

Answers to the Medical Quiz

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A.1 Semi-lobar holoprosencephaly. The patient presented with hypotelorism, cleft lip and polydactyly. The CT scan showed fused cerebral cortex, which is only seen in the anterior part of the brain and fused thalami. Only the posterior portion (splenium) of the corpus callosum is formed with no evidence of inter-hemispheric fissure. The lateral ventricles are replaced by a single crescent shaped holoventricle which opens into a large dorsal cyst that occupies the posterior fossa. There is no third ventricle due to fusion of the thalami.

DISCUSSION

Holoprosencephaly is failure of differentiation or cleavage of the prosencephalon or forebrain.

During the fourth intrauterine week, the neural folds expand and fuse to form three primary brain vesicles: the forebrain (prosencephalon), the midbrain (mesencephalon) and the hindbrain (rhombencephalon)¹.

The prosencephalon further differentiates into the telencephalon (precursor for cerebral cortex, caudate nucleus and putamen) and the diencephalon (precursor for thalamus, hypothalamus and globus pallidus).

Around the 35th day of gestation the cellular elements of the telencephalon and diencephalon start to differentiate and form the two cerebral hemispheres, two thalami, etc; in holoprosencephaly, this fails to occur and in severe cases even the pre-maxillary facial segments are hypoplastic².

Causes:

- Teratogens (maternal DM, Ethanol, Plant alkaloids, anti-epileptics).
- Genetic mutations.
- Chromosomal abnormalities (Trisomy 13 and 18).
- Sporadic.
- Infection (TORCH).

Types:

- Alobar
- Semilobar
- Lobar

Alobar Holoprosencephaly:

Severely abnormal child (seizures, abnormal neonatal reflexes) with severe midline facial deformities (absent or hypoplastic pre-maxillary segment).

Possible imaging findings: Fused thalami leading to absence of the third ventricle. No inter-hemispheric fissure, falx cerebri or corpus callosum. Cerebrum simulates a pancake-like mass in the rostral-most portion of the brain. The lateral ventricles are fused forming a crescent shaped holovertricle continuous with a large dorsal cyst. A Single anterior cerebral artery supplies both hemispheres².

Semi-lobar Holoprosencephaly:

Facial anomalies may be mild or absent. Affected individuals may have macro or microcephaly. Some may have developmental delay.

Possible Imaging findings: Posterior parts of the Falx and inter-hemispheric fissure may be formed leading to separation of the hemispheres. The temporal horns of the lateral ventricles are rudimentary and the third ventricle may be partially formed³. The hippocampus is incompletely formed, and the septum pellucidum is absent. Only splenium of the corpus callosum is present. A dorsal cyst may be seen².

Lobar Holoprosencephaly:

Mild to moderate developmental delay. Hypothalamo-pituitary dysfunction and possibly some visual problems.

Possible Imaging findings: The third ventricle is fully formed. There is some frontal horn formation. The temporal horn is well defined, but the ventricles are still morphologically abnormal due to absence of the septum pellucidum³. The posterior half of corpus callosum is formed. The Inter-hemispheric fissure and falx extend to frontal area (anterior falx may be hypoplastic).

The frontal lobes are hypoplastic. Hippocampi may be normal or almost normal².

Incidence: Holoprosencephaly is present in 1 in 10,000-20,000 neonates at birth and occurs at a rate of 1 in 250 during embryogenesis⁴.

In general, holoprosencephaly results in substantial early morbidity and mortality with a significantly reduced survival. However, individual reports describe long-term survival in all forms of holoprosencephaly. The strongest correlation is a direct relationship between the severity of facial anomalies and increased mortality. In individuals with cyclopia or ethmocephaly, survival is rare beyond one week.

Patients with alobar holoprosencephaly have a survival rate of about 50% by 4-5 months of age and about 20% at 12 months of age. Isolated semilobar and lobar holoprosencephaly have survival rates of about 50% to 12 months of age.

Virtually all surviving individuals have some degree of developmental delay often persisting as mental retardation; this generally occurs in direct correlation to the severity of holoprosencephaly. However, case reports do describe individuals with lobar holoprosencephaly who have normal or near-normal development. In addition, feeding difficulties leading to aspiration pneumonia and/or failure to thrive frequently occur in individuals within all subtypes⁴.

No standard course of treatment is available, only symptomatic and supportive.

REFERENCES

١. Moore KL, Persaud TVN. Before We Are Born, Essentials of Embryology and Birth Defects, Saunders; New York, 6 edition.
٢. Barkovich A.J. Pediatric Neuroimaging. Lippincott Williams & Wilkins, New York: Raven Press, 3rd Edition (2000).
٣. Holoprosencephaly. <http://hpe.stanford.edu/research/neuroimaging.html> (Neuro imaging). Access Date 24 October 2007.
٤. Tegay DH. Holoprosencephaly. <http://www.emedicine.com/radio/topic347.htm> Access Date 24 October 2007.

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