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Case Report

Cyclopia: A Rare Congenital Malformation

Sunil Kumar Yadav, Arun Giri and Vijay Kumar Shah
Department of Pediatrics and Neonatology, Nobel Medical College and Teaching Hospital
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Abstract
Cyclopia is a rare and lethal congenital anomaly of the forebrain system, resulting from incomplete cleavage of prosencephalon into right and left hemispheres occurring between the 18th and the 28th day of gestation. Approximately 1.05 in 100,000 births are identified as infants with cyclopia, including stillbirths. Many teratogenic factors are identified as the causative factors for this anomaly which include irregular cholesterol biosynthesis, radiation exposure, viruses, alcohol intake and maternal diabetes. Many authors also suggest genetic etiology of this illness. We report a case of 35 year old lady $G_7P_6L_5$ with previous history of normal vaginal delivery who presented to us in second stage of labor. She delivered a male baby with a large head, a median single eye and absent nose with intact mouth. The baby died soon after the birth. This case is presented because of its rarity. Early ultrasound diagnostics and proper management of this anomaly must be emphasized most strongly to prevent complication associated with this condition.
Key words: *Cyclopia, single eye, large head*

Introduction

Cyclopia is a rare congenital anomaly characterized by a single midline orbit that contains ocular structures that could be monophthalmic, synophthalmic, or anophthalmic [1]. It results from incomplete cleavage of prosencephalon into right and left hemispheres occurring between the 18th and the 28th day of gestation [2]. Approximately 1.05 in 100,000 births are identified as infants with cyclopia, including stillbirths [3].

Three levels of increasing severity are described: alobar holoprosencephaly (cyclopia being the most severe form), with a single brain ventricle and no interhemispheric fissure; semi lobar holoprosencephaly with a partial separation; and lobar holoprosencephaly, where the right and left ventricles are separated, but with some continuity across the frontal cortex [4].

Cyclopia typically presents with a median single eye or a partially divided eye in a single orbit, absent nose, and a proboscis above the eye. Extra cranial malformations described in stillbirths with cyclopia include polydactyly, renal dysplasia, and an omphalocele.

The etiology of this rare syndrome, which is incompatible with life, is still largely unknown. Most cases are sporadic [5]. Heterogeneous risk factors have been implicated. Possible risk factors include: maternal diabetes [6]. The only formally recognized environmental factor with a 1% risk and a 200-fold increase in fetal holoprosencephaly), drugs during pregnancy [7, 8] (alcohol, aspirin, lithium, anticonvulsants, hormones, retinoic acid, anticancer agents, and fertility drugs), radiation exposure, chromosomal abnormalities [2] (mostly trisomy 13) and genetic causes (familial occurrences in

*Corresponding Author: **Dr. Sunil Yadav,** | E-mail: dr.sunil_yadav@yahoo.com

twins and in consanguineous marriages have been documented) [9]

Case presentation

We report a case of 35 year old unbooked $G_7P_6L_5$ at 34^{+2} weeks of gestation presented to the labor room of Nobel Medical College and Teaching Hospital (NMCTH) in second stage of labor. She had normal vaginal delivery in her previous and present pregnancies. She belongs to lower socioeconomic status with irregular antenatal check-up and no antenatal ultrasound scan was done in this pregnancy. There was no history of diabetes in mother or any teratogenic, radiation or drug exposure in first trimester. She delivered a male baby vaginally weighing 2.5 kg with congenital anomalies. The baby died after 15minutes of birth. On examination, the newborn was found to have a pink face and a trunk with peripheral cyanosis. Heart rate was 134 beats/minute and respiratory rate 32/minute, but Apgar score was not calculated because of congenital malformations. Head circumference was 38 cm, with a dysmorphic face, a median single eye, absence of nose, and micrognathia. In the face, there was no nasal aperture or proboscis in the midline. The external ears were normal. No cleft lip or cleft palate was noted, but there was micrognathia (Figure 1). In postnatal period, while reviewing the history, it was found that the baby was the product of consanguineous marriage which may be the etiological factor for this anomaly. Brain MRI could not be done, because baby expired after 15minutes of birth.

Chromosomal analysis and postmortem autopsy were not carried out as consent to these two procedures was not given by the father.

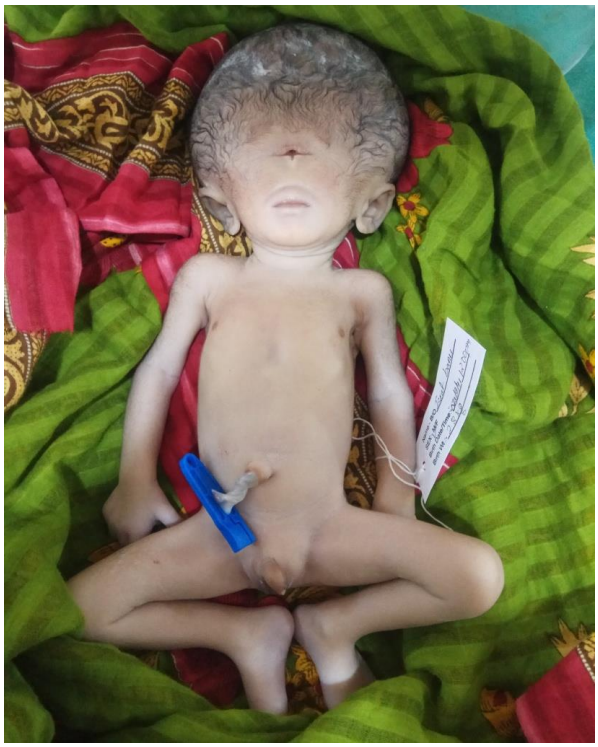

Figure 1: Cyclopic baby

Discussion

During the 4th week of gestation, the neural tube forms the three primary brain vesicles (prosencephalon, mesencephalon, and rhombencephalon) and by the 5th gestational week, the prosencephalon further divides into the telencephalon and diencephalon. The two cerebral hemispheres and the lateral ventricles arise from the telencephalon, whereas the thalami, hypothalamus and the basal ganglia arise from the diencephalon.

Holoprosencephaly refers to a group of disorders arising from failure of normal forebrain development during embryonic life. There are three forms of holoprosencephaly: alobar, semi lobar and lobar varieties, with alobar holoprosencephaly (cyclopia) being the most severe form and characterized by undifferentiated holosphere of the cerebral parenchyma with a central monoventricle, fused thalami, and absence of midline structures, such as corpus callosum and the midline falx cerebri [10,11,12,13].

*Corresponding Author: **Dr. Sunil Yadav,** | E-mail: dr.sunil_yadav@yahoo.com

Ultrasonography is the most helpful in the prenatal diagnosis of cyclopia [14,15,16] Holoprosencephaly can be expected to present in 16% or more of all cases of fetal hydrocephalous [17]. Even about 17% of fetuses with alobar holoprosencephaly reported by DeMyer[17] and 29% reported by Nyberg [14,18] had a nondiagnostic face at delivery, but when holoprosencephaly is suspected by sonography to be the case, careful intrauterine scanning of the face will allow a more definitive diagnosis of cyclopia. One has to remember the well-known phrase, "the face predicts the brain." 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.

In our case, a severe hydrocephalous and other facial features were missed because sonography was not done in antenatal period. At birth, our case was found to have the typical facial features of cyclopia including a median single eye, absence of nose, micrognathia. (Fig 1)

Apart from the facial features of the infant with cyclopia, extra facial features were reported and could include polydactyly, renal dysplasia, and an omphalocele, all of which can be detected by sonography if looked for them carefully. The presence of extra facial abnormalities carries a very poor prognosis and almost always associated with stillbirth [14,19].

Most live infants with cyclopia at birth were reported to have the typical facial features but no extra cranial ones. During literature review, we found only two reports of live newborn infants with cyclopia having extra facial malformations in addition to facial features: a live newborn with cyclopia and bladder exstrophy was reported by Mc Gahan et al.[14] and another baby with polydactyly was reported by Corsello et al [20].

The originality of our case is that it is the first case report of a live preterm infant with cyclopia, with typical facial features. Even it is allowed by medical law in many countries to terminate the pregnancy if major congenital abnormalities are detected during pregnancy, but in many other countries it is still not allowed for cultural, religious, and other reasons. In our case, because of poor antenatal visits and check-ups, this lethal anomaly could not be diagnosed early and hence could not be terminated medically. This case calls for urgent worldwide legitimization of pregnancy termination in indexed cases.

The last but not the least important fact is that even Holoprosencephaly is a syndromic malformation with many genetic causes, both with and without an associated chromosomopathy, and chromosomal analysis and postmortem autopsy can add to the diagnosis of cyclopia, but in our case they were not carried out as consent to these two procedures was not given by the father.

Conclusion

The prenatal diagnosis of cyclopia can be made early by ultrasound and the awareness of the spectrum of sonographic findings of cyclopia can improve the accuracy of prenatal diagnosis. Early ultrasound diagnostics and proper management of this anomaly must be emphasized most strongly to prevent complication associated with this condition. However, in developing countries where women do not receive regular antenatal care and do not undergo prenatal diagnosis, such cases will go undetected. The legitimization of pregnancy termination for indexed cases in many countries around the world should be revised.

*Corresponding Author: **Dr. Sunil Yadav,** | E-mail: dr.sunil_yadav@yahoo.com

Consent

Written informed consent was obtained from patient's father for publication of this case report.

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Conflict of Interest: None

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*Corresponding Author: **Dr. Sunil Yadav,** | E-mail: dr.sunil_yadav@yahoo.com