METABOLIC DISORDERS

CONGENITAL GLYCOSYLATION TYPE Ic DISORDER

Clinical and biochemical characteristics of congenital disorder of glycosylation type Ic (CDG-Ic) are reported in 8 patients studied at Heinrich-Heine University Dusseldorf, Germany; University of Leuven, Belgium; University of Zurich, Switzerland; University Hospital Nijmegen; Sophia Children's Hospital, Rotterdam; and Ignatius Hospital, Breda, The Netherlands. All children had been referred for neurologic examination in the first 2 years of life because of developmental delay, muscular hypotonia, and/or epilepsy. Inverted nipples, abnormal fat distribution, and cerebellar hypoplasia, findings reported in CDG-type Ia cases, were not present. The diagnosis of CDG was established between 4 months and 8 years of age by serum transferrin isoelectric focusing pattern. Patients with CDG-Ic have a milder phenotype than those reported with CDG-Ia. All the cases of CDG-Ic were homozygous for the A333V mutation in the a-1,3 glucosyltransferase gene. (Grunewald S, Imbach T, Huijben K et al. Clinical and biochemical characteristics of congenital disorder of glycosylation type Ic, the first recognized endoplasmic reticulum defect in N-glycan synthesis. Ann Neurol June 2000;47:776-781). (Respond: Dr RA Wevers, University Hospital Nijmegen, Laboratory of Pediatrics and Neurology, Institute of Neurology, PO Box 9101, NL-6500 HB Nijmegen, The Netherlands).

COMMENT. Congenital disorders of glycosylation (CDGs) were formerly known as carbohydrate-deficient glycoprotein syndrome. Diagnosis is established by testing for the isoelectric focusing (IEF) pattern of serum transferrin. Developmental delay, muscular hypotonia, and epilepsy are the common neurologic manifestations of CDG-Ic. Additional characteristics of CDG-Ia include cerebellar hypoplasia, retinitis pigmentosa, abnormal fat distribution, inverted nipples, hepatomegaly, hypoalbuminemia, coagulopathy (also in CDG-Ic), transaminemia, and tubular proteinuria.

MITOCHONDRIAL NEUROGASTROINTESTINAL ENCEPHALOPATHY

The syndrome of mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) was identified in 21 probands and 35 patients studied at Columbia University College of Physicians and Surgeons, New York; Northwestern University School of Medicine, Chicago; and other centers in the USA, Greece, UK, Canada, Belgium, Portugal, Switzerland, Japan, Italy, and Israel. The most prominent and debilitating symptom is gastrointestinal dysmotility, with decreased small intestine motility, delayed gastric emptying, and recurrent diarrhea, borborygmi, and intestinal pseudo-obstruction. Patients usually die in early adulthood (mean 38 years; range, 25-58 years). Neurologic manifestations included peripheral neuropathy, ptosis, ophthalmoparesis, areflexia, hearing loss, and infrequent pigmentary retinopathy and mental retardation. Homozygous or compound heterozygous thymidine phosphorylase mutations were present in all patients examined. Severe reduction of leukocyte thymidine phosphorylase activity is diagnostic. (Nishino I, Spinazzola A, Papadimitriou A et al. Mitochondrial neurogastrointestinal encephalomyopathy: an autosomal recessive disorder due to thymidine phosphorylase mutations. Ann Neurol June 2000;47:792-800). (Respond: Dr Hirano, Department of Neurology, Columbia University College of Physicians and Surgeons, P&S 4-443, 630 West 168th Street, New York, NY 10032).

COMMENT. The syndrome of mitochondrial neurogastrointestinal encephalomyopathy is an autosomal recessive disorder characterized clinically by severe gastrointestinal dysmotility, cachexia, ptosis, ophthalmoparesis, peripheral neuropathy, leukoencephalopathy, and mitochondrial abnormalities. The disease is caused by mutations in the thymidine phosphorylase gene.

SEIZURE DISORDERS

NEURONAL DYSFUNCTION AND TEMPORAL LOBE EPILEPSY

The relation of the neuronal dysfunction in the temporal lobes of children with temporal lobe epilepsy (TLE) to intractable seizures was investigated at the Montreal Neurological Institute and Hospital, and Montreal Children's Hospital, Canada. Reduction in N-acetylaspartate/creatine (NAA/Cr) ratios in the temporal lobes, as measured by proton magnetic resonance spectroscopic imaging, was used as an indicator of neuronal dysfunction. No significant differences were observed in the NAA/Cr ratios in 5 consecutive children with newly diagnosed TLE compared to 5 with long-standing intractable TLE. The patients had bilateral or unilateral reductions in NAA/Cr ratios of equal severity and extent in both groups. The results imply that the temporal lobe neuronal dysfunction in children with TLE is not specifically related to the intractable seizures and is present before seizures begin. (Miller SP, Li LM, Cendes F et al. Neuronal dysfunction in children with newly diagnosed temporal lobe epilepsy. Pediatr Neurol April 2000;22:281-286). (Respond: Dr Douglas L Arnold, Montreal Neurological Institute and Hospital, 3801 University Street, Montreal, Quebec H3A 2B4, Canada).

COMMENT. N-acetylaspartate/creatine ratio is a marker of the epileptogenic process and neuronal dysfunction in temporal lobe epilepsy, and reductions in the ratio are not specifically related to effects of refractory seizures.

EPILEPTIC SYNDROMES, COGNITION AND CLASS PLACEMENT

A retrospective statistical analysis of IQ and school placement in 251 children with epilepsy, aged 3 to 17 years, is reported from the Hopital-Saint-Vincent-de-Paul, Paris, France. Age at onset and seizure frequency are associated with poor outcome. Children with idiopathic generalized or localization-related epilepsy have higher IQ scores and a greater likelihood of normal school placement than those with symptomatic or cryptogenic generalized epilepsies. IQ and schooling are related to the epileptic syndrome, age at onset and duration of epilepsy, and number of antiepileptic drugs. Cognitive deficits vary with the localization of an epileptic focus. (Bulteau C, Jambaque I, Viguier D et al. Epileptic syndromes, cognitive assessment and school placememnt: a study of 251 children. Dev Med Child Neurol May 2000;42:319-327). (Respond: Dr C Bulteau, Hopital Saint Vincent de Paul, Service de Neuropediatrie, 82 Avenue Denfert-Rochereau, 75674 Paris Cedex, France).

COMMENT. Epileptic syndromes vary in their association with impairments in IQ and school performance. IQ scores and class placement are least affected in children with idiopathic, generalized or localization-related epileptic syndromes.

Autistic regression with Landau-Kleffner syndrome is reviewed by Mantovani JF, Washington University School of Medicine, St Louis, MO (Dev Med Child Neurol May 2000;42:349-353). A cause and effect relationship between autism and EEG abnormalities is not established, and therapies for LKS, including