The Middle Interhemispheric Variant of Holoprosencephaly

Simon, E. M. ¹ * Barkovich, A. J. ²
¹The Children’s Hospital of Philadelphia, Philadelphia, PA; ²University of California, San Francisco, San Francisco, CA

Purpose
The middle interhemispheric variant of holoprosencephaly (MIH) is a rare malformation in which the cerebral hemispheres fail to divide in the posterior frontal and parietal regions. We report the morphologic abnormalities of the brain in a large group of patients with MIH, compare these features with those of classical holoprosencephaly (HPE), and propose a developmental mechanism, based on current knowledge of developmental neurogenetics, by which MIH develops.

Materials & Methods
Neuroimaging studies of 21 patients (MR imaging of 16 patients and high quality X-ray CT of 5 patients) with MIH were reviewed retrospectively in order to categorize the cerebral abnormalities. The cerebral parenchyma, hypothalami, caudate nuclei, lentiform nuclei, thalami, and mesencephalon were evaluated for the degree midline separation (cleavage) of the two hemispheres. The orbits, olfactory apparatus, and presence or absence of a dorsal cyst were also assessed.

Results
In all patients, by definition, middle portions of the cerebral hemispheres were continuous across the midline, without an intervening interhemispheric fissure. The sylvian fissures were abnormally connected across the midline over the vertex in 18 (86%) of 21 patients. Two patients had relatively normal appearing sylvian fissures; one had no sylvian fissure due to the presence of large subcortical heterotopia. Heterotopic gray matter or dysplastic cerebral cortex was also seen in 18 of 21 cases. MIH differed from classical HPE as follows: (1) hypothalamus and lentiform nuclei were separated by the midline third ventricle in all subjects; (2) the caudate nuclei were separated by the cerebral ventricles in 89% of cases; (3) the most commonly affected basal nucleus was the thalami (noncleavage in 33% of cases, abnormal alignment in 5%); (4) 18% of cases showed some degree of mesencephalic noncleavage; (5) no patients were hypoteloric, four were hyperteloric, the remainder demonstrated normal intraocular distances. Dorsal cysts were present in 5 (25%) of 20 patients where it could be assessed, and, as in classical HPE, were associated with severe thalamic noncleavage (3 of 5).

Conclusion
MIH appears to cause lack of cleavage of midline structures in a completely different pattern than does classical HPE. MIH can be conceptualized as resulting from impaired induction or expression of genetic factors influencing the embryonic roof plate, whereas in classical HPE, induction or expression of the embryonic floor plate seems to be affected.
References