

DOMINANTLY INHERITED NEMALINE MYOPATHY

A locus on chromosome 15q21-23 for a dominantly inherited nemaline myopathy with core-like lesions is reported in two unrelated families evaluated at University Medical Center, Nijmegen, The Netherlands. TPM1 considered the strongest candidate gene had no identified disease-associated mutations. Patients have muscle weakness in neck flexors and proximal limb muscles without involvement of facial, respiratory, foot dorsiflexors or cardiac muscles. Muscle weakness is very slowly progressive and is manifested by the inability to perform fast movements such as running, and failure to break a fall when stumbling. Quadriceps biopsies showed type I fiber predominance with granular appearance suggestive of nemaline rods with Gomori trichrome stain. Zones devoid of ATPase and oxidative staining resembled central cores (pseudocores). Ultrastructural fiber examinations showed nemaline rods. (Gommans IMP, Davis M, Saar K et al. A locus on chromosome 15q for a dominantly inherited nemaline myopathy with core-like lesions. Brain July 2003;126:1545-1551). (Respond: BGM van Engelen MD PhD, Neuromuscular Centre, Nijmegen Institute of Neurology, University Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands).

COMMENT. A novel nemaline core-like myopathy is described in two unrelated families with an uncharacterized genotype. Muscle weakness is manifested by slowness of movement and inability to break a fall.

HEREDITARY MOTOR AND SENSORY NEUROPATHY WITH AGENESIS OF THE CORPUS CALLOSUM

The epidemiological, clinical, and molecular genetic aspects of hereditary motor and sensory neuropathy and agenesis of the corpus callosum (HMSN/ACC) are reviewed by neurologists at McGill University, Montreal, Canada. Rarely reported worldwide, HMSN/ACC is prevalent in the Saguenay-Lac-St-Jean region of Quebec, Canada. In this area, the incidence at birth is 1 in 2,117 live births and the carrier rate is 1 in 23 inhabitants. A set of 22 founders originating from France was common to all of the cases. First described in 1966 (LeBlanc et al), the autosomal recessive inheritance was recognized in 1972 (Andermann et al). The clinical manifestations have an early onset with delay in developmental milestones, a severe sensory-motor polyneuropathy with areflexia, agenesis of the corpus callosum, amyotrophy, hypotonia, cognitive impairment, and psychoses. The average age of walking is 3.8 years, scoliosis appears at age 10.4 years, the ability to walk is lost by 13.8 years, and the average age of death is 24.8 years (33 years in a more recent unpublished study by the authors). The gene defect is a mutation in SLC12A6, which codes for the cotransporter protein KCC3. (Dupre N, Howard HC, Mathieu J et al. Hereditary motor and sensory neuropathy with agenesis of the corpus callosum. Ann Neurol July 2003;54:9-18). (Respond: Dr Guy A Rouleau, Centre for Research in Neurosciences and Department of Neurology and Neurosurgery, McGill University, 1650 Cedar Ave, Montreal, Quebec, H3G 1A4 Canada).

COMMENT. HMSN/ACC is rare but is considered of interest because the SLC12A6 gene defect is causing both developmental (callosal agenesis) and degenerative abnormalities (progressive neuropathy, cognitive deficits, and psychoses) of central and peripheral nervous systems.

INFECTIOUS DISORDERS

HERPES SIMPLEX ENCEPHALITIS RELAPSE

The clinical, biological, and radiological features of 8 episodes of herpes simplex encephalitis (HSE) relapse are reviewed from the Hopital Saint Vincent de Paul, Paris. Of 42 children diagnosed with HSE between 1990 and 1997, 6 (7 months to 13 years of age) were referred for relapse and were followed for at least 5 years. Relapses occurred from 5 days to 26 months after acyclovir treatment (30-60 mg/kg/day, initiated at 0-3days after onset and continued for 9-21 days). Two patients had 2 relapses. Clinical presentation of the relapses were of 2 types: bilateral choreoathetoid movements and fever in 2 presenting within one month following the initial HSE; and other neurologic symptoms with fever in 6. The cases of movement disorder had no CT evidence of basal ganglia disease, they failed to respond to acyclovir, and symptoms persisted for 1.5 to 3 months. The 6 with no athetosis showed new lesions on CT and MRI, and a marked clinical improvement occurred with acyclovir. CSF showed increased leukocytes in all relapses, protein was elevated (>0.4 g/L) in 4, and HSV PCR was negative in all samples. Cases with extrapyramidal symptoms most likely represent a postinfectious immuno-inflammatory mechanism, and no virus is isolated in those with reported brain biopsy. In cases without extrapyramidal symptoms, resumption of viral replication is suspected based on new MRI lesions, detection of CSF interferon and HSV antibody synthesis, and marked response to acyclovir. Relapse is related to initial acyclovir treatment for too-short duration and too-low a dose. A minimum of 15 days course of acyclovir in a dose of 45 mg/kg/day is recommended to prevent relapse. Some cases of relapse may be due to a familial HSV-specific immune deficiency and inherited susceptibility to HSV disease. (De Tiege X, Rozenberg F, Des Portes V et al. Herpes simplex encephalitis relapses in children: differentiation of two neurologic entities. *Neurology* 22 July 2003;61:241-243). (Reprints: Dr B Heron, Department of Pediatric Neurology, Hopital Saint Vincent de Paul, 82 avenue Denfert Rochereau, 75674 Paris Cedex 14, France).

COMMENT. These authors have recently reported on the limitations of early diagnosis of HS encephalitis in children (De Tiege X et al; May 2003; see *Ped Neur Briefs* June 2003;17:44-46). A negative HSV PCR when testing CSF samples at 0-3 days after onset of symptoms should not delay initiation of acyclovir therapy in suspected cases of HSE. A repeat lumbar puncture is advised after a few days, without interruption of therapy. The EEG may be superior to CT in early diagnosis of neonatal HSE. A normal CT or MRI and absence of fever may sometimes lead to misdiagnosis.

A case of atypical herpes type 2 encephalitis with normal MRI is reported in an immuno-compromised adult. (Harrison NA et al. *J Neurol Neurosurg & Psychiatry* July 2003;74:974-976). Treatment with acyclovir was started after a positive PCR for HSV type 2 was obtained on CSF. Recovery followed prolonged valaciclovir for several relapses.