SEIZURE DISORDERS

3-PGDH DEFICIENCY, SEIZURES, AND MICROCEPHALY

The beneficial effects of oral L-serine (up to 500 mg/kg/day) and glycine (200 mg/kg/day) in 2 siblings, aged 7 and 5 years, with 3-phosphoglycerate dehydrogenase (3-PGDH) deficiency are reported from University Children's Hospital, Utrecht, The Netherlands. The patients were born with microcephaly, development was retarded, and seizures started at 1 year, 10 to 50 daily, and were refractory to sodium valproate and clonazepam. EEG's showed multifocal epileptiform discharges. MRI showed cortical atrophy and hypomyelination. Laboratory tests showed megaloblastic anemia, thrombocytopenia, low plasma concentrations of serine and glycine, and low CSF methyltetrahydrofolate concentration. 3-PGDH activity in cultured skin fibroblasts was deficient (3.9 and 1.7 mU/mg protein). The parents 3-PGDH activity was normal (23 and 27 mU/mg of protein). Amino acid treatment resulted in complete control of seizures in 2 weeks, and the EEG abnormalities resolved in 6 months. Plasma serine and glycine concentrations also became normal during therapy, and no adverse effects were noted during 12 months of follow-up. (de Koning TJ, Duran M, Dorland L et al. Beneficial effects of L-serine and glycine in the management of seizures in 3-phosphoglycerate dehydrogenase deficiency. Ann Neurol Aug 1998;44:261-265). (Respond: Dr de Koning, Department of Metabolic Diseases, University Children's Hospital "Het Wilhelmina Kinderziekenhuis," Nieuwegracht 137, 3512 LK Utrecht, The Netherlands).

COMMENT. 3-Phosphoglycerate dehydrogenase (3-PGDH) deficiency is a rare inborn error of serine biosynthesis recently recognized and manifested by congenital microcephaly, seizures, and psychomotor retardation. Low concentrations of serine and glycine are found in plasma and CSF during fasting. Whereas serine supplements alone correct the anemia and are partially effective against seizures, the addition of glycine results in complete seizure control and improves behavior and alertness. Serine metabolism should be checked by fasting plasma amino acid determinations in infants with microcephaly and seizures.

BRAIN NEOPLASMS

POST-CHEMOTHERAPY SECONDARY BRAIN TUMORS IN INFANTS

The longterm outcome of 198 infants with malignant brain tumors treated postoperatively with prolonged chemotherapy (vincristine, cyclophosphamide, cisplatinum, and etoposide) is evaluated by a Pediatric Oncology Study Group. Four of 132 children, 7 to 23 months at diagnosis, and 1 of 66 who were diagnosed between 24 and 36 months developed second malignancies. The primary tumors were choroid plexus carcinomas (2), ependymoma (1), ganglioglioma (1), and medulloblastoma (1). Secondary neoplasms were myelodysplastic syndrome (2), acute myelogenous leukemia (1), sarcoma (1), and meningioma (1). The risk of developing a second malignancy 8 years after diagnosis was 11% in the total group; in children younger than 24 months at diagnosis the risk was 19%, and in children diagnosed at 24 to 36 months it was 5%. The high rate of secondary malignancies, especially leukemia, in infantile brain tumor patients may be attributed to the oncogenic potential of prolonged alkylating chemotherapy and etoposide, with or without irradiation. (Duffner PK, Krischer JP, Horowitz ME et al. Second malignancies in young children with primary brain tumors following treatment with prolonged postoperative chemotherapy and delayed irradiation: a pediatric oncology group study. Ann Neurol Sept 1998;44:313-316). (Respond: Dr

Patricia K Duffner, Department of Neurology, Children's Hospital of Buffalo, 219 Bryant Street, Buffalo, NY 14222).

COMMENT. The authors conclude that the longterm chemotherapy regimen for infantile brain tumors may delay and decrease the risk of irradiation-induced neurotoxicity at the expense of increasing the risk of secondary malignancies.

In an editorial, "Rethinking brain tumors in babies and more," Fisher PG of Stanford University comments that these discouraging results of prolonged chemotherapy should stimulate research in the clinical biology of brain tumors and prompt a more selective approach to aggressive oncology (Ann Neurol Sept 1998;44:300-302).

NEUROMUSCULAR DISORDERS

HEREDITARY INCLUSION BODY MYOPATHY

A new familial, autosomal dominant, myopathy and variant of hereditary inclusion body myopathy (HIBM) is described in 19 members of a large Swedish family followed in the Departments of Pediatrics, Genetics, and Pathology, Sahlgrenska University Hospital, Goteborg, Sweden. Onset was in the newborn period with congenital joint contractures in 14, hip dislocation in 4, limb-girdle weakness and muscular atrophy, external ophthalmoplegia, and decreased tendon reflexes. The course was nonprogressive in childhood, and joint contractures resolved. From 30 to 50 years of age, most patients showed deterioration, with progressive muscle weakness and atrophy, especially of quadriceps. EMG showed myopathic changes, and serum CK was elevated. Muscle biopsy showed focal disorganization of myofilaments in childhood cases, and dystrophic changes in adults, with rimmed vacuoles and cytoplasmic and intranuclear inclusions. (Darin N, Kyllerman M, Wahlstrom J, Martinsson T, Oldfors A. Autosomal dominant myopathy with congenital joint contractures, ophthalmoplegia, and rimmed vacuoles. Ann Neurol Aug 1998;44:242-248). (Respond: Dr N Darin, Department of Pediatrics, Sahlgrenska University Hospital-East, S-416 85 Goteborg, Sweden).

COMMENT. Inclusion body myopathies are sporadic and inflammatory or familial and hereditary. The above Swedish family appears to suffer from a unique form of autosomal dominant HIBM that presents at birth and shows a progressive deterioration in adult life.

PROGNOSIS OF BENIGN CONGENITAL HYPOTONIA

Twenty five children diagnosed with benign congenital hypotonia (BCH) between infancy and 2 years of age were examined at 6 to 8 years of age and compared to 26 controls, matched for sex, age, and weight, in a study at the School of Occupational Therapy, Hebrew University-Hadassah Medical School, and Child Development Institute, Jerusalem. Sensory, visual-perception, visual-motor integration, and behavioral measures were similar in the 2 groups, but the BCH group showed impairments in gross motor performance, bilateral coordination and strength on the Oseretsky Test of Motor Proficiency, despite recovery of near normal muscle tone. (Parush S, Yehezkehel I, Tenenbaum A et al. Developmental correlates of school-age children with a history of benign congenital hypotonia. Dev Med Child Neurol July 1998;40:448-452). (Respond: Dr Shula Parush, School of Occupational Therapy, Hebrew University-Hadassah Medical School, PO Box 24026, Mount Scopus, Jerusalem, Israel 91240).