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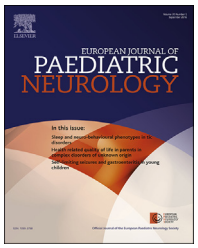

Original Article

Clinical and neuroimaging findings in children with gray matter heterotopias: A single institution experience of 36 patients

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ABSTRACT

Objective: To describe the clinical spectrum and neuroimaging features of childhood gray matter heterotopias in a single tertiary hospital in Taiwan.
Methods: We retrospectively reviewed the medical records and magnetic resonance images (MRI) of 36 patients with gray matter heterotopias, 19 females and 17 males, between July 1999 and June 2014. The MRI morphologic findings of gray matter heterotopias were recorded along with the presence of associated cerebral malformations. The clinical, electrophysiological and associated systemic malformation data were also recorded.
Results: A total of 36 patients were included in the study. Their ages ranged from 1 month to 18 years with a mean age of 3 years 6 months. According to the location of gray matter heterotopias, patients were classified into two groups: periventricular (26) and band (10). The phenotypic spectrum in our population differed from that described previously. In the periventricular group, additional cerebral malformations were found in 18/26 (69%) and systemic malformations in 14/26 (54%). In the band group, additional cerebral malformations were found in 5/10 (50%) and systemic malformations in 2/10 (20%). The majority of patients had developmental delay and intellectual deficit. Twenty-two patients suffered from epileptic seizures with 12 developing refractory epilepsy.
Conclusions: In periventricular heterotopias, the most common associated cerebral malformation was ventriculomegaly, followed by agenesis of corpus callosum. Congenital heart disease was the most common additional systemic malformation. However, the most common associated cerebral malformation was pachygyria in band form. The majority of patients had developmental delay, intellectual deficit, especially in band heterotopias.

Abbreviations: EEG, electroencephalography; MRI, magnetic resonance imaging.

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1. Introduction

Gray matter heterotopias are common forms of cortical development malformations characterized by the presence of cortical neurons in abnormal positions. They are caused by failure of neuronal migration from the germinal matrix in the wall of the lateral ventricle to the developing cerebral cortex between 6 and 16 weeks of gestation.[1] In addition, a defect in neural stem cell proliferation as an etiology has also been identified recently.[2,3] It is usually found during the evaluation of children or young adults with epilepsy, neurodevelopmental abnormalities, or an incidental finding.[1,4] The pathogenesis of gray matter heterotopias are not fully understood, but they lead to distinct clinicoradiologic syndromes. Gray matter heterotopias may occur in isolation, in association with other developmental anomalies of the brain, or as part of a multiple congenital anomaly syndrome.[5]

Three forms of gray matter heterotopias are classified on the basis of location and configuration of ectopic gray matter tissue on magnetic resonance imaging (MRI).[4] Periventricular heterotopias are described as nodule masses of gray matter adjacent to or protruding into the walls of the lateral ventricles.[5] Periventricular heterotopias are the most common.[4,6] Band heterotopias are characterized of heterotopic gray matter located in the white matter between the lateral ventricular wall and the cortex.[5] Subcortical heterotopias occur as masses of gray matter within the deep and subcortical white matter.[5] The purpose of this study is to evaluate the clinical and neuroimaging features of gray matter heterotopias over a 15-year period in a single tertiary hospital in Taiwan.

2. Materials and methods

The medical records of patients diagnosed with gray matter heterotopias at Chang Gung Memorial Hospital, a tertiary medical center in Taiwan, between July 1999 and June 2014, were retrospectively reviewed. This study was approved by our Institutional Review Board. Diagnosis of gray matter heterotopias was confirmed based on brain MRI. Clinical histories were reviewed and the following information was systematically collected from the medical charts: intellectual evaluation, motor developmental milestones, and associated cerebral and systemic malformations. In addition, presence of seizures was recorded, including seizure type, location of epileptic discharges on electroencephalography (EEG), and response to antiepileptic medications. Brain MRI studies included T1-weighted, T2-weighted, fluid-attenuated inversion recovery, diffusion-weighted and post-contrast T1 imaging. The hard copies of brain MRI of all patients were reviewed by an experienced pediatric neuroradiologist (AMC W). MRI morphologic findings of gray matter heterotopias were recorded along with the presence and type of associated cerebral malformations. Because we had no subcortical heterotopias, patients were subdivided into two groups: periventricular and band. Full systemic and neurologic examinations were performed during the visits to the pediatric neurology clinic. EEG was carried out for each patient using the international 10–20 system.

3. Results

During the study period, we included 36 patients with MRI diagnosis of gray matter heterotopias. Their ages ranged from 1 month to 18 years with a mean age of 3 years 6 months. Nineteen patients were females and 17 were males. Twenty-two patients (61.1%) had a history of epileptic seizures. Patients were classified into two groups.

3.1. *Periventricular heterotopias*

This group included 26 patients (14 females and 12 males), aged 1 month to 18 years with a mean age of 3 years 5 months. Details of the clinical seizure, EEG, heterotopic category, outcome, and associated systemic and cerebral malformations of these patients are shown in Table 1. The heterotopic nodules were isointensity to the cortical gray matter on MRI (Fig. 1). In our series, the nodules were bilateral in 14 patients with diffuse 10 and focal 4. Unilateral was noted in 12 patients with focal 8 and diffuse 4. The frontal horns of lateral ventricles were the most common location. Eighteen patients had associated cerebral malformations with ventriculomegaly found in 11, followed by agenesis of corpus callosum found in 7, and cortical dysplasia and hemispheric cyst each found in 3. In 11 patients with ventriculomegaly, we found 4 patients in unilateral focal, 3 each in bilateral diffuse and bilateral focal, and 1 in unilateral diffuse. Additional systemic malformations were noted in 14 patients with the most common being congenital heart disease in 6. Four patients had both atrial septal defect and patent ductus arteriosus, 1 had atrial septal defect only, and 1 had patent ductus arteriosus only. Sixteen patients (female:male = 11:5), including 12 with associated cerebral malformations, experienced epileptic seizures. Infantile spasms and partial seizure were the most common, each found in 6 patients. EEG abnormalities were found in 19 patients, with focal epileptiform being most common. Eight patients, including 5 with associated cerebral malformations, were refractory to anti-epileptic drugs. The majority of patients (19/26) had developmental delay and intellectual deficit.

3.2. *Band heterotopias*

This group included 10 patients (5 males and 5 females), aged 1 month to 16 years 1 month with a mean age of 3 years 8 months. Details of the clinical, EEG, heterotopic category, outcome, and associated systemic and cerebral malformations of these patients are shown in Table 2. The heterotopias had the same MRI signal intensity as the cortical gray matter (Fig. 2). Seven patients had bilateral involvement and the other 3 were unilateral. Associated cerebral malformations were detected in 5 patients, with pachygyria found in 3 patients, followed by ventriculomegaly in 2 patients. Six patients (male:female = 4:2), including 3 with associated cerebral malformations, experienced epileptic seizures. Infantile spasms, partial seizure and generalized seizure were each found in 2 patients. All 6 patients with seizures showed abnormal EEG with focal epileptiform being most common.