] Milder HPE forms are more compatible with life.[14]

The differential diagnosis includes hydranencephaly. However, the absence of midline structures exclaims this diagnosis.[12]

In severe cases, pregnancy termination should be discussed with the parents as soon as the diagnosis is clear. Pregnancy continuation is another option, considering the need for consultations with pediatric neurology, neurosurgery, and neonatology services.[11]

The mode of delivery depends on the presence of extra-facial abnormalities and other factors, as in any normal delivery. Our case had a special presented part, which was the posterior aspect of the neck and the shoulder, possibly due to the fetal head malformations.

The limitations of our management approach include the lack of prenatal and postnatal diagnostic testing. The case remained undiagnosed until delivery due to inadequate pregnancy follow-ups. Moreover, no serological or genetic tests were performed to identify the underlying etiology. Unfortunately, in resource-limited settings, diagnostic tests are not always readily available and may need to be prioritized for more urgent cases.

Conclusion

Early diagnosis of cyclopia is crucial due to the significant emotional impact on the family. Also, it allows them to make an informed decision about whether to continue the pregnancy. Many factors have been accused in causing holoprosencephaly; therefore, it is essential to investigate the potential causes using genetic and serological tests, including toxoplasma gondii tests if possible. Unique head malformations may lead to atypical presentations during delivery; however, vaginal delivery still be possible.

Abbreviation

HPE, Holoprosencephaly.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

This study is exempt from ethical approval in our institution.

Consent for Publication

Written informed consent was obtained from the parents for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Acknowledgments

We would like to thank the patient's parents for consenting to publish this case.

Funding

No funding was received for this research.

Disclosure

The authors declare that they have no conflicts of interest to disclose for this work.

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