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Case Report

# A Case Report: Alobar Holoprosencephaly

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## Abstract

Holoprosencephaly (HPE) is a developmental disorder. It's a rare congenital and the most common human forebrain malformation, occurs in 1 in 250 fetuses and 1 in 16,000 live births. Occurring due to incomplete cleavage of the prosencephalon. It is seen between the 18th and the 28th day of gestation. It is affecting face and forebrain and is associated with multiple midline facial anomalies. Herewith we report an antenatal case of such patient. Patient was evaluated and because of the lethal anomalous fetus, induction was done which led to a stillborn baby. The focus of this article will be on the pathophysiology of findings visible in fetal manifestation of the HPE spectrum.

**Keywords:** Pathophysiology of Holoprosencephaly; Environmental factors; Antenatal Detection; Developing Countries; Prognosis.



## INTRODUCTION

De Myer *et al*. determined Holoprosencephaly (HPE) is a developmental field defect caused primarily by impaired or incomplete midline division of the prosencephalon into distinct halves[1]. Classically, HPE brains were classified into the alobar, semi lobar and lobar types, depending on the degree of the interhemispheric division, but recent studies have identified less severe brain phenotypes, such as absent olfactory tracts and bulbs (arrhinencephaly) and agenesis of the corpus callosum [2]. HPE is often associated with characteristic facial dysmorphism, such as cyclopia, ethmocephaly, cebocephaly, median cleft lip, and single maxillary central incisor [1, 2].

Abnormalities of formation are rare, consisting of aprosencephaly and atelencephaly. The disorders of cleavage result into classic HPE spectrum.

Midline development abnormalities includes agenesis of the corpus callosum, septo-optic dysplasia (SOD), and isolated absence of the cavum septum pellucidum. In early human brain development process, the forebrain is divided into telencephalon and diencephalon. Telencephalon develops into cerebral hemispheres and subcortical structures such as basal ganglia, amygdala, and hippocampus. Thalamus and hypothalamus develop from Diencephalon [3].

## CASE REPORT

A 25-year-old, gravida 1 underwent antenatal ultrasonography. The indication for this US examination is to rule out any structural anomalies in the current pregnancy.

The ultrasound examination revealed a singleton intra-uterine live fetus in unstable lie. The biometric parameters correspond to 19-20Weeks.There is polyhydramnios. AFI-20.1cms. Biometric parameters are S/O fetal growth restriction.

### HEAD, NECK

There is Alobar Holoprosencephaly. Evidence of fused thalamus with absence of third ventricle, Cavum septum pellucidum, corpus callosum and interhemispheric fissure. There is single ventricle with horseshoe configuration.

### SPINE

The spine is well visualized from cervical to sacral region, within resolution of the ultrasound equipment without any evidence of a neural tube defect.

### FACE

Fetal face was seen in the coronal and profile views. There are close-set eyes with hypertelorism, Nose appears flattened, Evidence of proboscis.

**THORAX**

Anatomy of fetal thorax appears normal. Both lungs are seen. No any pleural effusion / pericardial effusion are noted.

**HEART**

The cardiac size and structures appear sonographically normal at four-chamber view, outflow tracts are seen and cardiac rhythm is regular. The FHR was 151 bpm. (This is not complete cardiac study report)

**ABDOMEN**

Anterior abdominal wall is intact. Stomach is seen on left side. Fetal liver showed normal echogenic pattern. Small bowels are forming.

**KIDNEYS BLADDER**

Both kidneys are well visualized. The pelvi-calceal differentiation and Renal pelvis is normal. Bladder is well visualized.

**EXTREMITIES**

All extremities are seen at the time of examination and showed normal size and shape. Mineralization appears normal for the gestational age. Both feet are seen and do not show any abnormality. Active movements of the extremities is seen and fetal body motion was also observed during this examination.

**FETAL ENVIORNMENT**

The placenta is forming over the anterior wall. There is no placenta previa. Retro placental area appears normal. Cord shows 3 vessels. Abdominal cord insertion is normal.

**LIQUOR**

There is polyhydramnios. AFI-20.1 cms.

**CERVIX**

The cervical length is measured trans-abdominally and is 4.5 cm**.** No funneling was seen at the internal os.

**FETAL GROWTH**

Biometric parameters are S/O fetal growth restriction. 3D and 4D study

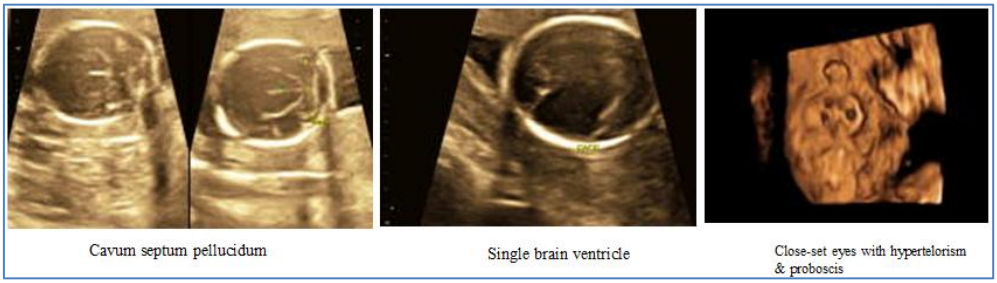


**Fig-1**

## CONCLUSION

There is single viable gestation of 19-20 weeks.

USG finding S/O Alobar Holoprosencephaly

There is polyhydramnios

Based on the ante-natal sonographic findings a diagnosis of alobar holo-prosencephaly was made.

As it was a lethal anomaly, preterm induction of vaginal delivery was done which resulted in a stillborn fetus. Examination of the fetus demonstrated gross facial anomaly. Brain morphology could not be assessed due to autolysis.

**Fig-2**

## DISCUSSION

It has been found that genetic and environmental factors are responsible for the pathogenesis of holoprosencephaly. Defective sterol metabolism leading to abnormalities in the sonic hedgehog (SHH) signaling pathway may have a role in its causation [4-7]. However, many genes besides SHH have also been associated with holoprosencephaly[8].

It can be diagnosed prenatally by karyotype analysis, microarray testing, ultrasonography, and magnetic resonance imaging (MRI) [9-11]. Abnormal Karyotype is found in about a third of holoprosencephaly cases, with trisomy 13 being the most common such anomaly [12, 13].

Recently, gene dosage methods like Quantitative Multiplex PCR of Short Fluorescent Fragments (QMPSF) or Multiplex Ligation Probe Amplification (MLPA) (MRCHolland), were added to the molecular diagnosis process14.

Large deletions in *SHH*, *ZIC2*, *SIX3* and *TGIF* are found in 8% of the cases (4% in alive children and 12% in fetuses) [15,16].

While the proportion of point mutations is higher in living children than in fetuses, part of deletions is, on the contrary, higher in fetuses than in living patients, which may explain the more severe phenotype in fetuses leading to termination of pregnancy.

Monogenic inheritance of nonsyndromic HPE includes autosomal dominant transmission with variable expressivity and incomplete penetrance; autosomal recessive transmission; and X-linked transmission [17]. Cohen and Shiota *et al*. explained, some environmental factors have been implicated in human HPE, and it is accepted that maternal diabetes mellitus, ethyl alcohol, and retinoic acid can cause HPE in humans.

In addition, polygenic mechanisms and gene–environmental interactions probably play a major role in the genesis of human HPE [18, 19].

A systematic search for gains or losses in the subtelomeres by MLPA led to the identification of about 4.3% novel rearrangements involving known but also novel HPE loci.But, at the moment, this approach still concerns research.

## CONCLUSIONS

In general, the severity of any facial defect depends on the severity of the brain defect. However, the case here shows facial alteration and important brain defects, therefore the type of HPE could be described as alobar form of HPE.

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