Paediatric neuro-imaging: Diagnosis

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We congratulate Professor Savvas Andronikou of the Department of Radiology, University of Pretoria, for his spot-on diagnosis, for which he receives the award of R1 000 from the RSSA. Dr Misser elaborates below on the images and findings. Please refer to page 45 of the March 2013 issue of the *SAJR* (http://dx.doi.org/10.7196/SAJR.843) for the investigative images.

Diagnosis

Imaging and findings

A 2-year-old boy presented with microcephaly and developmental delay. The MRI images referred to above, were obtained.

The sagittal T1 (Fig. 1) sequence shows an abnormal appearance of the corpus callosum. The entire body of the corpus callosum is remarkably thin. Only the splenium and part of the genu is relatively spared. Along with the posterior frontal and parietal lobe cerebral fusion, note the absence of the septum pellucidum and fused frontal horns of the lateral ventricles (Figs 2 - 4). The sylvian fissures appear continuous across the hemispheres. MRA of the intracranial vessels (Fig. 5) demonstrates an azygous anterior cerebral artery. The combination of features is compatible with a syntelencephaly subtype of holoprosencephaly.

Discussion

Holoprosencephaly (HPE) is perhaps one of the more complex and captivating congenital brain malformations, with its striking imaging phenotype abnormalities and complex neurological impairment. It is characterised by failure of cleavage of the prosencephalon, a process that usually occurs between the 18th and 28th days of gestation. The overall incidence is much higher than expected, with up to 1 in 250 conceptions affected. With the immense improvement in neuro-imaging, particularly in magnetic resonance imaging, we are now able to delineate the specific areas of involvement including cerebral frontal and parietal lobes, basal ganglia, thalami, orbits and facial structures. There are four subtypes of this malformation. The spectrum includes the classic HPE subtypes in the De Myer classification (viz. alobar, semilobar and lobar HPE), in addition to the fourth subtype known as the middle interhemispheric variant of holoprosencephaly (MIH) or syntelencephaly (Table 1). Solitary median maxillary central incisor is one of several microforms of autosomal dominant HPE not usually included in the classification.

MIH is a relatively milder clinical form of holoprosencephaly, first described in 1993 by Barkovich *et al.*[1] Although akin to other forms of holoprosencephaly, MIH is thought to develop on a somewhat different pattern of midline non-cleavage. The classic subtypes of HPE all involve induction of the embryonic floor plate, and *SHH* is the primary gene abnormality described among several others. In contrast, in the pathogenesis

Table 1. Subtypes of holoprosencephaly and differentiating features[1,4,5]

	Alobar	Semilobar	Lobar	MIH
Degree of prosencephalon non-separation	Almost complete non-separation with holosphere of cerebral parenchyma.	Posterior cerebral hemispheres near normal. Fused anterior aspect with undeveloped frontal lobes.	Rostral and ventral frontal lobe fusion. Rest of cerebral hemispheres separated.	Posterior frontal and parietal lobe fusion. Caudate and thalami often incompletely cleaved.
Falx cerebri and interhemispheric (IH) fissure	Absent IH fissure. Dorsal cyst present.	Partial formation of shallow IH fissure and falx posteriorly. ± Dorsal cyst. Falx absent anteriorly.	Hypoplastic anterior falx. Fissure is present.	Anterior falx is normal or mildly dysplastic. Posterior aspect of falx is absent. Azygous ACA.
Corpus callosum abnormality	Agenesis of corpus callosum.	Genu and anterior body absent. Splenium almost normal.	Genu mildly dysplastic. Body and splenium well-formed.	Absent body of corpus callosum with normal splenium and genu.
Severity, additional features and prognosis	Lethal subtype. Stillborn or short lifespan. Severe facial dysmorphism. Cyclopia. Olfactory aplasia. Monoventricle.	Intermediate severity. Dorsal cyst seen when thalami are fused. Frontal horns absent. Occipital horns normal.	Mild subtype. Present later with visual difficulties or developmental delay. ± Mild olfactory bulb and tract hypogenesis.	Mild cognitive and vision impairment. Facial features similar to lobar subtype. Best prognosis.

of MIH it is the embryonic roof plate that is involved. Mutations of the *ZIC2* gene on chromosome 13, which plays a critical role in differentiation of the roof plate of the developing embryo, have been implicated in MIH.[2]

The affected children present with a variety of deficits including spasticity, dystonia and oromotor dysfunction affecting feeding and speech. Seizures as well as mild cognitive and visual impairment are noted in these children. Endocrinopathy is not a common feature owing to sparing of the hypothalamus and basal forebrain. When compared with other forms of HPE, the overall functional levels including mobility, hand/arm function and speech are better in patients with MIH.

On MR imaging, MIH is characterised by abnormal fusion of the posterior frontal and parietal regions of the cerebral hemispheres. The anterior portions of the frontal lobes, olfactory tracts and the occipital lobes are usually normal. There is frequent incomplete cleavage of the heads of the caudate nuclei and thalami, but the hypothalamus and lentiform nuclei are well-separated. Almost all patients with MIH have a single or azygous anterior cerebral artery. There is a coronal configuration of the sylvian fissures which are continuous across the cerebral vertex. Frequent association with heterotopias and malformations of cortical development have been reported.[3]

In the presence of typical MRI features, a reasonably confident diagnosis of syntelencephaly may be made even antenatally.[4] This radiological diagnosis may serve as a valuable tool in prognostication and in the counselling of parents.

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