## AUTOIMMUNE DISORDERS

#### NEUROLOGIC COMPLICATIONS OF CELIAC DISEASE

Patients with celiac disease (CD) [n=111] and controls (n=211) were questioned regarding neurologic disorders, their charts were reviewed, and they received neurologic evaluations, including brain imaging or EEG if indicated, in a study of neurologic complications of CD at Carmel Medical Center, Technion-Israel Institute of Technology, Haifa, Israel. The mean age of patients and controls was 20.1 +/- 9 years, and the ratio of male to female was 2:3. The CD was classical infantile and diagnosed at 1.8 years in 58 (52.3%), and later in onset (diagnosed at 14.8 years) in 53 (47.7%). Neurologic disorders were found in 57 (51.4%) of patients with CD, whereas only 42 (19.9%) control subjects had abnormal neurologic findings. Patients with late-onset CD had more neurologic complications than the classical CD group (54.7% vs 48.3%) but the difference was not significant. Neurologic abnormalities and their frequency compared to controls included: hypotonia, 21.6% vs 3.8% (p<0.01); developmental delay, 15.5% vs 3.3% (p<0.01); seizures, 7.2% vs 0.8% (p<0.09); learning disabilities and ADHD, 20.7% vs 10.5% (p<0.01); headache. 27.9% vs 8.1% (p<0.01); ataxia, 5.4% vs 0% (p<0.01); and tics, 0.9% vs 2.4% (p=0.67). Seizure disorders were increased with CD but not significantly, and tic disorders showed no increased prevalence. The gluten-free diet benefited those CD patients with infantile hypotonia and migraine headache. (Zelnik N, Pacht A, Obeid R, Lerner A, Range of neurologic disorders in patients with celiac disease. Pediatrics June 2004;113:1672-1676). (Reprints: N Zelnik MD, Department of Pediatrics, Carmel Medical Center, 7 Michel St, Haifa 34362, Israel).

COMMENT. The range of neurologic disorders associated with celiac disease is wider than previously reported and includes chronic migraine headache, developmental delay, hypotonia in infants, learning disabilities and ADHD. Apart from cases of epilepsy with occipital calcifications, recurrent seizures were not significantly correlated with CD. In occipital lobe seizures related to CD, the CD may be clinically asymptomatic (Ambrosetto G et al. **Epilepsia** 1992;33:476-481; **Ped Neur Briefs** Aug 1992). The benefit derived from a gluten-free diet in CD patients with migraine is of interest, and gluten as a trigger for migraines with proven CD. (Millichap JG and Yee M. The diet factor in pediatric and adolescent migraine. **Pediatr Neurol** Jan 2004).

# FAMILIAL HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS WITH CEREBELLAR SWELLING AND TONSILLAR HERNIATION

A 3 year-old male child who presented with fever and cerebellar ataxia two weeks after varicella was subsequently diagnosed with hemophagocytic lymphohistiocytosis in a report from the Hospital de Cruces, Barakaldo, Bizkaia, Spain. CSF showed a slight increase in protein and pleocytosis of 36 cells/mL, 97% lymphocytes. CT scan of the brain was normal. Fever recurred 1 week later and was associated with hepatosplenomegaly and pancytopenia. At one month after varicella was diagnosed he became comatose and

developed status epilepticus. An EEG was compatible with diffuse encephalopathy or encephalitis. Treatment with acyclovir was without benefit, MRI revealed cerebellitis with swelling and multiple enhancing lesions. Severe increased intracranial pressure with tonsillar herniation and hvdrocephalus responded to dexamethasone. Hemophagocvtic lymphohistiocytosis (HLH) was suspected, and treatment with dexamethasone, etoposide, and cyclosporin A (HLH-94 protocol) resulted in a dramatic clinical response, with normal CSF and EEG, and improvement in the MRI. Cord blood stem cell transplantation was performed 10 months later, with initial infectious complications and neurologic sequelae (seizures, behavior disorder, and visual field defects), but subsequent clinical improvement. Genetic studies with DNA sequencing showing a mutation in the perform gene confirmed the diagnosis of familial HLH. (Astigarraga I, Prats JM, Navajas A et al. Near fatal cerebellar swelling in familial hemophagocytic lymphohistiocytosis. Pediatr Neurol 2004;30:361-364). (Respond: Dr Astigarraga, Pediatric Oncology Unit, Department of Pediatrics, Hospital de Cruces, 48903 Barakaldo, Bizkaia, Spain).

COMMENT. Familial histophagocytic lymphohistiocytosis (HLH) is often triggered by infection, and varicella preceded the onset of neurologic symptoms in this case. The disease is characterized by activation of T cells and macrophages leading to an inadequate immune response. CNS involvement is common and symptoms include bulging fontanel, neck stiffness, seizures, ataxia, visual disturbance, hemiplegia, and coma with increased intracranial pressure. In the above report, cerebellar signs preceded the systemic presentation with hepatosplenomegaly and cytopenia. HLH should be suspected in children with progressive encephalopathy and pancytopenia of unknown cause, and therapy instituted early. Dexamethasone, etoposide, and cyclosporine followed by stem cell transplantation are effective, and result in a 3-year probability survival in 62% cases.

HLH or 'hemophagocytic syndrome' with lamotrigine. (Yang Y-C, Jou S-T, Chang Y-H et al. Pediatr Neurol 2004;30:358-360). An 8 year-old male with pornecephaly and epilepsy unresponsive to topiramate and valproate developed a skin rash 2 weeks after beginning antiepileptic treatment with lamotrigine. One month later, impaired liver function, pancytopenia and hemophagocytosis without evidence of infection led to a diagnosis of HLH. The blood count and liver function improved dramatically when AEDs were discontinued and IV immunoglobulin and steroid were administered. Pancytopenia during treatment with new AEDs such as lamotrigine should alert to a possible HLH. Phenytoin may also trigger HLH, and valproate, also suspect in this case, may elevate blood levels of lamotrigine.

## TRAUMATIC DISORDERS

### RISKS OF BRAIN INJURY AFTER BLUNT HEAD TRAUMA

The association of loss of consciousness (LOC) and/or amnesia with traumatic brain injury (TBI) identified on CT and TBI requiring acute intervention was evaluated in 2043 children <18 years old enrolled prospectively in a level 1 trauma center ED at University of California, Davis School of Medicine, CA. A documented history of LOC and/or amnesia was obtained in 801 (39%). Of 745 with LOC and/or annesia and CT, 70 (9.4%) had TBI