

Prenatal diagnosis of a possible new middle interhemispheric variant of holoprosencephaly using sonographic and magnetic resonance imaging

O. PICONE*, R. HIRT*, B. SUAREZ†, A. COULOMB‡, G. TACHDJIAN§, R. FRYDMAN* and M.-V. SENAT*

*Service de Gynécologie-Obstétrique, ‡Service d'Anatomopathologie and §Service d'Histologie, Embryologie, Cytogénétique, (à orientation biologique et génétique de la reproduction), Hôpital Antoine Béchère, Clamart, Assistance Publique des Hôpitaux de Paris (AP-HP), Université Paris XI, Paris and †Service de Radiologie, Hôpital Privé de Thiais, France

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ABSTRACT

A peculiar subtype of holoprosencephaly, middle interhemispheric variant (MIH), which is characterized by a partial posterior interhemispheric fusion of the brain, has been described in children. We describe the features of a case of a possible new MIH at 26 weeks of gestation, diagnosed using prenatal sonography and magnetic resonance imaging and confirmed by postmortem examination. This malformation of the brain was associated with an unusual appearance of the corpus callosum and rare chromosomal abnormality: a 45X/46,XX/47,XX,+18 mosaicism. Copyright © 2006 ISUOG. Published by John Wiley & Sons, Ltd.

CASE REPORT

A 21-year-old woman, gravida 2 para 2, was referred at 26 weeks of gestation with suspected absence of the fetal septum pellucidum and corpus callosum following routine ultrasound examination.

We performed a detailed ultrasound examination of the fetal brain. In the coronal view, anteriorly, the interhemispheric fissure (IHF) was present and deviated, and the frontal horns were separated; in the median part, the ventricles communicated and the deep gray nuclei appeared normal (Figure 1a); posteriorly, the IHF was present and the occipital posterior horns were separated. In the axial view, the septum pellucidum could not be identified; the

posterior portions of the frontal lobes and the parietal region of the ventricles were not separated; bilateral colpocephaly (10 and 12 mm) was also diagnosed. The third ventricle was considered normal. In the sagittal view (Figure 2a), callosal dysgenesis was noted. The corpus callosum was present but was abnormally thin and straight, with a stick-like appearance and no evidence of the genu and splenium. The posterior fossa was normal.

Magnetic resonance imaging (MRI) was performed to complete the morphological examination of the fetal brain. This confirmed interhemispheric fusion of the atria with colpocephaly and a normal separation of frontal and occipital lobes. The falx cerebri was present (Figure 1b). The corpus callosum was also confirmed as being abnormal (Figure 2b). The separation of the hypothalamus and basal ganglia was normal. The myelination and gyration were normal for gestational age. Cytogenetic analysis of cells obtained from the amniotic fluid revealed a 45,X/46,XX/47,XX,+18 karyotype.

The parents were informed of the poor prognosis associated with such anomalies¹. Termination of pregnancy was performed at their request in accordance with French legislation.

Pathological examination of the fetus was performed. External examination showed a eutrophic female fetus without facial anomalies. The autopsy showed no visceral malformations. The brain weighed 189 g (50th centile). Gyration was consistent with that of a fetus 3 weeks later in gestation (Figure 3a). The olfactory bulbs were present. The brain stem and cerebellum were normal. The IHF

Correspondence to: Dr O. Picone, Service de Gynécologie-Obstétrique, Hôpital Antoine Béchère, 157, rue de la porte de Trivaux, 92140 Clamart, France (e-mail: olivier.picone@abc.ap-hop-paris.fr)

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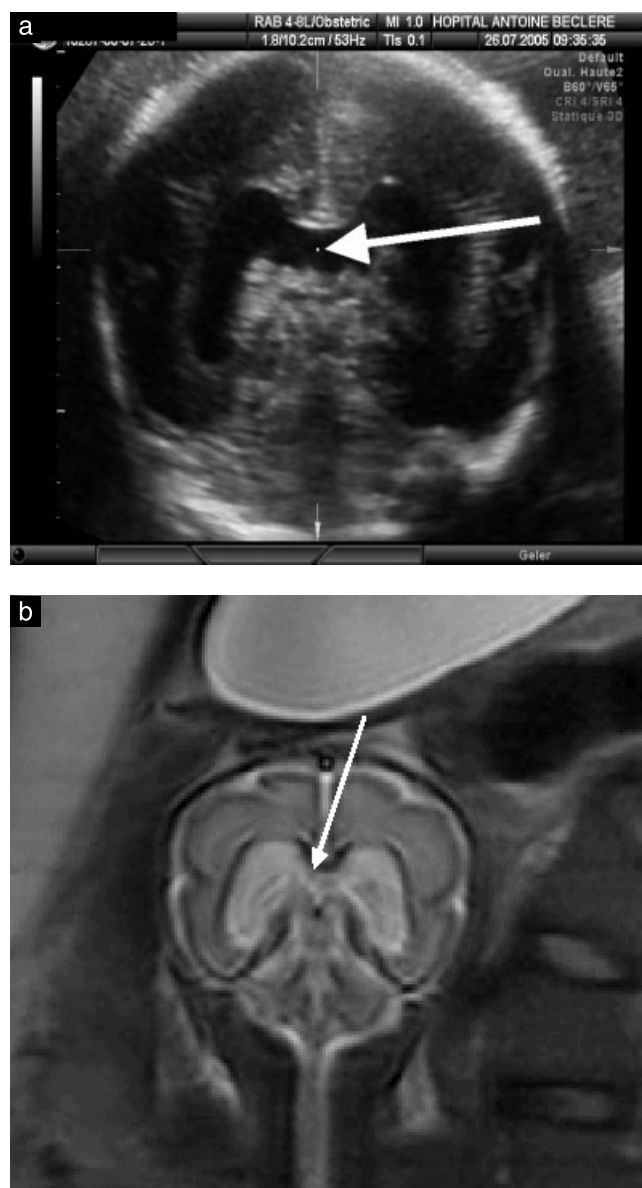


Figure 1 Median coronal view of the fetal brain showing opening of the septum pellucidum (arrow); (a) ultrasound and (b) magnetic resonance images.

was present in the anterior and posterior parts of the brain but was fused in the median part over a distance of 3.5 cm. Coronal sections (Figure 3b) demonstrated deviation of the anterior IHF, and communication of the lateral ventricles with the third ventricle. The cavum and septum pellucidum were absent and the corpus callosum was thickened, measuring 4 mm. The thalami were not fused.

On microscopic examination, with the exception of hypoplastic ovaries, no visceral anomalies were observed. The cerebral cortex was normal, without neuronal migration anomalies. Heterotopic neurons were observed in the vermis. The germinal matrix was normal. The main anomaly was a dysplastic corpus callosum with fusion of the two hemispheres in the median part of the brain, corresponding to a middle interhemispheric fusion (also called syntelencephaly).

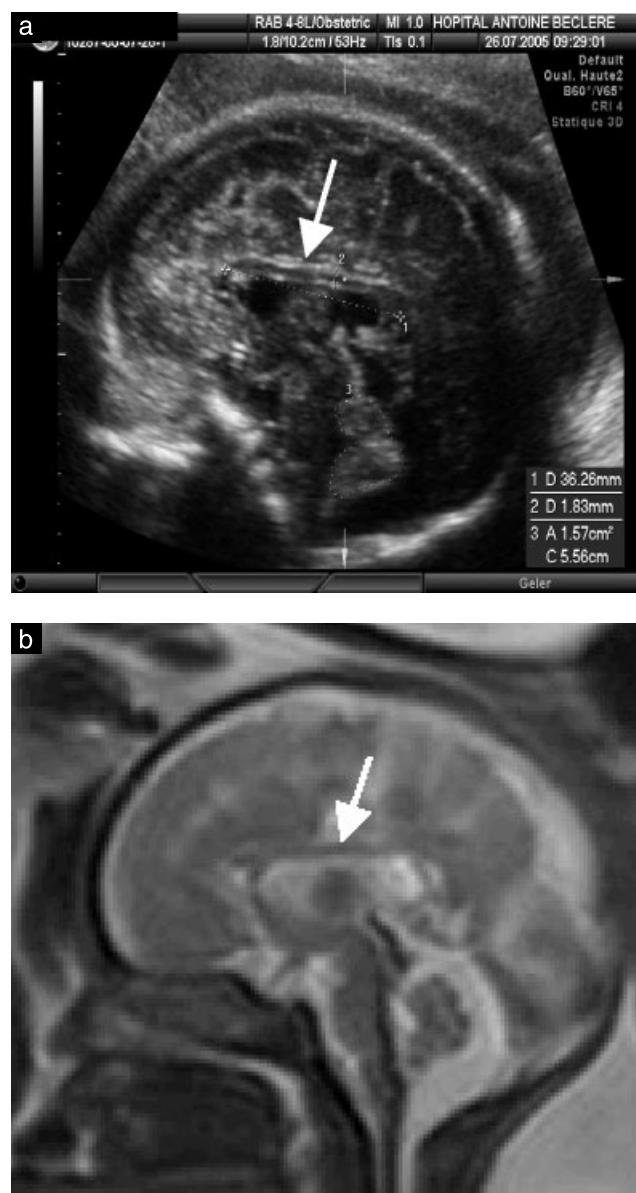


Figure 2 Sagittal view of the fetal brain showing the abnormal corpus callosum (arrow); (a) ultrasound and (b) magnetic resonance images.

DISCUSSION

This case illustrates the prenatal appearance of a likely new middle interhemispheric variant (MIH) associated with an uncommon chromosomal abnormality, 45,X/46,XX/47,XX,+18. Holoprosencephalies (HPE) are complex anomalies of the forebrain that are postulated to derive from a failure in the diverticulation of the embryonic prosencephalon. This malformation is classically divided into three subtypes: alobar, semilobar and lobar, but the precise prenatal classification may sometimes be difficult. In the alobar variety, the IHF and the falx cerebri are totally absent, there is a single primitive ventricle (holoventricle), the thalami are fused in the midline, and there is absence of the third ventricle, neurohypophysis, olfactory bulbs and tracts. In semilobar HPE, the two hemispheres are

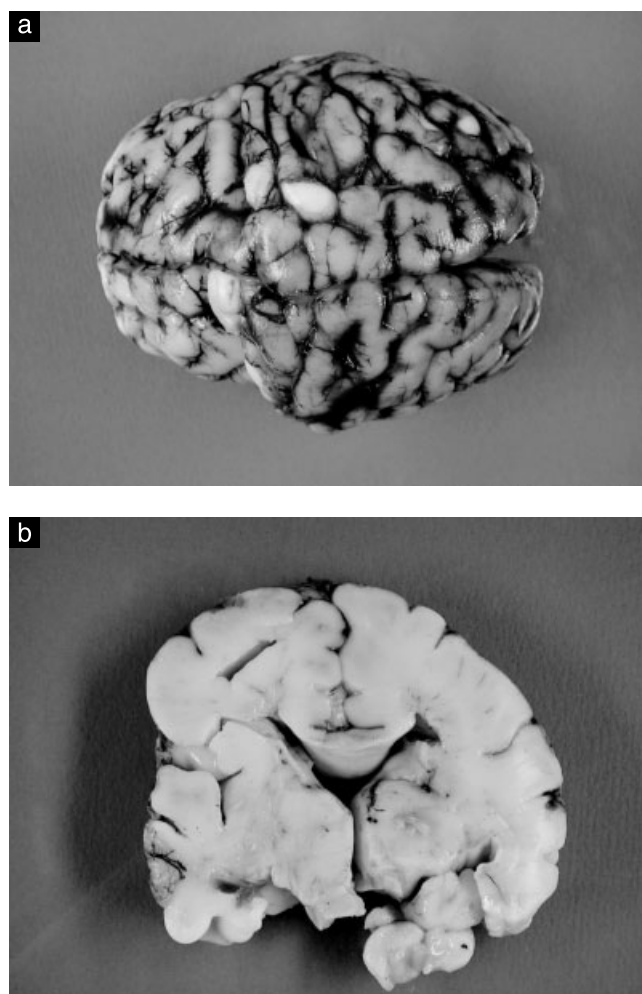


Figure 3 (a) External appearance of the fetal brain postmortem. (b) Median coronal section showing absence of the septum pellucidum.

partially separated posteriorly, but there is still a single ventricular cavity. In the lobar variety, the IHF is well developed posteriorly and anteriorly, but there is still a variable degree of fusion of the cingulate gyrus and the lateral ventricles, and the septum pellucidum is absent.

The differential diagnosis between lobar HPE and MIH may be difficult. MIH consists of an abnormal midline continuity of the posterior frontal and parietal regions of the cerebral hemispheres, with separation of the basal forebrain, anterior frontal lobes and occipital regions^{1,2}. Maligner *et al.*³ reported two such fetuses with lateral ventricles communicating only in their middle portion,

with normal anterior horns and non-cleavage of the midbrain. These findings were confirmed by autopsy in only one of the two fetuses. All 15 MIH infants described by Lewis *et al.*¹ had normal separation of the lentiform nuclei and hypothalamus, unlike the ubiquitous non-separation of varying severity seen in classic HPE. The most commonly affected deep gray nucleus in MIH was the thalamus, which had not separated in 33% of cases¹. This study presented the clinical manifestations of MIH compared with classic subtypes of HPE and concluded that MIH is similar to the lobar subtype for functional measures but differs in the absence of endocrine dysfunction and choreoathetosis¹. To Simon *et al.*⁴, MIH appears to be the non-cleavage of midline structures in a completely different pattern from that of classic HPE: 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.

Our case has two features that distinguish it from previously reported cases of classic MIH or lobar HPE: i) the sylvian fissures were not connected across the midline over the vertex, with a sylvian angle of Barkovich that was almost normal, and ii) the callosal dysgenesis consisted of a stick-like rudimentary corpus callosum with an absent genu and splenium. Furthermore, in MIH, as in our case, myelination is normal, and the olfactory bulbs are present, in contrast to classic HPE.

Prenatal classification of HPE and its variants is difficult, and it may be that a wide range of varieties exists within the classical subtypes. Studying these anatomical variations, together with their chromosomal and genetic abnormalities, will help us to better understand the mechanisms of these malformations.

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