

Holoprosencephaly Alobar: A Case Report and Literature Review

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Abstract

Case Report

Holoprosencephaly is a rare congenital brain malformation resulting from failure of diverticulation and cleavage of primitive prosencephalon which occurs at 4 - 8th week of gestation and is usually associated with multiple midline facial anomalies. It is the most common forebrain developmental anomaly in humans and a worldwide distribution. The etiology of HPE is very heterogeneous. Clinical expression is variable, extending from a small brain with a single cerebral ventricle and cyclopia to clinically unaffected carriers in familial holoprosencephaly. Here, we report neonatal case of holoprosencephaly alobar of premature girl 34t week, with microcephaly, flat nose, a single nostril, midline cleft lip palate and choanal atresia.

Keywords: Holoprosencephaly alobar, imaging CT.

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INTRODUCTION

Holoprosencephaly (HPE) is a rare congenital anomaly, which occurs due to the failure of prosencephalon to develop into two hemispheres, occurring at a very early embryonic stage, between the 18th and 28th days of gestation [1]. Three anatomical forms of varying severity have been described: alobar, semi-lobar and lobar HPE. It can be the cause of facial abnormalities, neurological manifestations and various endocrine disorders [2]. We report a case of alobar holoprosencephaly associated with multiple facial deformities.

CASE REPORT

This was the fourth pregnancy of non-consanguineous parents, aged 41 and 48 years, respectively. The other pregnancies was normal. There was a no history of neither hereditary disease nor chromosome disorders in either family. The mother had received no regular prenatal checkups, including ultrasound examination; hence, no diagnosis was made during the prenatal stage. In the 34th week, a female baby weighing 2700 g was born via cesarean section; she was immediately admitted to the pediatric emergency for respiratory distress, Physical examinations showed lethargy, choanal atresia, cebocephaly and cleft palate. A brain CT performed on the first day of admission showed fused thalamus and a

single large U-shaped ventricular cavity, with a thin rim of peripheral cerebral parenchyma, the falx cerebri and septum pellucidum were not visualized, The posterior fossa structures were normal, The median facial structures were dysmorphic with single nostril, choanal atresia, midline cleft palate and solitary median maxillary central incisor, Thespine, thoracic cage, and heart were scannographically normal. The newborn died on the seven day of her life.

DISCUSSION

Holoprosencephaly is a spectrum of cerebrofacial anomalies resulting from the complete or partial failure of the diverticulation and cleavage of the primitive forebrain [3], During the third week of embryonic life, the prechordal mesoderm migrates into the area prior to the notochord and affects midline facial development; hence, before 4 weeks of embryonic age, the varying degrees of loss or disruption in the development of prechordal mesoderm cause abnormal forebrain development and midfacial defects [4].

The epidemiology of holoprosencephaly is poorly described before, partly because milder forms may go unrecognized; on the other hand, there is marked natural loss of the fetus, while. Consequently, the prevalence rate differs in various study groups. During early embryogenesis it is about 1 in 250; due to

the high rate of spontaneous abortion, the prevalence rate in live births ranges from 1 in 14,736 to 1 in 26,730 according to different studies [5].

The etiology of HPE includes genetic and environmental factors. Among the environmental causes, there are: maternal diabetes mellitus, maternal alcoholism, in utero infections with CMV, rubella or toxoplasma, some drugs (retinoic acid, cholesterol synthesis inhibitors). HPE can be transmitted in an autosomal dominant way. Mutation of SHH gene is the most frequent cause of familial HPE. Also, HPE is associated in 40% of cases with numerical chromosomal anomalies, the most frequent one being trisomy 13 [6], in the presented case, no risk factors were identified in the mother's history. No genetic studies were made on the infant.

HPE is classified into three types:

1. Alobar, which means the complete absence of division of the prosencephalon structures, resulting in completely absent interhemispheric fissure and corpus callosum, fused thalami, fused cerebral hemispheres with only one cerebral ventricle, and facial dysmorphism which include such abnormalities as cyclopia, proboscis, ethmocephaly and cebocephaly. It is the most severe form.



Fig-1: Anterior view of the face: single nostril and hypotelorism (cebocephaly)

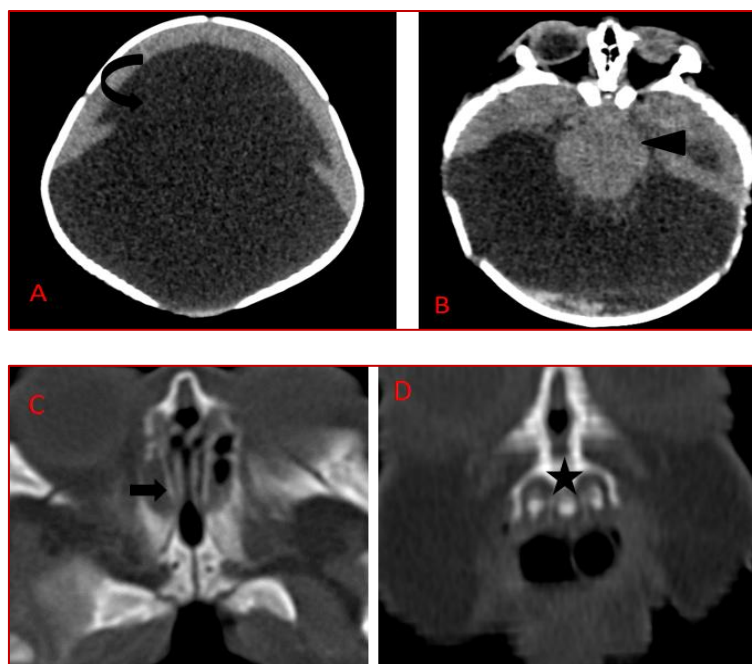


Fig-2: A et B: Axial CT images showing fused thalamus (arrow head) and a single large U-shaped ventricular cavity (curved black arrow), with a thin rim of peripheral cerebral parenchyma, the falx cerebri and septum pellucidum were not visualized. **C:** choanal atresia (black arrow). **D:** solitary median maxillary central incisor (star).

2. Semilobar, consisting in incomplete separation of the cerebral hemispheres: there are two cerebral hemispheres connected in the frontal area, with a singular ventricular cavity and partially fused thalami.
3. Lobar, in this case interhemispheric fissure is present, septum pellucidum is absent and frontal horns of lateral ventricles communicate, corpus callosum is absent hypoplastic or normal, with midline fusion of cingulate gyrus. It is the least severe form.

There is a fourth type described in the literature, the middle interhemispheric variant (MIH), which means a defect of separation of the posterior portions of frontal lobes and the parietal lobes, with varying lack of cleavage of the basal ganglia and thalami and absence of the body of the corpus callosum but presence of the genu and splenium of the corpus callosum [7].

Clinical findings are variable and depend on the degree of severity of holoprosencephaly. Midfacial defects occur in most cases and have a prognostic significance. These include: absence of the eyes, cyclopia, proboscis, cebocephaly (hypotelorism associated with a single nostril), cheilo/palatoschisis, agnathia or micrognathia. Cyclopia, proboscis and cheilo/palatoschisis are associated with severe forms of HPE. Microcephaly, or, rarely, macrocephaly, suggesting the presence of hydrocephaly. Mental retardation directly correlated with the severity of HPE. Neurologic manifestations are also frequently encountered: seizures, hyper/hypotonia, dysphagia, dysphonia, extrapyramidal disorders, like chorea or dystonia. Endocrine dysfunctions: hypopituitarism, diabetes insipidus [6-7].

Prenatal diagnosis of HPE is mainly made by ultrasonography, which can show: polyhydramnios, hypotelorism, arinia, cyclopia, proboscis, cheilo/palatoschisis, single cerebral ventricle. The diagnosis could be made in most cases of alobar and semilobar holoprosencephaly after 17 weeks of gestation, when the production of cerebrospinal fluid starts. In lobar cases diagnosis could be difficult because the antenatal picture of septo-optic dysplasia is almost identical to that of lobar holoprosencephaly [8]. The role of fetal MRI is in the confirmation of the sonographic findings and detection of any other additional anomaly [9].

If the pregnancy was not followed, as in the case of our patient, the diagnosis is made by transfontanel ultrasound, which will be confirmed by a CT scan or by a magnetic resonance image. An angiographic study can also be contributory [10].

The treatment of HPE is supportive and is oriented towards different malformations associated. Prognosis is dependent upon the degree of fusion and malformation of the brain, as well as other health complications that may be present. Alobar and semilobar HPE are lethal. Children born with lobar HPE can survive for years, but encounter a lot of neurologic manifestations and severe mental retardation [6].

CONCLUSION

Holoprosencephaly alobar is a rare fatal pathology with great etiological heterogeneity, which can be revealed at birth by a polymalformative syndrome. It results from an anomaly in the cleavage of the forebrain into cerebral hemispheres, occurred during the second gestational month. The prenatal diagnosis of HPC is established by fetal ultrasound. Postnatal, imaging (ETF, CT and MRI) allows an exhaustive lesional assessment of this pathology, which had an extremely reserved prognosis.

REFERENCES

- Amirshahi, M., Sanagoo, A., Salehi, A., Kerami, A., Abdollahimohammad, A., Mirshekari, F., ... & Mirshekari, L. (2015). Alobar holoprosencephaly: A case report. *Journal of Nursing and Midwifery Sciences*, 2(4), 70-74.
- Chang, L. H. (2003). Alobar holoprosencephaly: report of two cases with unusual findings. *Chang Gung medical journal*, 26(9), 700-706.
- Chellaoui, M., Chat, L., Najid, A., & Amour-Ammar, B. H. (1999). Holoprosencephalie alobaire a propos d'un cas, *Médecine du Maghreb*, n°75.
- Dubourg, C., Bendavid, C., Pasquier, L., Henry, C., Odent, S., & David, V. (2007). Holoprosencephaly. *Orphanet journal of rare diseases*, 2(1), 1-14.
- Evans, M.I., Johnson, M.P., Yaron, Y., & Drugan, A. (2006). eds. *Prenatal diagnosis*. New York (NY): McGraw Hill Publishing Co, 289-308.
- Funk, K. C., & Siegel, M. J. (1988). Sonography of congenital midline brain malformations. *Radiographics*, 8(1), 11-25.
- Muenke, M., & Beachy, P. A. (2000). Genetics of ventral forebrain development and holoprosencephaly. *Current opinion in genetics & development*, 10(3), 262-269.
- Poenaru, M. O., Vilcea, I. D., & Marin, A. (2012). Holoprosencephaly: two case reports. *Romanian Journal of Medical Practice*, 7(1).
- Raman, R., & Mukunda Jagadesh, G. (2014). Antenatal diagnosis of alobar holoprosencephaly. Case reports in *Radiology*, 2014.
- Seck, N., Basse, I., Keita, Y., Boiro, D., Thiam, L., Ndongo, A. A., & Diagne, I. (2017). Holoprosencéphalie alobaire avec diabète insipide et hypothyroïdie chez un nourrisson de 10 mois. *Pan African Medical Journal*, 28(1).