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Synophtalmia on a newborn

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Abstract

Synophtalmia or cyclopia is a rare presentation of alobar holoprosencephaly. Cases which have been reported are stillborn or dead in post-delivery period. We are presenting a 3000-g live full-term newborn girl delivered by caesarean section with a well-marked cyclopia, but who died 30 min post-delivery. The case did not present with other abnormalities. The literature showed that genetic disorders are associated with cyclopia. A prenatal anomaly scan can help in the early detection of the condition and timely termination of the pregnancy can be conducted.

Keywords

Cyclopia, synophtalmia, newborn, Democratic Republic of the Congo

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Introduction

Synophtalmia or cyclopia is the most extreme sign associated with alobar holoprosencephaly, most severe form of holoprosencephaly (HPE); it's a rare birth defect with an incidence of 1 in 100,000 in newborns.[1] The condition was named after the single-eyed giant 'Cyclops' in Greek mythology. Various hypotheses and different causes have been investigated about the genesis of HPE. Clinically, the condition is characterized by one eye or double eyes in one orbit with a nose either missing or replaced with a non-functioning nose in the form of a proboscis which generally appears above the central eye providing a characteristic form of cyclopia called rhinencephaly. Different extracranial malformations (polydactyly, renal dysplasia and an omphalocele) have been reported to be associated with cyclopia depending on its underlying cause.[2,3]

Cyclopia has been reported to be associated with different risk factors including maternal diabetes, infections and genetic abnormalities.[4,5] The diagnosis of cyclopia is mostly established after 20 weeks of gestation by ultrasonography (USG).[1] To our knowledge, this is the first case of cyclopia reported in Democratic Republic of the Congo (DRC) and especially in eastern rural region of the country. We are presenting a case of synophtalmia term female newborn from a non-consanguineous marriage.

Case presentation

A 3000-g live full-term newborn girl delivered by caesarean section due to severe foetal distress. The baby was the second born from a 27-year-old female who attended four antenatal consultations without any prenatal ultrasound scan done and did not have any history of disease nor drugs abuse during the pregnancy. Moreover, the mother did not state any history of exposure to teratogens during pregnancy, especially in the first trimester. During history-taking at admission, the parents did not mention the history of congenital anomalies or close family marriages with their relatives. The newborn had a microcephalus with dysmorphic face, well-marked two corneum, absence of nose, micrognathia and a proboscis without other external abnormalities (Figure 1). The newborn's skin was cyanotic, possibly due to hypoxia. Her vital signs at birth were as follows: temperature: 36.0, heart rate: 176 beats per minute (bpm), respiration rate: 66 breaths per minute, and oxygen saturation: 80%. The baby succumbed 30 min post-delivery from respiratory failure. The parents did not consent for post-mortem examination; however, the parents of the baby were counselled, and a date

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Figure 1. Newborn baby with well-marked cyclopia with a proboscis and without any other visible external abnormalities.

of follow-up was given to continue psychological support and family planning for the next pregnancy.

Discussion

During the embryological period, primary neurulation is responsible for forming the neural tube. The neural tube forms three important structures: the forebrain, midbrain and hindbrain.[6] Holoprosencephaly results from incomplete separation of the forebrain into the right and left hemispheres between days 18–28 of pregnancy.[7] Pathogenesis of HPE requires an in-depth knowledge about relationship between the developing brain and the facial structures during embryogenesis. A number of signalling pathways control and coordinate the development of brain and face, including Sonic hedgehog (SHH), Bone Morphogenetic Protein (BMP), Fibroblast Growth Factor (FGF) and Nodal signalling.[8] *SHH* mutations are the most common genetic cause of HPE in humans and many of the HPE genes encode proteins that either directly or indirectly regulate SHH expression or signalling. Signalling from the ventral midline is critical for normal midface development, a process in which SHH plays a key role. Some environmental factors like retinoic acid or ethyl alcohol plays a role in SHH signalling. However, *SHH* mutations account for only a minority of overall HPE cases and carrying a mutation alone does not mean that an individual will manifest HPE.[9] Only about 37% of human carriers of *SHH* mutations develop HPE, while others display mild signs or no signs at all highlighting the complexity of HPE pathogenesis and complicating the process of genetic counselling.[8,9]

HPE is categorized into three types: lobar HPE, semilobar HPE and alobar HPE being the most severe form.[7] Cyclopia or synophtalmia is a clinical presentation associated with alobar HPE, a rare and lethal congenital malformation resulting from incomplete separation of prosencephalon into two halves of hemispheres during organogenesis leading to failure of cleavage of orbit into two cavities of eyes.[2,3] To our knowledge, this is the first case reported from the rural area of the eastern DRC. The face is either missing the nose or the nose is replaced with a proboscis which is a non-functional nose which appears above the central eye.[10]

Rare reported cases of cyclopia were associated with Patau Syndrome (trisomy 13), a rare chromosomal condition.[4] Although not proven, the SHH gene regulator was found to be involved in the separation of the single eye field into two bilateral fields resulting in cyclopia development.[11] Most cases are stillborn or dead few minutes post-delivery. Maternal exposure to teratogenic drugs (such as amidopyrine, corticosteroids, aspirin, lithium, anticonvulsants, retinoic acid and anticancer agents); alcohol; toxoplasmosis, rubella, cytomegalovirus, and herpes simplex (TORCH) infections; ionic radiation; and maternal diabetes have been reported to be associated with cyclopia.[1,12]

Knowing that 'the face predicts the brain', the cardinal facial features of cyclopia may include a median single eye or a partially divided eye in a single orbit, absent nose, and a proboscis above the eye. Other facial features are absent philtrum, otocephaly, and astomia or microstomia.[5,10] In this case, at birth, we found to have the typical facial features of cyclopia including a median single orbit with two corneum (synophtalmia), absence of nose, micrognathia and a proboscis above the eye (Figure 1).

Apart from facial features of cyclopia, there are other extra facial features reported and could include polydactyly, renal dysplasia, and omphalocele all of which can be detected by sonography if present and this depends on the underlying cause.[3,5] The presence of extra facial abnormalities carries a very poor prognosis and almost always associated with stillbirth.[1,3,5]

Sonography and magnetic resonance imaging (MRI) are the most helpful in the prenatal diagnosis of cyclopia and associated abnormalities;[1,13] however, for this case report, none of the abovementioned investigations was done due to their unavailability and that the anomaly was diagnosed after birth.

In terms of management, termination of the pregnancy should be offered in all cases after a detailed prenatal examination and appropriate genetic counselling. Postnatal chromosomal analysis and gross examination of the specimen can further contribute to the diagnosis of cyclopia.[1]

Since most of reported cases are either still birth or newborn dies just a few minutes post-delivery, there is a need to emphasize the need for awareness and education about the importance of antenatal check-ups about risk factors and investigations such as sonography and genetic tests.

Conclusion

Synophtalmia is a rare congenital anomaly. Its clinical appearance is a psychological trauma to parents and family members. Early and timely detection can prevent such trauma. A need of prenatal sonography should be encouraged to all pregnant women to detect such abnormality.

Author contributions

L.B.B. managed the patient and F.K.S. wrote the case report. M.M. and J.F. helped in editing the paper. F.K.S. contributed scientifically to this .paper. All authors read and approved the final version to be published.

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series

Informed consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article. 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.

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