Holoprosencephaly

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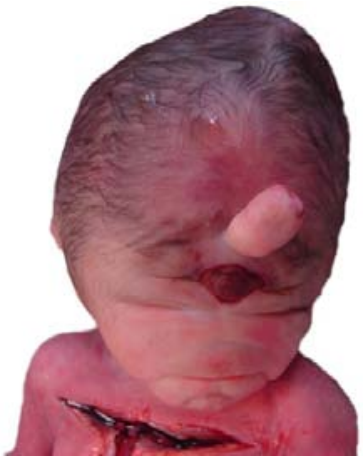

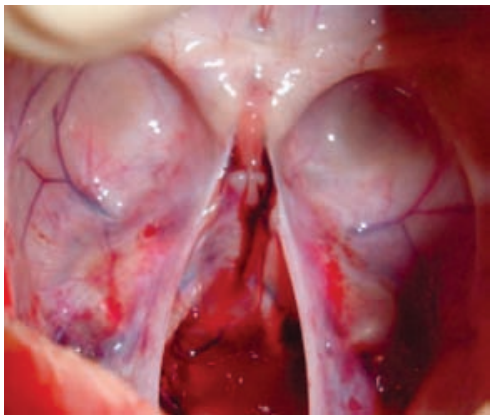

Received: Nov 17,2012
Acepted: Dic 23,2012

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Images ilustrate synophtalmia and a proboscis in a patient with alobar holoprosencephaly.

Holoprosencephaly (HPE) is the most common structural anomaly of the development of human's forebrain, resulting from incomplete midline cleavage of the prosencephalon, associated with neurologic impairment and dysmorphism of the brain and face, due to disturbance of the delicate balance of signals required for proper separation of the cerebral hemispheres.[1-2]

HPE occurs rather frequently, having been observed in 1:250 conceptions.[3] Due to a high rate of fetal demise, the birth prevalence is 1:8000-10000 live births.[3,4]

Its etiology is extremely heterogeneous and it is still being elucidated.[1] Chromosomal defects, genetic mutations and environmental teratogenic factors have been suggested, with varying levels of evidence.[5] including maternal diabetes, ethanol, cytomegalovirus infection, salicylates, antiepilectic medications, retinoic acid and maternal hypocolesterolemia. Abnormalities of chromosome number occur in aproximatly 32-42% of patients with HPE, most commonly trisomy 13,[2] followed by trisomy 18 and 21.[5]

The clinical suspicion of HPE is typically based upon compatible craniofacial features, developmental delay, seizures, or specific endocrinological abnormalities.[2] The diagnostic process is typically initiated by abnormal prenatal brain imaging, positive physical examination findings, and/or positive family history.[1] Magnetic resonance imaging provides better characterization of malformations than prenatal ultrasounds,[2] providing the highest quality data for this purpose, allowing detailed analysis of cortical white matter and structural abnormalities of the deep gray nuclei.[1] However, advances in high-resolution prenatal ultrasound have allowed improved consistency between prenatal ultrasound and prenatal confirmation, being able to diagnose this disease before 16 weeks of gestation, and before 12 weeks transvaginally.[6]

The forebrain maldevelopment alterations produce facial malformations, ranging from the presence of a single upper central incisor to cyclopia. These phenotypic facial characteristics predict up to 80% brain findings.[7]

Based on the degree of nonseparation of the precencephalon, HPE is classically divided into four types. These types, in order of increasing cortical separation, include the alobar form, semilobar, lobar and the mittle interhemispheric variant.[1] It is also classified according to the gene mutated in 7 types.[7]

Medical complications include hydrocephalus, seizures/epilepsy, motor impairment, pulmonary issues, poor gastric emptying, gastroesophageal reflux, constipation, central diabetes insipidus, hypothalamic dysfunction and ophthalmologic problems.[2] Medical management of HPE is complex. Coordinated multidisciplinary care can help ensure that a child receives optimal treatment.

Prognosis is dependent upon the degree of fusion and malformation of the brain.[8] Mortality is high in newborns; however, some children survive beyond the neonatal period. Although survival typically correlates with the severity of brain malformation, there is significant survival variability within each type of HPE.

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