term antibacterial therapy, careful follow-up and monitoring with spinal x-ray and neurologic evaluation, as indicated in the Great Ormond Street experience of spinal TB.

# METABOLIC DISORDERS

## CLINICAL CHARACTERISTICS OF 5 PHENOTYPES OF COENZYME Q10 DEFICIENCY

Researchers at Columbia University Medical Center, New York; University of Genoa, Italy; and University of Granada, Spain reviewed 149 cases of coenzyme Q10 (ubiquinone) deficiency, including their own cohort of 76 patients diagnosed from 1997-2010. Cerebellar ataxia was the principal phenotype and the presenting symptom in 94 children (63%). Less frequent phenotypes included encephalomyopathy in 4 patients, isolated myopathy in 14, infantile-onset multisystemic disease in 17, nephropathy (with or without sensorineural hearing loss) in 11, and atypical presentations in 9. Other manifestations include neuropathy, seizures, congenital hypotonia, dystonia, ophthalmoplegia, retinitis pigmentosa, optic atrophy, agenesis of corpus callosum, and hypogonadism. Onset was primarily in childhood; 82% were aged < 13 years including 23% in infancy (<12 months). Mortality rate was 8%.

Direct measurement of CoQ10 in skeletal muscle by liquid chromatography is the most reliable test for diagnosis of CoQ10 deficiency. Morphological and biochemical findings differ in the various clinical forms. Family history suggests autosomal recessive inheritance. Pathogenic mutations are described in patients with the infantile multisystemic syndrome and some juvenile-onset cerebellar ataxia cases. Response to oral supplementation with CoQ10 is frequent but variable; one patient with infantile spasms failed to respond. (Emmanuele V, Lopez LC, Berardo A, et al. Heterogeneity of coenzyme Q10 deficiency. Patient study and literature review. **Arch Neurol** 2012 Aug;69(8):978-83). (Respond: Michio Hirano MD, H Houston Merritt Clinical Research Center, Department of Neurology, Columbia University Medical Center, 630 W 168th St, P&S 4-423, New York, NY 10032. E-mail: mh29@columbia.edu).

COMMENT. The occurrence of primary and secondary CoQ10 deficiencies adds to the difficulty in study of the molecular classification of this heterogeneous disorder. (Quinzii CM, Hirano M. **Biofactors** 2011 Sep;37(5):361-5). Pathogenic mutations are identified in genes involved in the biosynthesis of CoQ10 (primary CoQ10 deficiencies) or in genes not directly related to CoQ10 biosynthesis (secondary CoQ10 deficiencies). Respiratory chain defects may contribute to the pathogenesis of primary CoQ10 deficiencies.

# HEADACHE DISORDERS

## MANIFESTATIONS OF FAMILIAL HEMIPLEGIC MIGRAINE

Researchers at University of Arkansas, Little Rock, AR report 3 cases of familial hemiplegic migraine complicated by reversible cerebral edema and followed by

neurocognitive impairment. Patient 1, a 13-year-old girl developed a severe headache during a volleyball game and on neurologic examination she had global aphasia, right-sided weakness, and ataxia. The initial MRI was normal, but the initial EEG revealed generalized slowing, 1-2 Hz, in the left hemisphere. Follow-up MRI 9 days after onset of signs revealed increased T2 signal involving the left hemisphere, with mild mass effect and midline shift. Her mother and brother had frequent migraine episodes accompanied by confusion, aphasia and hemiplegia. Treatment included verapamil, valproic acid, methylprednisolone, and IV immunoglobulin. The diagnosis of familial hemiplegic migraine was supported by CACNA1A gene mutations. She was maintained without further migraine episodes while taking verapamil as prophylactic. MRI and EEG repeated at 4 months follow-up were normal, but she had attention and memory problems in school. Two male patients, ages 8 and 15 years, with similar histories to that of case 1 had EEGs that revealed slowing in one hemisphere, 1-2 Hz, consistent with the MRI finding of unilateral cerebral edema. Mutation was located on ATP1A2 gene in case 2, and gene mutation was lacking in case 3; minor head trauma may have precipitated this patient's migraine attack. Neuropsychological evaluation and/or school reports at follow-up revealed cognitive impairment, memory and attention problems in all 3 patients. (Asghar SJ, Milesi-Halle A, Kaushik C, Glasier C, Sharp GB. Variable manifestations of familial hemiplegic migraine associated with reversible cerebral edema in children. **Pediatr Neurol** 2012 Sep;47(3):201-4). (Respond: Dr Asghar, Section of Pediatric Neurology, University of Arkansas Children's Hospital, Little Rock, AR 72202. E-mail: asgharsheilaj@uams.edu).

COMMENT. Genetic heterogeneity and persistent cognitive impairment are illustrated by these case reports of variable manifestations of familial hemiplegic migraine. EEG slowing was consistent with the temporary cerebral edema as a feature of FHM. A triad of prolonged hemiplegic migraine, cerebellar ataxia, and epileptic seizures is linked to CACNA1A gene mutations and may be complicated by status epilepticus. (Zangaladze A et al. **Epilepsy Behav** 2010 Feb;17(2):293-5). This report recommends that patients with prolonged hemiplegic migraine attacks and confusion be tested with continuous EEG to rule out electrographic status.

**Sporadic hemiplegic migraine presenting as acute encephalopathy.** A 10-year-old boy with psychomotor delay and cerebellar vermis atrophy developed right hemiplegia with vomiting, loss of consciousness, convulsions, and fever. EEG showed delta activity over the left hemisphere, and MRI revealed swelling of the left temporo-occipital cortex. Interleukin-6 was elevated in the CSF. Acute symptoms resolved after 3 weeks and recurred 7 months later with migraine attacks. A de novo mutation in the CACNA1A gene was identified. Family history was negative for migraine. Both familial and sporadic hemiplegic migraines are genetically heterogeneous, the majority caused by CACNA1A mutations. (Ohmura K, et al. **Brain Dev** 2012 Sep;34(8):691-5).

## SEX DIFFERENCES IN BRAIN OF MIGRAINEURS

Researchers at Children's Hospital Boston and other Harvard Medical School centers studied alterations in brain structure in male and female age-matched interictal