

Cyclop deformity born to an eclamptic mother: a case report and literature review

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Abstract: Cyclopia is a rare congenital craniofacial abnormality considered the severest form of alobar holoprosencephaly. It is aetiopathogenically heterogeneous and incompatible with life. We report the case of a phenotypically female preterm stillbirth whose mother was severely pre-eclamptic. Prenatal ultrasonography revealed multiple congenital anomalies including microcephaly, fused sutures, hypotelorism, absent nasal opening and polyhydramnios. Postmortem confirmed cyclopia comprising a deformed face having a single central slit-like orbital groove possessing two eyes with a superiorly attached blind-ending proboscis, absent nose, and well-formed mouth. The brain consists of a non-cleaved frontal lobe overlying a single large ventricle with a membranous roof and absent olfactory tracts and bulbs. There is also absence of corpus callosum.

Keywords: Cyclopia, holoprosencephaly, proboscis, hypotelorism.

INTRODUCTION

Cyclopia is a rare congenital craniofacial anomaly presenting with a single median eye and varying degrees of duplication of the ocular structures [1]. There is usually a single palpebral fissure and a blind-ending proboscis as well as severe brain malformation. It is incompatible with life. Globally, Cyclops constitute approximately 1.05 in 100 000 births including stillbirths [2, 5].

CASE REPORT

The patient is a preterm female newborn delivered of a 32 year old Para ¹⁺² mother with pre-eclampsia. The baby was delivered by Caesarean section at 31 weeks of gestation owing to the condition of the mother. Prenatal ultrasonography revealed multiple congenital anomalies including microcephaly, fused sutures, hypotelorism, absent nasal opening and polyhydramnios.

Post mortem findings

Postmortem reveals a phenotypically female newborn with a deformed face having a single

central slit-like orbital groove possessing two eyes with a superiorly attached blind-ending proboscis, absent nose, and well formed mouth. The entire brain weighs 100g and consists of a non-cleaved frontal lobe overlying a single large ventricle with a membranous roof and absent olfactory tracts and bulbs. There is absence of corpus callosum and there is no pituitary gland in the sella tursica. The superior colliculi are enlarged while the inferior ones are unremarkable. There is grossly unremarkable brainstem and cerebellum. The two eyes are separated by periorbital adipose/connective tissue but they fuse posteromedially with a single third cranial nerve which bifurcate shortly and enter the brain. The irides are separate and there are no colobomata. The heart shows a large atrial septal defect with bilateral atrial dilatation. Other organs are grossly normal and located in the appropriate anatomical spaces.

Microscopically, the cerebral cortex is made of mass of hypocellular tissue with wavy pattern. The medial and lateral geniculate nuclei are absent and the thalamus and hypothalamus are compressed.



Fig 1: Cyclop showing a single central slit-like orbital groove possessing two eyes with a superiorly attached blind-ending proboscis, absent nose, and well-formed mouth.

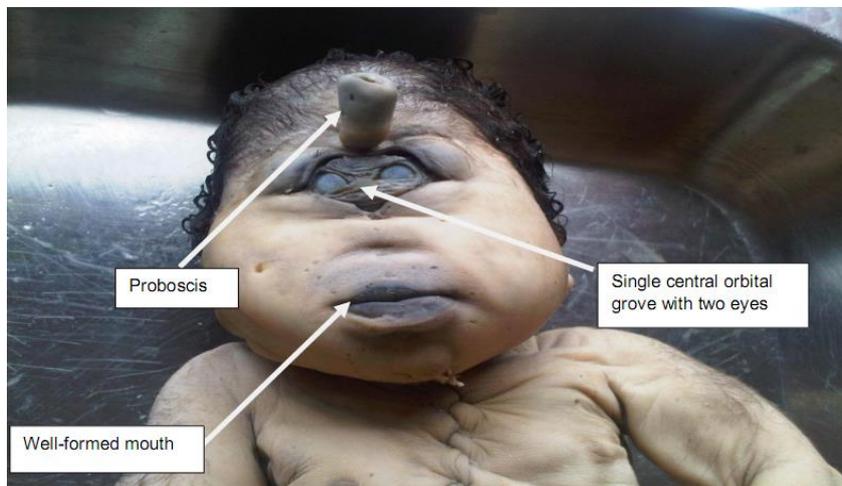


Fig 2: Close up of key facial features.

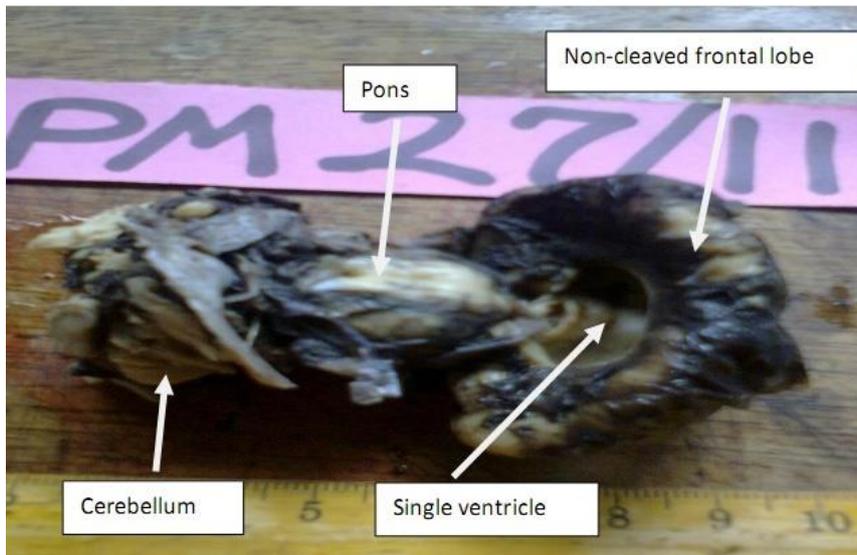


Fig 3: The brain showing a non-cleaved frontal lobe overlying a single large ventricle with a membranous roof and absent olfactory tracts and bulbs.

DISCUSSION

Holoprosencephaly (HPE) is a rare developmental craniofacial anomaly with failure of midline “cleavage” of the embryonic forebrain. Contrary to previously held belief that it was due to defective cleavage, it is now well understood that the forebrain anomalies result from primary defects in induction of growth of the affected midline structures [6, 13].

It can be classified into two groups namely (a) classic and (b) middle interhemispheric (MIH). Based on severity, the classic HPE is sub classified into alobar, semi lobar, and lobar subtypes, with alobar being the most severe. All classic HPE subtypes exhibit severe neuropathology of ventral predominance with variable affection of the rostral, dorsal, and posterior domains [6]. In alobar holoprosencephaly, the prosencephalon fails to cleave sagittally into cerebral hemispheres, transversely into telencephalon and diencephalon, and horizontally into olfactory tracts and bulbs [8,10]. Depending on the configuration of the dorsal lip of the holotelencephalon covering the membranous ventricular roof, alobar holoprosencephaly is further subdivided into the pancake type, the cup type, and the ball type [10]. In semi lobar holoprosencephaly, rudimentary cerebral lobes with incomplete mostly posterior interhemispheric fissure are present. The olfactory tracts and bulbs are usually absent. In lobar holoprosencephaly, the brain has largely well formed cerebral hemispheres that may be normal in size. There may be some midline continuity of the cingulate gyrus. The olfactory tracts and bulbs may be absent or hypo plastic and the corpus callosum may be absent, hypo plastic, or normal [10].

The MIH type (also called syntelencephaly) is defined by midline failure that is restricted to the dorsal forebrain, mainly affecting the posterior frontal and parietal lobes [6]. Syntelencephaly is characterized by segmental fusion of the cerebral hemispheres and thalamus as well as hypo plastic corpus callosum with variable septum pellucidum. Severe facial pathologies such as or facial clefts and hypotelorism are absent [6, 7].

The aetiopathogenesis involves chromosomal defects, genetic mutations and environmental teratogenic factors. Trisomy 13 is probably the most frequently associated chromosome aberration followed by 18p- and triploidy. Trisomies 18 and 21 as well as ring chromosome 18 also occur among other aberrations. Known mutations commonly found in association with holoprosencephaly involve the following genes; *Sonic Hedgehog (SHH)*, *ZIC2*, *SIX3*, *TGIF*, *PTCH*, *GLI2*, *FAST1*, *TDGF1*, *DHCR7* [10]. The environmental risk factors include ethanol, diabetic embryopathy, retinoic acid, viruses especially Cytomegalovirus (CMV) and salicylates [9,14,20].

CONCLUSION

Cyclopia is considered the severest form of alobar holoprosencephaly. Holoprosencephaly(HPE) is a developmental anomaly characterized by impaired midline “cleavage” of the embryonic forebrain. It is aetiopathogenically heterogeneous and incompatible with life.

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