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INFECTIOUS DISEASES

ENCEPHALITIS LETHARGICA: AN AUTOIMMUNE DISEASE

Twenty patients (16 from 2-16 years old, mean 10.4 years; 4 from 17-69, mean 47.5 years) with an encephalitis lethargica (EL) syndrome resembling that reported in the 1916-1927 epidemic, and presenting between 1999 and 2002, are reported from Great Ormond Street Hospital, London, and other tertiary neurology centers in the UK. The EL syndrome consisted of a sleep disorder (somnia, sleep inversion, or insomnia), lethargy, parkinsonism, dyskinesia (dystonia, oculogyric crises, hemiballism, chorea or tics), and neuropsychiatric symptoms (mutism (10 patients), anxiety, depression (6), agitation, catatonia, obsessive-compulsive disorder, ophthalmoplegia or pupillary abnormalities (7), headache (6), and seizures (3)). Eleven patients (55%) had a pharyngitis infection before onset of symptoms, 10 had a monophasic illness, and 7 a relapsing course. Five made a complete recovery at mean follow-up of 5 months (range 2-14 months), and 15 have persistent impairments (movement disorder in 6 and neuropsychiatric illness in 10). CSF was abnormal in 13 of 16 tested (elevated protein [>0.3 g/dl] in 75%, and oligoclonal bands in 69%). MRI was abnormal in 40%, with inflammatory changes localized to the basal ganglia, midbrain and thalamus. ASOT was elevated in 65% and normal in 35%; 2 had positive throat cultures for group A *Streptococcus*. Western immunoblotting showed autoantibodies reactive against human basal ganglia antigens in 95% of EL patients compared to 2-4% of child and adult controls ($P<0.0001$); they were also present in the CSF of 4 EL patients. Immunohistochemistry localized antibody binding to neurons. This EL-like syndrome appears to be secondary to a postinfectious autoimmunity against deep grey matter neurons. (Dale RC, Church AJ, Surtees RAH, et al. Encephalitis lethargica syndrome: 20 new cases and evidence of basal ganglia autoimmunity. *Brain* January 2004;127:21-33). (Respond: Dr Russell Dale, Neurosciences unit, Mecklenburgh Square, Institute of Child Health, London WC1N 3JJ, UK).

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COMMENT. This report of an encephalitis lethargica (EL) syndrome, with similar characteristics to that of von Economo's EL first described in 1916, may now be added to the growing list of immune-mediated movement and neuropsychiatric disorders linked to group A streptococcal infections. Sydenham's chorea is the classic phenotype and more recently, pediatric autoimmune neuropsychiatric disorder (PANDAS) and post-streptococcal dystonia (Dale et al, 2001). That anti-basal ganglia antibodies are pathogenic in this spectrum of autoimmune disorders is suggested but not yet proven. Questions regarding the regional specificity of the antibodies, and the possibility that they may be markers for a destructive process, secondary to T cell-mediated or direct toxicity from the streptococcus infection, need to be clarified (Vincent A. Editorial comment. *Brain* 2004;127:2-3). A response of EL to plasma exchange or other immunotherapies (Blunt et al, 1997), as sometimes reported in PANDAS, would be of interest. Behavior disorders, resembling those of attention-deficit-hyperactivity and oppositional defiant disorders, and termed 'organic drivenness,' were described as complications of encephalitis following the influenza pandemic of 1918 (Hohman, Ebaugh, 1922, 1923; Kahn, Cohen, 1934).

CORONAVIRUS AND ADEM

A boy aged 15 years with acute disseminated encephalomyelitis (ADEM) found to have human coronavirus (HCoV) in the cerebrospinal fluid (CSF) and nasopharynx is reported from the Children's Hospital of Buffalo, SUNY at Buffalo, NY. The child presented with a 5-day history of numbness that began in the lower extremities and progressed to the umbilicus. He had difficulty in walking, clumsiness in the right hand, and increased irritability. An upper respiratory infection had occurred one week before the onset of numbness, and the brother had recently recovered from a sore throat. The neurologic examination revealed normal optic discs and cranial nerves, mild distal weakness (4/5) in the right hand and foot, patchy loss of vibration and temperature sensation below T10, normal proprioception and pinprick sensation, negative Romberg test, mild dysmetria of the left hand, and an impaired tandem and antalgic gait. Symptoms resolved over several weeks without therapy. MRI of brain and spinal cord on admission showed lesions on T-2 weighted imaging at C4-C5 and T7-T8, and patchy hyperintensities in the white matter, especially the centrum semiovale and left cerebellum. Coronavirus OC43 was detected in CSF and nasopharyngeal secretions by PCR, and antibody titers rose from 1:160 in acute serum to 1:640 in convalescent serum at 3 weeks. Tests for other viruses were negative. CSF showed 10 red cells and 38 white blood cells, 92% lymphocytes, protein 40 mg/dL, and glucose 58 mg/dL. Immunoglobulin G index was 0.77 (normal <0.70). A test for oligoclonal bands was omitted. MRI at 6 weeks showed improvement, but follow-up MRI at 3 months revealed a new asymptomatic lesion in the left cerebellar hemisphere, and periventricular lesions in the right cerebral hemisphere were brighter and larger. ADEM was the presumed diagnosis, the first reported case associated with coronavirus in a child, but multiple sclerosis could not be ruled out. (Yeh EA, Collins A, Cohen ME, et al. Detection of coronavirus in the central nervous system of a child with acute disseminated encephalomyelitis. *Pediatrics* January 2004;113:e73-e76). (Respond: E Ann Yeh MD, Women's and Children's Hospital of Buffalo, Department of Neurology, 219 Bryant St, Buffalo, NY 14222).