Case Report

Fetal Alobar Holoprocencephaly

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Abstract

Alobarh holoprocencephaly is a very rare fetal congenital malformation. It is a disorder caused by the failure of procencephalon (forebrain) to sufficiently divide into the double lobed cerebral hemisphere. The result is a single lobed brain with skull and facial defects. Here we report a case of alobar holoprocencephaly detected by USG at 29 week of gestation though the routine 22 week anomaly scan was normal. She was counseled regarding the poor outcome of fetus with such disorder but she decided to continue the pregnancy up to term. She was admitted at her 38 weeks of pregnancy and delivered a male baby with congenital birth defects - alobar holoprocencephaly with cleft palate, cleft lip and absence of nasal bone.

Keywords: *Alobar; Holoprocencephaly; Congenital anomaly.*

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Introduction

Holoprocencephaly is a very rare fetal congenital malformation. It is a disorder caused by the failure of procencephalon (forebrain) to sufficiently divide into the double lobed cerebral hemisphere.[1] The result is a single lobed brain structure and skull and facial defects. There are three types of holoprocencephaly. Most serious form is the alobar holoprocencephaly in which the cerebral hemispheres fail to separate and is usually associated with severe facial deformities. It is estimated to be 1 in 16000 live births and 1 in 250 spontaneous abortions.[2,3] Mutations in genes encoding the sonic hedgehog protein is thought to be responsible for such anomaly. There are some non-genetic risk factors like diabetes mellitus, transplacental infections, previous history of miscarriage, drugs like aspirin, lithium, retinoic acid, anticonvulsants, oral contraceptive, etc.[4] Prognosis is dependent on the extent of cerebral and facial deformities.[5] Moderate to severe defects may cause mental retardation, spastic quadriparesis, athetoid movements, endocrine disorders, epilepsy, etc.[6] There is no definitive modality of treatment for children with such

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conditions and treatment is often symptomatic. However treatment of deformities i.e. cleft lip may increase the quality of their life.[7-9]

Case report

Mrs. X, 34 years of age, Para-2 (LUCS)+1(abortion), a known case of diabetes mellitus for 8 years, got admitted on 30th August 2019, with pregnancy for 38 weeks and 2 days. This patient was not on regular antenatal checkup. On her first visit at 22 weeks anomaly scan report was normal but at about 29 weeks an ultrasonogram showed suggestive of semi lobar holoproencephaly. Repeat ultrasonogram confirmed alobar holoprocencephaly. The cerebral hemispheres appeared thin and undivided with bilateral cleft lip, dysmorphic fetal face.

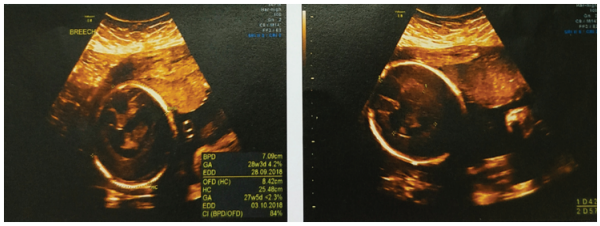

Fig. 1: USG at 29 weeks of pregnancy showing undivided cerebral hemisphere

At this point, she was counseled about the fetal deformity and its bad prognosis and was advised to get admitted for further evaluation and management. The patient however did not comply and went abroad for treatment. She got admitted again at her 34 week of pregnancy and was referred to department of Paediatric Neurology for consultation regarding the fate of the fetus. Their opinion was that despite the rate of survival in such cases are usually low and survived fetus may suffer from severe neurological defects, termination should be done if only the parents want. But the patient wished to carry the fetus upto term. A male baby with severe form of congenital birth defects (cleft palate, cleft lip with absence of nasal bone) was delivered by Cesarean section at 38 week 2 days gestation with APGAR score 8/10.

Fig. 2: Newborn with cleft lip, cleft palate and absent nasal bone

The baby was admitted to NICU. On 7th day of puerperium, patient was discharged on request with the baby and after 2 days the baby died.

Discussion

In this study, we presented a unique case of a neonate, born with severe holoprocencephaly. The fetus was diagnosed with alobar holoprocencephaly at 29th week of gestation, while the routine ultrasound performed at 22 week revealed no abnormalities in the fetus. Earliest diagnoses for alobar, semi-lobar and lobar holoprocencephaly are reported during weeks 13 and 21 week of pregnancy in previous studies.[10,11] In one study, Poenaru et al. described two fetuses diagnosed with alobar holoprocencephaly and lobar holoprocencephaly phalydiagnosed at 29 week of gestation.[12] Therefore, it could be concluded that time of holoprocencephaly diagnosis is not restricted and it may vary depending on ultrasound devices and radiologists involved in the process.

To date, the exact origin of holoprocencephaly remains unknown, and no specific causes could be identified in the majority of cases. In this regard, several risk factors have been proposed, including smoking habits, alcoholism, maternal diabetes

mellitus, pregnancy with infections (e.g., syphilis, toxoplasmosis, rubella, herpes and cytomegalovirus) and use of medications during pregnancy (e.g., aspirin, lithium, anticonvulsants, birth control pills and retinoic acid).[4] According to the literature, bleeding during the first trimester of pregnancy and history of miscarriage in women could result in the birth of neonates with holoprocencephaly; however, no significant correlation has been reported between the incidence of holoprocencephaly and maternal age.[13,14] In this case, the mother was a 34-year-old multiparous woman with some of the suggested risk factors for such condition like diabetes mellitus, history of taking aspirin for ischaemic heart disease and history of miscarriage.

Although many children with holoprocencephaly have normal karyotypes, specific chromosomal abnormalities have been identified in some patients, the most frequent of which is trisomy 13. Evidence suggests that holoprocencephaly could be hereditary in some families; however, degree of severity is variable among the affected individuals in the same family. In this regard, several genes have been recognized to play a role in the development of holoprocencephaly.[15,16] In their study, Niknejadi et al. reported a case of holoprocencephaly in one of the fetuses in a twin pregnancy, while the other fetus was diagnosed with Down syndrome.[17] According to their findings, karyotyping of both fetuses would be warranted if one of the twins had major malformations. In the study by Saeidi et al., chromosomal analysis was indicative of a normal karyotype in an infant diagnosed with alobar holoprocencephaly.[18]

Clinical findings of holoprocencephaly are variable depending on the severity of the condition.[19] Cyclopia, proboscis and cheilo/palatoschisis are associated with severe holoprocencephaly. On the other hand, mental retardation is known to have a direct correlation with the severity of holoprocencephaly.[20] In the current report, the baby was diagnosed with severe holoprocencephaly, and clinical findings were absence of nasal bone and presence of cleft palate with cleft lip. Several studies conducted by Thakur et al.[21], Tokmak et al.[22], Gawrych et al.[23], Gupta et al.[24] and Abubakar et al.[25] and National Institutes of Health Clinical Center have reported cases of holoprocencephaly accompanied by the aforementioned clinical manifestations.[26]

Conclusion

Prenatal diagnosis of holoprosencephaly is usually established commonly by ultrasonography or occasionally by MRI in the 2nd trimester. We thus recommend detailed sonographic evaluation of fetal anomaly in all pregnant women with significant risk factors such as diabetes mellitus, inappropriate drug use, etc. between the 18-24 weeks of gestation for prenatal diagnosis and timely intervention. Also proper antenatal care and drug education of potential mothers/couple will reduce the incidence from prescription/ nonprescription drugs. Patients diagnosed with holoprocencephaly should receive individualized treatment despite possible complications.

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