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CNS INFECTIONS

HUMAN PARECHOVIRUS AND NEONATAL ENCEPHALITIS

Clinical presentation, cranial ultrasound (cUS) and MRI findings, and neurodevelopmental outcome of 10 neonates (70% term) with human parechovirus (HPeV) encephalitis are described by researchers at University Medical Center, Utrecht, The Netherlands; University of Toronto, Ontario, Canada; and Universitaire de Quebec, Canada. Between Jan 1997 and Jan 2008, 14 infants with encephalitis were admitted to the NICU of the Wilhelmina Children's Hospital, Utrecht. Enterovirus was isolated in 3 infants, rotavirus in 1, and HPeV RNA in 9; the organism was unidentified in 1 infant. One infant with HPeV encephalitis presented at the Hospital for Sick Children, Toronto. Prospective diagnosis by viral molecular typing was made in 4 infants, and retrospective diagnosis in 6. The site of isolation of HPeV RNA was CSF in 7, blood in 2, and stool in 1. Type 3 HPeV was identified in all of 8 infants having adequate viral loads, None showed enterovirus or herpes simplex virus. Age at onset of symptoms varied from 6 to 90 days; <10 days in 60% patients. Clinical symptoms were fever, associated with seizures in 9 patients and a rash in 6. All seizures were prolonged, and repetitive in 5 patients, lasting >24 hours in 3. Cranial US showed periventricular echogenicity, and MRI and diffusion-weighted imaging, performed between 1 and 14 days after onset of symptoms, showed diffuse high signal intensity in the white matter on T2-weighted sequences, reduced diffusion in periventricular white matter, optic radiation, and internal capsule, and extensive white matter loss and severe gliosis in periventricular white matter on repeat MRI at 3 months to 7 years. Outcome assessed at term, 6, 15, and 24 months after birth, and longer in some, found cerebral palsy in 1 child, learning disabilities at 7 years of age in 1, epilepsy in 1, and mild hypertonia at 18 months in 1. Six patients were normal in development. Amplitude-integrated EEG continuous monitoring showed discontinuous normal voltage background in 2 of 4 infants with adverse outcome and

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repetitive seizures, and continuous normal voltage background in the other 2. (Verboon-Maciolek MA, Groenendaal F, Hahn CD, et al. Human parechovirus causes encephalitis with white matter injury in neonates. **Ann Neurol** Sept 2008;64:266-273). (Respond: Dr de Vries, Department of Neonatology, KE 04.123.1, University Medical Center, Lundlaan 6, 3584 EA Utrecht, The Netherlands. E-mail: l.s.devries@umcutrecht.nl).

COMMENT. Human parechoviruses (HPeV) types 1 and 2, formerly known as echoviruses 22 and 23 and belonging to the genus *Enterovirus,* have been reclassified in the new genus *Parechovirus.* HPeV 1 and 2 have not been isolated from neonates with encephalitis, but type 3 and CNS neonatal encephalitis have been reported. HPeV 4 has been found in an infant with fever only, and types 5 and 6 are also identified. The reverse transcription PCR test for HPeV became available in 2006.

Of the 10 neonates with HPeV encephalitis in the above study, only 1 showed CSF pleocytosis, and protein and glucose levels were always normal. Five showed normal neurodevelopment at ages 15 months to 7 years. Repetitive seizures correlated with poor developmental outcome. Neonatal HPeV-related seizures cannot be differentiated clinically from those caused by enterovirus infection; and both viruses should be investigated by PCR tests. The diagnosis of HPeV infection is made by a positive RT-PCR in CSF or blood. HPeV type 3 was identified in 8 of 10 patients tested.

In an editorial, Dr Joseph J Volpe of Boston Children's Hospital (**Ann Neurol** 2008;64:232-236) points out that Verboon-Maciolek and colleagues findings indicate that HPeV3 is a major cause of neonatal encephalitis and seizures, and 3 times more common than enterovirus, accounting for 64% of encephalitis cases admitted to the NICU at Utrecht University Medical Center. Major viral infections of the developing nervous system include rubella, cytomegalovirus, varicella-zoster, and lymphocytic choriomeningitis, acquired intrauterine (transplacental), and herpes simplex, enteroviruses, human parechovirus, and HIV, primarily parturitional or perinatal. Since CSF is normal in 90% cases of HPeV3 encephalitis, diagnosis may be overlooked. PCR analysis for HPeV3, enterovirus, and HSV is important in newborns presenting with unexplained seizures, especially if associated with rash and MRI evidence of white matter lesions.

CSF findings in herpes simplex, varicella zoster, and enterovirus infections in adults with viral meningitis are reported from Sheffield Teaching Hospitals, UK. (Ihekwaba UK, et al. **Clin Infect Dis** Sept 2008;47:783-789). Enterovirus was the most common cause of viral meningitis. CSF white cell and protein levels were significantly higher in patients with HSV type 2 than in those with enterovirus meningitis. Rash occurs after meningitis symptoms in varicella zoster infection (median delay 6 days). PCR provides a rapid, specific diagnosis.

NEUROPSYCHOLOGICAL OUTCOMES OF NEONATAL HERPES ENCEPHALITIS

Neuropsychological outcome and the relation to neuroimaging findings are studied in a cohort of 9 children between 2.5 and 13 years of age with neonatal herpes encephalitis, examined at Karolinska University Hospital, Sweden. Diagnosis, established by CSF PCR analysis, was triggered by seizures that occurred in 7 patients. All exhibited EEG abnormalities; and all received acyclovir. CSF showed a high protein content, and CT