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INFECTIOUS DISORDERS

SUBACUTE SCLEROSING PANENCEPHALITIS RESURGENCE

Five cases of subacute sclerosing panencephalitis (SSPE) are reported from the California Department of Health Services, Richmond, CA. They were identified among 1000 cases of encephalitis referred by physicians and enrolled in the California Encephalitis Project (CEP) from June 1998 to December 2003. Median age was 12 years (range, 9 to 13 years). Time from onset of behavioral and neurologic manifestations to first hospital admission ranged from 1 day to 2.5 years. The CEP was designed to identify the causes and clinical features of encephalitis in California. Case selection included patients older than 6 months, immunocompetent, with encephalopathy and one or more of the following: fever, seizure, focal neurologic signs, and EEG or neuroimaging findings consistent with encephalitis or CSF pleocytosis. The diagnosis of SSPE is based on 1) elevated measles virus (MV) immunoglobulin (Ig) G antibody in CSF, and absent antibody to herpes simplex virus and varicella zoster virus, and 2) clinical or neurodiagnostic manifestations of SSPE. Patients diagnosed with SSPE had a median MV IgG antibody level of 22.5 in serum and 18.2 in CSF; significantly lower antibody levels for MV [8.6 and <0.5; $p=0.0004$ and 0.0001] were reported in patients referred with alternative diagnoses [eg HSV, rabies]. The differential diagnoses on referral included mitochondrial disorder and ADEM, and a history of an illness compatible with measles was obtained only after positive antibody tests were reported. As of January 2004, 3 patients had died, after intervals of 20, 40, and 96 days from time of hospital admission. The 2 survivors have severe neurologic impairments. (Honarmand S, Glaser CA, Chow E, et al. Subacute sclerosing panencephalitis in the differential diagnosis of encephalitis. *Neurology* October (2 of 2) 2004;63:1489-1493). (Reprints: S Honarmand MS, Viral and Rickettsial Disease Laboratory, California Department of Health Services, 850 Marina Bay Parkway, Richmond, CA 94804).

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COMMENT. The authors found 1 case per year of SSPE in California and they stress the need to include SSPE in the differential diagnosis of encephalitis, especially among pediatric patients. SSPE was suspected only after the results of measles testing were known. SSPE is rare in the United States and the diagnosis may be missed or delayed because of nonspecific clinical manifestations at onset. Early signs include behavioral changes, deteriorating school performance, slurred speech, and hyperactivity. These are followed by aphasia, ataxia, tremors, myoclonic jerks, or choreoathetosis. Progression is variable, but the disease is usually fatal in 1 to 3 years. The risk of SSPE is highest in patients with measles contracted in the first 2 years of life. The EEG characteristically shows periodic high amplitude sharp and slow-wave bursts, associated with myoclonic jerks. The MRI may show increased T2 signal in cerebral white matter and brainstem. Laboratory testing is necessary for diagnostic confirmation (elevated MV IgG antibody in CSF; or MV protein or RNA in brain biopsy). The course is usually progressive, but acute fulminant cases occur. The history of an illness with rash is usually obtained subsequent to SSPE diagnostic confirmation, in patients who have entered the US from developing countries. Treatment with oral inosiplex (isoprinosine) in a recent international multicenter study provided a 34% rate of stabilization or improvement at 6 months (better than the expected 5 to 10% remission rate in untreated patients); the addition of intraventricular interferon had no added benefit (Gascon CG. **J Child Neurol** 2003;18:819-827; cited by Bale JF. Editorial. **Neurology** 2004;63:1352-1353). Prevention by measles immunization is the only effective treatment. Some reports of SSPE related to measles vaccination are now considered doubtful, since the genome of wild MV has been identified rather than the vaccine strain (Kawashima H, et al. **Brain Dev** 1996;18:220-223).

SSPE after intrauterine measles infection in the mother is reported in an infant infected shortly before delivery. The infant developed focal seizures at 5 months of age, and SSPE was diagnosed at 14 months by characteristic findings on EEG and MRI and confirmed by elevated CSF and serum MV IgG antibodies. Despite treatment with intraventricular interferon and oral isoprinosine, the child's condition progressed to a vegetative state and he died at 3 years of age by aspiration pneumonia (Dasopoulou M, Covanis A. **Acta Paediatr** 2004;93:1251-1253).

Familial SSPE in two siblings who had not been immunized is reported from Germany (Tuxhorn IEB. **Pediatr Neurol** 2004;31:291-294). A 7-year-old boy had behavioral problems and school difficulties for 1 year before referral and 2 years following measles, contracted at the same time as his father and younger brother. The diagnosis was confirmed in both children by CSF and serum measles specific immunoglobulin G synthesis and brain biopsy. Both children showed progressive myoclonic and partial complex seizures, and characteristic EEG and MRI findings.

Measles inclusion body encephalitis complicating stem cell transplantation is reported in a 13-year-old Mexican-American immunocompromised boy treated at Children's Memorial Hospital, Chicago, for an X-linked chronic granulomatous disease (Freeman AF, Jacobsohn DA, Shulman ST, et al. **Pediatrics** November 2004;114:e657-e660). Neither the patient nor the donor had known recent measles exposure or vaccination. Measles virus, genotype D3, was confirmed by reverse transcriptase-polymerase chain reaction and viral growth in brain

biopsy. Early brain biopsy is recommended in cases of obscure encephalitis in afebrile immunocompromised patients who present with focal status epilepticus.

NEUROLOGIC COMPLICATIONS OF INFLUENZA A INFECTION

Eight children aged 5 months to 9 years with neurologic complications associated with influenza A were identified by a review of records of patients admitted to Texas Children's Hospital, Houston, during an early and severe outbreak in October and November 2003. None had received the influenza vaccine. Presenting symptoms included seizures in 4 patients, altered mental status in 3, and mutism in 1; all occurred within 3 weeks of an upper respiratory infection onset, and all had symptoms and signs of influenza. The seizure manifestations were not typical of febrile seizures; 3 patients had laboratory or imaging evidence of direct CNS involvement, one was 9 years of age, and 1 had several afebrile seizures 3 days after the first seizure. Influenza A viral antigen (H3N2 A/Fujian/411/2002-like) was detected in nasal wash samples of 7 patients, and the virus was isolated in cultures of 6 nasal wash specimens. The virus was also isolated from the CSF of 1 of these patients. None had serum metabolic abnormalities or other CSF abnormalities. Brain imaging was abnormal in 3 patients. Antiviral treatment was used in 5. All 8 recovered, 6 completely and 2 with sequelae. (Maricich SM, Neul JL, Lotze TE, et al. Neurologic complications associated with influenza A in children during the 2003-2004 influenza season in Houston, Texas. *Pediatrics* November 2004;114:e626-e633). (Reprints: Stephen M Maricich PhD MD, Fellow in Child Neurology, CCC 17.10, 6621 Fannin St, Houston, TX 77030).

COMMENT. During the 2003-2004 influenza season in the United States, 142 deaths occurred in children infected (CDC *MMWR* 2004;52:1286-1288). The influenza A (H3N2) Fujian strain identified in the Houston outbreak was found in the majority of encephalopathy cases reported in Japan, and this strain may have an affinity for the CNS (Morishima T, et al. *Clin Infect Dis* 2002;35:512-517). Influenza A infection is an important cause of febrile seizures, especially in Japan (Kawada J-I, et al. *J Infect Dis* 2003;188:690-698) and China (Chiu SS, et al. *Pediatrics* 2001;108:e-63), but the association is less frequent in the United States, where herpesvirus (HHV)-6 accounts for one-third of all first time febrile seizures in children <2 years old (Hall CB, et al. *N Engl J Med* 1994;331:432-438). Seizures were the most common presenting neurologic complication of influenza A infection in the Houston outbreak. In this series, the seizure manifestations were not typical of febrile seizures and were classified as encephalopathic. The distinction between encephalopathy with seizures and complex febrile seizures is often difficult, but systemic cytokine responses may be involved in both (Kawada J-I, et al. 2003; Millichap JG, Millichap JJ. Influenza virus and febrile convulsions. *J Infect Dis* 2004;189:564). Studies of the role of viral infections in the cause of febrile convulsions is a relatively neglected field of research in pediatric neurology, and further work is needed to elucidate the mechanism of the seizure and the differentiation of simple and complex febrile convulsions. More severe neurologic complications of influenza A infection have included acute disseminated encephalomyelitis, transverse myelitis, Guillain-Barre syndrome, frontal lobe syndromes, and acute necrotizing encephalopathy (Studahl M. *J Clin Virol* 2003;28:225-232).