

atrophy caused by valproic acid. Pediatr Neurol May 2003;28:382-384). (Respond: Dr Yamanouchi, Department of Pediatrics, Dokkyo University School of Medicine, 880 Kitakobayashi, Mibu, Shimotsuga, Tochigi 321-0293, Japan).

COMMENT. Reversible dementia and pseudoatrophy of the brain associated with valproate treatment have been reported previously (McLachlan RS (1987), Papazian O et al (1995), and Guerrini R et al (1998) – authors' citations). The differential diagnosis includes VPA-related encephalopathy with hyperammonemia, mitochondrial disorders, cytochrome c deficiency, carnitine deficiency with hepatic failure, and paradoxical VPA-induced status absence. Changes in consciousness during treatment with VPA should suggest possible drug toxicity and reversible cerebral atrophy.

**The safety and efficacy of IV valproate in pediatric status epilepticus** is reported in 18 patients from Harbor-UCLA Medical Center, Torrance, CA (Yu K-T et al. Epilepsia May 2003;44:724-726). All 18 patients regained baseline mental status within 1 hour of seizure cessation. Post-infusion plasma VPA levels ranged from 51 to 138 mcg/ml.

## **NEUROMUSCULAR DISORDERS**

### **MYOPATHIC MITOCHONDRIAL DNA DEPLETION SYNDROME**

Three siblings with the myopathic form of mitochondrial DNA depletion syndrome and a homozygous mutation in the TK2 gene are reported from Columbia University College of Physicians and Surgeons, New York, NY. They developed normally until 12 to 16 months of age, when walking was delayed, limb muscles became progressively weak and hypotonic, and death from respiratory failure occurred at ages 23 to 40 months. Muscle biopsy showed 40% to 60% ragged-red cytochrome c oxidase negative fibers. All affected siblings had decreased activity of respiratory chain complexes. Southern blot analysis showed reduction of mitochondrial DNA-nuclear DNA ratio in muscle, indicating severe mitochondrial DNA depletion. Sequencing of the TK2 gene showed a homozygous mutation in exon 5. (Mancuso M, Filosto M, Bonilla E et al. Mitochondrial myopathy of childhood associated with mitochondrial DNA depletion and a homozygous mutation (T77M) in the TK2 gene. Arch Neurol July 2003;60:1007-1009). (Reprints: Salvatore DiMauro MD, Department of Neurology, 4-420 Columbia University College of Physicians and Surgeons, 630 W 168<sup>th</sup> St, New York, NY 10032).

COMMENT. Patients with the myopathic form of mitochondrial depletion syndrome (MDS) present with progressive weakness, hypotonia, and areflexia at or shortly after birth. Death from respiratory failure occurs before 1 year of age in the congenital form and before 10 years in the juvenile form. Primary mitochondrial DNA depletion is inherited as an autosomal recessive trait. In patients with predominant muscle involvement and mtDNA depletion, the TK2 gene should be screened for mutations, making prenatal diagnosis possible.

The minimum birth prevalence for mitochondrial respiratory chain disorders presenting by 16 years of age is estimated at 6.2/100,000 in an Australian study at Royal Children's Hospital, Melbourne (Skladal D, Halliday J, Thorburn DR. Brain August 2003;126:1905-1912). Pathogenic mtDNA mutations were identified in 12% of diagnosed cases and pathogenic nuclear gene mutations in a further 12%.