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Case Report: A rare case of Alobar holoprosencephaly with Cyclopia and Proboscis

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Abstract: *Antenatal case report of a 28 year old woman with obstetric score of $G_3P_2L_2A_0D_0$ referred for routine obstetrical sonogram showing a single live intrauterine fetus of 25 weeks 0 days with features of Alobar Holoprosencephaly with Cyclopia and Proboscis. The incidence of holoprosencephaly is about 1 in 10,000 to 20,000 births. Alobar holoprosencephaly with Proboscis and a single midline eye (Cyclops) as in this case is a rare finding. The pregnancy was terminated and the gross specimen of the fetus confirmed all the external findings seen on imaging and the mother was counselled regarding the case and regarding the minimal risk of recurrence in subsequent pregnancies.*

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I. Introduction

Holoprosencephaly (HPE) results from a primary defect of ventral induction and patterning that results in total or partial failure of separation of the prosencephalon into two separate hemispheres. The incidence of holoprosencephaly is about 1 in 10,000 to 20,000 births[1,2]. Alobar holoprosencephaly with Proboscis and a single midline eye (Cyclops) as in this case is a rare finding. The holoprosencephalies are a group of disorders that develop as a result of abnormal differentiation and cleavage of the prosencephalon. Holoprosencephalies are commonly divided into three subcategories based on severity: alobar, semilobar, and lobar. In alobar holoprosencephaly, prosencephalic cleavage fails, resulting in a single midline forebrain with a primitive monoventricle often associated with a large dorsal cyst. Cyclopia, the most striking visual manifestation of HPE, has engendered a rich mythologic tradition [3].

II. Case Presentation

A 28 year old woman Gravida 3, Para 2,Live 2 was referred for a routine obstetrical sonogram. Her last menstrual period was unknown. Her biologic standard tests were normal. She and her husband are not from the same family. The patient was scanned on a Samsung Ultrasound System. Sonography revealed a singleton male fetus of 25 weeks 0 days with following findings:

FETAL HEAD:

- Fetal cranium shows fused Thalami and a large monoventricle, Falx cerebri and Cavum septum pellucidum are absent[Figure 1 and 2].
- Transcerebellar Diameter measures 27m corresponding to 24 weeks 04 days [Figure 3]

FETAL FACE:

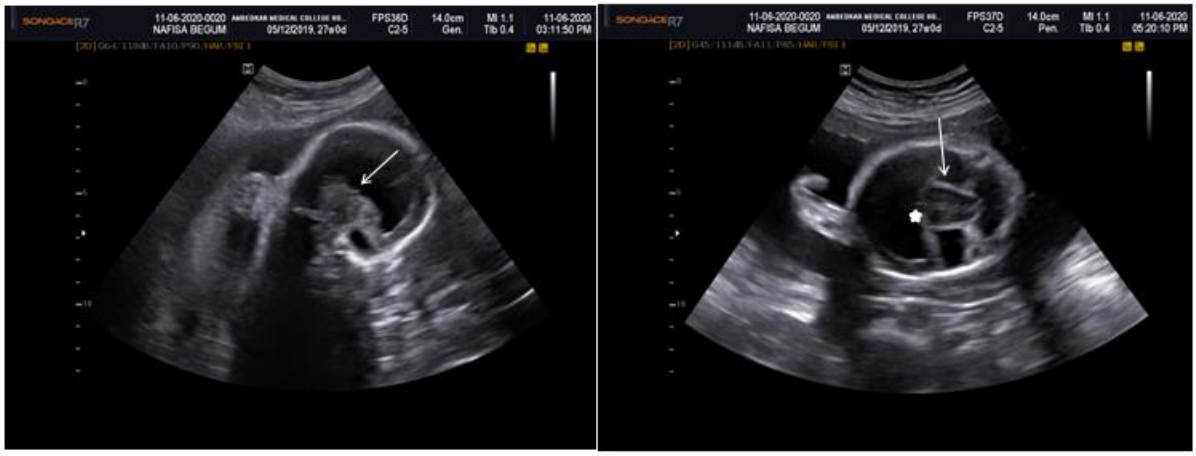
- Nasal bone not visualized.
- Midface appears hypoplastic with a midline Proboscis [Figure 4 and 5].A single midline Orbit is seen [Fugure 6].
- Fetal lips appears to be normal [Figure 7].

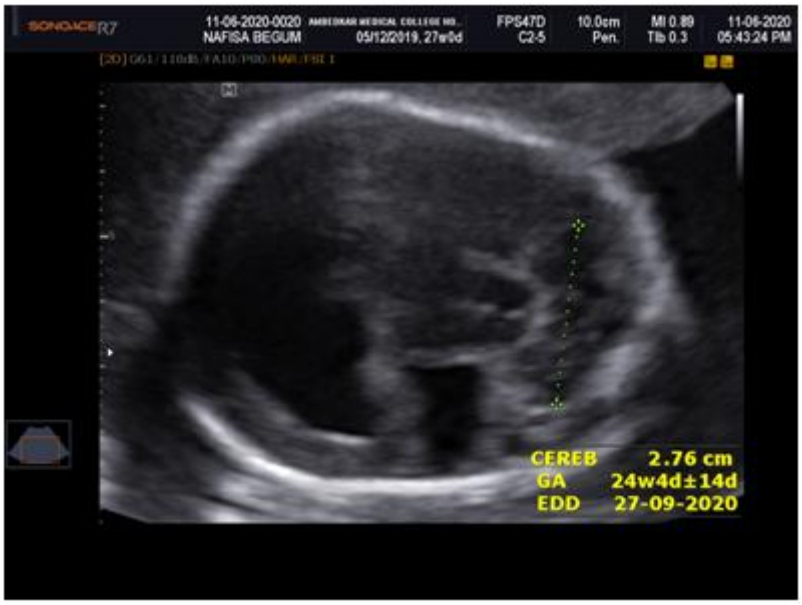
FETAL THORAX:

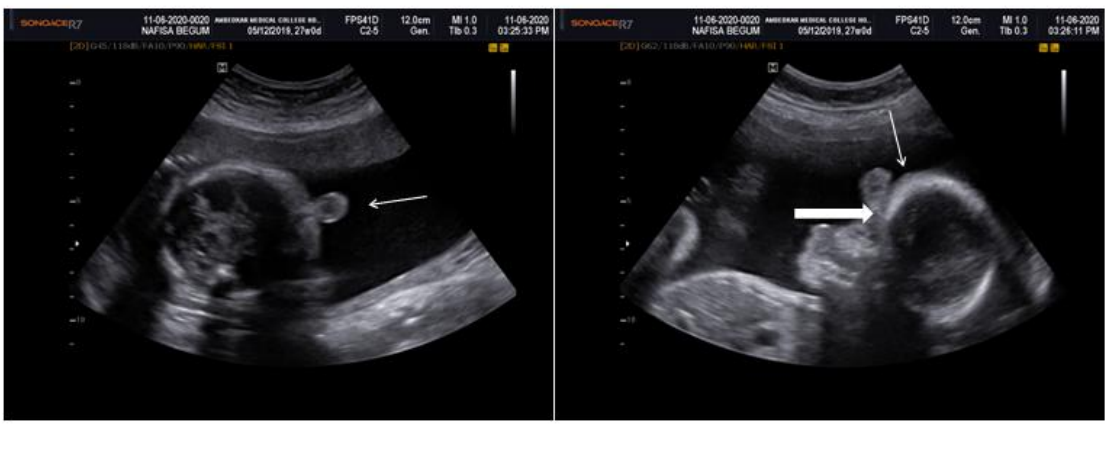
- Four chamber view of the heart shows hypoplastic Left Ventricle (LV) and Left Atrium [Figure 8].
- Left Ventricle shows an echogenic focus measuring 3mm [Figure 9].

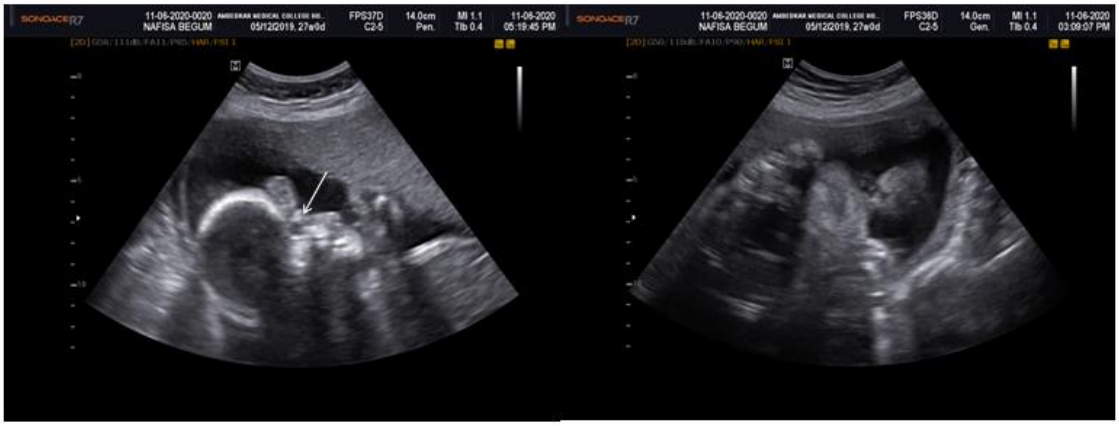
Fetal Abdomen, Spine and Limbs were normal to the extent visualized.
The pregnancy was terminated and the gross specimen of the fetus [Figure 10 and 11] confirmed all the external findings seen on imaging.

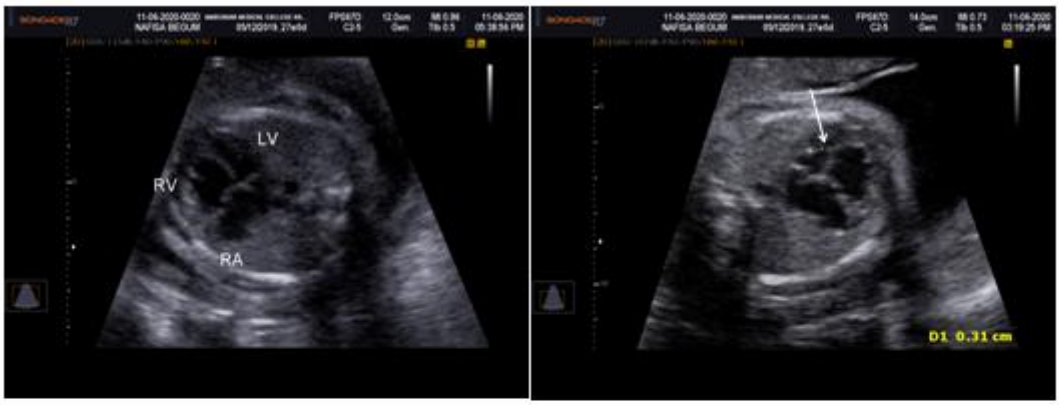
III. Figures










LV
RV
RA
D1 0.31 cm

IV. Discussion

The incidence of holoprosencephaly (HPE) is about 1 in 10,000 to 20,000 births [1,2]. Holoprosencephaly is usually sporadic, and the cause is unknown in most cases[4]. However, the disorder can be associated with a variety of chromosomal abnormalities such as trisomy 13, ring chromosomes and deletions [5-8].The risk of recurrence is estimated at 13%[9]. As the majority of cases of HPE are sporadic and clinically unsuspected[10], routine obstetric sonography is a potentially important means of prenatal diagnosis[11].

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 sonologist to search for the CNS anomalies. This has led to the popular statement "face predicts the brain" by DeMeyer[12].

There are three main forms of holoprosencephaly, namely, alobar, semilobar, and lobar holoprosencephaly. In Alobar HPE, prosencephalic cleavage fails, resulting in a single midline forebrain with a primitive monoventricle often associated with a large dorsal cyst [13,14]. It is the most severe from among the three variants of holoprosencephaly. In alobar HPE, the olfactory bulbs and tracts, the corpus callosum and anterior commissure, the cavum septum pellucidum, and the interhemispheric fissure are absent, while the optic nerves may be normal, fused, or absent [13,15]. Cyclopia or synophthalmia, severe ocular hypotelorism with divided orbits, and a proboscis-like nasal structure are mostly associated with alobar HPE[16,17]. The alobar form of holoprosencephaly is incompatible with life.

Semi lobar holoprosencephaly shows a rudimentary falx, partial interhemispheric fissure, partial separation of thalami, absent septum pellucidum and large H-shaped Monoventricle. The basal ganglia may show variable amount of fusion. The facial anomalies associated with this type are cleft lip, cleft palate, and hypertelorism.

Lobar holoprosencephaly is characterized by near total cleavage of cerebral hemispheres, presence of falx, interhemispheric fissure, and absent cavum septum pellucidum. The frontal horns appear box like due to absence of cavum septum pellucidum. The thalami and the basal ganglia are separated. It may be associated with hypertelorism.

In 1993, a new variant of HPE called "middle interhemispheric" (MIH) variant or syntelencephaly was described by Barkovich and Quint[18]. Here the interhemispheric fissure is formed in the frontal and occipital regions but is absent in the parietal region with fusion of the hemispheres. Children with semilobar, lobar, and middle hemispheric variants have variable survival with seizures being the most common presentation after birth.

The etiology of the holoprosencephalies is Heterogeneous and has been attributed to both environmental and genetic causes. These malformations are associated with microdeletions or duplications within the genes responsible for forebrain development. Holoprosencephaly has also been associated with triploidy, trisomy 13, trisomy 18, and a number of other syndromes. Holoprosencephaly has been associated with autosomal- dominant, recessive and monogenic inheritance, infections (cytomegalovirus, toxoplasmosis), toxins (hydantoin), maternal diabetes, first trimester bleeding and dizygotic twins[19].

V. Conclusion

Alobar Holoprosencephaly with Cyclopia and Proboscis is a rare congenital malformation which is due to failure of formation of prosencephalic cleavage. Most of infants born with such anomalies are still born or die immediately after birth. The Prognosis is poor for severe malformation. It can be diagnosed by screening ultrasound and if it is detected at an early stage of pregnancy, termination can be performed and maternal psychological trauma can be minimized.

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