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,