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INFECTION-RELATED DISORDERS

ACUTE DISSEMINATED ENCEPHALOMYELITIS

The literature on acute disseminated encephalomyelitis (ADEM) is reviewed in an update by researchers at the University of San Francisco, CA; University of Texas Southwestern Medical Center, Dallas; and Universities in Germany. The clinical onset of ADEM is preceded by a febrile infection, usually upper respiratory, in about 50% to 75% of cases. Viral infections include herpes simplex, in 10% of cases in one series; measles (1/1000); rubella (1/10,000 to 1/20,000); varicella zoster (1/10,000 to 1/20,000); varicella, mumps, HIV, human herpesvirus 6, hepatitis virus (A and C), Epstein-Barr, coronavirus, cocksackie B, and dengue viruses. Bacterial infections include streptococcus, *mycoplasma pneumoniae*, and *rickettsia rickettsii*. Vaccinations include hepatitis B (2 of 31 patients vaccinated 3-6 weeks prior to onset of ADEM); pertussis (0.9/100,000 following DPT-triple vaccine); measles (0.1/100,000 for live measles vaccination); polio, and rabies. Neurologic symptoms and signs appear days to weeks after an infection or vaccination, with an average latency of 4 to 13 days; these include fever, headache, lethargy, ataxia, obtundation, and brainstem involvement. Bickerstaff encephalitis and postinfectious transverse myelitis, where inflammation and demyelination are confined to the brainstem and spinal cord, respectively, are considered subgroups of ADEM. Bilateral optic neuritis is characteristic of varicella-related ADEM. The clinical diagnosis usually requires confirmation by MRI, showing disseminated CNS demyelination, and follow-up MRI after 6 months to exclude new lesions suggestive of MS. CSF to rule out acute viral, bacterial, or parasitic meningoencephalitis may show lymphocytic pleocytosis and elevated albumin. Oligoclonal banding occurs in an average of 12.5% cases in children (range 0-29%), often transiently. PCR results may be positive for an inciting pathogen, but proof of a causative relation to ADEM is difficult. Brain biopsy is considered in cases with insidious onset and mass effect. The most common differential diagnosis is MS. ADEM is considered a monophasic disease, but 25% to 33% of patients have relapses, usually within 1 year of the initial event, and significantly shorter than

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MS relapse interval of 3.1 years. Treatment consists of IV high-dose corticosteroids, and if necessary, the addition of IV immunoglobulin and plasmapheresis, and immunosuppressive agents. Prognosis today is favorable, and contrasts with 25% mortality and 35% morbidity reported in pre-vaccination, measles-induced ADEM cases. Early use of high-dose steroids has also contributed to the improved outcome. (Menge T, Hemmer B, Nessler S et al. Acute disseminated encephalomyelitis. An update. *Arch Neurol* December 2005;62:1673-1680). (Olaf Stuve MD, Department of Neurology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390).

COMMENT. Although ADEM is considered a relatively rare disorder, with an estimated annual prevalence rate of 0.8/100,000 of the population (Leake JA et al. *Pediatr Inf Dis J* 2004;23:756-764), the diagnosis is increasingly important because of the expanded usage of vaccination, the need for early steroid therapy, and the risks of permanent neurologic sequelae. The poor prognosis of patients with measles-related ADEM should be a warning to parents who are persuaded to forego immunization of a child because of unsubstantiated reports of potential risks of autism.

Patients with onset of ADEM before 5 years of age have a lower mean intelligence quotient ($p<0.01$), significantly lower scores on reading and spelling tests ($p<0.001$), and a higher incidence of severe behavioral and emotional problems, compared to controls of the same age and socioeconomic status (Jacobs RK et al. *Pediatr Neurol* 2004;31:191-197). This study finds standard scores on spelling significantly lower in a young onset group compared to older onset patients with ADEM ($p<0.05$). Long-term neuropsychological dysfunction may occur in children who develop ADEM in early childhood, despite the absence of persisting neurologic deficits. (see *Ped Neur Briefs* 2004;18:66).

KLEINE-LEVIN SYNDROME

A systematic review of all published cases of Kleine-Levin syndrome (KLS) described in 195 articles since 1962 is presented from Stanford University Center for Narcolepsy, Palo Alto, CA; the Kleine-Levin Syndrome Foundation, Boston, MA; and Hôpital Pitie-Salpetriere, Paris, France. KLS is primary or infrequently, secondary to stroke, brain trauma and other disorders. Of 168 primary cases, 68% occurred in males, and the median age of onset was 15 years (range 4-82 years). Onset was preceded by infection in 43% of cases, commonly a nonspecific fever or flu-like illness, upper respiratory tract infection or tonsillitis, and less often, gastroenteritis, Epstein-Barr virus, varicella-zoster virus, Asian influenza, and *streptococcus*. Hypersomnia is the characteristic symptom, occurring in 100% cases. Other common symptoms include mental disorders (confusion, amnesia, derealization, hallucinations) in 98%, eating disorders (80%), hypersexuality (masturbation, inappropriate sexual advances) (43%), compulsions (29%), and depression (48%). Episodes of hypersomnia lasted 10 days, recurred every 3.5 months, and recovery followed in 8 years. Women had a longer disease course than males (9+/-8.7 years vs 5.4+/-5.6 years, $p=0.01$). Treatment with stimulants (mainly amphetamines) relieved somnolence in 40%. Lithium prevented relapses in 41% cases cf to 19% with no relapse in untreated cases ($p=0.02$). CSF was normal. EEG showed only nonspecific diffuse slowing in 70% patients. Brain CT and MRI were normal. Hormonal tests showed no consistent abnormality. In 18