St Louis Encephalitis

A Review of 11 Cases in a 1995 Dallas, Tex, Epidemic

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Objective: To update some of the clinical features of St Louis encephalitis (SLE), a common arboviral infection that occurs in epidemic patterns in the south-central and midwestern United States.

Methods: Eleven patients with SLE from a 1995 epidemic in Dallas, Tex, were studied clinically, radiologically, neurophysiologically, and neuropathologically (in 1 case).

Results: The electroencephalograms and magnetic resonance imaging (MRI) scans of our patients revealed features that have received little attention in previous studies. Of the 9 patients who were examined with electroencephalography, all 9 had seizures or other abnormalities, and 1 had nonconvulsive status epilepticus. Two of 6 patients who had MRIs showed substantia nigra edema. Finally, 2 (18%) of our patients had coinfection with the human immunodeficiency virus.

Conclusions: The MRI findings of substantia nigra edema in patients with SLE have not been previously reported. Nonconvulsive status epilepticus can occur in patients with SLE and should be considered in patients with prolonged encephalopathy. Finally, human immunodeficiency virus coinfection may be a risk factor for symptomatic SLE infection.

Arch Neurol. 2000;57:114-118

The St Louis encephalitis (SLE) virus, a member of the Flavivirus (group B) arthropod-borne viruses, is a common cause of epidemic encephalitis. Several epidemics in the eastern and central United States have been reported over the past decades. These epidemics typically occur between July and September and are associated with significant mortality and morbidity. Early recognition of cases is rewarding, since aggressive mosquito-control measures in high-risk areas may abort the spread of the epidemic. Most of the patients with SLE are seen by neurologists because of the prominence of central nervous system (CNS) signs and symptoms; while CNS findings are usually nonspecific, certain features should prompt definitive serologic testing.

We reviewed the clinical characteristics, cerebrospinal fluid (CSF) analysis results, electroencephalograms (EEGs), computed tomographic (CT) and/or magnetic resonance imaging (MRI) scans, and autopsy findings of 11 patients who were diagnosed as having SLE in a recent (August-September 1995) epidemic in Dallas, Tex.
PATIENTS AND METHODS

PATIENTS

Thirty-five patients were admitted to Parkland Memorial Hospital, Dallas, between July and September 1995 with a diagnosis of acute CNS infection. Eleven of these patients were confirmed to have SLE by serologic analysis criteria. All patients underwent neurological examination by one of us (M.W. or R.D.-A.), as well as a lumbar puncture. Laboratory evaluations, including complete hemogram, chemistry, and coagulation studies, were performed on all patients. Electroencephalography studies were performed on 9 patients. Nine patients had unenhanced CT scans of the brain. Six patients underwent MRI scans using a high-field (1.5-T) magnet, 4 of these with gadolinium administration.

SERологIC ANALYSIS

Serologic analysis was performed on specimens from 33 patients in whom physicians suspected an acute CNS infection. Specimens were stored at −20°C. Antibodies were isolated by Arbovirus IgG-IgM-IF diagnostic kit (MRL Diagnostics, Cypress, Calif). The diagnosis of SLE was made by finding an IgM-IgG titer of 1:236 or higher, or IgG levels in acute titers with a 4-fold change in titers during the convalescent period. For viral cultures, the specimen was stored at −70°C. The specimen was inoculated to Vero cells and stored at 37°C. Cells were examined for 2 weeks for cytopathic effect. Diagnosis was confirmed using immunocytochemical stains.

cytic. Protein levels were elevated in 7 patients (mean, 0.67 g/L; range, 0.39-1.43 g/L). Cerebrospinal fluid glucose level was normal in all patients (range 2.2-9.0 mmol/L [40-163 mg/dL]). Anti-SLE IgM levels were elevated in serum from 6 patients (range, >1:32 to 1:640) and serum IgG was elevated in all patients (range, >1:32 to 1:32 678). Viral cultures were submitted from the CSF of 6 patients, but virus was only isolated from the cerebellum of 1 patient who came to autopsy. Further laboratory evaluation revealed serologic evidence of infection with HIV (2 patients), hepatitis C virus (1 patient), and herpes simplex virus 1 (1 patient).

Four patients had generalized tonic-clonic seizures. One patient developed status epilepticus and required pentobarbital anesthesia. Electroencephalograms were obtained for 9 patients and results on all were abnormal, showing status epilepticus (1 patient) (Figure 1), bilateral periodic lateralized epileptiform discharges (1 patient), and background diffuse slowing (7 patients).

Ten patients had CT scans of the brain; the films showed atrophy and chronic ischemic changes (4 patients), atrophy alone (3 patients), or no abnormality (3 patients). Six patients had MRI scans of the brain (4 with gadolinium administration), of which 5 (3 with gadolinium administration) were reviewed by one of the authors (R.A.S.). Two showed T2-weighted signal hyperintensity that was thought to represent edema in the substantia nigra (SN) (Figure 2). There were no significant T1-weighted findings before or after gadolinium administration. The MRI scans of 3 other patients showed atrophy, chronic ischemia, or both; 1, by report only, was normal.

Six patients required mechanical ventilation. Three patients died, 5 were discharged home, 2 were discharged to rehabilitation units, and 1 to a nursing home. The average length of hospital stay was 17 days. The cause

Figure 1. Electroencephalogram obtained when patient 5 was unresponsive but without clinically apparent manifestations of seizures. Referential Cz montage.

Figure 2. Left, Magnetic resonance imaging scan for patient 6 (MRI SE [magnetic resonance imaging spin echo] 2550/80); substantia nigra shows T2-weighted signal hyperintensity bilaterally and symmetrically. These lesions were not enhanced with the use of gadolinium. Right, Magnetic resonance imaging scan for patient 3 (MRI SE 3300/120). Right substantia nigra shows T2-weighted signal hyperintensity; gadolinium was not administered for this scan.
of death for the 3 who died was sepsis (2 patients) and basilar artery thrombosis (1 patient). An autopsy was performed on 1 patient, and SLE virus was cultured from the cerebellum. The brain was diffusely involved, but inflammatory and gliotic changes were most marked in SN and cerebellum. The autopsied patient did not have an MRI scan during life. Details of clinical and laboratory evaluation of our patients are summarized in the Table.

**Comment**

The clinical presentation and neurological findings of our patients, although not markedly different from other reported series, have some unique features that have not been well described in previous epidemics. The most novel feature is the MRI scan abnormality, which, to our knowledge, is the first to be reported in patients with SLE. The crescentic zones of T2-weighted signal hyperintensity conforming anatomically to the SN, bilaterally in one patient and unilaterally in the other (Figure 2), correlate with the predominant involvement of the SN in SLE that has been reported pathologically. This pattern is geometrically simpler and more nearly coextensive with a specific substructure of the brain and in 1 patient more symmetric than the findings reported in other kinds of encephalitis, such as eastern equine, Japanese, herpes simplex, and influenza A; however, it is subtle and may be difficult to evaluate prospectively in a clinical case. The SN hyperintensity is more specifically abnormal on a second echo or “strongly” T2-weighted sequence, while a slightly fuller, apparent, or subtle hyperintensity of the SN on a first echo (“proton–density-weighted”) sequence is nonspecific because it is also seen in some normal studies. While we believe that this abnormality is relatively specific for SLE, its sensitivity may be low, since we found it on only 2 of 6 MRI scans available for our review. Furthermore, we were unable to obtain a direct correlation between the radiologic and pathologic findings, since our patient who came to autopsy did not have an MRI scan during life.

<table>
<thead>
<tr>
<th>Patient No./Age, y/Sex</th>
<th>Race</th>
<th>Presenting Features</th>
<th>Clinical Findings</th>
<th>Seizures</th>
<th>Cerebrospinal Fluid Analysis</th>
<th>Serology Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nucleated Cells, No.</td>
<td>Protein Level, g/L</td>
</tr>
<tr>
<td>1/78/M White</td>
<td></td>
<td>Tremor, rigidity, and confusion</td>
<td>Unresponsive and respiratory failure</td>
<td>Tonic-clonic</td>
<td>5</td>
<td>0.51</td>
</tr>
<tr>
<td>2/47/M Black</td>
<td></td>
<td>Headache and fever</td>
<td>Tremor</td>
<td>None</td>
<td>14</td>
<td>0.48</td>
</tr>
<tr>
<td>3/21/M Hispanic</td>
<td></td>
<td>Headache and fever</td>
<td>Tremor and gait ataxia</td>
<td>None</td>
<td>446</td>
<td>1.02</td>
</tr>
<tr>
<td>4/49/M Black</td>
<td></td>
<td>Confusion and fever</td>
<td>Tremor and respiratory distress</td>
<td>Tonic-clonic</td>
<td>126</td>
<td>0.44</td>
</tr>
<tr>
<td>5/49/F Black</td>
<td></td>
<td>Fever, headache, and myoclonic jerks</td>
<td>Unresponsive and myoclonic seizures</td>
<td>Status epilepticus</td>
<td>68</td>
<td>0.60</td>
</tr>
<tr>
<td>6/37/M Black</td>
<td></td>
<td>Headache, fever, and leg weakness</td>
<td>Confusion and paraparesis</td>
<td>None</td>
<td>54</td>
<td>1.43</td>
</tr>
<tr>
<td>7/49/M White</td>
<td></td>
<td>Lethargy and fever</td>
<td>Tremor and dysarthria</td>
<td>None</td>
<td>29</td>
<td>0.43</td>
</tr>
<tr>
<td>8/24/F Hispanic</td>
<td></td>
<td>Headache and lethargy</td>
<td>Lethargy</td>
<td>None</td>
<td>30</td>
<td>0.45</td>
</tr>
<tr>
<td>9/44/F Hispanic</td>
<td></td>
<td>Back pain and leg weakness</td>
<td>Paraparesis, bilateral VI palsies, opsoclonus, and ocular bobbing</td>
<td>None</td>
<td>319</td>
<td>1.07</td>
</tr>
<tr>
<td>10/50/M Black</td>
<td></td>
<td>Dizziness and right hemiparesis</td>
<td>Confusion, right hemiparesis, and tremors</td>
<td>Tonic-clonic</td>
<td>45</td>
<td>0.39</td>
</tr>
<tr>
<td>11/82/M Black</td>
<td></td>
<td>Fever and lethargy</td>
<td>Unresponsive</td>
<td>None</td>
<td>42</td>
<td>0.53</td>
</tr>
</tbody>
</table>

*CT indicates computed tomography; MRI, magnetic resonance imaging; EEG, electroencephalogram; NA, not available; HIV, human immunodeficiency virus; HCV, hepatitis C virus; HSV-1, herpes simplex virus 1; SN, substantia nigra; SIADH, syndrome of inappropriate secretion of antidiuretic hormone; and RPR, rapid plasma reagin.*
The EEG features of SLE have received some attention.\textsuperscript{1} In our series, convulsions were common, affecting 4 (36\%) of our patients, including 1 patient who developed nonconvulsive status epilepticus and needed pentobarbital anesthesia (Figure 1). To our knowledge, this is the first reported case of nonconvulsive status epilepticus resulting from SLE infection. As indicated in previous reports,\textsuperscript{1,3} prognosis was worse among patients with seizures. Of 4 patients with seizures, 2 died and 2 had a prolonged hospital course. We believe that EEGs should be performed for all patients with SLE who present with altered mental status to exclude nonconvulsive seizures, even though our series cannot determine whether aggressive anticonvulsant therapy results in an improved outcome.

Two patients (18\%) in our series were HIV positive. The course of the illness was not more severe in these patients, including 1 patient who developed nonconvulsive status epilepticus and needed pentobarbital anesthesia (Figure 1). To our knowledge, this is the first reported case of nonconvulsive status epilepticus resulting from SLE infection. As indicated in previous reports,\textsuperscript{1,3} prognosis was worse among patients with seizures. Of 4 patients with seizures, 2 died and 2 had a prolonged hospital course. We believe that EEGs should be performed for all patients with SLE who present with altered mental status to exclude nonconvulsive seizures, even though our series cannot determine whether aggressive anticonvulsant therapy results in an improved outcome.

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Two patients presented with back pain and paraparesis; the spine MRI scans were normal for both patients. Although uncommon, myelopathy and transverse myelitis have been reported previously.\textsuperscript{7} Recovery was incomplete for both of our patients, and they were left with residual paraparesis. The common presenting features in our series were tremor, headache, and HIV coinfection. Although we do not know the background rate of HIV seropositivity in the community affected by this epidemic, HIV infection may be a risk factor for the development of symptomatic encephalitis after SLE infection. We suggest that SLE should be considered in patients who are febrile, HIV seropositive, and living in endemic areas with signs and symptoms of encephalitis in summer months. Additionally, patients with symptomatic SLE infection should be tested for infection with HIV. Given the low number of patients in the epidemic described here, further study will be needed to definitively establish this important issue.

<table>
<thead>
<tr>
<th>CT Scan Findings</th>
<th>MRI Scan Findings</th>
<th>EEG Findings</th>
<th>Course/Complication</th>
<th>Outcome</th>
<th>Discharge Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrophy and ischemia</td>
<td>Atrophy and ischemia</td>
<td>Diffuse slowing</td>
<td>Mechanical ventilation and sepsis</td>
<td>Died</td>
<td>Died</td>
</tr>
<tr>
<td>Atrophy</td>
<td>NA</td>
<td>NA</td>
<td>None</td>
<td>Discharged home</td>
<td>Normal</td>
</tr>
<tr>
<td>Normal</td>
<td>SN edema</td>
<td>Diffuse slowing</td>
<td>None</td>
<td>Discharged home</td>
<td>Normal</td>
</tr>
<tr>
<td>Atrophy and ischemia</td>
<td>NA</td>
<td>Diffuse slowing</td>
<td>Mechanical ventilation and HSV-1</td>
<td>Discharged home</td>
<td>Normal</td>
</tr>
<tr>
<td>Normal</td>
<td>Ischemia</td>
<td>Status epilepticus</td>
<td>Mechanical ventilation</td>
<td>Discharged to nursing home</td>
<td>Bed-bound and marked cognitive decline</td>
</tr>
<tr>
<td>Normal</td>
<td>SN edema</td>
<td>Periodic lateralized epileptiform discharges</td>
<td>Mechanical ventilation</td>
<td>Discharged to rehabilitation</td>
<td>Paraparesis</td>
</tr>
<tr>
<td>Atrophy and ischemia</td>
<td>Atrophy</td>
<td>Diffuse slowing</td>
<td>None</td>
<td>Discharged home</td>
<td>Normal</td>
</tr>
<tr>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>None</td>
<td>Discharged home</td>
<td>Normal</td>
</tr>
<tr>
<td>Atrophy</td>
<td>Atrophy</td>
<td>Diffuse slowing</td>
<td>HIV+, SIADH, RPR+</td>
<td>Discharged to rehabilitation</td>
<td>Paraparesis</td>
</tr>
<tr>
<td>Atrophy</td>
<td>NA</td>
<td>Diffuse slowing</td>
<td>Mechanical ventilation, rhabdomyolysis, and sepsis</td>
<td>Died</td>
<td>Died (autopsy done)</td>
</tr>
<tr>
<td>Atrophy and ischemia</td>
<td>NA</td>
<td>Diffuse slowing</td>
<td>Basilar artery thrombosis</td>
<td>Died</td>
<td>Died</td>
</tr>
</tbody>
</table>
lethargy, and fever, as reported in most previous epi-
demics.5,6 One patient presented with opsoclonus,
ocular bobbing, and other signs of brainstem involve-
ment, as has been documented in previous case
reports.7

Serologic testing was the most useful diagnostic tool
in our series, as in others.7 Cerebrospinal fluid viral cul-
tures were negative for all patients during life. There was
no correlation between outcome and CSF cell count or
SLE titers.

The neuropathologic findings in the 1 case that came
to autopsy (patient 10) included neuronal degeneration,
microglial proliferation, and perivascular mononuclear in-
filtmate with marked involvement of the SN. These find-
ings are similar to those previously reported.10

Only 11 patients were diagnosed as having SLE in
our epidemic. This modest number of affected individu-
als may be attributable to early recognition of cases and
a massive campaign of vector elimination mounted by
the Dallas County Health Department in affected high-
risk areas.

Accepted for publication May 3, 1999.

This study was supported by grant KO8 NS01763
from the National Institutes of Health, Bethesda, Md, and
a Neuropharmacology Research Fellowship from the
American Academy of Neurology, St Paul, Minn (Dr
Diaz-Arrastia).

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