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J. GORDON MILLICHAP, M.D., F.R.C.P., EDITOR

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NEUROMUSCULAR DISORDERS

COLQ-MUTANT CONGENITAL MYASTHENIC SYNDROMES

The clinical and molecular genetic findings of 22 COLQ-mutant congenital myasthenic syndromes (CMS) are reported from 14 centers mainly in Europe. They represented 10% of the total CMS patients with a genetic diagnosis at these centers. The mutations in acetylcholinesterase (AChE) collagen-like tail subunit gene (COLQ) are associated with end-plate AChE deficiency. The disease presents at birth (in 11 patients) with hypotonia, ptosis, ophthalmoparesis, facial weakness, weak cry and suck, and respiratory insufficiency. In 4 patients, initial symptoms of muscle weakness and fatigability were delayed until 2 to 7 years of age. Respiratory crises occurred in 10 patients, precipitated by infections in 5. None had arthrogryposis; one had congenital clubfeet. Diurnal fluctuation of symptoms was noted in 8 patients, and disease progression occurred in 9 (41%). Repetitive nerve stimulation caused a decremental response in all but 2. Myopathic potentials were recorded on EMG in 15. A characteristic double CMAP was observed in more than half the patients. None of 8 tested showed AChR antibodies. Serum CK levels were normal. Muscle biopsy in 11 patients was unremarkable in 4 and showed myopathic changes in 4. AChE inhibitor treatment (pyridostigmine) was generally ineffective long-term or caused worsening of symptoms. A surprising short-term beneficial effect was observed in 4 patients. Tensilon test performed in 4 patients was positive in 2. Ephedrine had a beneficial effect in 5 cases treated. Genetic analysis of family members was compatible with a recessive inheritance, nine belonging to consanguineous marriages. Clinical phenotypes were variable. Some patients differed from the classical phenotype, having a mild course without progression. Others had limb-girdle proximal weakness reminiscent of CMS with DOK7 gene mutation, with sparing of eye muscle involvement. (Mihaylova V, Muller JS, Vilchez JJ et al. Clinical and molecular genetic findings in COLQ-mutant congenital myasthenic syndromes. **Brain**

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March 2008;131:747-759). (Respond: Hanns Lochmuller MD, Institute of Human Genetics, University of Newcastle upon Tyne, International Centre for Life, Central Parkway, Newcastle upon Tyne NE1 3BZ, UK).

COMMENT. Molecular genetic testing is important in diagnosis and therapy of infants with CMS. The administration of esterase inhibitors in patients with COLQ mutations can result in serious complications, and an initial short-term beneficial effect may be misleading. Ephedrine (2 to 3 mg/kg/day) was the most effective therapy in the above study. Most patients with COLQ mutations are disabled from infancy, and muscle weakness is progressive and complicated by ventilatory insufficiency and scoliosis. Clinical diagnosis is supported by repetitive CMAP, and increased muscle weakness following administration of pyridostigmine. COLQ gene mutations are the third most common cause of CMS, and occur as frequently as DOK7 mutation cases.

HISTOCHEMICAL ABNORMALITIES IN VARIOUS FORMS OF CONGENITAL MUSCULAR DYSTROPHY

A large Australasian cohort of patients with congenital muscular dystrophy (CMD) was screened to determine the frequency of various forms, in a study at Children's Hospital at Westmead; the University of Sydney; University of Melbourne, Australia; and University of Nevada, Reno; and University of Illinois, Chicago. Of 101 patients, 45% were screened by immunofluorescence and showed abnormal staining for glycosylated-a-dystroglycan (DG) in 25%. Half of these had reduced DG by Western Blot test. All patients with abnormal DG staining had DNA sequencing of the fukutin-related protein, fukutin, POMGnT1 and POMT1 genes, and mutations were identified in one patient for each of the genes. Abnormalities in collagen VI immunofluorescence were identified in 12% of CMD patients, COL6 mutations in 8 of 9 patients tested, and laminin a-2 deficiency occurred in 8% of cases. (Peat RA, Smith JM, Compton AG et al. The diagnosis and etiology of congenital muscular dystrophy. **Neurology** Dec 26, 2007 (Epub ahead of print)).

COMMENT. Various histochemical and DNA sequencing abnormalities are identified in a large cohort of CMD cases. Patients with abnormal glycosylated a-dystroglycan immunofluorescence were most common in this cohort. Other studies have suggested that the cause of 50% of all CMDs is a primary deficiency in laminin a2, and Ullrich CMD is a second most common form. Molecular diagnostic testing is important for genetic counseling and an emerging new era of gene therapy (Rando TA. Get personal with gene therapy for muscular dystrophy. **Lancet Neurology** 2008;7:196-8).

MRI IN CONGENITAL FACIAL PALSY

Magnetic resonance (MR) findings in a 12-month-old boy with congenital unilateral facial palsy and a 9-month-old girl with atypical Moebius syndrome are reported from the National Center of Neurology and Psychiatry, Kodaira, Japan. In the boy with unilateral palsy, MRI showed an asymmetry of internal auditory channels with absence of the right facial nerve. MRI on the girl with Moebius syndrome showed a slightly hypoplastic