

INFECTIOUS DISORDERS

EPSTEIN-BARR VIRUS AND OPSOCLONUS MYOCLONUS SYNDROME

A new case of opsoclonus-myoclonus syndrome (OMS) secondary to Epstein-Barr virus (EBV) is reported in an adult, and five previously documented cases (3 children, 2 adults) are reviewed from the University of Miami, FL. In the current case, acute onset oscillopsia, tremulousness, and ataxia were preceded by a 10 day history of fever, sore throat, and macular-morbilliform rash. Examination showed multidirectional eye saccades, persisting on eye closure and in sleep, truncal ataxia, and limb myoclonus. Brain MRI and EEG were negative. Head, chest, abdomen and pelvic CT scan and whole-body PET scan were negative. EBV capsid antigen test was positive at 1:640. PCR for EBV genome in the CSF and blood were positive. Methylprednisolone and immunoglobulin IV for 3 to 5 days were without immediate effect, and recovery occurred over 7 weeks. Examination at 1 year follow up was normal. In the 5 previously reported cases of OMS and EBV, none showed EBV in the CSF. (Verma A, Brozman B. Opsoclonus-myoclonus syndrome following Epstein-Barr virus infection. Neurology April (1 of 2) 2002;58:1131-1132). (Reprints: Dr Ashok Verma, 1150 NW 14th St, Ste 701, Miami, FL 33136).

COMMENT. In children OMS is usually a sign of neuroectodermal tumor and rarely is associated with infection. In adults, lung, breast, or pelvic cancer is usually uncovered, and infection occurs in about 20% of cases (authors' citation of literature). The identification of an infectious cause is rare, and EBS has been reported in only 5 previous cases. A postinfectious or parainfectious process is suggested in the present case with EBV. See Ped Neur Briefs Nov 2001;15:87, for an article on neurobehavioral outcome of OMS.

CYTOTOXIC T LYMPHOCYTES IN RASMUSSEN'S ENCEPHALITIS

The role of cytotoxic T lymphocytes and other mechanisms in the pathogenesis of Rasmussen's encephalitis (RE) is reviewed at the University of Vienna, Austria, and the University of Bonn, Germany. The densities of T cells, microglial nodules and glial fibrillary acidic protein positive astrocytes in surgically collected brain specimens are inversely correlated with disease duration. Inflammation and T cells are most pronounced at the earlier stages of RE. Brain specimens tested by immunochemistry and polymerase chain reaction for the presence of viruses such as enterovirus, Epstein Barr, cytomegalovirus and herpes simplex have failed to show a causal link between a specific virus and RE. Some patients with RE have high-titre anti-GLuR3 antibodies, and treatment with plasma exchange may result in a decrease in seizure frequency. However, anti-GLuR3 antibodies are not specific for RE, but may occur with noninflammatory focal epilepsy. The recent recognition of cytotoxicity by CD8/granzyme-B-positive T lymphocytes in brain biopsies or surgical specimens suggests that an autoimmune response mediated by cytotoxic T lymphocytes may be a key mechanism in the etiology of RE. (Bauer J, Bien CG, Lassmann H. Rasmussen's encephalitis: a role for autoimmune cytotoxic T lymphocytes. Current Opinion in Neurology 2002;15:197-200). (Respond: Dr Hans Lassmann, Brain Research Institute, Div of Neuroimmunology, University of Vienna, Spitalgasse 4, A-1090 Vienna, Austria).

COMMENT. Rasmussen's encephalitis is characterized by intractable seizures of focal onset, usually an *epilepsia partialis continua*, and chronic inflammation with progressive hemispheric neurologic deterioration. In the final residual, atrophic stage of the disorder, seizures decrease in frequency and the neurologic deficit becomes static. The differentiation between a viral cause or an autoimmune mechanism remains to be determined.

PROSPECTIVE DIAGNOSIS AND TREATMENT OF PANDAS

Twelve school-aged children with new-onset pediatric autoimmune neuropsychiatric disorder with group A streptococcal infection (PANDAS) were identified over a 3-year period (1998-2000) at the University of Rochester, NY. An acute onset of severe obsessive-compulsive disorder was associated with an acute group-A beta-hemolytic streptococcal (GABHS) pharyngitis, confirmed by positive throat culture and/or rapid antigen detection, and in 3 cases, very high antideoxyribonuclease antibody titers. All patients were treated with penicillin, amoxicillin or a cephalosporin for 10 days, and eradication of GABHS was followed by immediate resolution of the OCD symptoms. Recurrence of OCD in 6 patients was associated with acute GABHS that responded to antibiotic therapy. The age at onset of OCD was 5-12 years, predominantly in boys (1.4:1), and the initial OCD episode occurred from September through April, the peak seasonal occurrence of GABHS. Symptoms of OCD, meeting DSM-IV diagnostic criteria, included compulsive hand washing or excessive toilet hygiene, compulsive daytime urinary urgency without infection, and age-inappropriate separation anxiety when leaving their mothers. Four children (33%) had neurological disorders in addition to OCD, including recurrent tics, transient ADHD, or choreiform movements. This is the first prospective study to confirm the PANDAS syndrome and its response to treatment with penicillin. (Murphy ML, Pichichero ME. Prospective identification and treatment of children with pediatric autoimmune neuropsychiatric disorder associated with group A streptococcal infection (PANDAS). Arch Pediatr Adolesc Med April 2002;156:356-361). (Reprints: Michael E Pichichero MD, Elmwood Pediatric Group, University of Rochester Medical Center, 601 Elmwood Avenue, Box 672, Rochester, NY).

COMMENT. This study corroborates the association between streptococcal infection and the acute onset of neuropsychiatric symptoms. It also demonstrates the benefit of treatment with penicillin for the tonsillitis or pharyngitis with concomitant recovery from the OCD, tics and sometimes ADHD symptomatology. A possible diagnosis of PANDAS should be considered in new cases of OCD or tics, especially when symptoms are acute in onset.

SEIZURE DISORDERS

SCN1A GENE MUTATIONS IN SEVERE INFANTILE MYOCLONIC EPILEPSY

Ten novel mutations of SCN1A were found in in a pair of monozygotic twins and 12 unrelated Japanese infants with severe myoclonic epilepsy in infancy (SMEI) examined at the Brain Science Institute, Saitama; and National Epilepsy Center, Shizuoka, Japan. Of the 10 heterozygous mutations, 3 were frameshift and 7 nonsense mutations. These rather than missense mutations are the major causes of SMEI. Missense mutations of the same gene result in generalized epilepsy with febrile seizures plus (GEFS plus). (Sugawara T, Mazaki-Miyazaki E, Fukushima K et al. Neurology April (1 of 2) 2002;58:1122-1124). (Reprints: Dr K Yamakawa, Laboratory