

## CLINICAL AND NEURORADIOGRAPHIC MANIFESTATIONS OF EASTERN EQUINE ENCEPHALITIS

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### ABSTRACT

**Background** Eastern equine encephalitis occurs principally along the east and Gulf coasts of the United States. Recognition of the neuroradiographic manifestations of eastern equine encephalitis could hasten the diagnosis of the illness and speed the response to index cases.

**Methods** We reviewed all cases of eastern equine encephalitis reported in the United States between 1988 and 1994. The records of 36 patients were studied, along with 57 computed tomographic (CT) scans and 23 magnetic resonance imaging (MRI) scans from 33 patients.

**Results** The mortality rate was 36 percent, and 35 percent of the survivors were moderately or severely disabled. Neuroradiographic abnormalities were common and best visualized by MRI. Among the patients for whom MRI scans were available, the results were abnormal for all eight comatose patients as well as for all three noncomatose patients who subsequently became comatose. The CT results were abnormal in 21 of 32 patients with readable scans. The abnormal findings included focal lesions in the basal ganglia (found in 71 percent of patients on MRI and in 56 percent on CT), thalami (found in 71 percent on MRI and in 25 percent on CT), and brain stem (found in 43 percent on MRI and in 9 percent on CT). Cortical lesions, meningeal enhancement, and periventricular white-matter changes were less common. The presence of large radiographic lesions did not predict a poor outcome, but either high cerebrospinal fluid white-cell counts or severe hyponatremia did.

**Conclusions** Eastern equine encephalitis produces focal radiographic signs. The characteristic early involvement of the basal ganglia and thalami distinguishes this illness from herpes simplex encephalitis. MRI is a sensitive technique to identify the characteristic early radiographic manifestations of this viral encephalitis. (N Engl J Med 1997;336:1867-74.)

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**E**ASTERN equine encephalitis is a life-threatening mosquito-borne arboviral infection found principally along the east and Gulf coasts of the United States.<sup>1</sup> It was first recognized in humans in 1938.<sup>2-4</sup> Cases have occurred sporadically and in small epidemics: 223 cases were reported to the Centers for Disease Control and Prevention (CDC) between 1955 and 1993,<sup>5,6</sup> including a peak of 36 in 1959.<sup>7</sup> About one third of those affected die of the infection.

Diagnosing eastern equine encephalitis is difficult

because its symptoms are nonspecific and confirmation requires either specific serologic findings or the demonstration of the virus in cerebrospinal fluid or brain tissue.<sup>1</sup> Since cranial computed tomographic (CT) scans or magnetic resonance imaging (MRI) scans are obtained for most patients with encephalitis, the identification of neuroradiographic findings suggestive of eastern equine encephalitis could hasten its recognition. Although no specific treatment is available, rapid diagnosis is important for the institution of public health controls.<sup>8</sup>

Little is known about the neuroradiographic manifestations of eastern equine encephalitis. Cranial CT findings have been reported in 16 patients.<sup>6,9-14</sup> Most were studied with early-generation scanners, and the results were considered either normal or indicative of cerebral edema. Two of the 16 patients had frontal lesions; 2 others had abnormalities of the thalami and basal ganglia. In two of these four patients, MRI confirmed the CT findings.<sup>6,14</sup>

To define the neuroradiographic manifestations of eastern equine encephalitis more clearly, we collected clinical and radiographic data on all 38 cases reported in the United States between 1988 and 1994.

### METHODS

#### Identification of Cases

The CDC identified states reporting cases between 1988 and 1994. Reporting physicians or institutions either obtained informed consent for the release of records or provided confidential copies of records after removing any identifying information. The information available on each patient included a comprehensive clinical narrative, laboratory data at admission, specific documentation of the means by which eastern equine encephalitis was diagnosed, and if available, copies of the neuroradiographic studies.

Putative cases were assigned to one of three diagnostic categories according to the CDC criteria.<sup>15</sup> A confirmed case was one in which the IgM capture enzyme immunoassay of cerebrospinal fluid was positive, there was a fourfold rise in the titer of serum antibody against eastern equine encephalitis virus, or eastern equine encephalitis virus was isolated from cerebrospinal fluid or brain tissue. A probable case was one in which serum IgM capture enzyme immunoassay was positive or there was a single serum hemagglutination-inhibition titer of at least 1:320, a complement-fixation titer of at least 1:128, an immunofluorescence titer of at least 1:256, or a neutralization titer of at least 1:160. All other cases were considered unconfirmed.

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This study was approved by the human research committee of Brigham and Women's Hospital. When requested, approval was also obtained from state or local research committees.

### Abstraction of Clinical Data

The charts of all patients were reviewed independently by two clinicians, who abstracted the data. The prodrome was defined as the period between the onset of symptoms that were reasonably attributable to eastern equine encephalitis and the first major neurologic manifestation (altered mental status, seizure, hemiparesis, or severe headache and a temperature of at least 103°F). The severity of clinical sequelae was classified according to the patient's functional status on discharge from an acute care facility: a designation of normal indicated that no deficits remained; a designation of mild sequelae indicated that self-care was possible outside an institutional setting; a designation of moderate sequelae indicated that institutional care was required to manage the activities of daily living; a designation of severe sequelae indicated that the patient was in a permanent vegetative state; and a designation of death indicated that the patient had died before discharge.

### Interpretation of Radiographic Films

The radiographic films were assessed independently by two neuroradiologists. One was unaware of the study's objectives, and both were unaware of the patients' histories. Differences in interpretation were resolved by consensus. The quality of the films was assessed subjectively. Poor-quality films were not analyzed. Radiographically evident lesions were scored as follows: 1+, less than 1 cm in diameter; 2+, 1 to 2.5 cm in diameter; and 3+, more than 2.5 cm in diameter.

### Statistical Analysis

Univariate analyses were performed to correlate specific clinical or laboratory findings with the outcome. For contingency tables, Fisher's exact test was used. For unpaired nonparametric data, the Mann-Whitney rank-sum test was used. Two-tailed P values were calculated, and all values below 0.05 were considered to indicate statistical significance.

## RESULTS

### Identification of Cases

Records were obtained for 38 patients with putative cases of eastern equine encephalitis, including all 36 reported to the CDC during the study years. Two cases did not meet diagnostic criteria and were eliminated. Of the remainder, 26 were defined as confirmed and 10 as probable. Three have been described in detail previously,<sup>6,14,16</sup> and nine others briefly.<sup>17</sup>

### Demographic and Epidemiologic Characteristics

Cases were recognized in 11 states. Twenty-five of the 36 patients were male, and 29 were white. The median age was 59 years (range, 6 months to 85 years). Seven patients were under 20 years of age. None were seriously impaired before their illness.

### Clinical and Laboratory Characteristics

Thirteen of the 36 patients died (36 percent). Of the survivors, 1 recovered fully, 14 had mild impairments, 3 had moderate impairments, and 5 had severe impairments. The median duration of acute care hospitalization was 18 days (range, <1 to 89).

**TABLE 1. PREVALENCE OF CLINICAL SIGNS, SYMPTOMS, AND LABORATORY ABNORMALITIES ON HOSPITALIZATION AMONG 36 PATIENTS WITH EASTERN EQUINE ENCEPHALITIS.**

VARIABLE	PREVALENCE (% OF PATIENTS)
<b>Symptoms and signs</b>	
Fever	83
Headache	75
Nausea and vomiting	61
Malaise and weakness (nonfocal)	58
Confusion	44
Myalgia and arthralgia	36
Neck stiffness*	36
Plantar reflex	29
Chills	25
Seizures†	25
Weakness (focal)	23
Abdominal pain	22
Respiratory symptoms	11
Cranial-nerve palsies‡	8
Sore throat	8
Diarrhea	8
Photophobia	3
<b>Laboratory findings§</b>	
Pleocytosis	97
Elevated protein concentrations in cerebrospinal fluid	94
Elevated red-cell count in cerebrospinal fluid	77
Leukocytosis	69
Hyponatremia	60

\*This category includes all patients with neck stiffness, regardless of the severity.

†Seizures were included if they occurred either before or on the day of admission.

‡All patients with palsies on admission had a central abnormality of the seventh cranial nerve.

§Complete data were not available for all patients. The numbers of patients for whom data were available are as follows: cerebrospinal fluid white-cell count, 34; cerebrospinal fluid protein level, 32; cerebrospinal fluid red-cell count, 31; peripheral-blood white-cell count, 35; and serum sodium level, 35. All cerebrospinal fluid values refer to the patients' first lumbar punctures. For 29 of the studies, the sample was obtained within 24 hours after hospitalization. A normal red-cell count was considered to be  $\leq 5$  cells per milliliter. For other laboratory data, the reference ranges for normal values were obtained from Isselbacher et al.<sup>18</sup>

Among the patients who died, the median duration of hospitalization was 16 days. Only three patients died during the first week of hospitalization.

For most patients, the illness began with a short prodrome (median, 5.0 days; range, 0 to 28), typically mimicking a benign viral illness; fever, headache, and abdominal distress were common (Table 1). Two patients were admitted during the prodromal period for presumptive abdominal emergencies. Neurologic symptoms (confusion, somnolence, focal weakness, seizures, and meningeal signs) prompted evaluation in all others. Once the neurologic symptoms began, the condition of the patients de-

teriorated rapidly. Four were stuporous or comatose when first evaluated; 21 others (for a total of 69 percent) became stuporous within two days after admission. In all, 32 of the 36 patients (89 percent) eventually became stuporous or comatose. The median ( $\pm$ SD) duration of coma in patients with a favorable outcome (no, mild, or moderate sequelae) was  $5 \pm 4.7$  days. One patient recovered with mild sequelae after nine days of coma.

Seizures occurred in 18 patients: 15 had generalized seizures (tonic-clonic in most, and twitching in 2), 3 had focal events (1 of whom also had a generalized seizure), and 1 had partial complex seizures. Focal weakness, ranging from subtle to severe, occurred in 16 patients. Paresthesias accompanied paresis in one patient. Cranial-nerve palsies developed in nine patients (cranial nerve VII was affected in five, cranial nerve XII was affected in one, and five had oculomotor phenomena). The course in one patient was indistinguishable from that of aseptic meningitis.

Leukocytosis and hyponatremia were common (Table 1). At the time of admission, the median white-cell count was 14,500 cells per cubic millimeter (range, 3800 to 23,900), and the median serum sodium concentration was 134 mmol per liter (range, 123 to 146). Thirty-four patients (94 percent) had at least one lumbar puncture. The median initial cerebrospinal fluid white-cell count was 370 cells per cubic millimeter (range, 0 to 2400; median of 70 percent neutrophils), and the median protein concentration was 97 mg per deciliter (range, 31 to 297). Hypoglycorrhachia was typically absent.

Electroencephalographic results were available for 24 patients. All showed generalized slowing and disorganization of the background initially. Epileptiform discharges were noted in six patients, including four who had periodic lateralizing epileptiform discharges. No correlations could be drawn between specific clinical events and electroencephalographic patterns.

#### Neuroradiologic Findings

Thirty-five of the 36 patients underwent CT scanning at least once. We obtained 57 of the 76 scans that were performed and at least 1 study from 33 of the 35 patients who underwent CT (94 percent). Sixteen patients underwent MRI at least once. We obtained 23 of the 25 MRIs that were performed and at least 1 set from 15 of the 16 patients who had MRI (94 percent). One CT scan and one MRI were of poor quality and were not analyzed. Overall, we reviewed at least one CT scan from 89 percent of the patients and at least one MRI from 39 percent (Table 2).

The interval between the onset of neurologic symptoms and the initial radiographic study that we reviewed ranged from 1 to 14 days (median, 2). In all but one patient, CT was the initial study performed.

**TABLE 2.** RESULTS OF NEURORADIOGRAPHIC STUDIES IN 32 PATIENTS WITH EASTERN EQUINE ENCEPHALITIS.

ANATOMICAL SITE OR ABNORMALITY	CT SCAN (N=32)	MRI SCAN (N=14)
Basal ganglia†	18	10
Thalamus	8	10
Brain stem	3	6
Cortex	4	5
Periventricular area (focal lesions)	0	2
Meninges	2	0‡
Hydrocephalus	1	0
Any abnormality	21	13

\*These values are the numbers of patients in whom the finding was unequivocally present.

†An area was scored as abnormal only once per patient, regardless of the number of scans demonstrating the abnormality.

‡MRI was not performed in the two patients whose CT scans showed meningeal enhancement. Parenchymal enhancement was unequivocally present on MRI in five of the nine patients with abnormal results of MRI in whom contrast-enhanced imaging was attempted.

In general, the CT and MRI findings were similar, but MRI was more sensitive.

#### MRI Findings

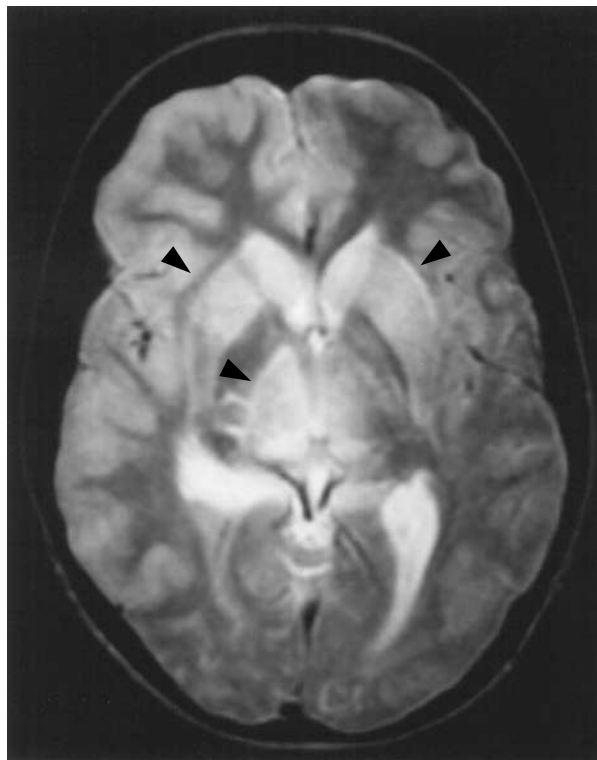
For 13 of the 14 patients included in this analysis, every MRI (21 studies altogether) revealed abnormalities. Five patients first underwent MRI within three days after the onset of neurologic symptoms; the results of all five scans were abnormal. In three of the five, the abnormal results preceded the onset of coma. Lesions were best seen on T<sub>2</sub>-weighted images, appearing as areas of increased signal intensity. Larger lesions were also visible on unenhanced T<sub>1</sub>-weighted images. The basal ganglia and thalami were most commonly involved. Noncontiguous abnormalities were also seen in the brain stem, cortex, and periventricular white matter. With the exception of white-matter changes, all abnormalities were evident early in the course of illness and diminished with clinical improvement.

Lesions of the basal ganglia ranged in size from 2+ to 3+, were either unilateral or asymmetric, and sometimes involved the adjacent internal capsule (Fig. 1A). Large lesions were associated with a mass effect. Thalamic and brain-stem lesions were smaller and either unilateral or asymmetric. The midbrain was the portion of the brain stem most often involved. Cortical lesions varied in location: in three cases they were in the temporal lobe, in two cases they were in

the insula, and in one case each they were in the frontal lobe and cingulum (Fig. 1C).

Two young, previously healthy women had periventricular white-matter changes. In each, MRI revealing these abnormalities was performed well after the onset of neurologic disease (12 and 19 days later). The first woman had patchy abnormalities of the posterior periventricular white matter; the second had punctate lesions adjacent to the lateral ventricles that were reminiscent of those seen in multiple sclerosis (Fig. 2).

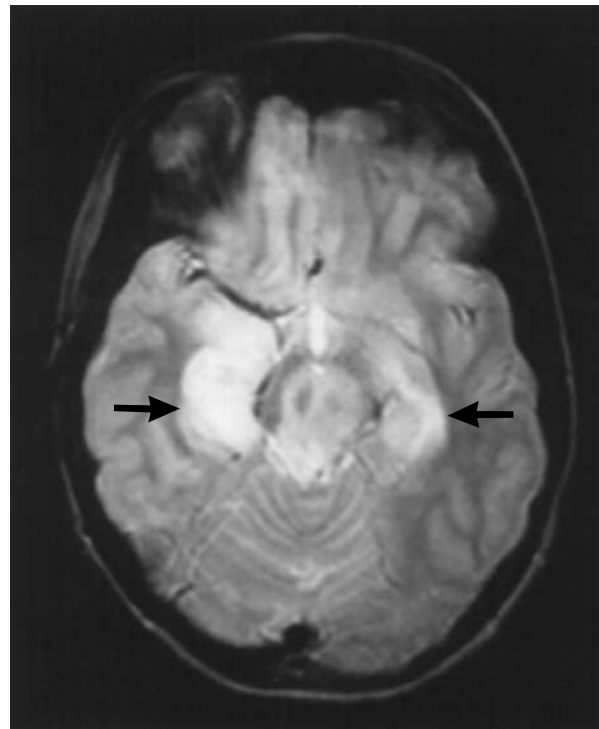
Imaging with contrast medium was attempted in



A



B



C

**Figure 1.** Lesions of the Basal Ganglia and Cortex in a 14-Year-Old Boy Who Died of Eastern Equine Encephalitis.

Panel A shows an MRI scan taken three days after the onset of neurologic symptoms. Large, asymmetric lesions are present in the caudate nuclei, putamina, and thalami (arrowheads). Panel B shows a CT scan taken seven days after the onset of neurologic symptoms. Large lesions of the basal ganglia and thalami are again evident (outlined by arrowheads). There is diffuse swelling of the brain. Panel C shows an image from the same MRI as shown in Panel A. Lesions are present in the medial temporal lobes (arrows) and right insula (not shown). Autopsy revealed diffuse encephalomalacia, marked perivascular chronic inflammatory changes, and focal intraparenchymal perivascular hemorrhage in the caudate nucleus and putamen. Several microglial nodules were evident. A necrotic and hemorrhagic area measuring 3 cm by 2 cm was present in the anterior portion of the right temporal lobe.

nine patients with abnormal imaging results. Definite enhancement was seen in five patients, and equivocal enhancement in one. When present, enhancement was confined to areas of abnormal T<sub>2</sub>-weighted signal.

A single patient in this series had no abnormalities on MRI scanning. His examination was performed 12 days after the onset of neurologic symptoms and 4 days after the resolution of coma.

#### CT Findings

Of the 32 patients whose scans were analyzed, 21 (66 percent) had abnormal findings at some point in their illness. Abnormalities were detected in 2 of 8 patients who underwent scanning after the onset of neurologic symptoms but before the onset of coma and in 9 of 15 others who underwent scanning at the onset of coma. Two of four patients who never became comatose also had abnormal results. Only 3 of 15 patients studied after the first day of the coma, but while still comatose, had normal results. In 11 patients, no specific abnormalities were seen.

As with MRI, lesions of the basal ganglia were the most common finding on CT scanning (Table 2). The putamen and the caudate head were particularly likely to be involved (Fig. 1B). The lesions ranged from subtle to obvious. Intermediate or large lesions were common, the latter associated with a mass effect. In patients with subtle findings, serial studies often showed evolution of the lesions (Fig. 3A and 3B). Thalamic and midbrain lesions were 1+ to 2+ in size. In all patients for whom both CT and MRI results were available, MRI was more sensitive, revealing more abnormalities and better detail (Fig. 3C).

Meningeal enhancement was unequivocally detected in two patients. In one, the appearance of the suprasellar cistern and the intensity of enhancement after the administration of contrast medium suggested the presence of subarachnoid hemorrhage or meningitis.

#### Characterization of Prognostic Factors

To identify prognostically important variables, we correlated the presence or absence of certain features with the outcome. Information on all features was not available for every patient. Sequelae were categorized in each of two ways: survival as opposed to death, and a favorable outcome (no, mild, or moderate sequelae) as opposed to an unfavorable outcome (severe sequelae or death). The prognostically important variables that were identified by the two categorization schemes were concordant.

Neither the age of the patient nor the duration of the prodrome was a statistically significant predictor of outcome, although patients with favorable outcomes tended to be younger and to have longer prodromes. No clinical variables correlated with out-



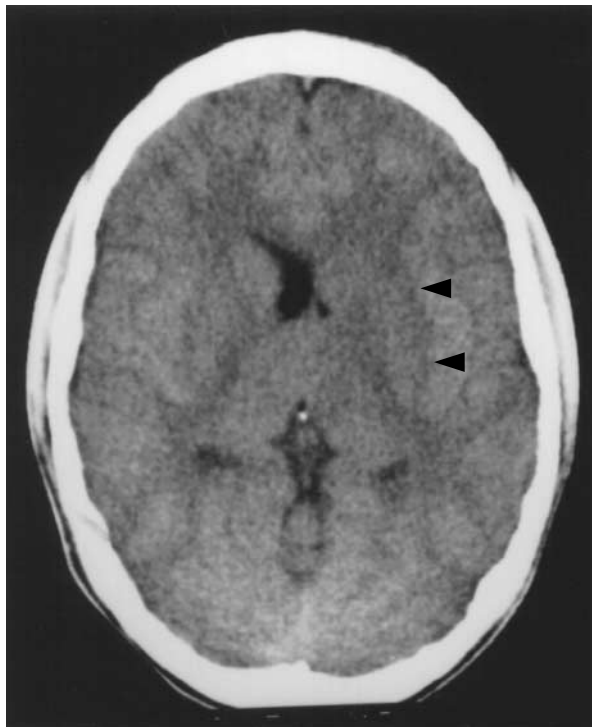
**Figure 2.** Periventricular White-Matter Lesions in a 33-Year-Old Woman Who Contracted Eastern Equine Encephalitis during Her Seventh Month of Pregnancy.

The patient survived with mild sequelae and delivered a normal child at term. This MRI scan was obtained 19 days after the onset of neurologic symptoms. A punctate area of increased T<sub>2</sub>-weighted signal is present in the right periventricular area (arrow). Similar lesions were seen in several other sections.

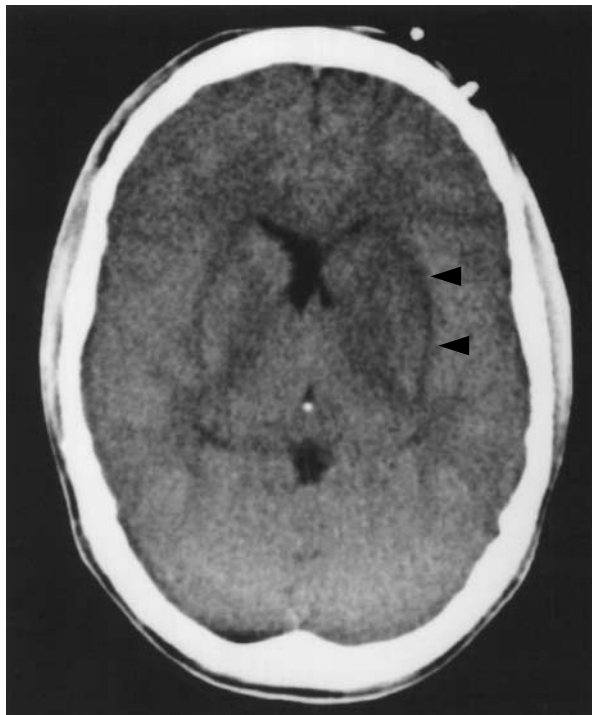
come, including the temperature at admission or the presence of neck stiffness, seizures, focal weakness, or a plantar reflex.

Two laboratory variables did predict outcome: the initial white-cell count in cerebrospinal fluid and the severity of hyponatremia during hospitalization. Ten of 13 patients with initial cerebrospinal fluid white-cell counts of at least 500 cells per cubic millimeter had unfavorable outcomes, as compared with 6 of 21 with counts below 500 cells per cubic millimeter ( $P=0.01$ ; relative risk, 2.7; 95 percent confidence interval, 1.3 to 5.6). Similarly, 12 of 14 patients whose lowest serum sodium concentration was  $\leq 130$  mmol per liter had an unfavorable outcome, as compared with 4 of 16 whose lowest value exceeded 130 mmol per liter ( $P<0.01$ ; relative risk, 3.4; 95 percent confidence interval, 1.4 to 8.2).

We could not correlate the severity of neuroradiographic lesions with outcome, although our attempt was undoubtedly confounded by uneven film quality and the disparate times of the radiographic studies



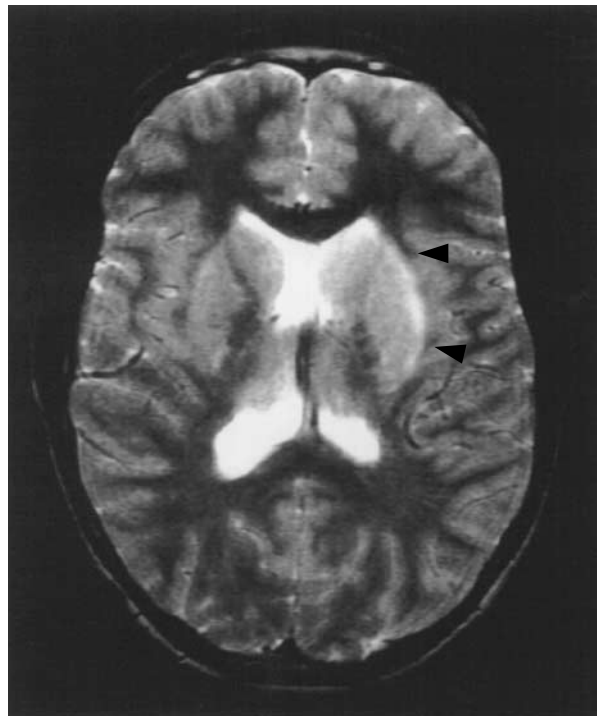
A



B

during each patient's course. All three patients whose CT scans showed no abnormalities on day 2 of coma or beyond had favorable outcomes. We could not correlate the severity of lesions with any clinical variables. Patients with larger lesions tended to be older and to have higher cerebrospinal fluid white-cell counts than those with smaller lesions, but the differences were not significant.

Eight of 21 patients treated with anticonvulsants did well, as compared with 9 of 13 who were not treated with anticonvulsants ( $P=0.16$ ). Three of 12 patients who were given corticosteroids for cerebral edema did well, as compared with 13 of 20 who were not given corticosteroids ( $P=0.07$ ).



C

**Figure 3.** The Evolution of Subtle Changes on CT and MRI Scanning in a 14-Year-Old Boy Who Survived Eastern Equine Encephalitis with Mild Sequelae.

Panels A and B show CT scans without contrast medium that were taken one day (Panel A) and five days (Panel B) after the onset of neurologic symptoms. Initially, there was a subtle loss of the normal demarcation between the left caudate nucleus and internal capsule (arrowheads in Panel A). Later, the abnormality was unmistakable (arrowheads in Panel B). There are poorly marginated, low-density, bilateral putaminal, pallidal, and capsular lesions. Panel C shows an MRI scan taken two days after the onset of neurologic symptoms. The higher sensitivity of the MRI, as compared with CT, is obvious (arrowheads). The MRI showed several other lesions (pontine, mid-brain, and thalamic) that were not suspected on CT scanning.

## DISCUSSION

We studied all cases of eastern equine encephalitis that were reported in the United States from 1988 through 1994, making this the largest case series since 1957.<sup>19</sup> Radiographically, eastern equine encephalitis is a focal disease, with a predilection for early involvement of the basal ganglia, thalami, and brain stem. The prevailing view of the radiographic manifestations of the disease was shaped by just 14 cases studied with older-generation CT scanners.<sup>1,13</sup> Accordingly, the prevalence of focal neuroradiographic abnormalities in eastern equine encephalitis has not been recognized. Focal clinical signs are well described in the illness,<sup>4,13,19</sup> and occurred at some point in 59 percent of the patients in our series.

Gross inspection of the brains of patients who died early in the course of eastern equine encephalitis reveals edema, leptomeningeal vascular congestion, hemorrhage, and encephalomalacia. Pyogenic meningial exudate is rare.<sup>4</sup> On cut sections, small necrotic foci are widely distributed.<sup>4,20,21</sup> Histopathological manifestations include vascular, neuronal, and glial components. Vascular findings include arteriolar and venular inflammation, endothelial proliferation, small-vessel thrombosis, and perivascular cuffing. An inflammatory meningeal infiltrate is variably present.<sup>4,12,20-22</sup> Focal parenchymal infiltration by neutrophils and macrophages causes neuronal destruction, neuronophagia, focal necrosis, and spotty demyelination. Glial proliferation results in glial nodules. In the brains of patients who died later in the course of illness, cortical atrophy predominates.<sup>3,4,11,20-22</sup>

The results of autopsy series differ on whether certain areas of the brain are particularly vulnerable to eastern equine encephalitis virus. Farber et al. suggested that the basal ganglia and brain stem are the most severely affected<sup>4</sup>; Hauser suggested the mid-brain.<sup>21</sup> Dent studied Hauser's patients but found no predilection for any particular areas.<sup>20</sup> Our findings, like those of Farber et al., suggest that although focal lesions are variably distributed, involvement of the basal ganglia and thalami is prominent. These changes are evident early in the course of eastern equine encephalitis and often resolve with recovery. Accordingly, we suspect that they represent ischemia, inflammation, or edema, at least initially, rather than necrosis.

We cannot explain the predilection for this anatomical pattern, but it has also been described in other viral encephalitides. Basal ganglionic and thalamic lesions were identified radiographically in 7 of 13 patients with Japanese encephalitis.<sup>23</sup> At autopsy, one had focal necrosis of the basal ganglia. Changes in the basal ganglia are also seen radiographically in measles,<sup>24</sup> mumps,<sup>25,26</sup> and echovirus 25 encephalitides<sup>27</sup>; in Creutzfeldt-Jakob disease<sup>28,29</sup>; and in non-infectious conditions, including cyanide and carbon monoxide poisoning.<sup>30</sup> Influenza A encephalitis is associated with cortical, subcortical, thalamic, and

pontine abnormalities.<sup>31,32</sup> As was true in our series, MRI is a more sensitive method of identifying these changes than CT.

A minority of the patients in our series had cortical or subcortical lesions, predominantly involving the frontal lobes and anterior and medial portions of the temporal lobes. Herpes simplex encephalitis, which resembles eastern equine encephalitis clinically, typically also produces abnormalities of the frontal and temporal lobes.<sup>33,34</sup> Unlike eastern equine encephalitis, however, herpes simplex encephalitis rarely involves the basal ganglia. When it does, the involvement is usually lateral and late<sup>34</sup>; in eastern equine encephalitis, the involvement is usually medial and early. The two diseases can be remarkably similar electroencephalographically. A minority of patients with eastern equine encephalitis have changes that are characteristic of herpes simplex encephalitis.<sup>35,36</sup> Thus, a diagnosis based on isolation of the herpes simplex virus is imperative, even in apparently classic cases of herpetic encephalitis.

CT showed meningeal enhancement in two patients, presumably reflecting the meningeal component of infection.<sup>4,19-22</sup> In two young patients, MRI showed late white-matter changes. Neither patient was studied early, so the changes cannot be definitively attributed to eastern equine encephalitis. Nevertheless, demyelination is a known sequel of the illness.<sup>4,20-22</sup>

MRI was exceedingly sensitive to the central nervous system manifestations of eastern equine encephalitis. The results of every MRI obtained from a comatose patient or a patient who subsequently became comatose were abnormal. Thus, the diagnosis of eastern equine encephalitis should be questioned in comatose patients with normal findings on MRI. Because CT remains the initial radiologic tool in suspected cases of encephalitis, physicians must be familiar with the subtle early CT changes of eastern equine encephalitis (Fig. 3) that mimic early infarction or nonspecific findings common in elderly patients. Clinicians who encounter such findings should consider a diagnosis of eastern equine encephalitis in the appropriate setting, especially during mosquito season in areas in which the disease is endemic.

Our patients' courses closely matched those in earlier clinical descriptions. The median age in our series was older than in previous reports,<sup>13,19,21,37</sup> possibly reflecting regional or temporal differences in demographics and human habitat. In contrast to an earlier series,<sup>13</sup> neither the age of the patient nor the duration of the prodrome significantly predicted outcome.

High initial white-cell counts in cerebrospinal fluid and the development of severe hyponatremia during hospitalization each predicted a poor outcome. Both are probably markers of intense cerebral inflammation. Surprisingly, patients who were treated with either an

ticonvulsants or corticosteroids had poorer outcomes than those not so treated, associations that bordered on statistical significance. These results are probably confounded by unidentified variables, such as the severity of illness. We would not withhold corticosteroids or anticonvulsants from patients with eastern equine encephalitis solely on the basis of our findings.

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