

# Syntelencephaly, a lesser known variant of holoprosencephal

G Khandelwal, G Bathla, R Jain, P Sharma, V Maller

## Citation

G Khandelwal, G Bathla, R Jain, P Sharma, V Maller. *Syntelencephaly, a lesser known variant of holoprosencephal*. The Internet Journal of Radiology. 2007 Volume 9 Number 1.

## Abstract

Holoprosencephaly has been traditionally classified in to three types: alobar, semi lobar and lobar forms. A lesser known variant of holoprosencephaly, known as Midline Interhemispheric Fusion (MIH) variant was described in 1993. We present a case of MIH along with a review of imaging findings and review of literature, correlating the differences in presentation with the underlying differences in neuroanatomy.

## CASE REPORT

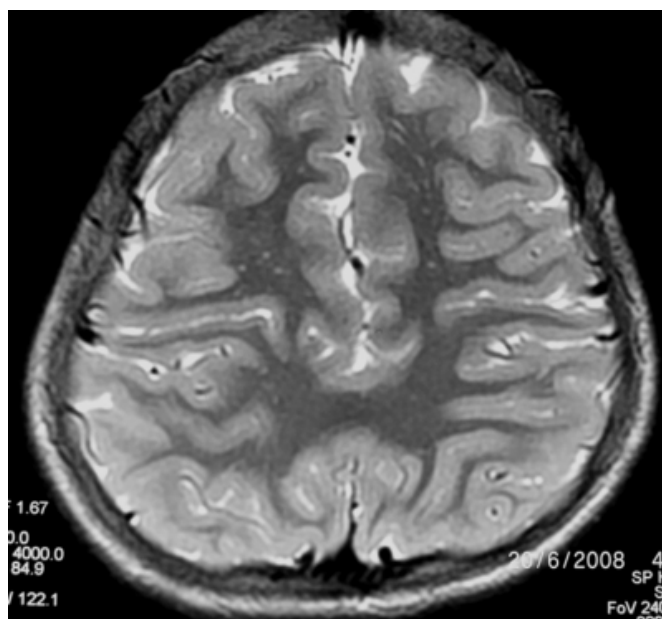
A six year old child presented with a history of seizures since birth and developmental delay. There was no significant ante or peri natal history. No history of any familial disorder or similar complaints in siblings was forthcoming.

MR imaging revealed fusion of cerebral hemispheres in parietal region along with partial agenesis of corpus callosum. There was associated azygous ACA along with abnormal orientation of sylvian fissures which appeared to meet in the midline. No evidence of any heterotopic gray matter was seen.

Based on the imaging appearances, a diagnosis of MIH variant of holoprosencephaly was made.

## Figure 1

Figure 1,2,3: T2W axial, sagittal and coronal MR images showing fusion of cerebral hemispheres across the midline, along with partial agenesis of corpus callosum and an azygous ACA.



**Figure 2**



**Figure 3**



## DISCUSSION

HPEs have traditionally been classified according to the system of DeMyer and coworkers<sup>1,2</sup> into alobar, semi lobar, and lobar forms. A fourth subtype, called the middle interhemispheric variant (MIH) of holoprosencephaly or syntelencephaly, was first identified in 1993<sup>3</sup>.

Neuroimaging in MIH reveals presence of anterior and posterior inter hemispheric fissure without separation of cerebral hemispheres in the posterior frontal and parietal regions. The sylvian fissures have an abnormal orientation and appear to connect across the midline in majority of the

patients. Associated heterotopic gray matter and cortical dysplasia are also common, including abnormal thickening of the cortex lining the anterior IHF<sup>7</sup>.

The thalami are the most common deep nuclei affected in MIH and their abnormalities may be associated with dorsal midline cysts. The corpus callosum is malformed with variable presence of splenium, genu or body. A complete corpus callosum is not seen in either MIH or HPE. There may also be an associated azygous cerebral artery in MIH patients.

Associated Chiari malformations, cerebellar hypoplasia, cephaloceles and polymicrogyria have also been reported in MIH.

Classic holoprosencephaly (HPE) includes the alobar, semi lobar and lobar forms and is characterized by variable degree of formation of anterior and posterior IHF, corpus callosum, septum pellucidum and deep cerebral nuclei. It results from a primary defect in basal forebrain patterning during the first 4 weeks of embryogenesis<sup>4</sup>. This defect results in incomplete separation of the cerebral hemispheres.

Children with HPE have many neurologic problems including mental retardation, spasticity, athetoid movements, seizure disorders, and endocrinologic dysfunction.<sup>5,6</sup> Patients with the most severe type (alobar) make minimal developmental progress and have shortened life spans<sup>6</sup>.

MIH differs from classic HPE in certain key aspects. In MIH, impaired induction or expression of genetic factors appears to influence the embryonic roof plate, whereas in classic HPE, induction or expression of the embryonic floor plate seems to be affected<sup>7</sup>. In contrast to HPE, patients with MIH have a relative sparing of the basal forebrain, with a well formed interhemispheric fissure and normal or nearly normal caudates, hypothalami and basal ganglia. However, they have more severe involvement of the thalami, and the IHF in the region of the posterior frontal lobes and parietal lobes<sup>8</sup>.

This translates into a slightly different clinical profile of patients with MIH as compared to HPE. Various authors<sup>9,10</sup> have found absence of endocrinopathy in MIH as compared with the classic subtypes which likely correlates with the lack of hypothalamic abnormalities. Choreoathetosis in MIH is also lower than that for semi lobar HPE, likely secondary to lack of caudate and lentiform nuclei abnormalities. Mobility, upper extremity function, and language have

similarly been correlated with the degree of non separation of the caudate, lentiform and thalamic nuclei, and grade of HPE.

However, both MIH and classic HPE share a fundamental similarity: non-cleavage of a substantial portion of the supratentorial brain into two separate hemispheres<sup>7</sup>. The fact that mutations in ZIC2 cause classic HPE as well as MIH provides further evidence that MIH is a variant of HPE<sup>11</sup> which differs from classical HPE by lack of endocrine abnormalities and choreoathetosis.

## LEARNING POINT

Due to differences in pattern of neuroanatomic abnormalities in MIH, there is a very low incidence of endocrinopathies, hypothalamic dysfunction, and choreoathetosis, while there is a relative high incidence of dorsal cysts and spasticity. Advances in neuroimaging have made possible the differentiation between the two subtypes hence allowing accurate diagnosis and predicting the overall outcome with greater certainty

## References

1. DeMyer W, Zeman W. Alobar holoprosencephaly (arhinencephaly) with median cleft lip and palate: clinical, nosologic, and electroencephalographic considerations. *Confin Neurol* 1963;23:1-36
2. DeMyer W, Zeman W, Palmer CG. The face predicts the brain: diagnostic significance of median facial anomalies for holoprosencephaly (arhinencephaly). *Pediatrics* 1964;34:256-263
3. Barkovich AJ, Quint DJ. Middle interhemispheric fusion: an unusual variant of holoprosencephaly. *AJNR Am J Neuroradiol* . 1993; 14: 431-440
4. Golden JA. Towards a greater understanding of the pathogenesis of holoprosencephaly. *Brain Dev* . 1999; 21: 513-521.
5. Ming JE, Muenke M. Holoprosencephaly: from Homer to Hedgehog. *Clin Genet*. 1998; 53: 155-163.
6. Barr M Jr, Cohen MM Jr. Holoprosencephaly survival and performance. *Am J Med Genet*. 1999; 89: 116-120
7. Simon EM, Hevner RF, Pinter JD, et al. The middle interhemispheric variant of holoprosencephaly. *AJNR Am J Neuroradiol*2002; 23 :151 -155
8. Takanashi J, Barkovich AJ, Clegg NJ, Delgado MR. Middle interhemispheric variant of holoprosencephaly associated with diffuse polymicrogyria. *AJNR Am J Neuroradiol*. 2003; 24:394-397.
9. Plawner LL, Delgado MR, Miller VS, et al. Neuroanatomy of holoprosencephaly as predictor of function: beyond the face predicting the brain. *Neurology*. 2002; 59: 1058-1066.
10. Lewis AJ et al. middle interhemispheric variant of holoprosencephaly: a distinct clinicon neuroradiologic subtype. *Neurology*.2002; 59:1860-65.
11. Brown LY, Odent S, David V, et al. Holoprosencephaly due to mutations in ZIC2: alanine tract expansion mutations may be caused by parental somatic recombination. *Hum Mol Genet* . 2001; 10: 791-796.

**Author Information**

**G. Khandelwal**

**G. Bathla**

**R. Jain**

**P. Sharma**

**V. Maller**