HEREDODEGENERATIVE DISEASES

GENETICS OF X-LINKED ADRENOLEUKODYSTROPHY

An 8.5-year-old girl with cerebral X-linked adrenoleukodystrophy is reported from Ben-Gurion University, Beer Sheva, Israel, and Johns Hopkins University, Baltimore, MD. Early development was normal, she could read by 6 years, but severe behavioral problems and deterioration of academic performance developed by 8 years of age. The symptoms of "school phobia" included separation anxiety, oversensitivity to noise, and isolation from peers and teachers. Neurologic exam was normal and intelligence scores by WISC-R were low normal. Achievement was impaired by distractibility and visuospatial defects. Cortisol response to IV ACTH was normal, ruling out adrenal insufficiency. MRI revealed diffuse white matter involvement, most prominent in frontal regions. Very long chain fatty acids in plasma and skin fibroblasts were elevated. Cytogenetic analyses on peripheral lymphocytes showed a deletion at Xq27.2-ter and the unexpected demonstration of a de novo deletion in her paternal X chromosome, involving all of Xq28 and part of Xq27. In combination with the abnormality on the maternal X chromosome, this caused failure of expression of functional ALDP, similar to that in affected males. Neurological and psychological status was stable at 18 months after bone marrow transplant. (Hershkovitz E, Narkis G, Shorer Z et al. Cerebral X-linked adrenoleukodystrophy in a girl with Xq27-ter deletion. Ann Neurol August 2002;52:234-237). (Respond: Eli Hershkovitz MD. Pediatric Department, Soroka University Medical Centre, Beer Sheva, Israel).

COMMENT. Cytogenetic studies are recommended in severely symptomatic X-linked adrenoleukodystrophy heterozygotes. Treatment with bone marrow transplant as recommended in boys with ALD can be beneficial in affected girls.

SEIZURE DISORDERS

IRON INSUFFICIENCY AND FEBRILE SEIZURES

The significance of iron status as a possible risk factor for a first febrile seizure (FFS) was investigated at Jordan University and King Hussain Medical Center, Irbid, Jordan. Mean ferritin level in this prospective study of 75 children with FFS (29,5 +/- 21.3 mcg/L) and 75 matched controls (53.3 +/- 37.6 mcg/L) was significantly decreased (P=0.0001). A plasma ferritin level of <30 mcg/L was significantly more prevalent among children with FFS (49 of 75) than controls (24 of 75). Mean levels of Hgb, MCV, and MCH were lower in FFS cases, and a higher proportion of FFS cases had an Hgb <110 g/L, MCV <72 fL, and MCH <24 pg, but differences were not significant. The findings suggest a possible role for iron insufficiency in FFS. (Daoud AS, Batieha A, Abu-Ekteish F et al. Iron status: A possible risk factor for the first febrile seizure. Epilepsia July 2002;43:740-743). Dr A Daoud, Department of Pediatrics, Jordan University of Science and Technology, Irbid, Jordan).

COMMENT. Plasma ferritin is used as a reliable measure of iron deficiency and total body iron status. Decreased plasma ferritin levels in children with a first febrile seizure are not explained by fever, since the mean peak temperature on admission was similar in patients and controls. Other neurologic disorders in which iron-deficiency anemia may play a role include breath-holding spells, developmental delay, and behavior and attention disorders.

Iron metabolism and Hallervorden-Spatz syndrome are reviewed in Ped Neur Briefs October 2001;15:75-76.

Genetics of febrile seizures. A splice-site mutation in the GABRG2 gene has been described that causes a nonfunctional truncation of the GABA receptor g-subunit, and contributes susceptibility to childhood absence epilepsy and febrile convulsions in a single family. (Kananura C, Haug K, Sander T et al. Arch Neurol July 2002;59:1137-1141). The association of a missense mutation in the GABRG2 gene and susceptibility to febrile seizures is a rare finding, previously reported and cited by the authors in only one other family (Wallace RH et al. Nat Genet 2001;28:49-52).

VISUAL ATTENTION IN WEST SYNDROME

The maturation of visual attention is evaluated prospectively in a study of infants with West syndrome (WS) before, during and after the onset of seizures, followed until age 24 +/- 2 months at Catholic University, Rome, and University of Pisa, Italy. Thirteen infants with symptomatic WS and 22 normal control infants received a serial complete assessment at age 3 months, at the time of onset of spasms, and at 2 years. Visual attention assessment was clinical and also by means of a fixation-shift system, the ocular behavior monitored by video recordings. The median onset of spasms was 7.5 months (range, 3.5-12 months). EEG showed bilateral epileptic discharges, dominant in the occipital regions in 5; 7 had typical and 6 a modified hypsarrhythmia. Before onset of spasms, fixation and tracking were present in all infants, but only 4 (30%) could pass the fixation-shift test. At onset of spasms, the majority (70%) showed severe impairment of visual behavior; only 4 (30%) responded to fixation and tracking, and only one responded correctly to the fixation-shift test. At age 2 years, a general improvement in visual attention had occurred; fixation and tracking were possible in all cases, but only 2 could perform the fixation-shift test correctly. Cognitive development (DQ) paralleled the visual maturation: borderline DQ before onset of spasms, a general deterioration to a median score of 35 at onset of spasms, with minor improvement at age 2 year follow-up. In 2 cases with normal DQ at 3 months, a parallel deterioration of fixation-shift skills and cognitive development was observed even some months before onset of spasms. (Guzzetta F, Frisone MF, Ricci D, Rando T, Guzzetta A. Development of visual attention in West syndrome. Epilepsia July 2002;43:757-763). (Reprints: Dr F Guzzetta, Neuropsichiatria Infantile, Policlinico Gemelli, UCSC, Largo Gemelli 8, 1-00168 Rome, Italy).

COMMENT. A parallel defect of visual attention and cognitive development occurs in infants with West syndrome and sometimes precedes the onset of infantile spasms. In an infant with delayed development who presents with visual inattention, a diagnosis of West syndrome should be considered in the differential diagnosis and an EEG performed as part of the evaluation. The occipital preponderance of hypsarrhythia frequently reported in cases of WS appears to correspond to the common occurrence of visual inattention in this syndrome.

TOPIRAMATE AND METABOLIC ACIDOSIS IN INFANTS

The acid-base metabolism was investigated in 9 infants and toddlers, aged 5 months to 2.3 years (median, 6 months), treated with topiramate (TPM) for seizures at Johannes Gutenberg University, Mainz, Germany. TPM was used in maximal doses of 8.2-26 mg/kg/day (median, 11 mg/kg/day), as add-on therapy in 5 and monotherapy in 4 patients with refractory seizures. Diagnoses were infantile spasms in 5, epilepsia partialis continua in 1, infantile epileptic