NEUROMUSCULAR DISORDERS

CONGENITAL MUSCULAR DYSTROPHIES AND COGNITIVE IMPAIRMENT

Reserchers at the Department of Paediatric Neurology, Catholic University, Rome and other Italian centers specializing in neuromuscular disease studied the prevalence of congenital muscular dystrophy (CMD) in the Italian population, and the frequency of individual genetically defined forms, including de novo phenotypes. Clinical, brain MRI and morphological data were also obtained. Of 160 patients with CMD, 92 (58%) were cognitively impaired; 9 had borderline, 25 mild, 20 moderate, 19 severe, and 18 profound cognitive impairment. Brain MRI in 90 patients showed structural changes with cerebellar hypoplasia in 64 (71%), 4 (5%) had diffuse white matter changes only, and 22 (24%) had normal scans. Epilepsy was present in 35/92 (38%), and all had MRI abnormalities. Seventy-three (79%) of the 92 showed a-dystroglycan (a-DG) reduction in muscle biopsy, with 42/73 carrying mutations in the known genes. Another 6/92 (7%) showed a laminin a2 deficiency on muscle biopsy, and 5 of the 6 carried mutations in LAMA2. The remaining 13/92 (14%) patients had normal a-DG and laminin a2 expression on muscle. Cognitive impairment was not always associated with a-dystroglycanopathy or laminin a2 reduction. Patients with cognitive impairment but normal MRI more often carried mutations in POMT1 and POMT2 and had no mutations in known genes in 14% cases. Among patients with a-DG reduction but no mutations in known genes, a new phenotype was identified in 4, characterized by cognitive impairment, microcephaly, cerebellar hypoplasia, and severe myoclonic epilepsy. The severity of cognitive impairment was unrelated to mutations in individual genes but was more related to severity of MRI brain structural changes. Walker-Walburg syndrome and muscle-eye-brain phenotype were generally associated with most severe cognitive impairment. (Messina S, Bruno C, Moroni I, et al. Congenital muscular dystrophies with cognitive impairment: a population study. **Neurology** Sept 14, 2010;75:898-903). (Response and reprints: Dr Eugene Mercuri, Department of Child Neurology, Policlinico Gemelli, Largo Gemelli 00168, Rome, Italy. E-mail: mercuri@rm.unicatt.it).

COMMENT. Congenital muscular dystrophy is a heterogeneous group of autosomal recessively inherited diseases with various clinical phenotypes, mostly characterized by muscular dystrophy, structural brain abnormalities, and ocular involvement. Six causative genes are identified, including fukutin (FKTN) with mutations causing Fukuyama type CMD, the most prevalent alpha-dystroglycanopathy in Japan. (Murakami T, Nishino I. **Brain Nerve** 2008;60(10):1159-64) FKTN mutations can cause a broad spectrum of CMD, mainly associated with cognitive impairment and cobblestone lissencephaly, but rarely as a mild phenotype without brain involvement, occurring in a 4-year-old Italian patient. (Saredi S et al. **Muscle Nerv** 2009;39(6):845-848).