Case Report

Journal of College of Medical Sciences-Nepal, Vol-20, No.4, Oct-Dec 2024
ISSN: 2091-0657 (Print); 2091-0673 (Online) Open Access
DOI: 10.3126/jcmsn.v20i4.61740

Semilobar Holoprosencephaly with Cebocephaly: A Case Report

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ABSTRACT

Background

Holoprosencephaly is a rare congenital malformation affecting 6 to 12:10,000 live-born infants and is characterized by failure of separation of cerebral hemispheres. Recognised associations include midline facial defects - hypotelorism, cyclopia and cebocephaly. We report a case of semilobar holoprosencephaly with cebocephaly that presented at our hospital. This case is a rare presentation of holoprosencephaly along with facial abnormalities. Our case describes nasal and ocular abnormalities associated with holoprosencephaly. This may add new information regarding associated anomalies of holoprosencephaly. There are three categories of holoprosencephaly with alobar holoprosencephaly being the most severe, followed by semilobar holoprosencephaly and lobar holoprosencephaly being the mildest form. In women with a history of holoprosencephaly or holoprosencephaly in the current pregnancy, antenatal workup to rule out fetal chromosomal disorders and metabolic workup for maternal preeclampsia should be done.

Keywords: case reports; cebocephaly; holoprosencephaly; hypotelorism; malformation.

INTRODUCTION

The term holoprosencephaly (HPE) was proposed by DeMyer and Zeman. It is a developmental disorder resulting from failure of separation of the midline forebrain structures at various levels resulting in a defect of the embryonic forebrain. Based on the severity of incomplete cleavage of the mid and forebrain, HPE is commonly classified into three types: alobar, semi-lobar and lobar.[1] The overall prevalence of HPE in a multicentre study was 1 in 13,000 to 18,000 live births with female preponderance.[2] The rarity of semilobar holoprosencephaly with monoventricle combined with the presence of facial anomalies, makes this a remarkable case.

CASE REPORT

This newborn infant was the first child of healthy non-consanguineous 25-year-old mother and 26-year-old father. The mother did not undergo regular antenatal check-ups during pregnancy. She had no known teratogen exposure and there was no history of similar cases in the family. No anomaly scan was done for the patient. On admission, mother's vitals were stable and routine blood tests (hemogram, Liver function test (LFT), Renal function test (RFT), urine analysis revealed no abnormality. Ultrasound done at 27 weeks of gestation for assessment of fetal wellbeing revealed a single live fetus with monoventricle and no distinction between the cerebral hemispheres. The dilated monoventricle compressed the surrounding cerebral hemispheres to a chink of tissue displaced to the periphery, showing no sulcal-gyral pattern. No corpus callosum was seen. The thalami appeared fused. Rudimentary falx cerebri and an incomplete interhemispheric fissure were seen in the posterior part. A prominent cystic area in the posterior fossa (Figure 1) causing compression of the cerebellar hemispheres, possibly representing a Blake pouch cyst was seen. The mother had polyhydramnios (AFI ~ 30). Placenta was posterior walled. The fetal face showed normal bony orbits with hypotelorism. However single nostril was seen in fetal nose. There were no labial or palatal malformations. Fetal thorax, abdomen, limbs and spine revealed no abnormalities. Following the ultrasound, patient was advised

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Article received: 2024-05-26. **Article accepted**: 2024-11-09. **Article published**: 2024-12-31.

immediate termination but the patient refused. She was screened for retroviral infection, hepatitis, and syphilis and was documented nonreactive.

She came back after 3 weeks and a live female baby was delivered by caesarean section with a birth weight of 1.5 kg. On examination of the neonate, there was hypotelorism, proboscis-like nose with single nostril (Figure 2).

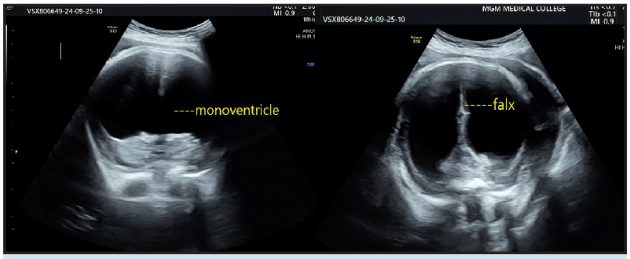

Figure 1. Antenatal ultrasound depicting monoventricle with no proper brain tissue. Neurosonogram depicting remnant of falx cerebri with residual brain tissue.

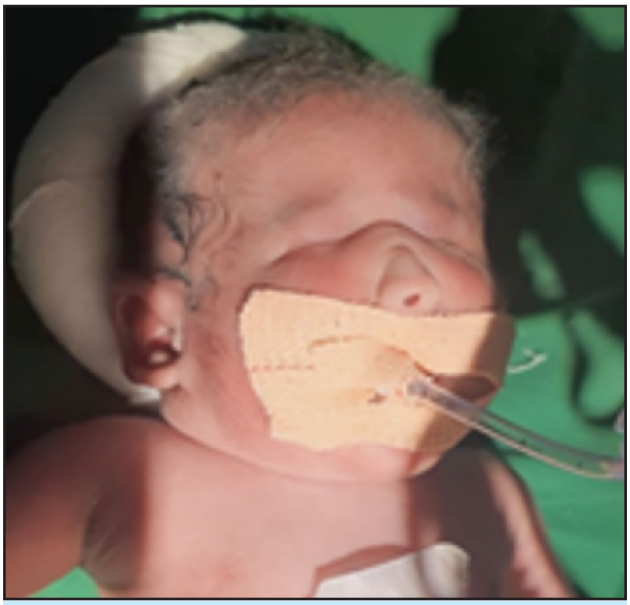

Figure 2. Hypotelorism,proboscis like nose with single nostril.

Neurosonography of neonate revealed monoventricle with partially formed falx cerebri and compressed brain tissue, similar to that seen on antenatal sonography. Orbital sonography revealed dysmorphic small globes with no definitive lens (Figure 3).

Abdominal sonography was normal. Both upper and lower limbs were normal. A diagnosis of Semilobar HPE with cebocephaly was made based on the aforementioned clinical and ultrasonography findings. The parents refused to give consent for brain MRI

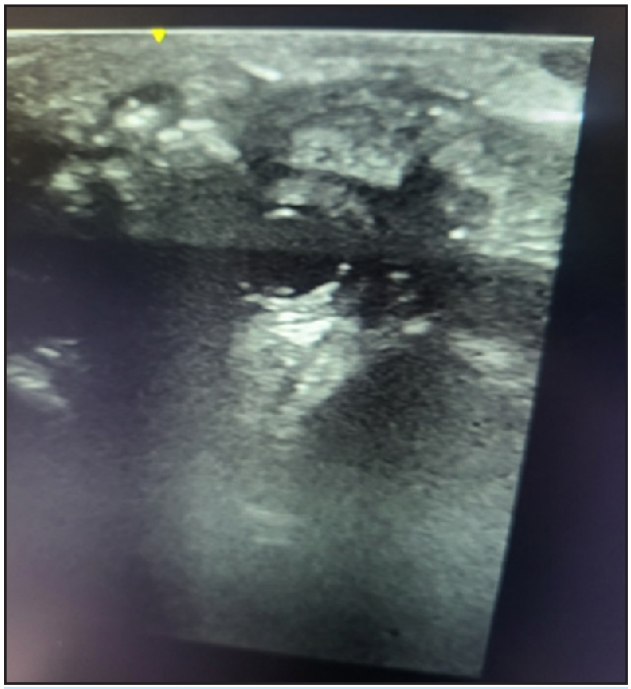

Figure 3. Orbital sonography showing dysmorphic small globe with no definitive lens.

of the neonate. After basic neonatal care was given (drying the baby, clearing the airway off secretions), the baby was transferred to the neonatal intensive care unit (NICU) but died 2 hours after admission. Following her death, further investigations were not possible due to parents' refusal.

DISCUSSION

Primary neurulation is responsible for forming the neural tube in embryological period. The neural tube forms three important structures: the forebrain, midbrain and hindbrain.[3] Incomplete separation of the forebrain into the right and left hemispheres between days 18 and 28 of pregnancy leads to HPE. It is commonly associated with mid facial defects and has a spectrum of presentations.[4]HPE is divided into three types: lobar HPE, semilobar HPE, and alobar HPE.[5] In lobar HPE, the interhemispheric fissure, falx are clearly developed though their most anterior aspect is shallow and dysplastic, third ventricle and lateral ventricle horns are generally well formed but the frontal horns are dysmorphic. Splenium and most of body of corpus callosum can be identified; however rostrum and genu are absent. Semilobar HPE has a rudimentary interhemispheric fissure and incomplete falx cerebri, thalami may be partially fused, temporal

horns of lateral ventricles may be partially formed, splenium of corpus callosum is present, but body and genu are absent. Alobar type is the most severe form of HPE characterised by monoventricle with small remnant of cerebral hemispheres, absent falx cerebri, interhemispheric fissure, corpus callosum and third ventricle with fusion of thalami.[1] The etiology of HPE is complex; multiple environmental and genetic factors have been reported in the pathogenesis.[2, 4] Alcohol and tobacco intake during pregnancy, maternal diabetes mellitus and Toxoplasmosis, rubella, cytomegalovirus, and herpes simplex (TORCH) infections, especially cytomegalovirus have been reported as environmental factors.[6, 7] HPE occurs in about 70% of patients with trisomy 13.[8] Antenatal ultrasonography helps in diagnosing the intracranial abnormalities and associated facial malformations of HPE. The intracranial findings include monoventricle, fused thalami and the absence of midline structures, whereas cebocephaly, cyclopia, hypotelorism, and cleft lip are important facial characteristics which help in the antenatal diagnosis of patients with HPE.[1, 9] The survival of an HPE new-born depends on its severity and associated anomalies. Most new-borns with alobar HPE have a poor prognosis. Children with other forms of HPE rarely survive into adulthood. HPE survivors can have developmental delay, profound intellectual impairment, and seizures.[10]

CONCLUSIONS

In women with a history of HPE or HPE in the current pregnancy, the antenatal genetic workup should be done to rule out fetal chromosomal disorders. Screening for pre-eclampsia should be done in a woman with HPE fetus and expectant management should be instituted. Severe forms of HPE warrant immediate termination owing to its poor prognosis. Patient and family members also need to be counselled about course of action in future pregnancies.

ACKNOWLEDGEMENTS

We would like to thank the paediatrics department of M.G.M Medical College and L.S.K. Hospital who were involved in the management of the new-born.

Conflict of interest: None

Funding: None

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Citation: Jyothish J, Das R. Semilobar Holoprosencephaly with Cebocephaly: A Case Report. JCMS Nepal. 2024; 20(4): 382-85.