MUSCLE DISORDERS

CONGENITAL MYASTHENIC SYNDROMES

A new syndrome associated with a deficiency of acethylcholine receptor (AChR) and a short open-time of the AChR channel in a 5 year-old girl with myasthenic symptoms since birth is reported from the Neuromuscular Research Laboratory, Mayo Clinic, Rochester, MN. She required ventilatory support for the first 24 days after birth, nasogastric feeding for 6 months, and was hypotonic and weak. She had fluctuating ptosis, head control was delayed until 5 months, she walked unsteadily at 16 months, and had slurred speech when tired, and difficulty in chewing and closing her mouth. Her parents were healthy and mother was not myasthenic. On examination at 5 years, her head was dolichocephalic, the palate was high-arched, and teeth malocclued. Myasthenic signs included ptosis, weakness of facial, laryngeal, and masticatory muscles, truncal and limb muscle weakness, and hypoactive deep tendon reflexes. Symptoms responded to pyridostigmine, 5 mg/kg/daily, and prednisone, 1 mg/kg, on alternate days. Tests for anti-AChR antibodies were negative. EMG studies with facial nerve stimulation evoked a 25% decremental response, and an intercostal muscle specimen for morphological and electrophysiological studies showed decreased numbers of endplate-specific I-BGT binding sites and attenuated immunostaining of endplates by anti-AChR antibodies. The neonatal onset, negative tests for anti-AChR antibodies, abnormal AChR kinetics, and other findings distinguished this case from autoimmune myasthenia gravis. (Engel AG et al. Congenital myasthenic syndromes: I. Deficiency and short open-time of the acetylcholine receptor. Muscle & Nerve Dec 1993;16:1284-1292). (Reprints: AG Engel MD, Department of Neurology, Mayo Clinic, Rochester, MN 55905).

COMMENT. Congenital myasthenia gravis is distinguished from the *neonatal transient* form by absence of the disease in the mother, less severe generalized muscle weakness, and a relatively poor response to anticholinesterase treatment. Ptosis relieved by sleep is the most common presenting sign, and ophthalmoplegia and weakness of facial and masticatory muscles occur frequently during childhood and adult life. A family history of myasthenia in brothers, sisters, and cousins has been described. (Millichap JG, Dodge PR. Diagnosis and treatment of myasthenia gravis in infancy, childhood, and adolescence; a study of 51 patients. Neurology 1960;10:1007).

Since this clinical description more than 30 years ago, and the later discovery of the autoimmune origin of myasthenia gravis, the absence of antibodies against the acethylcholine receptor further delineated the congenital syndrome. Subsequently, Engel and his colleagues have identified and characterized a number of different congenital myasthenic syndromes, including endplate acethylcholine and AChR deficiencies, a slow-channel syndrome, and defects in resynthesis of ACh rd kinetics f AChR. The investigation of congenital myasthenic syndromes is complex and requires studies of the kinetics of AChR, and ultrastructure of the endplate.

A further syndrome without endplate AChR deficiency, in which the defect of neuromuscular transmission is attributed to an abnormal interaction of acethylcholine with its receptor, is reported from the Mayo Clinic (Uchitel O, Engel AG et al. Muscle & Nerve Dec 1993;16:1293).