Department of Neurology, Hospital de Pediatria Dr JP Garrahan, Combate de los Pozos 1881 (1245), Buenos Aires, Argentina).

COMMENT. Childhood ADEM is an inflammatory demyelinating disease that is typically preceded by a viral febrile illness or vaccination, affects boys more frequently than girls, and usually follows a monophasic course with recovery in 90%. Significant residual disability in 10% is not related to MRI lesions at onset but it is correlated with the occurrence of optic neuritis. Absence of oligoclonal bands in the CSF and long-term MRI findings will distinguish ADEM from MS in the 10% of patients showing a biphasic course with single relapse.

In a previous report of 31 children with ADEM from Australia (Hynson JL et al. 2001; See Ped Neur Briefs June 2001;15:46), the most frequent presenting neurologic symptom was ataxia, in 65%. MRI showed bilateral, asymmetrical involvement of white matter of frontal and parietal lobes, with lesions in deep grey matter including the thalamus in 61%. Corpus callosum and periventricular demyelination, characteristic of MS, was present in 29%.

MUSCLE DISEASES

GENE EXPRESSION PROFILES OF INFLAMMATORY MYOPATHIES

The simultaneous expression of 10,000 genes was measured, using Affymetrix GeneChip microarrays, in muscle specimens from 45 patients with various myopathies (dystrophy, congenital myopathy, and inflammatory myopathy) examined at Brigham and Women's Hospital, and Children's Hospital, Harvard Medical School, Boston, MA. Bioinformatics techniques were also used to classify specimens from 14 patients with subtypes of inflammatory myopathy (IM) - dermatomyositis, polymyositis, and inclusion body myositis (IBM) - and to identify the gene profiles. Ten of 11 patients with IM, and 10 of 12 with Duchenne MD were correctly classified. The various subtypes of IM have distinct gene expression signatures. (Greenberg SA, Sanoudou D, Haslett JN et al, Molecular profiles of inflammatory myopathies. Neurology October (2 of 2) 2002;59:1170-1182). (Reprints: Dr Steven A Greenberg, Department of Neurology, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115).

COMMENT. Standard clinical and histopathological methods of differentiation of various inflammatory myopathies (IM) are not always conclusive, and misclassification may result in inappropriate management. The advent of molecular profiling techniques should provide a more accurate classification of the various subtypes of IM and other muscle diseases. An editorial comment points out that microarray analysis, while generating useful information, has methodological challenges that must be addressed before it realizes its potential in clinical research and practice (Thornton CA, Welle SL. Neurology 2002;59:1128-1129).

MITOCHONDRIAL DNA DEPLETION SYNDROME

Twenty patients with myopathic mitochondrial DNA (mtDNA) depletion syndrome (MDS) were screened for mutations in thymidine kinase 2 (TK2) and deoxyguanosine kinase (dGK) genes at Columbia University, New York, NY. Four patients from two families had TK2 mutations, and none had dGK mutations. Two siblings were compound heterozygous for a H90N and a T77M mutation. Other siblings had a homozygous I22M mutation, one having spinal muscular atrophy

(SMA) and lower motor neuron disease. Muscle TK2 activity was reduced compared to controls (28% cf 37%). All 20 patients had COX-negative fibers on muscle biopsies.

In Family I, Patient 1, a Hispanic boy, had nonconsanguinous parents. Normal until 12 months of age, he developed a progressive ataxic gait impairment, and was unable to walk or stand by 2 years. Muscle weakness and hypotonia involved shoulder and hip girdle muscles, respiratory insufficiency necessitating mechanical ventilation was present by 3 years of age, and he died at 40 months. Laboratory studies had shown an elevated CK level (1.238 U/L, n<200), and nonspecific organic aciduria. An older sister (patient 2) had a slower course, falling frequently at age 16 months, and was unable to walk by 4 years of age. Her CK was 950 U/L and she had lactic acidosis (12 mmol/L. n<2.2). A younger sister was asymptomatic. In Family 2, Patient 4 lost his ability to walk by 2 years, and had severe proximal weakness, muscle wasting, areflexia, and scoliosis at age 3 years. His cognitive function and language were normal for his age. EMG showed chronic partial denervation, fibrillations, and loss of motor unit potentials, compatible with SMA. Serum CK and lactate were mildly increased. He is alive at 48 months of age. His sister, who presented with weakness and hypotonia in early infancy, episodic vomiting, failure to thrive, and metabolic acidosis, had a primary myopathy. She died at 2 years of age, with respiratory infection and insufficiency. The clinical expression of TK2 mutations may be myopathic or neuropathic and the myopathic form is genetically heterogeneous. (Mancuso M, Salviati L, Sacconi S, et al. Mitochondrial DNA depletion. Mutations in thymidine kinase gene with myopathy and SMA. Neurology October (2 of 2) 2002;59:1197-1202). (Reprints: Dr Tuan H Vu, Department of Neurology, P&S Building 5-431, Columbia University, New York, NY 10032).

COMMENT. Mitochondrial DNA depletion syndrome (MDS) is an autosomal recessive disorder of early childhood that involves muscle (myopathic form) or liver and brain (hepatocerebral form). The myopathic form is characterized by progressive weakness, hypotonia, areflexia, and respiratory failure before 10 years of age. MDS is a heterogeneous disorder in which mtDNA depletion in affected tissues is generally proportional to the severity of symptoms. Mutations in the thymidine kinase gene (TK2), involved in deoxyribonucleotide metasbolism, can be manifested clinically by a pure myopathy or spinal muscular atrophy. Other genes may also be involved in the etiology of myopathic MDS.

MOVEMENT DISORDERS

MYOCLONUS-DYSTONIA SYNDROME

The clinical phenotypic features of myoclonus-dystonia (M-D), including motor symptoms, psychiatric disorders, and neuropsychological deficits, were evaluated in 50 subjects from three M-D families examined at Mount Sinai School of Medicine, New York, and other centers. Each family had different truncating mutations in the SGCE gene on 7q21 chromosome, and one had an additional missense alteration in the DRD2 gene on 11q23. The families had several motor features in common: symptoms began in the first or second decade and either myoclonus or dystonia or both involved the upper limbs, head, neck, or trunk. Psychiatric disorders, correlating with the motor symptoms, occurred in most patients and included depression, obsessive-compulsive disorder, and substance abuse, especially alcohol dependence. Whether the OCD and other psychiatric problems are specifically related to the M-D gene mutations or are secondary to the stress of the disease remains to be determined. Cognitive tests revealed