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Megalencephaly with Polymicrogyria: A Case Report

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Summary. **A male infant with bilateral megalencephaly, recognized in the 12th week of gestation, displayed polymicrogyria on magnetic resonance imaging. It is generally accepted that patients with polymicrogyria almost always have microcephaly.**

The present case is therefore unusual and is considered to be the first in which magnetic resonance imaging detected migrational disorders of the brain in a bilateral megalencephalic patient.

INTRODUCTION

With magnetic resonance imaging (MRI) permitting clear delineation of gray-white matter differentiation, it has become possible to diagnose with increasing frequency migrational disorders radiologically.[1,2] We here report a case of megalencephaly with polymicrogyria. This case is unusual because patients with polymicrogyria almost always have microcephaly. Moreover, this is considered to be the first case where MRI detected migrational disorders in bilateral megalencephaly.

CASE REPORT

The male patient presented megalencephaly at the age of 4 months. He was the third child born to nonconsanguineous parents after an uncomplicated pregnancy. However, increased biparietal diameter had been noticed from the 12th week of gestation. He was delivered at the 35th week of gestation. His head circumference at birth was 38.4 cm (+3.78 SD). At the age of 3 months, recurrent generalized tonic clonic seizures, occasionally associated with apnea, appeared.

On admission at the age of 4 months, his head circumference was 48.5 cm (+4.86 SD). Neither pigmented nor depigmented skin lesions were observed. Minor anomalies, such as frontal bossing, a saddle nose, long eyelashes and high-arched palate, were noticed. The anterior fontanelle was 5×6 cm, soft and flat. The cranial sutures were not dissociated. The optic fundi were normal. There was no social smile. Visual following of objects was not observed. Muscle tone was remarkably decreased and he had no head control. Deep tendon reflexes and primitive reflexes were not elicited. All laboratory examinations were unremarkable.

Regarding neuroradiological studies, computed tomography (CT) performed at a separate hospital at birth (Fig. 1A) revealed a thick cortex with attenuated gray-white matter interdigitations, especially in the frontal and temporal regions. A rounded, high-density spot was noted at the orifice of the right deep sulcus. Ventriculomegaly was regarded as mild. MRI performed at the age of 5 months (Fig. 1B-D) revealed broad-based gyri with a thick cortex, especially in the frontal and temporal cortex. Lateral ventricles, cavum septi pellucidi, and cavum vergae were large. Moreover, the cortex was remarkably thick in the right opercular region and a large vascular structure was detected at the orifice of the deep sulcus. Several small vessels ran centripetally within the deep sulcus from a large vascular structure. Several hyper-intense lesions lining the subcortical white matter of the frontal region and observed on long-TR images and low-signal intensity at the same site on short-TR images are presumably a result of gliosis.

Up to the age of 16 months, subsequent CTs and MRIs were performed. Although findings referred to the cerebral surface, cerebral contour and gray-white matter interdigitations showed no changes, and the

size of ventricles increased with age. The ventricular index was calculated by dividing the transverse diameter of the bilateral anterior horns by the transverse diameter of the total skull at the level of the third ventricle. As shown in Fig. 2, the ventricular index tended to increase with age. To evaluate ventriculomegaly, cisternography and a gradient-echo of MRI were performed at the age of 16 months. Cisternography using ^{111}In-DTPA showed a delay of ascent in cerebral convexities but no ventricular reflux. A gadientecho of MRI revealed periaqueductal flow void.

This patient is now 17 months of age. Although the seizures have been controlled by antiepileptics, both head control and the visual recognition of objects are absent. Neurological findings at present are not different from those at admission. Head circumference has gradually increased with age as shown in Fig. 2, but the patient does not show any manifestations of the increased intracranial pressure.

DISCUSSION

The findings of CT and MRI noted in this patient, such as cortical thickness, attenuated gray-white matter interdigitation and broad wide-based gyruses, correspond to migrational disorders of the brain.[1-3] Moreover, the remarkably thick cortex in the right opercular region, a large vascular structure located at the orifice of the deep sulcus, and gliosis in the white matter are considered evidence of polymicrogyria.[4]

However, according to reports on clinical manifestations and neuroimaging studies concerning migrational disorders, patients almost always show microcephaly, with the exception of Walker-Warburg syndrome, and schizencephaly, which both accompany hydrocephalus, and unilateral megalencephaly.[1-3,5]

Megalencephaly is defined as an oversized and overweight brain that exceeds the mean by more than 2.5 standard deviations for the respective age and sex with the exception of the presence of

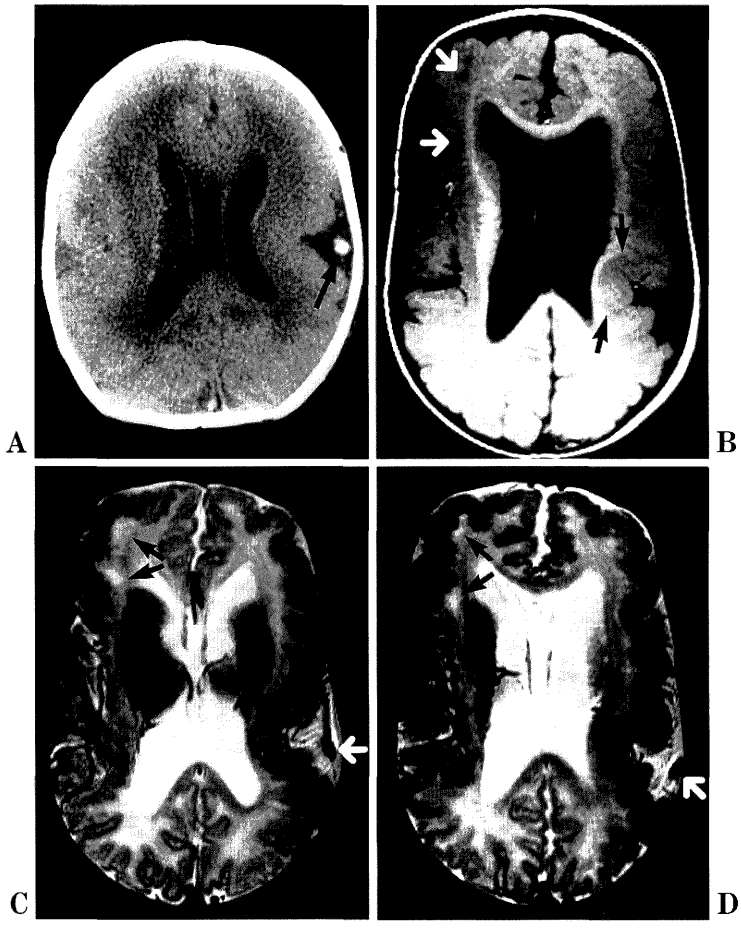

Fig. 1. CT at birth and MRI at the age of five months. **A.** Unenhanced CT shows a thick cortex with attenuated gray-white matter interdigitation. A high-density spot can be noted at the orifice of the right deep sulcus (black arrow). **B.** Axial T_1-weighted (SE, TR600/TE15) MRI shows a remarkably thick cortex in the right opercular region (black arrows) with thinning of the underlying white matter. Low intensity lesions of the subcortical white matter are noted in the frontal region (white arrows). **C** and **D.** Axial T_2-weighted (SE, TR2000/TE90) MRI shows a large vascular structure in the right opercular region. Several small vessels run from a large vascular structure (white arrows). Hyper-intense legions of the subcortical white matter are noted in the frontal region (black arrows).

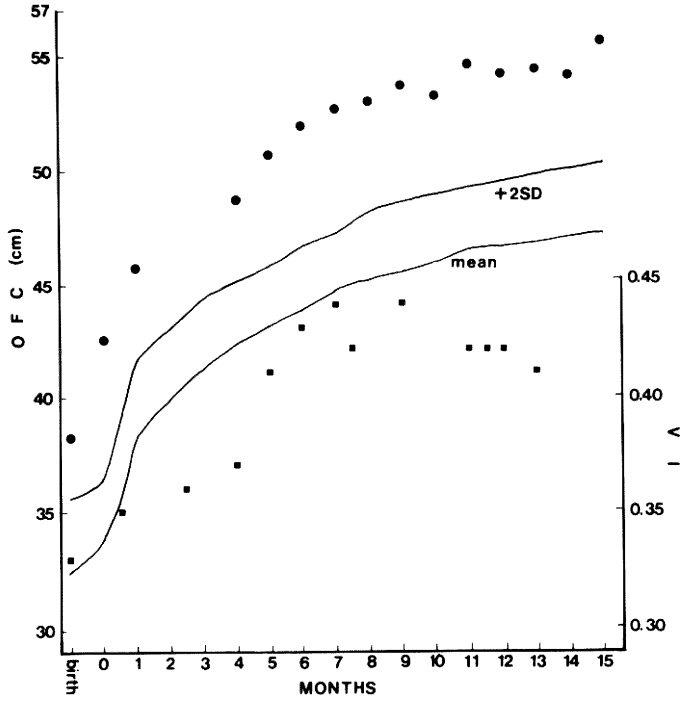

Fig. 2. Patient's growth in occipito-frontal circumference (OFC) and change of ventricular index (VI). = OFC; = VI. Solid lines are mean and 2SD of OFC. Age in months is expressed by corrected age from the expected date of confinement.

hydrocephalus. In living persons, occipito-frontal circumference (OFC) is available instead of brain weight.[6,7] The possibility that hydrocephaly is a cause of large head size seems unlikely because the large head size was evident at birth when the ventriculomegaly was still mild in this patient.

According to a review by Dekaban and Sakuragawa in 32 brains of primary megalencephaly, which implies bilateral megalencephaly without certain metabolic and degenerative disorders, severe malformations of the brain, such as pachygyria and polymicrogyria were noted in 32% of these patients by neuro-pathological examination.[6] Larroche also mentioned a case of bilateral megalencephaly with abnormal gyration of the cerebral cortex.[8] However, it is a fact that there are no reports of cases of megalencephaly with migrational disorder as detected by neuroimaging modalities.

Although the pathogenesis of megalencephaly is not clear, the disease is probably caused by disturbances in the regulation of cell proliferation.[7] However, the mechanism underlying the polymicrogyric brain accompanying megalencephaly remains unknown in this patient. The major neuronal migration is known to occur from the 7th week to the 16th week of gestation, and smaller waves of neuronal migration continue up to the 25th week of gestation.[4] Various types of migrational disorders are associated with the timing of the brain insults. It is generally accepted that agyria results from an insult at the 13th week of gestation, and polymicrogyria occurs during the middle-to-late second trimester.[4]

As for unilateral megalencephaly, heteroploidy of the cells and a biochemical defect in the control of the cell metabolism have been proposed as causes of hemispheric enlargement.[4,5] As Barkovich et al. described eight cases of polymicrogyria diagnosed by CT and MRI in a report of 12 cases of unilateral megalencephaly, polymicrogyria seems to be noted more often in unilateral megalencephaly in comparison with bilateral megalencephaly.[5] Moreover, it is interesting that there seemed to be an inverse relationship between the severity of hemispheric involvement and the degree of hemispheric enlargement.[5] Although the reason why polymicrogyria are noted more often in unilateral megalencephaly is not clarified, Barkovich postulated that a mild brain insult, which is not severe enough to destroy the developing neuronal and glial cells in the late second trimester, may cause both polymicrogyria and unilateral megalencephaly.[4,5] However, in our case, an increased biparietal diameter was noticed from the 12th week of gestation even though the mechanism of unilateral megalencephaly postulated by Barkovich can be applied to the bilateral megalencephaly. The mechanism of megalencephaly in our case can not be clarified, but there is a possibility that the severity of the brain insult, which was thought to occur before

the 12th week of gestation, influenced the cortical dysplasia and the cerebral enlargement.

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