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SEIZURE DISORDERS

PERIVENTRICULAR NODULAR HETEROTOPIA AND EPILEPSY

The clinical, MRI, and EEG findings in 54 patients (35 female, 19 male; aged 1 to 64 years) with periventricular nodular heterotopia (PNH) were analyzed in relation to epileptic outcome and genesis of epileptic discharges, in a study at the Neurological Institute and Epilepsy Surgery Center, Niguarda General Hospital, Milan, Italy. Five PNH groups were defined based on imaging and clinical findings: Group 1) bilateral and symmetrical (9 patients); 2) bilateral single-nodule (9); 3) bilateral asymmetrical (9); 4) unilateral (14); and 5) unilateral with neocortical extension (13). Focal interictal EEG abnormalities were related to PNH location and were frequently multifocal, except in group 2 patients. Ictal EEG and stereo-EEG recordings suggest that epileptic discharges and seizures originate from abnormal circuitries located close to or involving the PNH. Group 1 patients showed a female preponderance (8:1), normal neurologic and mental findings, and epilepsy preceded by febrile seizures; while group 2 showed male preponderance (7:2), large ventricles, and mental retardation, with a benign course of epilepsy. Groups 3, 4 and 5 had a worse epileptic outcome than groups 1 and 2. The outcome of groups 4 and 5 unilateral cases was similar, regardless of cortical involvement. Genetic factors are important in etiology of bilateral PNH cases, with mutations involving FLN1 and other novel genes. Acquired prenatal factors are important in unilateral heterotopias, with co-occurrence of genetic and environmental factors in some. (Battaglia G, Chiapparini L, Franceschetti S, et al. Periventricular nodular heterotopia: classification, epileptic history, and genesis of epileptic discharge. **Epilepsia** Jan 2006;47:86-97). (Reprints: Dr G Battaglia, Molecular Neuroanatomy Lab, Department of Experimental Neurophysiology and Epileptology, Instituto Neurologico "C Besta," Via Celoria 11, 20133 Milano, Italy).

COMMENT. Most PNH are associated with refractory epilepsy. Epileptiform activity

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is generated in the nodules or in the adjacent neocortex. The heterotopia are part of an abnormal circuitry involving surrounding cortex.

EEG-fMRI studies of grey matter heterotopia at the Montreal Neurological Institute showed metabolic responses in the heterotopia while spikes were generated in the neocortex (Kobayashi E et al. **Brain** 2006;129:366-374). Activation responses reflected excitation involving the heterotopia and surrounding cortex, and deactivation also reflected a distant, extra-lesional inhibition. EEG-fMRI is a non-invasive procedure that may explain the epileptogenicity of neuronal migration disorders and the involvement of areas of the brain distant from the heterotopia.

ANGELMAN SYNDROME AND EPILEPSY

Twenty-six patients with Angelman syndrome (AS), of which 19 had 15q11-13 maternal deletion, were studied and followed at the University of San Paulo, Brazil, with particular reference to the prevalence and type of epilepsy and its response to antiepileptic drugs. Epilepsy occurred in 22 patients (85%), 19 with deletion and 3 without positive genetic confirmation. All 19 patients with deletion had generalized seizures, and 10 (53%) had partial seizures. Video-EEG uncovered atypical absence and subtle myoclonic seizures, often missed by parents; it also recorded nonconvulsive status that is sometimes prolonged and associated with cognitive decline in 7. Mean age at onset of seizures was 1 year 1 month, and in 18 patients, epilepsy preceded the clinical diagnosis of AS. Five (26%) had their first seizure with fever, and 10 (53%) had epilepsy aggravated by fever. Sixteen (84%) had status epilepticus, associated with hyperthermia in 7. Valproic acid, alone or in combination with phenobarbital or clonazepam, improved seizure control while carbamazepine, oxcarbazepine, and vigabatrin caused aggravation of seizures. Refractory seizures occurred in 16 (84%) during infancy and early childhood, but seizure frequency decreased at a mean age of 5.3 years. Improvement in seizure frequency and severity continued through late childhood and puberty. (Valente KD, Koiffmann CP, Fridman C, et al. Epilepsy in patients with Angelman syndrome caused by deletion of the chromosome 15q11-13. **Arch Neurol** January 2006;63:122-128). (Respond: Kette D Valente MD PhD, Department of Psychiatry, University of Sao Paulo, R Jesuino Arruda, 901/51, 04532-082 Sao Paulo, SP Brazil).

COMMENT. Angelman syndrome is characterized by developmental delay, severe mental retardation, paroxysmal laughter, ataxia associated with hand flapping, seizures, and stereotyped jerky movements, regarded as cortical myoclonus (Guerrini R et al. **Ann Neurol** 1996;40:39-48). Physical signs include microcephaly, prominent jaw, wide mouth, pointed chin, and hypopigmentation. Seizures are mainly generalized, frequently partial, atypical absence, myoclonic, sometimes included as a cause of West, or Lennox-Gastaut syndromes, and, as shown in the above study, often febrile in type.

The typical interictal EEG abnormality shows rhythmic slow waves at 4-6 Hz and runs of 2-3 Hz slow spike-wave complexes anteriorly. Eye closure is accompanied by spikes and 2-4 Hz slow waves posteriorly (Robb SA et al. **Arch Dis Child** 1989;64:83-86; Sugimoto T et al. **Epilepsia** 1992;33:1078-1082). Status epilepticus is a frequent complication, sometimes precipitated by hyperthermia, and often recurrent. Age-related improvement in seizure frequency and severity is an additional characteristic.