SEIZURE DISORDERS

ABSENCE EPILEPSY WITH FAST RHYTHMIC ATYPICAL EEG

The medical files of 31 patients with absence epilepsy (AE) were reviewed at La Timone University Hospital, and Henri Gastaut/Saint Paul Hospital, Marseilles, France. Five having an atypical EEG pattern with fast rhythmic spikes (10-15 Hz) during slow-wave sleep were selected for further study. Age at onset of absence seizures was 3 to 12 years. Four developed generalized tonic clonic seizures with onset at 11 to 16 years. All had borderline intelligence, with social and l;earning handicaps. Neuroimaging was normal. AE was classified as juvenile absence epilepsy in 2. EEG recordings during absence seizures showed generalized spike or polyspike waves of 3-4 Hz. Sleep EEG showed fast rhythmic discharges during stage II slow-wave sleep, without clinical manifestations on video. Seizures were mostly refractory to valproate and lamotrigine, and one patient died a sudden unexplained death at 3 year follow-up. (Guye M, Bartolomei F, Gastaut JL, Chauvel P, Dravet C. Absence epilepsy with fast rhythmic discharges during sleep: an intermediary form of generalized epilepsy? Epilepsia March 2001;42:351-356). (Reprints: Dr F Bartolomei, Service de Neurophysiologie Clinique et Unite d'Epileptologie Clinique, Chu Timone, 264 rue Saint Pierre, 13385 Marseille CEDEX 05, France).

COMMENT. Children presenting with absence epilepsy associated with fast rhythmic spikes in sleep EEG are at risk of a relatively poor outcome, with development of generalized tonic clonic seizures, resistance to antiepileptic drugs, and learning handicaps. The authors classify these cases as a separate clinical entity, intermediary between idiopathic and cryptogenic/symptomatic generalized epilepsies, and different from the Lennox-Gastaut syndrome that also exhibits fast discharges during slow-wave sleep in the EEG. Previous reports have recognized the risk of poor outcome of idiopathic generalized epilepsies associated with polyspike waves and fast rhythmic discharges in slow wave sleep. (Gibbs FA, Gibbs EL, 1952; Lennox WG, 1960; Lugaresi E et al, 1974; Degen R, Rodin E, 1991; Michelucci R et al, 1995).

EEG IN WOLF-HIRSCHHORN/PITT-ROGERS-DANKS SYNDROMES

A characteristic electroclinical pattern is described in a child with Pitt-Rogers-Danks syndrome (PRDS) and in 14 reports of Wolf-Hirschorn syndrome (WHS) reviewed at the Division of Medical Genetics, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland. Both syndromes are caused by deletions of the short arm of chromosome 4.

A 13 month-old female child presented with persistent growth failure and developmental delay. She could not sit and exhibited stereotyped hand-wringing movements. Dysmorphic features included a triangular face, prominent eyes, hypertelorism, and micrognathia. A relative macrocephaly (50th percentile) contrasted with a height and weight below the 3rd percentile. At reevaluation at 3 years, the developmental level was at 18 months, and she had tonic and generalized myoclonic seizures, controlled by valproate. In video-EEG recordings, 2-3 Hz high-voltage spike-wave bursts were associated with myoclonic jerks, and some without clinical manifestations. The bursts were localized over the centro-occipital area and became diffuse and generalized in sleep. The parents karyotypes were normal. (Zanki A, Addor M-C, Maeder-Ingvar M, Schorderet DF. A characteristic EEG pattern in 4p-syndrome: case report and review of the literature. Eur J Pediatr Feb 2001;160:123-127). (Respond: Dr Andreas Zanki, Institut fur

Medizinische Genetik, Universitat Zurich, Ramistrasse 74, 8001 Zurich, Sweitzerland).

COMMENT. Wolf-Hirschhorn syndrome (WHS) is characterized by severe growth and psychomotor retardation, microcephaly, dysmorphic triangular facies ("Greek helmet" appearance), skeletal and cardiac defects. Pitt-Rogers-Danks syndrome (PRDS) shares features like microcephaly, growth and mental retardation, but is less severe than WHS, without skeletal and cardiac anomalies. Both syndromes are caused by 4p deletions. Seizures occur in the majority of patients reported, and the EEG findings appear to be characteristic and common to both syndromes, and similar to those in Angelman's syndrome (AS). Periodic bursts of 2-3 Hz high-voltage slow waves with spike wave activity are typically biparietal and associated with myoclonic jerks in sleep in WHS and PRDS, and are usually bifrontal or generalized in AS. Most cases of AS are caused by deletions on chromosome 15q11-13, involving GABA receptor genes. Other GABA receptor genes have been mapped to chromosome 4p. Electroclinical and genetic similarities in WHS and AS suggest a common epileptic mechanism involving GABA pathways. The EEG might be of value in early diagnosis of these syndromes.

TOPIRAMATE-INDUCED METABOLIC ACIDOSIS IN EPILEPSY

Serum bicarbonate (HCO3) levels were measured before, during, and after discontinuing topiramate (TPM) as adjunctive therapy for medically refractory epilepsy in 30 children treated at Children's Hospital, Boston, MA. TPM dose varied from 50 to 650 mg/day, and 2 to 32 mg/kg/day. Larger doses resulted in higher TPM levels and greater likelihood of low HCO3 levels. Two-thirds had a greater than 10% decrease in HCO3 levels; the reduction was by 8 and 10 mEq/L in 2 cases. None was symptomatic. TPM was discontinued in 7 because of ineffectiveness, and in 2 with anorexia. The serum HCO3 returned to pretreatment levels. Monitoring HCO3 levels may be indicated, especially in patients predisposed to acidosis. (Takeoka M, Holmes GL, Thiele E et al. Topiramate and metabolic acidosis in pediatric epilepsy. Epilepsia March 2001;42:387-392). (Reprints: Dr M Takeoka, Child Neurology Service, Department of Pediatrics, School of Medicine, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan).

COMMENT. Topiramate is a carbonic anhydrase inhibitor, and a decrease in serum HCO3 levels with metabolic acidosis may be expected. This study has documented the generally asymptomatic association of lowered HCO3 levels in children treated with adjunctive topiramate therapy for refractory epilepsy. Various mechanisms of action have been proposed for TPM. The carbonic anhydrase inhibitory activity is generally described as weak, but is obviously sufficient to lower HCO3 levels in a substantial proportion of patients treated.

The mechanism of the anticonvulsant action of acetazoleamide, a potent carbonic anhydrase inhibitor, was first demonstrated in 1954 in animal studies at the Department of Pharmacology, University of Utah (Millichap JG, Woodbury DM, Goodman IS. J Pharmacol & Exper Therap 1955;115:251-258; and Proceedings of the American Epilepsy Society meeting, New York, Dec 1954). The anticonvulsant effect is related to the direct inhibition of carbonic anhydrase in the brain, and is independent of the metabolic acidosis which results from inhibition of the enzyme in the kidney. The anticonvulsant effect is not abolished in nephrectomized animals. Metabolic acidosis secondary to acetazolamide (or topiramate) has a very weak anticonvulsant effect, as demonstrated by studies with ammonium chloride in animals tested with electroshock seizures and in the clinic (Millichap JG. Anticonvulsant action of Diamox in children. Neurology 1956;6:552-559). A supplement of bicarbonate, as proposed by Takeoka and