The Selective Value of Computed Tomography of the Brain in Cerebritis Due to Systemic Lupus Erythematosus

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Abstract. Systemic lupus erythematosus (SLE) and steroid effects on the brain were measured by computed tomography (CT). Of 14 patients with SLE cerebritis, 10 (71%) had marked cortical atrophy and 4 (29%) minimal atrophy. None were normal by CT. Controls included 22 patients with SLE without cerebritis receiving corticosteroids; this group had normal CT scans in 16 (73%) and minimal cortical atrophy in the remaining 6 (27%). Follow-up CT on 5 patients with cerebritis was unchanged. CT of the brain is a minimally invasive technique for documenting SLE cerebritis. CT may also help differentiate cerebritis from the neuropsychiatric side effects of corticosteroids. (J Rheumatol 9: 850-854, 1982)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS
CEREBRITIS
COMPUTED TOMOGRAPHY

The syndromes of central nervous system (CNS) dysfunction or cerebritis from systemic lupus erythematosus (SLE) have often presented difficulty in diagnosis and in differentiating side effects of therapy from complications of the disease itself1,2.

In some cases, neuropsychiatric illness may precede SLE and be unrelated3. However, in the past, most cases of abnormal CNS function in SLE had been ascribed to active SLE itself. More recently, there has been more concern about the neuropsychiatric complications of steroid therapy2. Antimalarials, not uncommonly used in therapy of SLE, have also been implicated as a cause of CNS dysfunction in SLE patients4. Further confusion as to the reasons for CNS dysfunction arises from complications of SLE itself, such as infection and uremia.

Since CNS involvement is the second leading cause of death in SLE5, a method or methods of differentiating these entities is needed. Consistent differentiation has not evolved with the use of clinical parameters, serology6,7, CSF analysis8,9, electroencephalogram (EEG)9, or radionuclide brain scans10. Enhanced computed tomography (CT) has been shown of benefit in differentiating intracerebral hemorrhage from infarction in patients with focal neurologic deficits11. Also response to higher dose steroids has not been consistently helpful in CNS lupus9.

To date, CT in patients with non-focal neurologic deficits has produced somewhat conflicting results12-14. We attempted to clarify the findings of CT of the brain in SLE patients with and without cerebritis. We also tried to determine the effects of corticosteroid therapy on CT of the brain. Our objectives were to determine if CT scanning can help decide which approach to therapy is needed in treating a patient with SLE who develops neurologic abnormalities.

MATERIALS AND METHODS

Thirty-four patients from the Jackson Memorial Hospital and Miami Veterans Administration Medical Center complex with 4 or more ARA criteria for SLE had CT of the brain. Of these patients with SLE, 14 had clinical features of cerebritis and 20 without cerebritis on longterm steroid therapy served as controls. Clinical examinations were performed by 1 of our group (NG). The CT of the brain was independently read by 2 neuroradiologists (SO and RQ), whose only knowledge of the patients was their age, sex and the diagnosis of SLE. The study covered an 18-month time period.
Cerebritis was defined as an abnormality of central neurological function identified by history/examination and noted as a change from a prior state in the absence of other possible etiologies. Longterm steroid therapy was defined as a minimum of prednisone 40 mg (or equivalent) daily for 3 months or continuous prednisone 20 mg (or equivalent) daily for at least 6 successive months prior to the evaluation. CT* was performed in the central plane parallel to Reid's baseline at 1 cm intervals. Contrast dye was used when not contraindicated.

Marked cortical atrophy by CT scan was defined as the presence of widening of cortical sulci and cerebral lateral ventricular dilatation—the ratio of the maximum diameter of the frontal horns to the greatest internal diameter of the skull being more than 0.2715. Minimal cortical atrophy included focal and diffuse widening of the cortical sulci in the presence of normal cerebral lateral ventricular size. A normal CT had neither widening of the cortical sulci nor the cerebral ventricles. The patient's age was limited to 50 years because of the occurrence of cortical atrophy with increasing age as an incidental finding. Dilatation of the lateral ventricles in the presence of normal cortical sulci was felt to represent increased intracranial pressure and not cortical atrophy, hence was not considered in this grading system.

Statistical analysis was carried out by the chi square method.

RESULTS

Some abnormality of the brain by CT was present in 11/14 patients during their 1st attack of SLE cerebritis. At the initial presentation with SLE cerebritis, 9 of 14 patients had marked cortical atrophy by CT and 2 had minimal cortical atrophy. At that time, a normal CT was found in 3 patients with SLE cerebritis. Two of these patients were on 30 and 40 mg prednisone at the time of the normal CT. The 3rd had been on corticosteroids previously but not in 4 months prior to the normal CT. Corticosteroids were administered in all 3 patients and after remission of the cerebritis, repeat CT demonstrated development of marked cortical atrophy in 2 of these patients and minimal cortical atrophy in the other. The role of corticosteroids in their cortical atrophy is unclear.

Ratios of frontal horns to the greatest diameter of the skull ranged from normal (0.23) to 0.31.

No patients with repeat attacks of SLE cerebritis had a normal CT of the brain (Table 1). After clinical remission of the cerebritis and a 1-15-month follow-up, repeat CT in 5 patients failed to show any regression of the existent cortical atrophy.

All patients had taken steroids at some time previously.

There was no significant difference between the groups of patients with cerebritis and those without cerebritis when comparing duration disease and time or mean dose on steroids (Table 2).

None of the SLE patients on corticosteroids without cerebritis had marked cortical atrophy by CT. Minimal cortical atrophy was present in 6 of 20 (30%). The majority (70%) had normal CT of the brain (Figure 1).

The neurologic features of our group were correlated with the CT results on Table 3. A psychosis of organic origin was present in 11 patients and seizures in 5 patients. Two patients had both an organic psychosis and seizures on the same presentation. Patient 5 had cortical atrophy with a temporal artery aneurysm and subsequent subarachnoid hemorrhage leading to death. There was no correlation between the type of clinical presentation and the presence of minimal or marked cortical atrophy.

Treatment with corticosteroids was beneficial in 11 of 14 patients with cerebritis. One patient responded to corticosteroids after the addition of cyclophosphamide. One patient (No. 1) was institutionalized with an irreversible organic mental syndrome.

Table 1. SLE findings by CT in patients with and without cerebritis

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Minimal Cortical Atrophy</th>
<th>Marked Cortical Atrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE with cerebritis*</td>
<td>0</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>SLE without cerebritis*</td>
<td>12</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>

*p < .001. See Methods.

Table 2. SLE comparison of duration disease and corticosteroid administration prior to cerebritis

<table>
<thead>
<tr>
<th>Duration SLE (Yr)</th>
<th>Time on Steroids (Yr)</th>
<th>Daily Dose* Steroids (Mean Daily Dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE with cerebritis</td>
<td>6.8</td>
<td>2.9</td>
</tr>
<tr>
<td>SLE without cerebritis</td>
<td>4.8</td>
<td>3.1</td>
</tr>
</tbody>
</table>

* Prednisone or equivalent.

*Jackson Memorial Hospital, GE CT178800 or EMI 1010. Miami Veterans Administration Medical Center, Ohio Nuclear FS50.
Fig. 1. CT scan at the level of the frontal horns.

Fig. 1a. Post contrast axial CT scan in Patient 1 shows no evidence of cortical atrophy or ventricular enlargement.

Fig. 1b. In Patient 2, CT shows minimal atrophy as evidenced by normal ventricular size but dilated cortical sulci.

Fig. 1c. In Patient 9 atrophy is demonstrated with enlarged ventricles and sulcal dilatation in addition to incidental right basal ganglionic calcification.
Table 3. Clinical characteristics of patients with SLE cerebritis: correlation of neurologic features with cortical atrophy (CoA) by CT

<table>
<thead>
<tr>
<th>Pts</th>
<th>Age</th>
<th>Sex</th>
<th>Neurological Features</th>
<th>1st Episode Cerebritis</th>
<th>2nd Episode Cerebritis</th>
<th>Convalescence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>F</td>
<td>Acute catatonia</td>
<td>Normal (Figure 1A)</td>
<td>Marked CoA</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>M</td>
<td>Seizures, movement disorder</td>
<td>Minimal CoA (Figure 1B)</td>
<td>Minimal CoA</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>19</td>
<td>F</td>
<td>Seizures</td>
<td>Marked CoA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>F</td>
<td>Hallucinations, coma</td>
<td>Normal CoA</td>
<td>Marked CoA</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>29</td>
<td>F</td>
<td>Coma, hemiplegia, seizures</td>
<td>Marked CoA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>26</td>
<td>F</td>
<td>Headache, lethargy, confusion, coma</td>
<td>Normal CoA</td>
<td>Marked CoA</td>
<td>Marked CoA</td>
</tr>
<tr>
<td>7</td>
<td>18</td>
<td>M</td>
<td>Seizures</td>
<td>Marked CoA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>14</td>
<td>M</td>
<td>Seizures, organic brain syndrome</td>
<td>Marked CoA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>16</td>
<td>F</td>
<td>Organic brain syndrome</td>
<td>Marked CoA</td>
<td></td>
<td>Marked CoA</td>
</tr>
<tr>
<td>10</td>
<td>22</td>
<td>F</td>
<td>Organic brain syndrome</td>
<td>Marked CoA</td>
<td></td>
<td>Marked CoA</td>
</tr>
<tr>
<td>11</td>
<td>21</td>
<td>F</td>
<td>Headaches</td>
<td>Marked CoA</td>
<td></td>
<td>Marked CoA</td>
</tr>
<tr>
<td>12</td>
<td>25</td>
<td>F</td>
<td>Headaches</td>
<td>Minimal CoA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>27</td>
<td>F</td>
<td>Schizophrenic depression</td>
<td>Minimal CoA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>34</td>
<td>F</td>
<td>Change in mental status</td>
<td>Marked CoA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Systemic manifestations of SLE included renal disease in 12 of 14 of the cerebritis group versus 9 of 20 in the noncerebritis group (p < 0.05), and systemic vasculitis in 6 of 14 with cerebritis versus 6 of 20 in the noncerebritis group (0.05 < p < 0.10).

Raynaud’s syndrome was present in 5 of 14 with cerebritis and 10 of 22 in the noncerebritis group. However, in the noncerebritis group, 5 of the 6 patients with minimal cortical atrophy had Raynaud’s phenomenon. Serologic tests and cerebrospinal fluid findings were not consistent or helpful in the evaluation of cerebritis in this group.

DISCUSSION

Our findings tend to indicate that CT scans of the brain are a sensitive but nonspecific means of evaluating SLE cerebritis. The presence of cortical atrophy seems to correlate with the presence of clinical SLE cerebritis. However, the clinical manifestations of cerebritis occurred before the changes of atrophy could be detected on the CT study in 3 of our patients. Once changes of atrophy occurred, they appeared to be irreversible in our group, persisting even when clinical remission had occurred. These findings may suggest that atrophy is most likely the end result of a presently undetermined pathological process in the brain. Possibly, as has been suggested before, this process is by the deposition of immune complexes in the choroid plexus and other small vessels of the brain. The relationship of cerebritis to vasculitis has been described, but true vasculitis with infiltration at all layers of the vessel wall has been an infrequent finding. Careful pathological studies by Johnson and Richardson support the concept that SLE of the nervous system is in most cases a vascular disease including very small blood vessels. In other studies, the persistent detection of precipitating antibodies to DNA has been correlated with the presence of cutaneous vasculitis and CNS disease. It is possible that immune complexes formed by these antibodies have an increased propensity to localize in the vasculature at these sites.

Gonzalez-Searano, et al recently reported on the results of CT of the brain on 20 patients with SLE. Twenty of 22 of their patients with cerebritis had abnormal CT studies compared to a small control group of 7 patients without clinical cerebritis — 1 of whom had an abnormal CT. These findings did not correlate with those of Betson, et al who studied CT of the brain of 15 patients on long term corticosteroids, 5 of whom had SLE. His patients demonstrated varying degrees of cortical atrophy unrelated to cerebral dysfunction and independent of their underlying diseases. Killian, et al felt that
CT of the brain was a useful technique for distinguishing CNS lupus from potential changes of corticosteroid therapy. Degree of cortical atrophy was not recorded in the above studies. The contradiction in those findings may indicate that there are wide variations in the interpretations of CT of the brain. One variable may be the type of CT equipment utilized.

Also minor degrees of cortical atrophy may receive different qualifying interpretations among neuroradiologists. Our neuroradiologists were consistent, but both were from the same institution.

Unlike other reports, our study does not indicate that steroid therapy is responsible for significant marked cortical atrophy; however, in our study, corticosteroid administration was felt to be associated with sulcal widening. This is an important distinction as it may help differentiate the problem of SLE cerebritis from that of steroid toxicity that may have very similar clinical features. This distinction could help the clinician to decide whether to increase or decrease the dosage of steroids being used when faced with a patient on steroids who develops neuropsychiatric symptoms.

It is emphasized that the diagnosis of SLE cerebritis is still a clinical syndrome and can be made after all other possible causes for the patient’s complaints have been excluded. However, CT of the brain in SLE may be of benefit in the following situations: 1) the presence of marked cortical atrophy at the time of the initial presentation of cerebritis indicates SLE induced CNS disease and 2) the absence of cortical atrophy on CT in a patient with CNS symptoms may suggest a non-SLE related CNS syndrome such as that induced by corticosteroids.

REFERENCES