

Case Report

Cyclopia-holoprosencephaly sequence: a rare entity

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ABSTRACT

Cyclopia is a congenital disorder, a rare form of holoprosencephaly, characterized by the failure of embryonic prosencephalon to properly divide the orbits of the eye into two cavities with grossly incomplete morphogenesis of fore brain. The severity has a marked variability and ranges from cyclopia to minimal craniofacial dysmorphism, such as microcephaly with a single central incisor. Reports of this anomaly are few and because of the rarity, the present case is being reported.

Keywords: Cyclopia, Holoprosencephaly, Proboscis, Single eye

INTRODUCTION

Cyclopia is been of much interest because it presents a striking deviation from the normal mode of human development, it is frequently observed in lower forms of life like cat, fish, etc. Cyclopia is a serious median faciocerebral development deformity and usually the baby is stillborn or dies soon after birth.¹ Approximately 1.05 in 100000 births, including stillbirths, are identified as cyclopean.² The prevalence of holoprosencephaly is about 1 in 11000 to 20000 live births and 1 in 250 embryogenesis.³

CASE REPORT

Mrs X, 24 years old 2nd gravida, married at 21 years of age, a non-consanguineous marriage, with a 1st conception ended as a 6 month spontaneous abortion due to pregnancy induced hypertension, then conceived after 1 year without any drugs. She is an unregistered mother now came with 6 months amenorrhea for the 1st AN visit, with no H/O of fever/drug intake/radiation/decreased foetal movements/bleeding per vagina in the past, she worked as a laborer in a cloth whitening chemical factory during her 1st trimester.

Her present ante natal ultra-sonogram showed a bicornuate uterus with conception in the left horn, single live intrauterine foetus consistent with 21 weeks 0 days, semi lobar holoprosencephaly (Figure 1), facial anomaly with single eyeball visualized, diaphragmatic hernia & polyhydramnios.



Figure 1: Ultra sound showing semilobar holoprosencephaly.

In view of poor prognosis, pregnancy was terminated. He was a stillborn, extremely preterm (22 weeks) boy, weighing 600 gm, length of 27 cm, with the following severe midfacial defects (Figure 2).



Figure 2: Cyclopia.

- 1) Single orbital cavity, elliptical in shape with two rudimentary eyes at the lateral end of the ellipse on the upper part of the face with upper and lower eyelids fused in the midline. Few eye lashes were present on the upper border, both the lower eyelids had the punctum in the midline.
- 2) No nose, a tubular pendular mass (Proboscis) of 2 cm length & 10mm in diameter was found above the eye, which had a single opening in the tip & patent throughout up to 2 cm, not extending above.
- 3) Low set ears and bilateral post axial polydactyly in all the four limbs.
- 4) Cranium appeared normal. Genitalia normal for GA.
- 5) Renal system normal (by USG), spine and back normal (by X-ray) (Figure 3).



Figure 3: Babygram showing spine.

DISCUSSION

Arrhirencephaly - cebocephaly - cyclopia

Is a primary birth defect in prechordal mesoderm? During the 3rd week of fetal development, the prechordal mesoderm migrates forward into the area anterior to notochord, necessary for development of midface with induction role in morphogenesis of the fore brain. Consequence of prechordal mesoderm defects are varying degrees of defects of midline facial development, median nasal process (pre maxilla) & incomplete morphogenesis of the forebrain.¹ One among them is cyclopia.

Cyclopia is a severe deficit in early midline facial development, eyes become fused, the olfactory phacodes consolidate into a single tube like proboscis above the eye, ethmoid & other midline bony structures are missing, failure in cleavage of prosencephalon with grossly incomplete morphogenesis of fore brain. Other less severe defects are hypotelorism, absence of philtrum or nasal septum, single central incisor, congenital nasal pyriform aperture stenosis, missing frenulum of upper lip and these defects suggest possible serious anomaly of brain development and structure (Table. 1).

Holoprosencephaly is heterogeneous with both genetical and environmental causes. Causes are usually unknown. The probable causes are aneuploidy trisomy 13 & 18, structural chromosomal syndromes including del 12p21, dup 3pter, del 17q36, del 13q, del 18p, del 21q22.3 and

an autosomal dominant type of holoprosencephaly with wide variability is *shh* at 7q36.⁴ Mutations in other genes that have been identified in both sporadic and functional causes include *ZIC 2* at 13q32, *SIX 3* at 2p21, *tgfr* at 18p11.3 as well as a number of genes involved in

signalling pathways, important for brain development including patched 1 (*ptch*) GL12, which is involved in *shh* signalling & *tgfr* & *fast i* which is involved in the nodal/transforming growth factor B (TGF-B) pathway.⁵

Table 1: Consequences of incomplete cleavage and incomplete mid facial development.

Gestation age of insult	Consequence	Features	Common
Day 28 of gestation	Incomplete cleavage & morphogenesis of fore brain	Single ventricle, Absent corpus callosum, Fused thalamus, Incomplete anterior and posterior pituitary, Microcephaly, Severe MR, Apneic episodes, Seizures, Abnormal EEG, Infant death, Absent olfactory nerves, Absent optic nerves.	Cyclopia, Anophthalmia, Microphthalmia, Coloboma iris, Retinal defect.
Day 35 of gestation	Missing or incomplete midfacial development	Cleft lip, Cleft palate, Absent philtrum, Absent nasal septum, Single naris, Proboscis, Hypotelorism.	

To account for the evolution of cases with normal karyotype,⁶ maternal rubella, toxoplasmosis, alcoholism, diabetes, and drug treatment have been implicated as the etiological agents.¹ Few authors have described the role of maternal ingestion of drugs like salicylates in the evolution of cyclopia and other anomalies.⁷

Various authors have observed that early diagnosis of this anomaly is possible by using the ultrasound examination, and the mother can be counselled in preparation for pregnancy termination.⁸

Parents of the affected child may have single central incisors, missing upper lip frenulum, absence of nasal cartilage. In general, the prognoses of these anomalies are very poor.

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