

encephalopathy; and 4) encephalopathy with cognitive deterioration and reversible cerebral atrophy. Brain pseudoatrophy and mental regression while taking valproate is reported in a child with a rare mitochondrial DNA mutation [1]. The current and 5 previously reported cases support a role of VPA in triggering a reversible dose-dependent mental deterioration with brain pseudoatrophy in children with epileptic seizures. Search for mtDNA mutation should be considered in a child treated with VPA who shows an unexplained clinical worsening and atrophic cerebral changes on MRI.

References.

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METABOLIC DISORDERS

5,10-METHYLENETETRAHYDROFOLATE REDUCTASE DEFICIENCY AND MYOCLONIC EPILEPSY

Investigators from the Children's Hospital of Philadelphia, PA, and McGill University, Montreal, Quebec, CA, report an adolescent learning-disabled girl who presented at age 14 years with an epilepsy syndrome initially diagnosed as juvenile myoclonic epilepsy. Her seizures initially resolved while taking valproic acid but later became refractory. At age 15 years she became ataxic and developed leg weakness and cognitive decline. Withdrawal of VPA and substitution of lamotrigine did not halt the mental deterioration, and testing revealed elevated plasma homocysteine and decreased plasma methionine. The diagnosis of 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency was confirmed by reduced fibroblast MTHFR activity, and mutation analysis revealing 2 variants in the MTHFR gene and splice site and missense mutations. Therapy with folinic acid, betaine, and methionine produced improvements in muscle strength, less severe ataxia, decreased seizures, and improved EEG and EMG. (D'Aco KE, Bearden D, Watkins D, Hyland K, Rosenblatt DS, Ficicioglu C. Severe 5,10-methylenetetrahydrofolate reductase deficiency and two MTHFR variants in an adolescent with progressive myoclonic epilepsy. *Pediatr Neurol* 2014 Aug;51:266-70).

COMMENTARY. MTHFR deficiency is an autosomal recessive inborn error of folate metabolism with defective remethylation of homocysteine to methionine. Elevated homocysteine and low methionine is a diagnostic marker for MTHFR deficiency. Infants typically present with seizures, microcephaly, neurological deterioration, and coma and death if untreated. Childhood presentation is milder, with developmental delay, and marfanoid appearance, but sometimes more severe with rapid neurological deterioration, seizures, and incoordination. MTHFR may also occur in adults, presenting as hereditary spastic paraplegia. Two unrelated families, each with 2 affected siblings, are reported from Hadassah Medical College, Jerusalem [1]. Treatment aims are normalization of plasma and CSF methionine levels and reduced homocysteinemia.

MTHFR deficiency should be considered in the differential diagnosis of progressive myoclonic epilepsy (PME). The most common causes of PME in a previously healthy adolescent are Unverricht-Lundborg disease, ME with ragged red fibers, neuronal ceroid lipofuscinosis, dentatorubro-pallidolusian atrophy (DRPLA), and

the sialidoses [2]. Investigators from University College, London, UK, and centers in Germany, examine the role of cerebellar pathology and alterations in inhibitory transmission in the pathogenesis of cortical myoclonus and ataxia [3].

References.

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2. Zupanc ML, Legros B. Progressive myoclonic epilepsy. Cerebellum. 2004;3(3):156-71.
3. Ganos C, et al. Mov Disord. 2014 Apr;29(4):437-43.

ELECTROMYOGRAPHY AND METABOLIC MYOPATHIES

Investigators at the Mayo Clinic, Rochester, MN, report the sensitivity and specificity of the pediatric EMG in the diagnosis of myopathic disorders in patients <18 years referred between 2009 and 2013. Referral diagnoses included myopathy, muscle weakness, neuromuscular disorders, myositis, myalgia, myoglobinuria, myasthenia, myotonia, cramps, periodic paralysis, hypotonia, and developmental delay. Only patients with both EMG and muscle biopsy were included for analysis. Patients with neurogenic EMG and neuromuscular disorders were excluded.

Myopathic EMG was defined as short duration, low amplitude, polyphasic motor unit potentials with rapid recruitment. Of 72 patients included (age range, 6 months-18 years), 32 had myopathic EMG with biopsy- or genetically-confirmed myopathy (Group A); 12 had myopathic EMG but normal biopsy (Group B); 3 had normal EMG but biopsy or genetically confirmed myopathy, all with metabolic myopathy (Group C); 25 had normal EMG and normal or nondiagnostic biopsy (Group D). The most common diagnoses were congenital myopathy (7 cases), metabolic myopathy (6 cases), muscular dystrophy (6 cases), genetically confirmed myopathy (5 cases), myopathy, undefined (5 cases), and inflammatory myopathy (4 cases). Pediatric EMG was 91% sensitive and 67% specific in myopathic disorders. Metabolic myopathies were commonly missed by EMG. (Ghosh PS, Sorenson EJ. Diagnostic yield of electromyography in children with myopathic disorders. **Pediatr Neurol** 2014 Aug;51(2):215-9).

COMMENTARY. Earlier studies show that the EMG has the highest concordance rate with neurogenic disorders but a lower concordance with myopathic disorders, especially in very young hypotonic infants [1]. More recent and the present studies show a higher rate of correlation in myopathic disorders but despite the exceptional expertise of the examiners, EMG frequently missed the diagnosis of a metabolic myopathy. Of 6 cases of metabolic myopathy, 3 had a normal EMG. Definitive diagnosis was made by muscle biopsy, biochemical analysis, and genetic testing of the muscle tissue. The metabolic abnormality was McArdle disease in 1 patient, mitochondrial myopathy in 1, mucopolisidosis type II in 1, and undefined in 3. The authors recommend that in cases presenting with a high degree of suspicion for metabolic myopathy, biopsy should be performed despite a normal EMG.

Electrophysiological Study of Mitochondrial Disorders. In 44 unselected mitochondrial disorder patients examined at the University of Pisa, Italy, motor nerve conduction studies were abnormal in 36.4%, consistent with a sensori-motor axonal multifocal neuropathy, mainly affecting the lower limbs. EMG evidence of myopathy