Focal Neurological Deficits and West Nile Virus Infection

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Our experience with West Nile virus infection revealed that 54% of 28 patients had a focal neurological deficit at presentation. A meningitis or encephalitis syndrome was absent in 47% of patients with focal deficits. Details of the variety of deficits, the time to development of deficits, and the associated radiological and laboratory findings are also discussed in the present report.

West Nile virus (WNV) infection first became epidemic throughout the United States in 2002, with the largest number of cases (884 cases that resulted in 64 deaths) occurring in the state of Illinois [1]. The rapid geographic expansion of this virus in 2003 (i.e., the occurrence of 9862 cases of WNV infection that resulted in 264 deaths) indicates that WNV may have become a permanent feature in the ecology of the United States [1]. Moreover, the Centers for Disease Control and Prevention (CDC; Atlanta, GA) case count for WNV infection in 2003 documented that neuroinvasive disease occurred in association with 2866 (29%) of 9862 reported cases of WNV infection [1].

Most cases of WNV infection in humans are subclinical, with 1 in 5 infected persons developing a mild febrile illness and with only 1 in 150 infected persons developing meningitis, encephalitis, or both [2]. However, focal symptoms, localized to an anatomical region of the peripheral nervous system or the CNS, were only described in a limited number of reports before the 2002 outbreak occurred [3–5]. In our experience in the Chicago area, focal neurological deficits were often seen among patients with WNV infection.

Patients and methods. After institutional review board approval had been received, patients with WNV infection were identified by laboratory audit at John H. Stroger Hospital of Cook County and Rush University Medical Center in Chicago, Illinois, and at Loyola University Medical Center in Maywood, Illinois. All patients in this series were seen in the hospital setting from August through October 2002. All patients had WNV IgM detected in serum and/or CSF samples by use of an IgM antibody ELISA performed at the Illinois Department of Public Health laboratories (in accordance with the accepted criteria for diagnosis of WNV infection in Illinois in 2002).

All available medical charts were reviewed by the authors of the present report, and the clinical characteristics of the patients were reported. If patients had localizing neurological deficits, such as a cranial nerve deficit or hemiparesis, on examination, then they were classified as having a “focal neurological presentation.” All examinations were performed by neurologists at the respective institutions that participated in the present study.

Patients were also classified on the basis of the clinical syndrome noted at presentation. Patients with a headache, stiff neck, and fever were classified as having a meningitis syndrome, and patients with confusion and an altered or depressed level of consciousness were classified as having encephalitis. The terms “meningitis” and “encephalitis” are, therefore, not used to localize neurologic pathology, other than to suggest a generalized meningeal or cortical process, respectively. Focal neurological deficits could, therefore, be noted in patients with meningitis, encephalitis, or fever alone. Laboratory and imaging data for each of the patients were then analyzed.

Results. Of the 884 patients with WNV infection in Illinois in 2002, 43 (5%) were seen at the 3 institutions that participated in the present study. Detailed medical records were available for 28 patients. We divided these 28 patients into 2 groups: patients who presented with a focal neurological complaint (examination by a neurologist was done to corroborate the deficit) and patients who presented with a nonfocal complaint (figure 1).

In our series, 15 (54%) of 28 patients presented with a focal neurological deficit, whereas 13 (46%) of 28 patients presented with nonfocal neurological findings (figure 1). Of the 15 patients with focal deficits, 7 (47%) presented with fever in the absence of an associated meningitis or encephalitis (M/E) syndrome. On the other hand, most patients with a nonfocal presentation had an associated M/E syndrome. There were also 2 patients with West Nile fever (which was defined by the CDC as febrile illness caused by WNV without associated complications).

In our series of patients, focal deficits that localized to the
Figure 1. Mode of presentation of infection with West Nile virus

CNS included aphasia (in 1 patient), optic neuropathy (in 4 patients), abducens nerve palsy (in 1 patient), facial nerve palsy (in 1 patient), bradykinesia (in 3 patients), parkinsonian tremor (in 2 patients), ataxia (in 1 patient), and dysmetria (in 1 patient). Manifestations of WNV infection in the peripheral nervous system included poliomyelitis-like illness (in 3 patients), Guillain-Barré syndrome (in 1 patient), and acute motor or sensory polyneuropathy (in 3 patients). Some patients had multiple deficits. The average age of these patients with focal neurological deficits was 58 years, and 73% of these patients were men. The details associated with each case of WNV infection are reported in table 1.

For the 15 patients with focal neurological deficits, we defined the “time to deficit” as the length of time from the onset of fever, meningitis, or encephalitis to the onset of the neurological problem. For these 15 patients, the median time to deficit was 7 days (range, 3–21 days). On the other hand, for the subgroup of 7 patients with fever alone, the median time to deficit was 14 days (range, 6–21 days), and, for the subgroup of 8 patients with an associated M/E syndrome, the median time to deficit was 5 days (range, 3–14 days). The difference in the time to deficit between the group of patients with fever alone and the group of patients with an associated M/E syndrome was statistically significant (14 days vs. 7 days, respectively; \( P < .012 \)).

Eleven of 15 patients with a focal neurological deficit had lumbar puncture performed. The median CSF protein level was 77 mg/dL, the median CSF glucose level was 88 mg/dL, and the median CSF WBC count was 65 cells/\( \mu L \) (80% lymphocytes). Eleven of 13 patients with a nonfocal presentation also had lumbar puncture performed. Their median CSF protein level and median CSF glucose level were identical (69 mg/dL), and their median CSF WBC count was 211 cells/\( \mu L \) (75% lymphocytes). When the CSF WBC counts for patients with focal deficits and fever alone, there was a nonsignificant difference (66 vs. 22 cells/\( \mu L \), respectively; \( P = .212 \)). There was no difference in the median CSF protein level between these 2 groups.

Eleven of 15 patients with focal deficits had MRI performed with and without contrast. Nine patients had brain MRIs that showed no acute pathological findings that corresponded to their clinical manifestations of WNV infection. Select orbital cuts were not performed on the patients with optic neuropathy. Two patients had MRI of the lumbosacral area performed. MRI of a patient who had poliomyelitis-like illness showed enhancement of intradural L1-2 and L2-3 roots only, as reported elsewhere [6].

Discussion. Since 1999, WNV infection has become a prominent public health issue in North America. In the initial report of WNV infection from New York State, clinical characteristics were reported for 59 patients [4]. Twenty-seven percent of patients had abnormal strength, 10% had flaccid paralysis, 32% had hyporeflexia, and 14% had axonal neuropathy documented by electrophysiological studies [4]. In a prospective review of a series of patients with WNV infection in St. Tammany Parish, Louisiana, in 2002, a total of 15 (94%) of 16 patients had tremor, 5 (31%) had myoclonus, and 11 (69%) had parkinsonism [5]. Acute flaccid paralysis was noted in 3 patients (19%) [7]. Experience with WNV infection in Canada in 2002 showed that 11 (42%) of 26 patients developed a neuromuscular complication due to WNV infection [8]. The authors of the study from Canada [8] noted that rhombencephalitis, parkinsonism, and myelopathy were less frequently seen in association with WNV infection. In each of these series, most patients presented with meningitis and/or encephalitis.

In our series, 54% of patients had a focal neurological deficit at presentation. A significant proportion of these patients (47%) did not have an associated M/E syndrome. Furthermore, there was a distinct difference in the time to deficit for patients with...
Table 1. Focal neurological deficits associated with West Nile virus infection.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, years</th>
<th>Sex</th>
<th>Focal deficit and findings of relevant workup</th>
<th>Time to deficit, days</th>
<th>Associated illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>70</td>
<td>F</td>
<td>Optic neuropathy of the left eye (visual acuity, 20/50), mixed aphasia, and EEG showing focal left-side slowing</td>
<td>3</td>
<td>M/E syndrome</td>
</tr>
<tr>
<td>2</td>
<td>65</td>
<td>M</td>
<td>Optic neuropathy of the left eye (visual acuity, 20/100)</td>
<td>7</td>
<td>M/E syndrome</td>
</tr>
<tr>
<td>3</td>
<td>48</td>
<td>F</td>
<td>Left greater than right sixth cranial nerve palsy</td>
<td>5</td>
<td>M/E syndrome</td>
</tr>
<tr>
<td>4</td>
<td>76</td>
<td>M</td>
<td>Bradykinesia and parkinsonian tremor in the left upper extremity</td>
<td>4</td>
<td>M/E syndrome</td>
</tr>
<tr>
<td>5</td>
<td>57</td>
<td>M</td>
<td>Dysmetria and ataxic gait</td>
<td>3</td>
<td>M/E syndrome</td>
</tr>
<tr>
<td>6</td>
<td>79</td>
<td>F</td>
<td>Bilateral optic neuropathy and flaccid monoplegia of the left upper extremity, with areflexia and normal sensation$^a$</td>
<td>7</td>
<td>M/E syndrome</td>
</tr>
<tr>
<td>7</td>
<td>75</td>
<td>M</td>
<td>Acute motor and sensory polyneuropathy</td>
<td>5</td>
<td>M/E syndrome</td>
</tr>
<tr>
<td>8</td>
<td>50</td>
<td>M</td>
<td>Bilateral facial weakness in peripheral nerve pattern</td>
<td>18</td>
<td>Fever only</td>
</tr>
<tr>
<td>9</td>
<td>56</td>
<td>M</td>
<td>Bradykinesia and intermittent parkinsonian tremor with mild rigidity in the right upper extremity</td>
<td>14</td>
<td>Fever only</td>
</tr>
<tr>
<td>10</td>
<td>79</td>
<td>F</td>
<td>Left optic neuropathy and bradykinesia</td>
<td>14</td>
<td>Fever only</td>
</tr>
<tr>
<td>11</td>
<td>29</td>
<td>M</td>
<td>Left gluteal pain with left leg paresis, areflexia, normal sensation, and positive straight-leg-raise test, but with intact sensation; MRI showed intradural root enhancement$^b$</td>
<td>6</td>
<td>Fever only</td>
</tr>
<tr>
<td>12</td>
<td>71</td>
<td>M</td>
<td>Left leg pain with paresis, areflexia, and normal sensation$^a$</td>
<td>18</td>
<td>Fever only</td>
</tr>
<tr>
<td>13</td>
<td>61</td>
<td>M</td>
<td>Ascending pain and weakness in the lower extremities that progressed to paraplegia with intact sensation and areflexia; CSF samples showed cytoalbuminological disassociation; EMG findings were consistent with an acquired demyelinating process$^b$</td>
<td>14</td>
<td>Fever only</td>
</tr>
<tr>
<td>14</td>
<td>46</td>
<td>M</td>
<td>Acute motor and sensory polyneuropathy</td>
<td>21</td>
<td>Fever only</td>
</tr>
<tr>
<td>15</td>
<td>55</td>
<td>M</td>
<td>Acute sensory polyneuropathy</td>
<td>7</td>
<td>Fever only</td>
</tr>
</tbody>
</table>

NOTE. EEG, electroencephalography; EMG, electromyography; M/E, meningitis or encephalitis. $^a$ Poliomyelitis-like illness with anterior horn cell or motor root localization. $^b$ Guillain-Barré syndrome.

focal neurological deficits after fever alone, compared with patients with focal deficits and an associated M/E syndrome (median time to deficit, 14 days vs. 5 days, respectively). This finding may suggest that a patient with an M/E syndrome due to WNV is more likely to develop focal deficits sooner rather than later. On the other hand, if the patient only has fever as an initial manifestation of WNV infection, then he or she may yet develop a focal deficit up to 2–3 weeks after the initial fever. The reasons for this difference between the 2 groups are currently unclear. Future studies should examine the time to deficit in a prospective fashion.

In our series of patients, we also noted several manifestations of WNV infection that previously had been described only in isolated case reports; these manifestations included Guillain-Barré syndrome, facial palsy, optic neuritis, and motor aphasia. As expected, the site of the attack on the nervous system by WNV predicts the clinical symptomatology of WNV infection. The virus infects neurons and glia causing inflammation with the development of mononuclear infiltrates, microglial nodules, perivascular cuffing, and edema [9]. Symptomatology of WNV infection may also be modified by intrinsic host factors. It is unclear whether susceptibility or symptomatology is altered by the degree of the response of the host to viral attack, because our patients with focal neurological deficits had CSF findings similar to those of patients with nonfocal presentation.

In a series of patients for whom autopsy findings were available, WNV was shown to have a predilection for deep nuclei, the cerebellum, the brainstem, and motor neurons within the CNS [10]. It is the destruction of motor neurons in the anterior horns of the spinal cord that leads to the presentation of WNV infection as poliomyelitis. Because electromyography and nerve conduction studies are unable to differentiate between anterior horn cell or ventral root lesions, we labeled 3 cases in our series as “poliomyelitis-like illness” (radiological or pathological confirmation of anterior horn cell involvement is lacking for these 3 cases) [6]. When clinical series have shown pathological and radiological evidence of anterior horn cell loss and inflammatory changes of nerve roots, the patients have been appropriately designated as having “WNV poliomyelitis” [10–12]. Also, in the present series, 2 of 3 patients who had poliomyelitis-like illness did not have an associated M/E syndrome. A review of the neuromuscular presentations of WNV infection also
noted that such deficits may develop without encephalitic symptoms [13].

The limitations of the present study are that it is hospital based and that it has selection biases intrinsic to a retrospective case series. There was incomplete ascertainment of cases, because we were able to obtain medical charts for only 28 of 43 patients with WNV infection. Our cohort is also subject to recall bias, because, although meningitis and encephalitis are noted by a physician, fever may be documented only on the basis of the medical history provided by a patient. Moreover, follow-up data is unavailable for our cohort. Nevertheless, focal neurological deficits occurred frequently and, therefore, are noteworthy manifestations of symptomatic WNV infection.

With WNV possibly becoming a recurrent feature in local ecologies, physicians need to maintain a high index of suspicion for WNV infection during the months of late summer and early fall. Physicians must be aware that the presentation of WNV infection can include focal deficits even in the absence of meningitis or encephalitis. Symptomatic WNV infection can present as an acute illness that mimics other common neurological diseases. The wide spectrum of neurological manifestations noted in the present study highlights the important role of neurologists in the diagnostic evaluation of patients with suspected WNV infection.

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References