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J. GORDON MILLICHAP, M.D., F.R.C.P., EDITOR

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SEIZURE DISORDERS

INFANTILE EPILEPTIC ENCEPHALOPATHIES

The phenotypic variability associated with sodium channel alpha 1 subunit gene SCN1A mutations was studied in 188 patients with various infantile epileptic encephalopathies referred to the Universities of Adelaide and Melbourne, Australia; and centres in Glasgow, UK; Wellington, New Zealand; Montreal and Vancouver, Canada; Worcester, MD, USA, Israel, and Denmark. All had seizure onset within the first 2 years of life. The total cohort contained 66 with severe myoclonic epilepsy of infancy (SMEI or Dravet syndrome). 36 had SMEI-borderland (SMEB), a syndrome that lacks myoclonic seizures or generalized spike-wave activity, 25 with cryptogenic generalized epilepsy, 18 with cryptogenic focal epilepsy, 10 with myoclonic-astatic epilepsy (MAE), and 12 with Lennox Gastaut syndrome (LAS). By molecular analysis, 90 (48%) had SCN1A mutations: 52 of the 66 (79%) patients with SMEI and 25 of 36 (69%) with SMEB had SCN1A mutations. Mutations were present in 24% of patients with cryptogenic generalized epilepsy and 22% of those with cryptogenic focal epilepsy. A small subgroup of 5 cases of severe infantile multifocal epilepsy (early onset seizures and later cognitive decline) had SCN1A mutations in 3. This broadening of the phenotypic spectrum of infantile epileptic encephalopathies allows early molecular diagnosis and genetic counseling. (Harkin LA, McMahon JM, Iona X et al. The spectrum of SCN1A-related infantile epileptic encephalopathies. Brain March 2007;130:843-852). (Respond: Prof Ingrid Scheffer, Epilepsy Research Centre, Neuroscience Bldg, Heidelberg Repatriation Hospital, Bansia St, West Heidelberg, Victoria 3081, Australia).

COMMENT. SMEI or Dravet syndrome is characterized by prolonged febrile hemiclonic or generalized tonic-clonic seizures with onset in the first year of life. Myoclonic,

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focal, absence and atonic seizures evolve between 1 and 4 years, and are accompanied by slow development and regression. Neurologic abnormalities include spasticity and ataxia. Some survive into adulthood, but seizures are refractory, and cognitive outcome is poor (Jansen FE et al. Neurology 2006;67:2224-6; cited by authors). In the current report, infantile.epileptic encephalopathies with SCN1A mutations now include, in addition to SMEI and SMEB, several infantile onset epileptic syndromes, previously thought to be cryptogenic.

EPIDEMIOLOGY AND OUTCOME OF CONVULSIVE STATUS EPILEPTICUS

The results of the North London Convulsive Status Epilepticus in Childhood Surveillance Study (NLCSESS) (Chin RF et al. Lancet 2006;368:222-229) are used to develop a new treatment protocol, by researchers at the Institute of Child Health, and Great Ormond Street Hospital for Children, London, UK, Status epilepticus is defined as a seizure or series of seizures that last for 30 min or more without regaining consciousness between seizures (ILAE Guidelines for epidemiologic studies on epilepsy. Epilepsia 1993;34:592-596). A definition used for treatment purposes includes continuous seizure activity lasting 5 min, and is termed potential status epilepticus. The study was for 2 years up to the 16th birthday and neonates were excluded. The incidence of CSE in this population was 17-23/100.000 children per year. Prolonged febrile seizures were the most common cause. occurring in 32% of the total of 304 episodes of CSE. Etiology was acute symptomatic in 17%, remote symptomatic in 16%, previous epilepsy in 12%, and unknown in 7%. Age incidence was mainly 0-4 years. Incidence was increased in Asian (Indian and Pakistani) ethnic groups, and with poor socioeconomic status. Acute bacterial and virus CNS infections accounted for 19% of CSE with fever. Seizures were focal in onset in 36%, becoming generalized in 95%; 60% lasted longer than 60 min, CSE recurred in 17% in 1 year. Mortality of 3.4% was related to the cause (bacterial meningitis, metabolic or neurodegenerative disorder).

Analysis of data extracted from the NLCSESS population-based study supported the use of iv lorazepam as first-line treatment of CSE in preference to rectal diazepam, and iv phenytoin as second-line treatment. Prehospital treatment is important, but doses of benzodiazepine should be limited to 2, to avoid respiratory depression. Management of an underlying acute symptomatic cause is as important as stopping the seizure in terms of long-term outcome. Treatment for possible bacterial meningitis should begin early in a child with febrile CSE and while the child is investigated. (Neville BGR, Chin RFM, Scott RC. Childhood convulsive status epilepticus: epidemiology, management and outcome. Acta Neurol Scand April 2007;115 (s186):21-24). (Respond: Dr Brian Neville, The Wolfson Centre, Mecklenburgh Square, London WC1N 2AP, UK).

COMMENT. This article was presented at an International Symposium on Status Epilepticus in Infants and Young Children in Japan, April 2006. Other papers presented and published in this supplement include "Treatment of convulsive status epilepticus (CSE)" by Sugai K, and "Hippocampal volumes and diffusion-weighted image findings in children with prolonged febrile seizures" by Natsume J et al. Sugai lists the causes of CSE in his tertiary hospital as intractable epilepsies (34-49%), CNS infections (14-28%), febrile seizures (13-23%), metabolic disorders (3-5%), and cerebrovascular (1-3%). In a city hospital in Japan,