PEDIATRIC NEUROLOGY BRIEFS
A MONTHLY JOURNAL REVIEW

J. GORDON MILLICHAP, M.D., F.R.C.P., EDITOR

Vol. 17, No. 4 April 2003

INFECTIOUS AND TOXIC DISORDERS

CAUSES AND CLINICAL FEATURES OF ENCEPHALITIS

The clinical and epidemiological features of encephalitis in California from June 1998 through December 2000 were studied at the Viral and Rickettsial Disease Laboratory, Richmond, CA, and CDC, Atlanta, GA. A core battery of tests, including PCR, serology, and virus isolation, for 13 potential causes of encephalitis was performed on CSF, and on acute- and convalescent-phase serum specimens from 334 enrolled patients who met the case definition of encephalitis. CSF showed an elevated WBC (median 61 cells/mm^3; range 6-5300/mm^3) in 228; elevated protein level (median 83 mg/dL; range 45-881 mg/dL) in 187; and a glucose level of <40 mg/dL (median 36; range 21-39 mg/dL) in 15 cases. Respiratory symptoms occurred in 133 patients (49%) and gastrointestinal symptoms in 145 (43%). A confirmed or probable infectious cause for the encephalitis was identified in 53; these were viral in 31 (9%), bacterial in 9 (3%), and parasitic in 2 cases (1%). A possible infectious cause was identified in an additional 41 (12%) patients. A noninfectious etiology was diagnosed in 32 cases (10%), and a nonencephalitis infection in 11 (3%). The etiology of 208 cases (62%) was unexplained. The most frequently identified viral agent was HSV-1 (11 patients); the remainder included enterovirus in 5 patients, Epstein-Barr virus (EBV) in 4, varicella zoster virus (VZV) in 3, human herpesvirus 6 (HHV-6) in 1, measles causing subacute sclerosing panencephalitis in 2, hepatitis C in 2, rotavirus in 2, and rabies in 1. No acute arbovirus infection was detected.

The 31 patients with confirmed or probable viral encephalitis ranged in age from 7 months to 81 years; 16 (50%) were children. Fever occurred in 25 (81%), gastrointestinal symptoms in 13 (42%), respiratory symptoms in 10 (32%), and seizures occurred in 9 (29%) patients. Sixteen (52%) were admitted to the ICU. Two-thirds (64%) of the HSV-1 encephalitis cases were adults, all having temporal lobe involvement. Three of the 4 with

PEDIATRIC NEUROLOGY BRIEFS (ISSN 1043-3155) © 2003 covers selected articles from the world literature and is published monthly. Send subscription requests ($65 US; $68 Canada; $75 airmail outside N America) to **Pediatric Neurology Briefs - J. Gordon Millichap, M.D., F.R.C.P.-Editor,** P.O. Box 11391, Chicago, Illinois, 60611, USA.
The editor is Pediatric Neurologist at Children's Memorial Hospital and Northwestern University Medical School, Chicago, Illinois. PNB is a continuing education service designed to expedite and facilitate review of current scientific information for physicians and other health professionals. Fax: 312-943-0123.

EBV infection and 4 of the 5 with enterovirus infection were children, and only 1 was admitted to the ICU. Bacterial causes for encephalitis (3% of cases) were *Bartonella* species in 7 (5 in children ages 4 to 16 years, and 6 with a history of exposure to cats), and *Mycoplasma pneumoniae* in 2 cases, ages 4 and 38 years. A parasitic cause was identified in 2, both having *Baylisascaris procyonis* infection, their ages 11 months and 17 years, and both showing peripheral blood eosinophilia and a history of raccoon exposure and dirt ingestion. (Glaser CA, Gilliam S, Schnurr D et al. In search of encephalitis etiologies: Diagnostic challenges in the California Encephalitis Project, 1998-2000. Clin Infect Dis March 2003;36:731-742). (Reprints: Dr Carol Glaser, Dept of Health Services, Viral and Rickettsial Disease Laboratory, 850 Marina Bay Pkwy, Richmond, CA 94804).

COMMENT. Despite comprehensive testing, the etiology of more than two-thirds of cases of encephalitis encountered in the state of California in a 2 year period (1998-2000) is undetermined. In those with a confirmed or probable infectious cause, a viral etiology is identified in 60%, bacterial in 17%, and parasitic in 4% of cases. Herpesviruses and enteroviruses are the most frequently identified agents. Arthropod-borne arbo viruses, and specifically California encephalitis, was not encountered. Children are affected in 50% of viral encephalitis cases, and in the majority of bacterial and parasitic cases.

Among 50 patients admitted to the Hospital for Sick Children, Toronto, because of an encephalitis-like illness, 1994-1995, a confirmed or probable infectious etiology is identified in 20 (40%) (Kolski H, et al. Clin Infect Dis 1998;26:398-409). This group of childhood cases has a much higher proportion of confirmed etiologies than the California study that involves all ages (50% children). A bacterial cause (*Mycoplasma pneumoniae)* is identified in 11 cases and herpes simplex virus in only 4. Whereas viral pathogens are more prevalent than bacterial agents in the California study (60% cf 17%), bacterial causes are identified in more than 50% of the Toronto cases. Seizures occur in 29% of California cases compared to 78% of the Toronto childhood patients.

In Finland a population-based study (Rantala H, Uhari M. Pediatr Infect Dis J 1989;8:426-430) of acute encephalitis in 95 children, 1973-1987, identifies only viral causes, and varicella is the most prevalent (25%); herpes simplex occurs in 7%, mumps in 8%, and measles in 4%. No cases of encephalitis caused by mumps, measles or rubella occur after 1982, when MMR vaccination is introduced. Another epidemiologic, multicenter, prospective study in Finland (Koskiniemi M, et al. Eur J Pediatr 1997;156:541-545) in the period 1993-1994 finds a change in the spectrum of encephalitis etiologies following vaccination programs. Varicella zoster, respiratory and enteroviruses occur in 61%, and herpes simplex, Epstein-Barr, adenovirus and rota viruses comprise 5% each. New causes are identified, especially *Chlamydia pneumoniae* and HHV-6. These reports emphasize the importance and value of new methods of identifying the etiologic agents for acute encephalitis, and the prompt introduction of antiviral, antibacterial or antiparasitic therapies when indicated. The prevalence of varicella as the cause of encephalitis in the Finland experience supports the AAP recommendation of varicella immunization at age 12 months. The AAP Red Book should include reference to *Baylisascaris procyonis*, warning of the risk of Raccoon roundworm eosinophilic encephalitis in young children with pica and geophagia. At least 12 cases of severe or fatal BP encephalitis are reported in the US since 1981 (MMWR, Jan 4, 2002;50:1153).