

PEDIATRIC NEUROLOGY BRIEFS

A MONTHLY JOURNAL REVIEW

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Vol. 20, No. 4

April 2006

INFECTIOUS DISEASES

VIRAL INFECTION AND ACUTE ENCEPHALOPATHY

An unselected series of 22 children (13 males; age range 1 mo to 13yr, median 2yr 4mo) with acute encephalopathy were studied prospectively at the Royal Manchester Children's Hospital, UK. Symptoms of a viral prodrome consistent with viral encephalitis were present in 17 (77%), and laboratory evidence of viral infection in 7, including adenovirus, HSV/CMV, Coxsackie, and varicella. Symptoms were respiratory in 7, rash in 4, malaise and fever 3, and diarrhea in 3; and neck stiffness was present in 3. All showed deterioration of consciousness over a few hours. One was diagnosed with herpes simplex encephalitis, and 1 had received rubella immunization 26 days before presentation. Neurologic symptoms and signs developed at a median of 8 days (range 3-28d) after presentation. Seizures occurred in 18 patients; they were focal in 10 and generalized in 8. CSF pleocytosis was found in 14/22, an elevated CSF:serum albumin ratio indicative of impaired blood-brain barrier in 18/21, a raised intrathecal immunoglobulin production and IgG index in 15, oligoclonal bands in 14/17, and elevated interferon-alpha (IFN- α) levels in CSF or serum or both in 16/18. An initial disruption of the blood-brain barrier was followed by intrathecal antibody production. A young age, a deteriorating electroencephalogram pattern with generalized slowing (grade 1) progressing to amplitude and burst suppression (grade 2) and finally, electrical silence (grade 3), and prolonged impairment of blood-brain barrier were associated with a poor prognosis. The persistence of intrathecal IFN- α was indicative of a good prognosis. A Glasgow Coma Score (GCS) of 7 or less in 15/22 at presentation did not predict outcome. Nine of 14 with a good outcome had low GCS vs 4/8 with a poor outcome. Of 20 survivors, 7 had moderate/severe impairment. Of 9 children aged 2 years or less, 6 were neurologically impaired. (Clarke M, Newton RW, Klapper PE, et al. Childhood encephalopathy: viruses, immune response, and outcome. *Dev Med Child*

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Neurol April 2006;48:294-300). (Respond: Richard W Newton MD FRCPCH, Department of Paediatric Neurology, Royal Manchester Children's Hospital, Pendlebury, Manchester M27 4HA, UK).

COMMENT. In the majority of young children with acute encephalopathy in this study, the earliest laboratory sign of CNS involvement was an abnormal CSF:serum albumin ratio and disruption of the blood-CSF barrier. This leads to CSF viral invasion, increased production of intrathecal antibodies by activated lymphocytes, and high levels of cytokines such as IFN- α , and CNS autoimmunity. As the authors suggest, early antiviral therapy could result in repair of the blood-brain barrier and attenuation of the immune response.

The value of the EEG in predicting outcome of encephalopathy is noteworthy. The EEG has been helpful in assessment of prognosis of complex febrile seizures (FS), sometimes difficult to distinguish from encephalopathy (Millichap JG et al. **Neurology** 1960;10:643-653). The CSF:serum albumin ratio found abnormal in encephalopathy may prove helpful in the diagnosis and distinction from prolonged, focal or multiple FS. Seizures occurred at onset in the majority of patients in the above study, but the seizure duration and degree of fever are not recorded. Six patients without CSF pleocytosis and 10 who recovered without sequelae might in some circumstances have been classed as complex FS.

CSF CULTURES AND BACTEREMIA IN NEONATAL MENINGITIS

Cerebrospinal (CSF) culture results were compared with results of blood cultures and CSF parameters (WBC, glucose, and protein) in 9111 neonates with culture-proven meningitis and a first lumbar puncture at >34 weeks' gestational age from 150 NICU's managed by the Pediatrix Medical Group. The concordance of these values was analyzed by researchers at Duke Clinical Research Institute, Durham, NC. Of 92 (1.0%) neonates with meningitis confirmed by CSF culture, only 62% had a concomitant positive blood culture within 3 days of LP; in 38% the blood culture was negative. In 57 with both positive blood and CSF cultures, the organisms were discordant in 2 (3.5%), the CSF pathogens requiring different antimicrobial therapy than the blood pathogen. In neonates with bacterial meningitis, CSF WBCs ranged from 0-15,900/mm³; 5% had 0-1 and 10% had <3 WBCs. Highest sensitivity (97%) and lowest specificity (11%) for prediction of meningitis was any WBCs in the CSF. When 21 WBCs were used as the upper limit of threshold, the sensitivity and specificity were 79% and 81%, respectively. CSF glucose and protein were variable and not of diagnostic value in the absence of a CSF culture. (Garges HP, Moody MA, Cotton CM, et al. Neonatal meningitis: What is the correlation among cerebrospinal fluid cultures, blood cultures, and cerebrospinal parameters? **Pediatrics** April 2006;117:1094-1100). (Respond: Daniel K Benjamin Jr MD PhD MPH, Department of Pediatrics, PO Box 17969, Duke Clinical Research Institute, Durham, NC 27715).

COMMENT. A suspected diagnosis of neonatal meningitis should not be dismissed by a negative blood culture or normal CSF cells, glucose or protein. The diagnosis must be established by a timely LP and positive CSF culture. The authors recommend that an LP should be included in the evaluation of sepsis in an infant. For patients pretreated with antibiotics who are asymptomatic and have negative blood and CSF cultures, and elevated