

Case Report

Holoprosencephaly with cyclopia: a rare case report

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ABSTRACT

Holoprosencephaly (HPE) with cyclopia is a rare congenital anomaly of the forebrain system where due to deformation and hypoplasia of the facial skeleton, one eye orbit is formed in the place where both eyes should be present. Many teratogenic factors are identified as the causative factors for this anomaly which include irregular cholesterol biosynthesis, viruses, alcohol intake and maternal diabetes. Many authors also suggest genetic aetiology of this illness. We report a case of 32 year old lady G₂P₁L₁ with previous history of normal vaginal delivery who presented to us in second stage of labour. She delivered a female fetus with multiple defects and later diagnosed as a case of holoprosencephaly with cyclopia. 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.

Keywords: Holoprosencephaly, Cyclopia, Micrognathia, Uncontrolled diabetes

INTRODUCTION

Cyclopia is a rare congenital fetal anomaly characterized by a single palpebral fissure and a proboscis associated with severe brain malformations. Approximately 1.05 in 100000 births, including stillbirths, are identified as cyclopean.¹ The prevalence of holoprosencephaly (HPE) is about one in 11000 to 20000 live births and one in 250 embryogenesis.² HPE results from incomplete cleaving of the telencephalic vesicles. Holoprosencephaly (HPE) with Cyclopia is a rare and life threatening median faciocerebral development deformity.³

CASE REPORT

We report a case of 32 year old unbooked G₂P₁L₁ at 37⁺² weeks of gestation presented to our labour room in second stage of labour. She had a previous normal vaginal delivery in her first pregnancy. 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 any teratogenic exposure in first trimester. She delivered a female fetus weighing 2.2 kg with multiple congenital anomalies. The baby died soon after birth. On gross examination, there was a single eye in mid-forehead (cyclopia) (Figure 1).



Figure 1: Cyclopic baby.

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. All other organs of the baby were normal and no other congenital malformations were found. In postnatal period, on evaluation the mother was found to have uncontrolled diabetes which may be the etiological factor for this anomaly. The fetal autopsy was denied by the parents because of religious beliefs.

DISCUSSION

During embryogenesis, the prechordal mesoderm not only forms the median facial bones but also induces rostral neuroectodermal differentiation and morphogenesis. Defects in the prechordal mesoderm can lead to the arrest or malformation of the facial bones and organogenetic cleavage of the prosencephalon.³ The mandible may also be affected along with other facial bones, leading to micrognathia as in our case.

HPE is classified into three types:

1. Alobar, which means the complete absence of division of the prosencephalon structures, resulting in completely absent interhemispheric fissure and corpus callosum, fused thalami, fused cerebral hemispheres with only one cerebral ventricle, and facial dysmorphism which include such abnormalities as cyclopia, proboscis, ethmocephaly and cebocephaly. It is the most severe form.
2. Semilobar, consisting in incomplete separation of the cerebral hemispheres: there are two cerebral hemispheres connected in the frontal area, with a singular ventricular cavity and partially fused thalami.
3. Lobar, in this case interhemispheric fissure is present, septum pellucidum is absent and frontal horns of lateral ventricles communicate freely, corpus callosum is absent hypoplastic or normal, with midline fusion of cingulate gyrus. It is the least severe form.

There are three types of eye deformities seen in cyclopia: one eye (monophthalmia), two fused eyeballs (synophthalmia) or complete absence of eyeballs (anophthalmia). The fetus in this case report had monophthalmia (Figure 1).

The etiology of HPE includes genetic and environmental factors. Among the environmental causes there are: maternal diabetes mellitus, maternal alcoholism, *in utero* infections with CMV, rubella or toxoplasma, some drugs (retinoic acid, cholesterol synthesis inhibitors).⁴ HPE can be transmitted in an autosomal dominant way. Mutation of SHH gene is the most frequent cause of familial HPE.⁵ Also, HPE is associated in 40% of cases with numerical

chromosomal anomalies, the most frequent one being trisomy 13.⁵

HPE can also be associated in about 25% of the cases with several defined multiple malformation syndromes with a normal karyotype, like Smith-Lemli-Opitz, Pallister Hall or velo-cardio-facial syndrome.⁴ In the presented cases, the mother had uncontrolled diabetes which may be the etiological factor.

The Clinical features are variable and depend on the degree of severity of holoprosencephaly. The midfacial defects include absence of the eyes, cyclopia, proboscis, cebocephaly (hypotelorism associated with a single nostril), cheilo/palatoschisis, agnathia or micrognathia. Cyclopia, proboscis and cheilo/palatoschisis are associated with severe and life-threatening forms of HPE.⁶ Microcephaly, or, rarely, macrocephaly, suggesting the presence of hydrocephaly.⁷ Mental retardation directly correlated with the severity of HPE. Neurologic manifestations like seizures, hyper/hypotonia, dysphagia, dysphonia, extrapyramidal disorders, like chorea or dystonia are frequently observed. Endocrine dysfunctions like hypopituitarism and diabetes insipidus also seen.⁵

In antenatal period HPE can be diagnosed by ultrasonography, which shows polyhydramnios, hypotelorism, cyclopia, proboscis, cheilo/palatoschisis, single cerebral ventricle. The diagnosis could be made in most cases of alobar and semilobar holoprosencephaly after 17 weeks of gestation, when the production of cerebrospinal fluid starts.⁵ In lobar cases diagnosis could be difficult because the antenatal picture of septo-optic dysplasia is almost identical to that of lobar holoprosencephaly.⁶ Unfortunately, our patient was not registered for antenatal care in our hospital; hence no ultrasound examinations could be performed earlier and diagnosis could not be made. Other diagnostic modalities include fetal MRI, Cytogenetic analysis and molecular analysis of fetal DNA.⁵

The management of HPE is supportive and is oriented towards different malformations associated. Prognosis is dependent upon the degree of fusion and malformation of the brain, as well as other health complications that may be present. Alobar and semilobar HPE are lethal. Children born with lobar HPE can survive for years, but encounter a lot of neurologic manifestations and severe mental retardation.

CONCLUSION

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.

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