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ATAXIA SYNDROMES

ATAXIA WITH IDIOPATHIC HYPOMYELINATION

A progressive ataxic diplegia syndrome of unknown etiology is reported in 4 unrelated girls evaluated at the National Institutes of Health, Bethesda, MD; Johns Hopkins University, Baltimore, MD; and Tufts, New England Medical Center, Boston, MA. Following normal early milestones, clumsiness and then progressive ataxia developed at 2 to 5 years of age. Seizures occurred in 3 of the 4 patients, some with fever. The ability to walk or sit independently was lost within one year of onset of ataxia. Other symptoms included progressive dysarthria and painful leg cramps. Two had optic atrophy. Deep tendon reflexes were markedly increased, plantar responses were extensor, and ankle clonus was elicited. Cognition was normal in two and mildly delayed in two. Early CTs and MRIs showed diffuse hypodensity of cerebral and cerebellar white matter, and later studies after clinical deterioration showed no progressive change or atrophy. Known metabolic and degenerative diseases were excluded. Open-brain biopsy specimens from two patients showed white matter hypomyelination, demyelination, and gliosis. Myelin-specific proteins and lipid analyses revealed decreased levels. Magnetic resonance spectroscopic imaging showed decrease of N-acetylaspartic acid, choline, and creatine in white matter, a diagnostic feature of the syndrome. (Schiffmann R et al. Childhood ataxia with diffuse central nervous system hypomyelination. Ann Neurol March 1994;35:331-340). (Respond: Dr Schiffmann, National Institutes of Health, Bldg 10, Rm 3D03, 9000 Rockville Pike, Bethesda, MD 20892).

> COMMENT. The MRSI findings appear to be unique to this childhood ataxic syndrome. The degree of white matter hypomyelination found early and before clinical deterioration and the absence of further white matter changes despite worsening of ataxia are remarkable findings.

SENSORY ATAXIA AND VITAMIN E DEFICIENCY

A progressive limb and gait ataxia, distal loss of proprioception and vibration sense, and areflexia, caused by a prolonged and severe vitamin E deficiency, are reported in four patients evaluated as adults at King's College,

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Hammersmith Hospital, and Institutes of Neurology and Child Health, London, UK. Two patients had abetalipoproteinemia and vitamin E was undetectable from birth. One had a familial vitamin E defiency, and had been diagnosed as Friedreich's ataxia at 13 years of age. One had Crohn's disease and fat malabsorption dating back to 16 years. Three had striking head tremor. Impaired nigrostriatal activity in the patients with abetalipoproteinemia, demonstrated by reduced dopa uptake using PET studies, was similar to that seen in Parkinson's disease. (Dexter DT et al. Nigrostriatal function in vitamin E deficiency: Clinical, experimental, and positron emission tomographic studies. Ann Neurol March 1994;35:298-303). (Respond: Prof AE Harding, University Dept of Clinical Neurology, Institute of Neurology, Queen Square, London, WC1N 3BG, UK).

COMMENT. Some children with typical signs of Friedreich's ataxia have familial vitamin E deficiency syndrome, with autosomal recessive inheritance. (Ped Neur Briefs Dec 1993;7:91). Early identification and supplementation with vitamin E may halt progression of the ataxia. A dose of 800 mg/day vitamin E in the 43-year-old male patient with this syndrome reported above had stabilized the neurologic status and his serum level of vitamin E was normal.

CEREBELLAR ATAXIA AND CSF FOLATE DEFICIENCY

A slowly progressive cerebellar syndrome associated with disturbed folate transfer across the choroid plexus is reported in an 18-year-old male who presented with incoordination of hands and feet at the Institute of Neurology, University Hospital of Nijmegen, The Netherlands. A rapidly progressive bilateral sensorineural hearing loss had preceeded the onset of ataxia which was complicated by dysarthria and dysphagia, and was followed at 21 years, with muscle cramps and at 26 years, with a distal spinal muscular atrophy and pyramidal tract signs of hyperreflexia and Babinski reflexes. Cranial CT showed cerebral and cerebellar atrophy and hypodensities in the basal ganglia. The serum (9.6-10.5 nmol/l) and red cell (371) folate levels were normal while the CSF folate was severely depleted (1.4-2.6 nmol/l; ref normal range 14-42). Analyses of folate binding protein in CSF performed at laboratories in Denmark showed abnormalities that indicate a defective folate transport into the CNS. (Wevers RA et al. Folate deficiency in cerebrospinal fluid associated with a defect in folate binding protein in the central nervous system. J Neurol Neurosurg Psychiatry Feb 1994;57:223-226). (Respond: Dr RA Wevers, Institute of Neurology, University of Nijmegen, PO Box 9101, 6500 HB Nijmegen, The Netherlands).

COMMENT. Folate occurs in higher concentrations in CSF than in plasma, and it enters the CSF against a concentration gradient. Folate binding proteins in the plasma membrane of the choroid plexus are essential in the transport of folate to the CSF and CNS. Low CSF folate has been reported in inborn errors of metabolism, Kearns-Sayre syndrome, and HIV infection. Neurologic manifestations of inherited disorders of folate metabolism include mental and motor retardation, ataxia, and seizures. Consanguinity of the parents of the above patient suggests an autosomal recessive inheritance.

In addition to folate and vitamin E deficiencies, other degenerative ataxias resembling Friedreich's ataxia that may be amenable to dietary supplements or modifications include vitamin B_{12} and biotin deficiencies and Refsum's disease, responsive to a diet low in