INFECTIOUS DISORDERS

ACUTE NECROTIZING ENCEPHALOPATHY WITH H1N1 INFLUENZA A VIRUS INFECTION

A case of acute necrotizing encephalopathy (ANE) associated with the novel H1N1 influenza A virus is reported in a 2-year-old European girl treated at the Catholic University, Rome, Italy. She was admitted with recurrent seizures, fever, sore throat, and altered mental status. She had nuchal rigidity and severe opisthotonus. Nasal swab was positive for the novel swine influenza A virus (H1N1). CSF showed no pleocytosis, and PCR was negative for influenza A, cytomegalovirus, Epstein-Barr virus, varicella-zoster, and enterovirus. EEG showed generalized medium-high voltage theta-delta waves. MRI hyperintense T-2 weighted lesions were present in the midbrain, brainstem meninges, and cervical cord, and swelling of subcortical white matter of insulae, thalami, geniculate bodies, and pons tegmentum. With diagnosis of H1N1 ANE the patient received antivirals, and after exclusion of herpes virus involvement, methylprednisolone (1 mg/kg/day for 5 days) was added with definite clinical improvement. Repeat MRI with contrast after 8 days showed ring-enhancement with central necrosis of lesions, and extension of spinal cord involvement to thoracic and lumbar regions. Clinical improvement of mental status and speech occurred by 20 days, but neurologic and eye examinations showed divergent strabismus of left eye, visual field abnormalities, and unsteady gait. (Mariotti P, Iorio R, Frisullo G, et al. Acute necrotizing encephalopathy during novel influenza A (H1N1) virus infection. Ann Neurol July 2010;68:111-114).

COMMENT. ANE is a potentially fatal subtype of influenza-associated encephalopathy, characterized by multiple, symmetrical brain lesions involving thalami, brainstem tegmentum, and cerebral white matter. The authors cite 3 previous reports of neurological complications of H1N1 virus infection, including one of fatal ANE in a 12-year-old child. (Lyon JB et al. Pediatr Radiol 2010;40:200-205). Another case of fatal H1N1-associated ANE in a 7-year-old girl of Chinese descent is recently reported from Children’s Hospital, Chattanooga, TN (Martin A, Reade EP. Clin Infect Dis April 2010;50:e50-e52). Increased intracranial pressure, herniation, and brain death occurred within 4 days of onset of fever and respiratory symptoms. A further case of H1N1-associated ANE in a 3-year-old Italian girl was complicated by tonsillar herniation and hydrocephalus. Consciousness improved after shunting and treatment with acyclovir and oseltamivir but voluntary movements and speech were impaired and MRI at 40 days showed residual evidence of cavitation in cerebellar hemispheres, thalami, corpus callosum, and frontal white matter.(Ormitti F et al. AJNR Am J Neuroradiol Mar 2010;31:396-400).

H1N1 influenza virus was complicated by acute hemorrhagic leukoencephalitis and hypoxic brain injury in a 40-year-old man who failed to respond to treatment and remained in a comatose state 2 months after onset. (Fugate JE et al. Arch Neurol June 2010;67:756-758).
The majority of children with pandemic H1N1 influenza-associated hospitalizations in Milwaukee, WI, April to August 2009, had uncomplicated illness. Of 75 admitted, neurological disorders included seizures in 5 (6.6%), febrile seizure in 1 (1.3%), cognitive dysfunction in 6 (8%), and neuromuscular disorder in 7 (9.3%). None had encephalopathy. (Kumar S et al. Pediatr Infect Dis J July 2010;29:591-594).

Abnormal behavior during influenza virus infection and use of Tamiflu. In Japan, oseltamivir (Tamiflu) is prescribed at the onset of influenza infection as prophylactic therapy for encephalopathy. The media has questioned whether the treatment might trigger the behavior disorder and suicidal thoughts sometimes associated with influenza virus infection. A study of 22 children admitted to hospital with abnormal behavior in Osaka, Japan, during the 2004-2007 influenza seasons, found the behavior appeared before treatment in 13 and after medication was started in 9. Oseltamivir was continued for 3-5 days after admission. Meaningless speech and involuntary movements were most frequent (16 children), and illusions, delusions, and altered awareness occurred in 14. Fear and excitement affected 6 children. All children recovered without development of severe encephalopathy. The clinical course was similar in the pre-Tami and post-Tami groups. The researchers concluded that abnormal behavior associated with some epidemics of influenza virus is not caused by oseltamivir, but further study is needed to determine the value of this treatment in prevention of encephalopathy. (Tanabe T et al. Brain Dev June 2010;32:440-444). Abnormal behavior complicating the presenting symptoms of influenza should warn of an impending encephalopathy.

CYTOMEGALOVIRUS Gn GENOTYPES, SYMPTOMS AT BIRTH, AND SEQUELAE

Researchers at St Orsola General Hospital, Bologna, Italy, monitored symptoms of cytomegalovirus virus (CMV) at birth and during long-term follow-up of 74 congenitally infected newborns, and analyzed the distribution of gN variants in relation to virological parameters, clinical signs at birth, and sequelae, psychomotor impairment and sensorineural hearing loss. The population examined consisted of 29 (39.2%) symptomatic and 45 (60.8%) asymptomatic infants at birth; 2 (2.7%) died in the first weeks, and follow-up data were available for 64 (86.5%) children. The asymptomatic group with a favorable long-term outcome was significantly associated with gN-1 and gN-3a genotypes. The symptomatic group, with abnormal imaging and sequelae was associated with gN-4 genotypes (p<0.05). gN-1 and gN-3A genotypes reduce the risk of sequelae 5 fold, whereas variants of gN-4 increase the risk of sequelae 8 fold. gN genotypes are markers for virulence of CMV wild-type strains and the risk of sequelae in CMV-infected newborns. (Pignatelli S, Lazzarotto T, Gatto MR, et al. Cytomegalovirus gN genotypes distribution among congenitally infected newborns and their relationship with symptoms at birth and sequelae. Clin Infect Dis July 2010;51:33-41). (Respond: Dr Sara Pignatelli, Department of Hematology, Oncology, and Laboratory Medicine, St Orsola Malpighi General Hospital, Bologna, Italy. E-mail: sarapignatelli@unibo.it).

COMMENT. Markers for the early identification of newborns with CMV at increased risk of developing neurological sequelae should assist in monitoring follow-up