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DEGENERATIVE DISORDERS

WOLFRAM SYNDROME

Two unrelated patients with Wolfram syndrome (diabetes insipidus, diabetes mellitus, optic atrophy, and deafness) in whom MRIs of the brain provide evidence of a diffuse neurodegenerative process are reported from the Departments of Neurology and Ophthalmology, University of California at San Francisco, CA. Patient 1 was mildly mentally retarded and had a 5-year history of ataxia. Diabetes mellitus and diabetes insipidus had developed at age 3, and bilateral optic atrophy was diagnosed at age 13. Deep tendon reflexes were diminished and plantar responses were extensor. An audiogram showed bilateral high frequency hearing loss. Her parents were first cousins. Patient 2 was admitted for treatment of diabetic ketoacidosis at age 21. She had severe bilateral optic atrophy and horizontal nystagmus. Her gait was ataxic. Deep tendon reflexes were diminished and the plantar responses were flexor. MRI showed atrophy of brain stem and cerebellum and ventricles were dilated. (Rando TA, et al. Wolfram syndrome: evidence of a diffuse neurodegenerative disease by magnetic resonance imagining. Neurology June 1992; 42:1220-1224.) (Reprints: Dr. Thomas A. Rando, Department of Pharmacology, Stanford University Medical Center, Stanford, CA 94305-5332.)

COMMENT. Wolfram syndrome is inherited as an autosomal recessive disorder or it may be sporadic. Reported neurologic features include ataxia, nystagmus, vertigo, dysarthria, dysphagia, mental retardation, seizures, psychiatric disorders, pigmentary retinopathy, tremor, dystonia, hyporeflexia and neurogenic bladder. Endocrine abnormalities include delayed sexual maturation, growth retardation, hypothyroidism, and testicular atrophy. Recurrent urinary tract infections are associated with bilateral hydronephrosis. The differential diagnoses include olivopontocerebellar atrophy, Friedreich's ataxia, Refsum's syndrome, Laurence-Moon-Biedl syndrome, and Alstrom syndrome. The childhood presentation of diabetes mellitus, diabetes

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insipidus, and optic atrophy together with gait ataxia should suggest the diagnosis of Wolfram syndrome and indicate the need for an MRI, audiogram and renal sonogram.

RETT SYNDROME

The late infantile regression period (stages I and II) was analyzed retrospectively in 91 girls and women at the Department of Pediatrics, University of Goteborg and Pediatric Clinic, Ostersund Hospital, Sweden. The median age at onset of developmental stagnation (stage I) was 11 months, and loss of acquired skills (stage II) began at 19 months and lasted for 19 months. The onset of regression was distinct in 43%, dramatic in 16%, and insidious in 41%. The first observed signs of disease were delay in reaching expected gross motor milestones, dissociation of motor development, and disequilibrium. A triad of manifestations characterized the deterioration or loss of acquired skills: contact/communication, hand use/skill, babble/words. End of regression occurred at mean age 2.5 years. The girls gradually became more alert and showed an interest to act and interact. Handedness showed a preference for the left hand compared to the right, and was associated with spike activity in the left central leads in the EEG in 13 of 20 girls. (Engerstrom IW. Rett syndrome: the late infantile regression period - a retrospective analysis of 91 cases. Acta Paediatr Feb 1992; 81:167-172.) (Correspondence: Dr. Ingegerd Witt Engerstrom, Pediatric Habilitation Center, Tallasvagen 4, S-83142 Ostersund, Sweden.)

COMMENT. This further delineation of the stages of Rett syndrome may help in the diagnosis and pathophysiology of the disorder. In a study involving the analysis of beta-endorphin, as well as lactate, pyruvate and metabolites of norepinephrine, dopamine and serotonin in CSF from 12 girls with Rett's syndrome, the most consistent and significant difference from a control group was the elevation of beta-endorphin immunoreactivity in the CSF. Myer EC et al. from the Department of Child Neurology, Medical College of Virginia, Richmond VA found increased levels of beta-endorphin immunoreactivity in lumbar CSF in 90% of 158 Rett syndrome patients. (Neurology Feb 1992; 42:357-360.) The authors note that the symptoms of Rett syndrome are similar to the effects of centrally administered beta-endorphin or other opioids in experimental animals.

SEIZURE DISORDERS

RECURRENT STATUS EPILEPTICUS

The risk of recurrent status epilepticus in 95 children followed prospectively for a mean of 29 months was determined at the Montefiore Medical Center and affiliated hospitals of Albert Einstein College of Medicine, Bronx, New York. Ages ranged from 1 month to 18 years (mean 4 years). The cause was idiopathic in 24, remote symptomatic in 18, febrile in 29, acute asymptomatic in 18 or a progressive neurologic disorder in 6. Neurologically abnormal children (34% of the study population) accounted for