

# Case Report

## Two Cases of Holoprosencephalies

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### Abstract

Two pregnant women with around 33-34 weeks of gestation were reported to Gynaecology and Obstetrics OPD of North Bengal Medical College Hospital, Bangladesh for last trimester antenatal checkup. They were primigravida with around 23-25 years of ages without previous antenatal check up. Both of them had normal course of pregnancy. Ultrasounds of pregnancy profile were done. It was observed in first case that septum pellucidum was absent in brain with partially formed falx cerebri, interhemispheric fissure. Occipital horn was rudimentary and thalami and basal ganglia were partially separated. This case was diagnosed as a case of semi lobar holoprosencephaly. In another case, septum pellucidum, falx cerebri and interhemispheric fissure were absent. Ventricle was monoventricular in appearance and thalami were fused. This case was diagnosed as a case of alobar holoprosencephaly. The importances of these classical cases of alobar and semi lobar holoprosencephalies are to make aware the radiologists to the imaging manifestations of holoprosencephalies and come to early diagnosis. If these cases are being diagnosed at an early stage of pregnancy, medical termination of pregnancy can be performed and maternal psychological trauma of bearing a deformed fetus can be avoided.

**Key words:** Alobar and semi lobar holoprosencephalies, Antenatal ultrasonography.

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### Introduction

Holoprosencephaly (HP) is a congenital anomaly occurs due to lack of cleavage of the prosencephalon. Although relatively rare, it is the most common anomaly that involves both the brain and the face. Prenatal diagnosis of this anomaly using ultrasonography is difficult and Magnetic resonance imaging (MRI) has recently become an important complement to ultrasound in prenatal diagnosis. HP is the most common anomaly affecting the ventral forebrain, occurring in 1/250 embryos and 1/8300-16,000 live births<sup>1,2</sup>. Modern ultrasound imaging devices have increasingly allowed sophisticated prenatal diagnosis of fetal disorders. Embryopathologic and ultrasound findings are reported in five cases of alobar holoprosencephaly that were

diagnosed prenatally, two cases as early as 23rd menstrual weeks<sup>3</sup>. Classically three subtypes of Holoprosencephaly have been recognized, however additional entities are now included in the spectrum of the disease. The three main subtypes, in order of decreasing severity are alobar holoprosencephaly, semilobar holoprosencephaly and lobar holoprosencephaly. It is usually obvious at birth even if antenatal diagnosis has not been made, due to associated midline facial anomalies including 3 proboscis, cyclopia, cleft lip and/or palate, ocular hypotelorism and solitary median maxillary central incisor. Additionally these children also have systemic problems, with poor feeding, hypothalamic/pituitary dysfunction and developmental delay<sup>4</sup>.

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The fundamental problem is a failure of the developing brain to divide into left and right halves (which normally occurring at the end of the 5th week of gestation). This results in variable loss of midline structures of the brain and face as well as fusion of lateral ventricles and the 3rd ventricle. Environmental factors such as maternal diabetes mellitus, alcohol use, and retinoic acid have been implicated in the pathogenesis, as has mutation of a number of genes including Sonic hedgehog and ZIC2, on chromosome 13q32<sup>5</sup>. Alobar holoprosencephaly is visible on all modalities, but in general is identified on antenatal ultrasound (if performed), and best characterized by MRI. On ultrasound there are monoventricle, fused thalami, absent corpus callosum, absent interhemispheric fissure, absent cavum septum pellucidum, absence of 3rd ventricle, middle and anterior cerebral arteries may be replaced by tangled branches of internal carotid and basilar vessels and severe facial malformations. On MRI, single midline monoventricle (or holosphere) with absence of lateral and third ventricles, absence of midline structures like absent septum pellucidum, agenesis or hypoplasia of the corpus callosum, interhemispheric fissure and falx cerebri, absent olfactory tract, dorsal cyst of holoprosencephaly, absent, fused or normal optic nerves and middle and anterior cerebral arteries may be replaced by tangled branches of internal carotid and basilar vessels. Associated craniofacial features may also be present which include proboscis, mono-orbit/cyclopia, mono-nostril, hypotelorism and cebocephaly<sup>6,7</sup>. As will most cerebral structural congenital abnormalities, semilobar Holoprosencephaly is visible on all modalities, but in general is identified on antenatal ultrasound, and best characterised by MRI. The basic structure of the cerebral lobes are present, but are fused most commonly anteriorly and at the thalami and there is partial diverticulation of brain (dorsal cyst). Features include<sup>8-9</sup> absence of septum pellucidum, monoventricle with partially developed occipital and temporal horns, rudimentary falx cerebri: absent anteriorly, incompletely formed interhemispheric fissure, partial or complete fusion of the thalami, absent olfactory tracts and bulbs, agenesis or hypoplasia of the corpus callosum and incomplete hippocampal formation. An easier approach might be to assess fusion of more than 50% of the frontal lobes which might be suggestive of semilobar HPE. In addition, this condition is associated with mild degree of facial abnormality such as hypotelorism and cleft lip.

## Case Report

Two pregnant women with around 33-34 weeks of gestation were reported to Gynaecology and Obstetrics OPD of North Bengal Medical College Hospital, Bangladesh for last trimester antenatal checkup. They were from shoal area from the bank of river Jamuna. Both parents were healthy and the marriage was nonconsanguineous. There was no family history of birth defects in both cases. They were primigravida with around 23-25 years of ages. None of them had previous antenatal check up. Both of them had normal course of pregnancy. On examination, they were normotensive, mildly anaemic, non-icteric. On per abdominal examination, fundal height corresponded to 30 weeks of pregnancy. With this findings they were advised for CBC, RBS, Blood Grouping and Screening for HbsAg and ultrasonography of pregnancy profile. Blood chemistries were unremarkable. Ultrasounds of pregnancy profile were done at Department of Radiology and Imaging. It was observed in first case that septum pellucidum was absent in brain with partially formed falx cerebri, interhemispheric fissure with presence of large dorsal interhemispheric cyst (Figure 1).

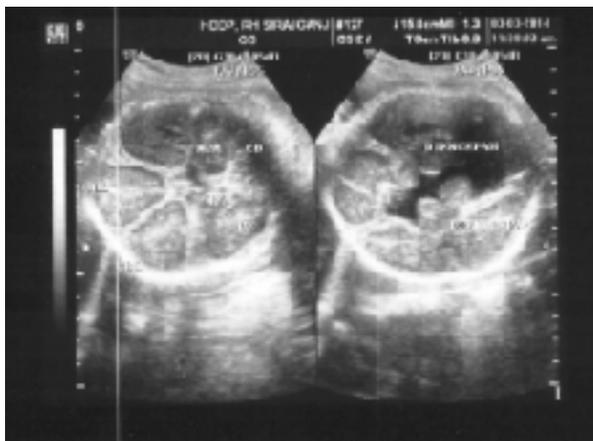


**Figure No. 1:** Ultrasonographic Scan of foetal head showing large dorsal interhemispheric cyst in semi lobar holoprosencephaly.

Occipital horn was rudimentary and thalami and basal ganglia were partially separated (Figure 2 and Figure 3). The spine, thoracic cage, heart, and limbs were sonologically normal. The posterior fossa structures were normal (Figure 3).

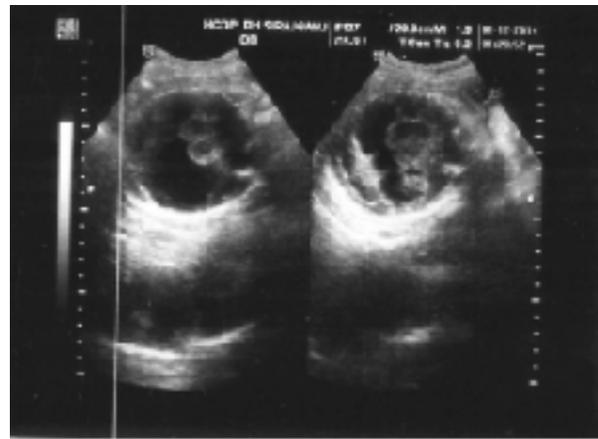


**Figure No. 2:** Coronal ultrasonography of foetal head of semi lobar holoprocencephaly showing absence septum pellucidum in brain with partially formed falx cerebri, interhemispheric fissure.

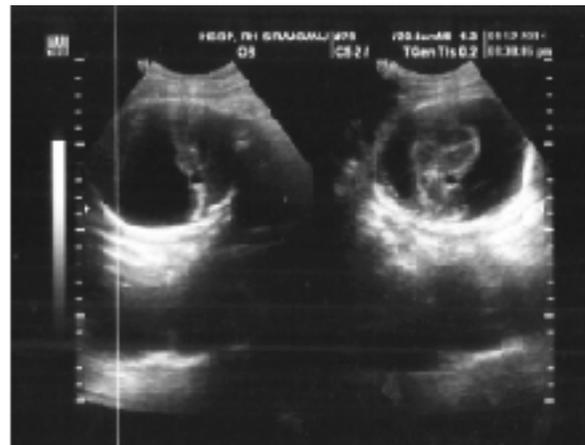


**Figure No. 3:** Ultrasound scan showing rudimentary occipital horn and partially separated thalami and basal ganglia in semi lobar holoprocencephaly.

This case was diagnosed as a case of semi lobar holoprocencephaly. In another case, septum pellucidum, falx cerebri and interhemispheric fissure were absent. Ventricle was monoventricular in appearance and thalami were fused (Figure 3 and figure 4).



**Figure No. 4:** Coronal scan of foetal head of Alobar holoprocencephaly showing mono ventricle with fused thalami and absence of septum pellucidum, falx cerebri and interhemispheric fissure.



**Figure No. 5:** Coronal scan of foetal head of showing mono ventricle and absence of falx cerebri in Alobar holoprocencephaly.

This case was diagnosed as a case of alobar holoprocencephaly. Amniotic fluid was adequate in both of the cases at ultrasonography. Further evaluation by other imaging modalities were not possible in these two cases as parents did not give consent to perform any test and also refused to take treatment for this unfortunate pregnancies.



**Figure No. 6:** Coronal ultrasound image showing the fused thalami in the centre and large monoventricle (thick white arrow). The amniotic fluid around the fetus is normal in quantity.

## Discussion

Holoprosencephaly is a spectrum of cerebrofacial anomalies resulting from the complete or partial failure of the diverticulation and cleavage of the primitive forebrain. During the 4th gestational week, the neural tube forms the three primary brain vesicles, namely, prosencephalon, mesencephalon, and rhombencephalon. By the 5th week of intrauterine life, the prosencephalon further divides into the telencephalon and diencephalon. The telencephalon forms the two cerebral hemispheres whereas the diencephalon forms the thalami, the hypothalamus, and the basal ganglia. The prechordal mesoderm takes part in the formation of the midline facial structures. The degree of facial dysmorphism is proportional to the severity of the intracranial abnormalities and should direct the radiologist to search for the CNS anomalies<sup>1,2,10</sup>. There are three main forms of holoprosencephaly, namely, alobar, semilobar and lobar varieties. The alobar holoprosencephaly is the most severe form and shows undifferentiated holosphere of the cerebral parenchyma with a central monoventricle and fused thalami<sup>1,3</sup>. The falx, interhemispheric fissure,

corpus callosum, optic tracts, olfactory bulbs, and the septum pellucidum are absent. Absence of septum pellucidum may be associated with septooptic dysplasia, holoprosencephaly, corpus callosal agenesis, schizencephaly, Chiari-II malformation, hydranencephaly, porencephaly, and cephaloceles (Figure 6)<sup>5,6,10</sup>. In present case of alobar holoprosencephaly septum pellucidum, falx cerebri and interhemispheric fissure were absent. Ventricle was monoventricular in appearance and thalami were fused. A dorsal cyst may be observed in the posterior cranial fossa in very severe forms of holoprosencephaly (alobar) and some of these cases may also be associated with Dandy Walker malformation, agyria, polymicrogyria, and heterotopias<sup>8,9</sup>. In present case reports dorsal cyst was seen in semi lobar holoprosencephaly. Alobar holoprosencephaly can be differentiated from hydrocephalus by the presence of midline echogenic falx, absent septum pellucidum, separated thalami, and distinct lateral ventricles in the latter. Hydranencephaly may also demonstrate absence or deviated falx but the thalami are not fused in this condition. In both hydranencephaly and Dandy Walker malformation, the falx cerebri, interhemispheric fissure, corpus callosum, and 3rd ventricle are present<sup>1</sup>. However, the role of maternal MRI is in the confirmation of the sonographic findings and detection of any other additional anomaly. Postnatal MRI with diffusion fiber tractography may detect rare association of brain stem and long tract abnormalities in holoprosencephaly<sup>10</sup>. The lobar and middle hemispheric variants are not associated with significant abnormalities of the white matter tracts whereas the alobar and semilobar forms are associated with abnormalities of the medial lemniscus and the corticospinal tracts<sup>10</sup>. Ultrasonography features of semilobar holoprosencephaly include<sup>8,9</sup> absence of septum pellucidum, monoventricle with partially developed occipital and temporal horns, rudimentary falx cerebri: absent anteriorly, incompletely formed interhemispheric fissure, partial or complete fusion of the thalami, absent olfactory tracts and bulbs, agenesis or hypoplasia of the corpus callosum and incomplete hippocampal formation. In present case of semilobar holoprosencephaly, the septum pellucidum was absent in brain with partially formed falx cerebri, interhemispheric fissure with presence of large dorsal interhemispheric cyst. Occipital horn was rudimentary and thalami and basal ganglia were partially separated. Fetal karyotyping is advisable in all the cases of holoprosencephaly as most of them are associated with chromosomal anomalies<sup>9,10</sup>.

However, karyotyping can not perform in all cases. Advanced investigations like fetal karyotyping is also not be available in all the places. So, antenatal diagnosis of holoprosencephaly by ultrasonography is essential in order to early diagnosis and to avoid the psychological pain of giving birth of a deformed baby at the end of pregnancy or delivering a still born baby.

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