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Research Article - Human anatomy case report

Alobar holoprosencephaly, proboscis and cyclopia in a chromosomally normal fetus: Prenatal diagnosis and fetal outcome

Mine Genç[1,*], Berhan Genç[2], Aynur Solak[2], Liya Alkılıç[3], Murat Uyar[4]

Departments of [1] Obstetric and Gynecology, [2] Radiology, [3] Pediatrics, and [4] Ophtalmology, Şifa University School of Medicine, İzmir, Turkey

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Abstract

Holoprosencephaly is a brain malformation that develops as a result of a defect in development of prosencephalon during early gestation. Holoprosencephaly can be diagnosed with prenatal ultrasonography and magnetic resonance imaging. We report herein a case with cyclopia and holoprosencephaly detected by prenatal ultrasonography.

Key words

3D sonography, Prenatal diagnosis, Magnetic resonance imaging, Prenatal ultrasonography

Introduction

Holoprosencephaly is a rare developmental disorder. During embryonic development the prosencephalon cannot be divided into cerebral hemispheres sagittally, telencephalon and diencephalon transversely, and olfactory and optic lobes horizontally. Based on the disease severity it is classified into 3 types: alobar, semilobar, and lobar. Severe brain anomalies are accompanied by severe face, extremity, and other organ anomalies. The aim of this study was, by using imaging modalities, to investigate the midline defects of a fetus diagnosed with alobar holoprosencephaly with 4D ultrasonography (USG) and magnetic resonance imaging (MRI) at 20th gestational week, and to discuss the disease under the light of the relevant literature data.

Case report

A 26-year-old woman (at her third pregnancy, with two healthy children delivered at term by cesarean section) who was in the 20th week of pregnancy according to last menstruation, was detected to have a fetus with alobar holoprosencephaly at obstetric ultrasonography examination. The patient had no history of consanguineous marriage, was not a smoker, had not made use of teratogenic drugs or alcohol nor had she suffered of any infectious disease during pregnancy. Ultrasonography showed

* Corresponding author. E-mail: doktorminegenc@gmail.com

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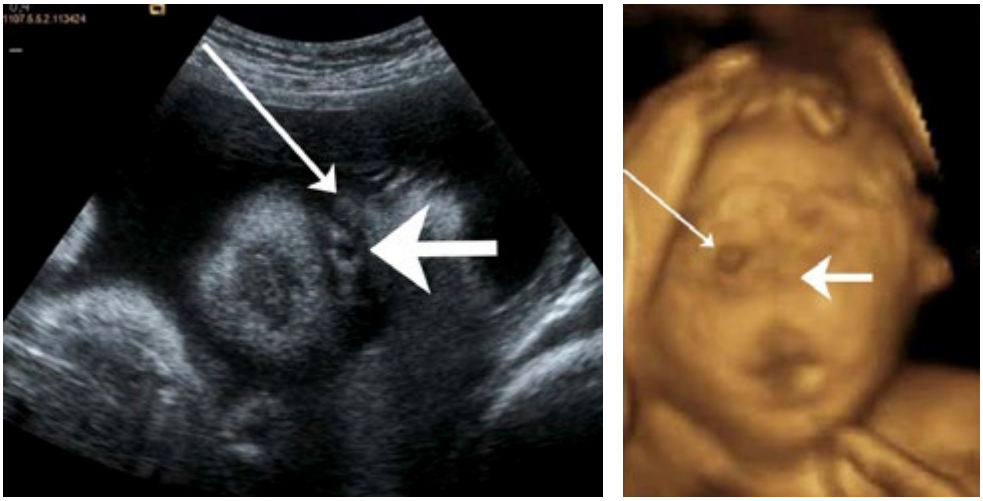

Figure 1a-b – B mode (a) and 3D ultrasonography (b) depicts proboscis (long, thin arrow), and only one eye is recognizable between the mouth and proboscis (short, thick arrow).

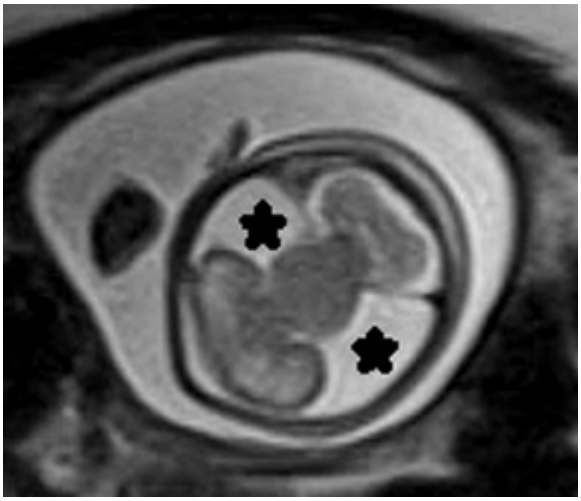

Figure 2 – Axial T2-weighted magnetic resonance image of the fetus shows fusion of the anterior and middle portion of cerebral hemispheres as well as major dilatation of subarachnoid spaces (black stars).

fused cerebral hemispheres in the anterior and middle portions, major dilatation of the cerebral ventricles, proboscis, microcephaly, bilateral microftalmia and hypotelorism; the single orbit was situated between the mouth and the proboscis. (Figs. 1, 2). A magnetic resonance imaging (MRI) examination performed during pregnancy showed fused cerebral hemispheres, a single ventricle, fused thalamic nuclei in their

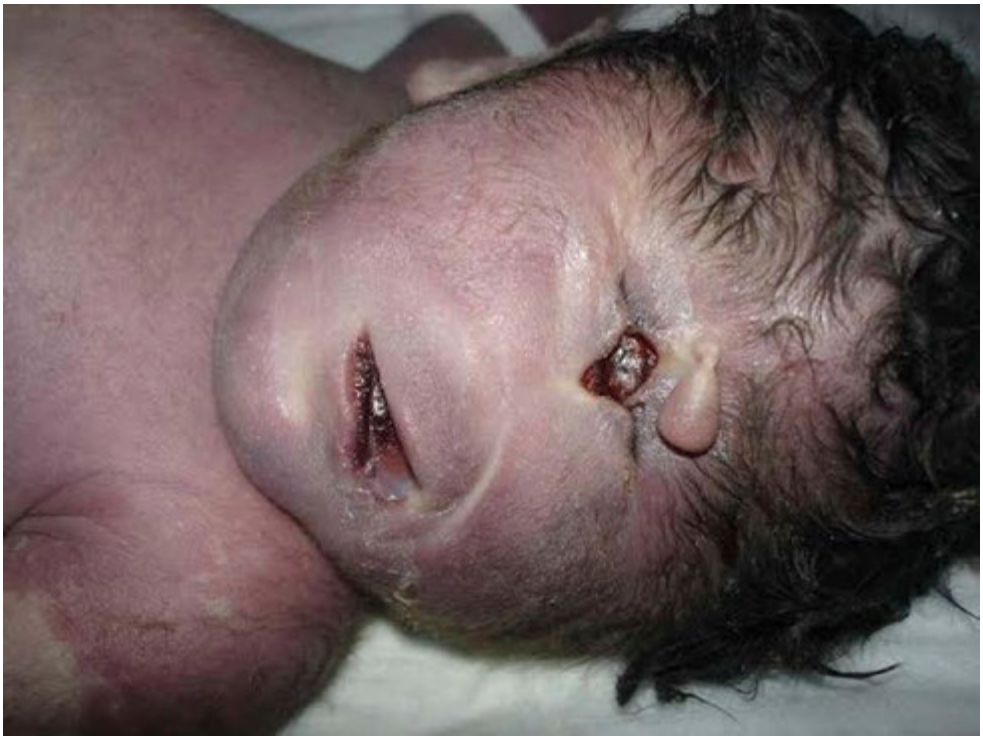

Figure 3 – Facial photograph of an infant with alobar holoprosencephaly shows proboscis, microcephaly, bilateral microftalmia, hypotelorism and a single orbit between the mouth and proboscis. There was no nose.

caudal portion (Fig. 3), and agenesis of suprarenal glands along with facial malformations. In the light of these findings the fetus was diagnosed with alobar holoprosencephaly.

The family was informed regarding the severity of the disorder. Owing to religious beliefs the family refused pregnancy termination. At 36th week of gestation a 2000 gr male infant was delivered with cesarean section. The gross examination of the infant after the delivery revealed cyclopia, a mobile proboscis-like nose on the normal nose position, and macroglossia (Fig. 4). There was no anomaly in either upper or lower extremities (Fig. 5). A postnatal MRI confirmed alobar holoprosencephaly (Fig. 6). The infant was intubated due to respiratory distress syndrome at 12 h of life and died at 24 h of life. The family refused autopsy examination. The chromosome analysis of the infant was normal (46, XY).

Discussion

Holoprosencephaly is a rare brain malformation resulting from a developmental anomaly of proencephalon between the 4th and 8th week of gestation, which is

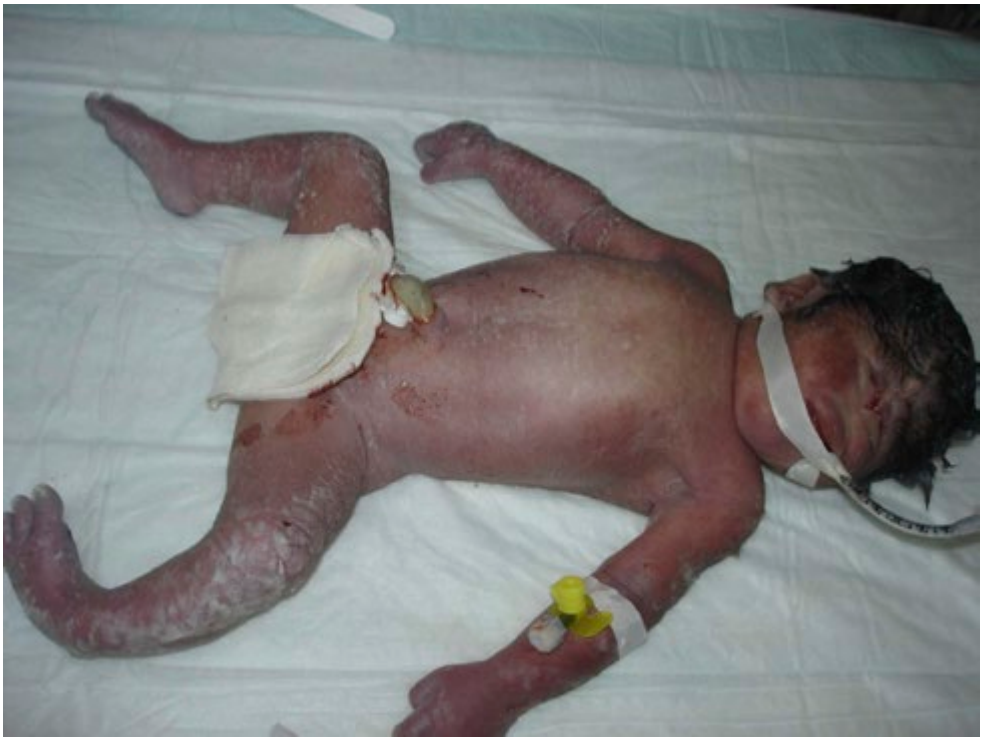

Figure 4 – Body profile of the baby with cyclopia.

seen in 1 of every 16000 live births and 1 of every 250 spontaneous abortion cases (Dubourg et al., 2007). Based on the division of prosencephalon, holoprosencephaly has three forms: alobar, semilobar, and lobar. In alobar holoprosencephaly, the most severe form, no division takes place in prosencephalon. The two lateral ventricles appear as a single ventricle. Thalamic fusion is observed. There exist no interhemispheric fissure, optic tracts, or olfactory processes. Corpus callosum does not exist either. Facial development may also be affected. There may be cyclopia, probocis, ethmocephaly, cebocephaly, and median cleft lip and palate. Midbrain, brain stem, and cerebellum are normal. The skull appears as water-filled on ultrasound examination, requiring differential diagnosis with hydrocephaly and hydranencephaly.

Semilobar holoprosencephaly is an intermediate form. There are partial segmentation of ventricles and partial fusion of thalami. Olfactory processes and corpus callosum are usually absent.

Lobar holoprosencephaly is the mildest form in which the hemispheres are well split. However, there is a fusion in the rostral portion. Lateral ventricles are interconnected, albeit dilated. Corpus callosum is either normal or hypoplastic. In 80% of the cases there are midline defects while 20% of the affected cases have a normally appearing face.

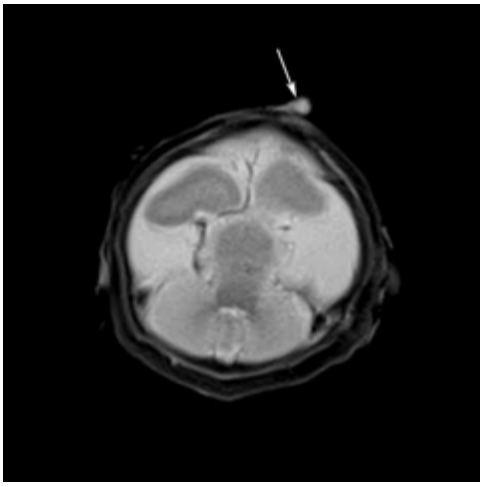

Figure 5 – Axial T2-weighted magnetic resonance imaging of a newborn with alobar holoprosencephaly shows fusion of midline structures and proboscis (arrow). Cerebellum appears normal.

In addition to cerebral and facial anomalies, severe cases with holoprosencephaly also have polydactyly, extremity deformations, exomphalos, renal dysplasia, and fetal hydrops. The majority of cases with additional anomalies are diagnosed to have chromosomal abnormalities. In the present case the mother, father and the baby had normal chromosomal analysis.

The diagnosis of the disease can be made with abdominal ultrasound examination and MRI during prenatal period (Poenaru et al., 2012). Our patient was diagnosed by prenatal abdominal 4D ultrasound and confirmed by MRI. The diagnosis was confirmed by cranial MRI postnatally. The prognosis of holoprosencephaly depends on disease severity and presence of accompanying anomalies.

The etiology of the disease is still unclear. Environmental and genetic factors may be be at work. Among environmental factors there are maternal diabetes mellitus, alcoholism, cytomegalovirus, rubella or toxoplasma infections, and some drugs (retinoic acid, cholesterol synthesis inhibitors, fenitoin, salicylates) (Ronen et al., 1991; Ming et al., 2002; Arathi et al., 2003; Capobianco et al., 2007; Dubourg et al., 2007; Krauss, 2007).

Holoprosencephaly may be transmitted as an autosomal dominant trait. Mutation of SHH (sonic hedgehog) gene is the most common cause of familial holoprosencephaly (Gupta et al., 2010). Trisomy 13 and trisomy 18 are the most frequently encountered chromosomal anomalies (Arathi et al., 2003; Chen, 2006). None of the above mentioned environmental and teratogenic factors was present in our patient. Her family history was non-remarkable, either. The etiopathogenesis of the disease is still unclear. Holoprosencephaly without a recognizable gene or chromosome defect has been already described occasionally (Garzozi et al., 1985).

In conclusion, this case underlines that the early diagnosis of holoprosencephaly is possible by observing hydrocephaly, a single ventricular cavity and facial abnor-

malities such as proboscis, microcephaly, and cyclopia at intrauterine obstetric ultrasonography. Although some genetic and teratogenic factors are known to play a role in the etiology of the disease, there may be no known risk factor, as in our patient. The family should be informed about the poor prognosis of severe forms.

References

Arathi N., Mahadevan A., Santosh V., Yasha T.C., Shankar S.K. (2003) Holoprosencephaly with cyclopia: report of a pathological study. Neurol. India 51: 279-282.

Capobianco G., Cherchi P.L., Ambrosini G., Cosmi E., Andrisani A., Dessole S., (2007) Alobar holoprosencephaly, mobile proboscis and trisomy 13 in a fetus with maternal gestational diabetes mellitus: a 2D ultrasound diagnosisand review of the literature. Arch. Gynecol. Obstet. 275: 385-387.

Chen H. (2006) Atlas of Genetic Diagnosis and Counseling. Humana Press, London.

Dubourg C., Bendavid C., Pasquier L., Henry C., Odent S., Veronique D. (2007) Holoprosencephaly. J. Rare Dis. 2: 8.

Garzozi H.J., Barkay S. (1985). Case of true cyclopia. Br. J. Ophthalmol. 69: 307-311.

Gupta A.O., Leblanc P., Janumpally K.C., Pattaporn T. (2010) A preterm infant with semilobarholoprosencephaly and hydrocephalus: a case report. Cases J. 3: **35-35**.

Krauss R.S. (2007) Holoprosencephaly: new models, new insights. Expert Rev. Mol. Med. 9: 1-17.

Ming J.E., Muenke M. (2002) Multiple hits during early embryonic development: digenic diseases and holoprosencephaly. Am. J. Hum. Genet. 71: 1017-1032.

Poenaru M.O., Vilcea I.D., Marin A. (2012) Holoprosencephaly: two case reports. Maedica 7: 58-62.

Ronen G.M., Andrews W.L. (1991) Holoprosencephaly as a possible embryonic alcohol effect. Am. J. Med. Genet. 40: 151-154.