

BILATERAL FRONTOPARIETAL POLYMICROGYRIA LINKED TO CHROMOSOME 16

Bilateral Frontoparietal Polymicrogyria: Clinical and Radiologic Features in 10 Families with Linkage to Chromosome 16

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Polymicrogyria is a common malformation of cortical development characterized by an excessive number of small gyri and abnormal cortical lamination. Multiple syndromes of region-specific bilateral symmetric polymicrogyria have been reported. We previously described two families with bilateral frontoparietal polymicrogyria (BFPP), an autosomal recessive syndrome that we mapped to a locus on chromosome 16q12-21. Here, we extend our observations to include 19 patients from 10 kindreds, all linked to the chromosome 16q locus, allowing us to define the clinical and radiologic features of BFPP in detail. The syndrome is characterized by global developmental delay of at least moderate severity, seizures, dysconjugate gaze, and bilateral pyramidal and cerebellar signs. Magnetic resonance imaging demonstrated symmetric polymicrogyria affecting the frontoparietal regions most severely, as well as ventriculomegaly, bilateral white-matter signal changes, and small brainstem and cerebellar structures. We have refined our genetic mapping and describe two apparent founder haplotypes, one of which is present in two families with BFPP and associated microcephaly. Because 11 of our patients initially were classified as having other malformations, the syndrome of BFPP appears to be more common than previously recognized and may be frequently misdiagnosed.

recurrent seizures. Magnetic resonance imaging (MRI) has allowed identification of these pathologic findings and has been used for classification. Patients may present with a localization-related or generalized seizure disorder. Polymicrogyria is a common malformation of cortical development that may be associated with intractable seizures and developmental delay. An “excessive number of small gyri” and an abnormality in cortical lamination characterize this disorder. Selected syndromes with bilateral polymicrogyria have been identified. The pathologic lesions are usually symmetric and involve the frontal, perisylvian, or parietooccipital regions.

Chang and colleagues presented the clinical and neuroimaging findings of an autosomal recessive disorder with bilateral frontoparietal polymicrogyria linked to chromosome 16q12-21. The 10 kindred included 19 affected individuals. The associated clinical disorders were highly stereotyped and included developmental delay, seizures, esotropia, and bilateral pyramidal and cerebellar signs. The patients were from the Middle East or Indian subcontinent. All individuals had a moderate-to-severe chronic global static encephalopathy. Fifteen (94%) of 16 patients had seizures. Most individuals experienced symptomatic generalized epilepsy with generalized tonic-clonic seizures or myoclonic seizures. Complex partial seizures were reported in only one patient. Information regarding seizure activity was not available in three patients. Dysconjugate gaze occurred in 15 (88%) of 17 patients, and MRI revealed bilateral frontoparietal polymicrogyria in all patients evaluated.

The present study reports an epileptic syndrome associated with a common genetic malformation and several stereotyped clinical features. The neuroimaging studies in these patients confirmed the presence of a bilateral frontoparietal polymicrogyria. The ictal semiology in most patients suggested a widely distributed epileptogenic disorder, probably reflecting the bi-hemispheric malformations of cortical development. Recognition of patients with stereotyped clinical and imaging findings, in association with bilateral frontoparietal polymicrogyria, will be important in identifying the underlying genetic factors.

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COMMENTARY

Malformations of cortical development represent an important symptomatic etiologic factor in patients with