SEIZURE DISORDERS

SEIZURES, PYRIDOXINE, AND HYPERPROLINEMIA TYPE II

A girl aged 20 months with hyperprolinemia type II, presenting with three convulsions within 15 hours precipitated by pneumonia, was evaluated at Southampton General Hospital, UK. She developed encephalopathy with back arching and purposeless movements. EEGs at first showed slow activity and later, generalized high voltage slow waves with sharp waves and spikes. Brain CT was normal. Urine analysis showed amino acid and organic acid abnormalities consistent with hyperprolinemia type II, and also xanthurenic acid and a metabolite of kynurenine, suggestive of vitamin B6 deficiency. Plasma analyses showed low levels of pyridoxal phosphate and pyridoxic acid, the end product of vitamin B6 catabolism. After 5 weeks of 50 mg pyridoxine/day orally, urine xanthurenic acid levels were normal. Pyrroline-5-carboxylate that accumulates in hyperprolinemia type II may link covalently with and inactivate vitamin B6. Maintenance treatment with vitamin B6 (10 mg/day), advised on discharge, was discontinued at home, and the child was readmitted with encephalopathy and seizures at 4 years of age. After IV pyridoxine 110 mg in divided doses, she recovered within 16 hours and was discharged in 36 hours, to continue daily oral vitamin B6 up to at least 10 years of age. Prior to the first admission, the only illness was a febrile seizure at 18 months, and after discharge she had developed a severe skin rash for 4 weeks in the diaper area. (Walker V, Mills GA, Peters SA, Merton WL. Fits, pyridoxine, and hyperprolinemia type II. Arch Dis Child March 2000;82:236-237). (Respond: Dr V Walker, Department of Chemical Pathology, Southampton General Hospital, Tremona Road, Southampton SO16 6YD, UK).

COMMENT. Hyperprolinemia type II is a rare autosomal recessive disorder caused by a deficiency of D-pyrroline-5-carboxylate dehyrogenase. It presents in childhood with convulsions, precipitated by infection, and sometimes a rash. Plasma analyses show a 10-fold increase in proline, pyrroline-5-carboxylate accumulation, and increased urinary proline, hydroxyproline, and glycine. The vitamin B6 deficiency diagnosed in the above case might account for seizures with hyperprolinemia. Vitamin B6 is inactivated by the proline metabolite pyrroline-5-carboxylate that accumulates in hyperprolinemia type II.

SEIZURES, RETARDATION, AND CREATINE SYNTHESIS DEFECT

Two unrelated boys, aged 2 and 5 years, with psychomotor retardation, hyperactive behavior, and epilepsy, associated with a creatine synthesis defect, are reported from Free University Hospital, Amsterdam, The Netherlands. Independent walking was achieved at age 2 years or later, and examination revealed hypotonia, autistic behavior, and delayed language development. EEG showed multifocal epileptic activity. Seizures were controlled with valproate in one child, and with creatine monohydrate in the other. Urinalyses showed a generalized elevation of amino acids, organic acids, sialic and uric acid expressed as mmol/mol creatinine. Serum creatinine was normal or low. Treatment with creatine monohydrate (500 mg/kg/day) resulted in control of seizures, and improved tone and motor development. While autistic behavior improved, the hyperactivity and inattentiveness persisted. Concentrations of guanidino-acetate in urine and plasma decreased with treatment but were not normal. Diagnosis of creatine synthesis defect was confirmed by absence of guanidinoacetate methyltransferase in fibroblasts. (van der Knaap MS, Verhoeven NM,

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 methylpredisolone (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.