

Maaswinkel-Mooij P, et al. Mental retardation and behavioral problems as presenting signs of a creatine synthesis defect. *Ann Neurol* April 2000;47:540-543). (Respond: Dr van der Knaap, Department of Child Neurology, Free University Hospital, PO Box 7057, 1007 MB Amsterdam, The Netherlands).

**COMMENT.** A deficiency of guanidinoacetate methyltransferase, an inborn error of metabolism of creatine synthesis, results in a decrease in body creatine, accumulation of guanidinoacetate, and decreased urinary excretion of creatine. This rare syndrome of creatine synthesis defect is characterized by psychomotor developmental delay or regression, behavioral abnormalities, muscle hypotonia, extrapyramidal movements, and intractable epilepsy. Diagnosis is suspected when urine amino acids and organic acids are increased generally, relative to creatine. Treatment with creatine monohydrate is followed by improvement but not complete resolution of symptoms.

### **BECTS WITH INTRACTABLE SEIZURES AND COGNITIVE DECLINE**

Two children, aged 2 and 4 years, with a characteristic onset of benign childhood epilepsy with centrotemporal spikes (BECTS), developed intractable seizures and cognitive decline, as reported from the Cleveland Clinic Foundation, OH. Seizures were repetitive clonic in one and hemifacial clonic in the second patient, and occurred more than 100 times daily. Some nocturnal generalized tonic-clonic seizures also occurred. Ictal EEGs showed focal sharp waves in central midline or centrotemporal regions, with or without evolution to generalized discharges. Interictal epileptiform, focal sharp wave, discharges were activated during drowsiness and sleep. MRIs were normal. Despite trials with five different antiepileptic drugs, including valproic acid (120 mcg/ml), carbamazepine, phenobarbital, phenytoin, ethosuximide, with prednisone and acetazolamide, seizures were uncontrolled. The IQ declined from 139 at 6 years, to 103 at 8 years, when surgery was considered but deferred in one. Seizures resolved spontaneously after 9 years of age in one, and they improved with the ketogenic diet after age 5 years in another. Cognition improved after seizures were controlled, or resolved spontaneously, in both patients. (Ong H-T, Wyllie E. Benign childhood epilepsy with centrotemporal spikes: Is it always benign? *Neurology* March (1 of 2) 2000;54:1182-1185). (Reprints: Dr Elaine Wyllie, Pediatric Epilepsy Program S51, The Cleveland Clinic Foundation, 9500 Euclid Ave, Cleveland, OH 44195).

**COMMENT.** BECTS is usually a benign disorder, characterized by infrequent seizures, with or without therapy, and spontaneous remission in later childhood. Rarely, seizures may be repetitive and frequent, refractory to medication, and associated with intellectual regression. The authors stress the need for a conservative approach to management, since spontaneous remission can be expected. The role of the antiepileptic medication in the cognitive decline of one of these patients is certainly suspect.

### **HIGH-DOSE IV STEROIDS IN LANDAU-KLEFFNER SYNDROME**

Intravenous therapy with methylpredisone (20 mg/kg daily) was effective in two six-year-old children with Landau-Kleffner syndrome treated at Jichi Medical School, Tochigi, Japan. A combination of valproate and a benzodiazepine had previously resulted in decreased seizures and EEG improvement, but speech and language were not improved. After 3 consecutive daily treatments with high-dose IV corticosteroids, speech was increased and receptive language improved. After a third course of therapy, the children could speak in sentences, and their subsequent language development was sustained.

(Tsuru T, Mori M, Mizuguchi M, Momoi MY. Effects of high-dose intravenous corticosteroid therapy in Landau-Kleffner syndrome. Pediatr Neurol 2000;22:145-147). (Respond: Dr Tsuru, Department of Pediatrics, Jichi Medical School, Kawachi-gun, Tochigi 329-0498, Japan).

COMMENT. High-dose corticosteroid therapy, administered early at the first appearance of symptoms, has been recommended in previous reports (Marescaux C et al. Epilepsia 1990;31:768-777; Lerman P et al. Dev Med Child Neurol 1991;33:257-266; Progress in Pediatric Neurology II, PNB Publ, 1994;pp221-226).

### **LOW-DOSE CLONAZEPAM EFFECT ON EPILEPTIFORM ACTIVITY**

The effect of low-dose clonazepam (CZP) on 24-hour long-term EEG recordings in 15 children with epilepsy was evaluated at the Karolinska Hospital, Stockholm, Sweden. A single IM injection of 0.02 mg/kg/bwt produced a highly significant decrease in epileptiform activity compared to placebo, in a double-blind study. Frequency of seizures decreased in parallel with the beneficial EEG response. Median plasma concentrations of CZP ranged from 18-<14 nM. (Dahlin M, Knutsson E, Amark P, Nergardh A. Reduction of epileptiform activity in response to low-dose clonazepam in children with epilepsy: A randomized double-blind study. Epilepsia March 2000;41:308-315). (Reprints: Dr M Dahlin, Neuropediatric Department, Astrid Lindgren's Children's Hospital, Karolinska Hospital, S-171 76 Stockholm, Sweden).

COMMENT. Low-dose clonazepam therapy (<0.02 mg/kg/day) can be effective in the control of focal and generalized epilepsy, while reducing the incidence of side effects commonly occurring with higher conventional doses (0.05 mg/kg/d). The development of tolerance is one of the greatest drawbacks of clonazepam therapy from a practical standpoint, an effect that usually leads to the necessity for larger doses and the occurrence of sedation, bronchial hypersecretion, and hyperactivity.

### **NEUROFIBROMATOSIS**

#### **MAGNETIC RESONANCE STUDIES IN NEUROFIBROMATOSIS 1**

Nine patients with neurofibromatosis type 1 (age, 6-19 years) and 9 controls were studied by quantitative magnetic resonance spectroscopic imaging (MRSI) at Johns Hopkins University School of Medicine, Baltimore, MD. Supratentorial UBO functional significance was studied using maps of the distribution of metabolites choline (Cho), N-acetylaspartate (NAA), and creatine. Metabolite concentrations were elevated or preserved in both UBOs and thalami of younger subjects (<10 years) and normal or reduced in older subjects. Decreases in NAA ratios were greatest in thalami of subjects with UBOs in the globus pallidus. (Wang PY, Kaufmann WE, Koth CW, Denckla MB, Barker PB. Thalamic involvement in neurofibromatosis type 1: Evaluation with proton magnetic resonance spectroscopic imaging. Ann Neurol April 2000;47:477-484). (Respond: Dr Barker, Department of Radiology, MRI 143C, Johns Hopkins University School of Medicine, 600 N Wolfe St, Baltimore, MD 21287).

COMMENT. The authors postulate that thalamic choline elevations in younger patients with NF-1 may reflect an increased myelin turnover in areas of intramyelinic edema, followed by neurophil injury and reduced N-acetylaspartate levels in older subjects.