Cerebrospinal Fluid Neutrophilic Pleocytosis in Hospitalized West Nile virus Patients

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A description of 7 consecutive patients admitted for various forms of neurological impairment. All these patients were found to have cerebrospinal fluid positive for West Nile virus IgM, and routine bacterial cultures were negative. Six of these patients did not present with the typical lymphocytic pleocytosis often quoted when discussing a viral meningitis/encephalitis; rather most presented with a cerebrospinal fluid neutrophilia. (J Am Board Fam Pract 2004;17:470–2.)

After the significant increase in West Nile virus (WNV) cases within the Rocky Mountain states1 during the summer of 2003, clinicians in the area have grown more familiar with the existence of West Nile virus.2 The virus, originally isolated in the West Nile region of Uganda in 1937, appeared for the first time in the United States in New York City during 1999. Its subsequent distribution has been called the “best documented spread of a vector-borne human pathogen in the past century.”3 In the summer of 2003, human cases of West Nile virus started to appear in significant numbers in the Rocky Mountain States.1 Further spread was expected in 2004 as West Nile virus entered the large population centers of the west coast.1 This single-stranded RNA virus has a mosquito vector and is amplified in avian hosts.4 Both avian and equine hosts experience significant morbidity and mortality.5 The vast majority of human infections are asymptomatic or exhibit mild febrile symptoms.2 Of those persons requiring hospitalization, there is significant morbidity. In severe disease, the greatest predictor for death is advanced age.6–8

Most discussions regarding the evaluation and diagnosis of neurological infection, including West Nile virus, regard the presence of lymphocytic pleocytosis in cerebrospinal fluid (CSF), as indicative of viral pathogenesis.3,8–10 We will describe 7 consecutive hospitalized patients presenting with neurological changes in whom the diagnosis of West Nile virus was made. Of these, only 1 patient presented with lymphocytic pleocytosis. Most presented with cerebrospinal fluid neutrophilic pleocytosis more generally associated with bacterial infections of the central nervous system (CNS).9

Case Reports

During July and August of 2003, the Montana Family Medicine Residency admitted a total of 7 patients who were eventually diagnosed with West Nile virus central nervous system infection. The information for this report was collected from retrospective chart review. All patients’ CSF samples were tested at the Montana State Public Health laboratory, in accordance with the CDC criteria for West Nile virus case determination. This lab used an IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA) to detect WNV-specific IgM antibody in CSF. IgM antibody in CSF strongly suggests recent CNS infection, because IgM does not readily cross the blood-brain barrier. IgM in serum may persist longer than 500 days after infection, so a single serum IgM is not considered diagnostic, in that it may indicate previous remote West Nile virus exposure.11,12 In addition, routine bacterial cultures were performed for all patients.

The 7 patients studied ranged in age from 24 to 74 years, with a median age of 55 years. There were 4 men and 3 women in the evaluation. All patients lived in south-central Montana except for 1 from northeast Montana. All patients recalled exposure to mosquitoes.

At presentation to the emergency department, all patients complained of headache. Five had symptoms of fever, chills, nausea, and vomiting. Two patients were brought in with decreased levels
of consciousness. One patient reported blurry vision (Table 1). One patient presented twice, the first time with headache, fever, and chills. This patient had an initial negative evaluation, including normal CSF cell count. The patient returned again 3 days later with persistent symptoms and an additional complaint of abdominal pain. At this time, repeat evaluation of this patient’s CSF was abnormal and indicative of CNS infection.

CSF samples were taken from all patients, and a cell count was obtained (Table 2). Total cerebrospinal fluid white blood cell counts ranged from 17 to 497. Five of the patients showed a neutrophilic predominance. In these patients, the average time from onset of symptoms to cerebrospinal fluid sampling was 3.6 days. Only 1 patient showed a lymphocytic predominance; his sample was obtained 2 days after initial onset of his symptoms. One patient’s sample showed a monocytosis, with 51%. All the patients’ cerebrospinal fluid samples demonstrated elevated protein levels and normal glucose levels.

<table>
<thead>
<tr>
<th>Test</th>
<th>Range (Median)</th>
<th>Reference Ranges</th>
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<tbody>
<tr>
<td>CSF</td>
<td></td>
<td></td>
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<tr>
<td>Leukocyte count</td>
<td>17–497 (141)</td>
<td>0–5</td>
</tr>
<tr>
<td>Protein</td>
<td>50–154 (73)</td>
<td>15–50</td>
</tr>
<tr>
<td>Glucose</td>
<td>51–120 (62)</td>
<td>50–80</td>
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<tr>
<td>Differential ≥50% neutrophils (n = 6 of 7)</td>
<td>6–100% (74)</td>
<td>All mononuclear cells</td>
</tr>
<tr>
<td>Blood</td>
<td></td>
<td></td>
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<tr>
<td>Leukocyte count</td>
<td>5.7–19.2 (10.5)</td>
<td>4.5–11</td>
</tr>
<tr>
<td>Hyponatremia, serum &lt;135 mmol/L (n = 6 of 7)</td>
<td>122–134 (132)</td>
<td>135–145</td>
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phocytic pleocytosis is not predictive regarding pathogenesis in the presence of West Nile virus CNS infections. Although it is unusual that cerebrospinal fluid cell counts were typical of viral infection in only one of these patients,3,4,8,10,17 other investigators have also noted the possibility of neutrophilic predominance of cerebrospinal fluid pleocytosis in subsets of patients during prior outbreaks of West Nile virus infections.7,10

It has been postulated that this neutrophilic predominance may be more evident earlier in the course of the infection.10 Our overall average from symptom onset to CSF sampling was 3.5 days. The cerebrospinal fluid finding of neutrophilic pleocytosis may be the result of earlier presentation to care by patients and increased vigilance by the medical community during a highly publicized outbreak of West Nile virus. With this in mind, it would seem most prudent for the evaluation of a patient presenting with neurological changes to consist of the full battery of cerebrospinal fluid laboratory tests, including West Nile virus CSF IgM, regardless of the initial cerebrospinal fluid white cell differential.

References


