MR Manifestations of the Brain in Neuropsychiatric Systemic Lupus Erythematosus Patients

Kyu Chan Oh, M.D., Woo Mok Byun, M.D., Han Won Jang, M.D., Kum Rae Kim, M.D.

Purpose: The primary goal of this study was to evaluate the MR findings of systemic lupus erythematosus (SLE) patients with neuropsychiatric symptoms.

Materials and Methods: The MR images of 38 patients with SLE were evaluated based on the presence of the following abnormal lesions: the locations of the abnormal signal intensity lesions in the white matter, infarctions, a small vessel vasculopathy, leukoencephalopathy, hemorrhage, abscess, and other lesions.

Results: The MR images showed an abnormality in 22 of 38 (58%) episodes. Abnormal signal intensities were noted in the subcortical and periventricular white matter in six cases, acute territorial infarctions in five cases, multiple small acute embolic infarctions in four cases and a brain abscess in two cases. A reversible posterior leukoencephalopathy was found in one case. In addition, another patient had vasogenic edema with focal central cytotoxic edema at the pons. The entire cerebral and corpus callosum volumes were significantly smaller in four patients with SLE as compared to the volumes in healthy control subjects.

Conclusion: SLE may induce variable MR imaging findings of the CNS. Recognition of the variable findings is helpful for easy diagnosis and prompt treatment.

Index words: Brain diseases
Lupus erythematosus, systemic
Central nervous system
Magnetic resonance (MR)

Systemic lupus erythematosus (SLE) patients frequently present with neuropsychiatric symptoms that vary from overt neurological and psychiatric disorders to more subtle signs, such as headache, mood disorders, and defects in cognitive function. Neurological and psychiatric illness occur in 25-70% of SLE patients and are responsible for significant morbidity and mortality [1].

Primary central nervous system (CNS) involvement (CNS lupus) results from a combination of factors related to an autoimmune response including vasculopathy, coagulopathy from the presence of antiphospholipid antibodies, and vasculitis. Five categories of mechanisms that underlie CNS manifestations in SLE are ischemia, hemorrhage, white matter damage, neuronal dysfunction and deficient psychological reactions [2]. MR imaging findings of neuropsychiatric SLE are highly variable.

Moritani et al. described that diffusion-weighted imag-
ing shows primarily two patterns of acute or subacute parenchymal lesions in patients with SLE: acute or subacute infarction and vasogenic edema with or without microinfarcts [3]. In 69% of cases, MRI demonstrated involvement of the CNS both in asymptomatic patients (64.3%) and in patients with neuropsychiatric manifestations (73.3%), including microembolic signals, cerebral infarctions (associated with antiphospholipid syndrome), atrophy, basal ganglia involvement, posterior leukoencephalopathy, subcortical calcification or hemosiderin deposits (T2*) and dilated perivascular spaces (4). Cerebral small vessel angiopathy is the predominant histopathological abnormality associated with SLE. On MRI, T2-weighted images of the brain reveal small punctuate lesions of increased signal intensity that are localized mainly in the periventricular and subcortical white matter in many SLE patients (2). As CNS changes resulting from hypertension or the aging process may reveal periventricular and subcortical lesions, the most common cerebral MR imaging findings due to small vessel angiopathy in SLE are not specific.

It is necessary to characterize and to evaluate the variable and unusual CNS manifestations of SLE on MR images to understand the pathogenic mechanisms and treatment. The aim of this study was to evaluate the CNS MR imaging findings of SLE.

Materials and Methods

A total of 38 patients that had SLE with neuropsychiatric symptoms were evaluated by the use of intracranial MRI. All patients fulfilled the American College of Rheumatology criteria for SLE [5, 6]. The patients included 27 women and 11 men, ages 11 to 81 years (mean age, 46 years). The symptoms of the patients are described in Table 1. MR examinations were performed using 1.5T (Vision; Siemens, Eralngen, Germany) imagers. Axial T1-weighted images [400- 600/25- 30 [TR/TE] were obtained before and after the administration of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany; 0.1 mmol/kg of body weight). Axial T2-weighted images [2000- 2500/100-120 [TR/TE]] or turbo-T2-weighted images [3000- 4000/90-100 [TR/TE]] were obtained before administration of gadopentetate dimeglumine. Fluid-attenuated inversion-recovery (FLAIR) images [10,000/140 [TR/TE]] were acquired. The section thickness was 3 mm, with an intersection spacing of 0%. A matrix size of 256×256 with a 20- to 24-cm field of view was used. The number of signal acquisitions was two. Axial diffusion-weighted images [4000- 5000/70- 80 [TR/TE]] were obtained with single-shot, spin-echo-type echo-planar imaging (field of view, 210×210 mm; image matrix, 256×256; section thickness, 5.0 mm with 3.0 mm gaps). The diffusion gradient strength was 66 mT/m. MR angiography (TOF-MRA: 16.8/6.9 [TR/TE], Contrast enhanced carotid MRA: 4.2/1.6 [TR/TE]) was performed in fourteen cases.

MR images were evaluated based on the presence or absence of abnormal lesions: locations of the abnormal signal intensity lesions in the white matter, territorial infarctions, small vessel vasculopathy, leukoencephalopathy, hemorrhage, abscess and other lesions. Apparent diffusion coefficient (ADC) and signal intensity changes on ADC and diffusion-weighted images were evaluated. We compared patients with SLE and control subjects in the same age range and sex for evaluation of brain atrophy, using examination of the images with visual inspection. Control subjects for comparison were selected in cases without apparent cranial symptoms, such as a routine MR examination for a health examination. An examination of antiphospholipid antibody was evaluated in eleven cases. The presence of antiphospholipid antibody was compared with the clinical and MR imaging findings. Follow-up MR examinations for the evaluation

<table>
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<th>Table 1. Clinical Symptoms of Patients with Neuropsychiatric SLE</th>
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<tr>
<td><strong>Symptom</strong></td>
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<td>Headache</td>
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<td>Motor weakness</td>
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<td>Mental change</td>
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<td>Seizure</td>
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<td>Neck stiffness</td>
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<td>Extremity tingling sensation</td>
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<td>Dizziness</td>
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<td>Dysarthria</td>
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<td>Tremor</td>
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<th>Table 2. MR Imaging Findings of Patients with Neuropsychiatric SLE</th>
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<td><strong>Finding</strong></td>
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<tr>
<td>Normal</td>
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<tr>
<td>Multiple small white matter lesions</td>
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<tr>
<td>Acute territorial infarctions</td>
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<tr>
<td>Multiple embolic infarctions</td>
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<tr>
<td>Brain abscess</td>
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<tr>
<td>Hematoma</td>
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<td>Aneurysm</td>
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<td>Reversible posterior leukoencephalopathy</td>
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<td>Diffuse reversible encephalopathy in the pons</td>
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<td>Brain atrophy</td>
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of disease progression or improvement were performed in ten cases.

**Results**

The MR images showed abnormalities in 22 of 38 (58%) episodes. The MR imaging findings of the patients are described in Table 2. Six patients had multiple punctuate lesions in both the cerebral subcortical and periventricular white matter (Fig. 1). Multiple small acute embolic infarctions were seen in four cases, and one case with embolic infarctions developed multiple brain abscesses (Fig. 2). Brain abscesses were found in two cases and were seen with multiple patterns. We supposed that one case with brain abscess developed from a septic embolic infarction. Another patient with an acute embolic infarction showed a combined multifocal small hematoma in both temporal lobes and an aneurysm in the right middle cerebral artery, distal to M2 (Fig. 3). A reversible posterior leukoencephalopathy was found in one case. Both basal ganglia, the thalamus, the occipital cortex, brainstem and left cerebellum showed iso signal intensity on a diffusion-weighted image and high signal intensity on an ADC image representing reversibility (Fig. 4). Vagogenic edema was caused by sudden hypertensive crisis. After treatment of hypertension, there was marked improvement of the lesions as seen on follow-up MR images after twelve days. In one patient, the pons on a diffusion-weighted image showed iso- or slightly hyperintense lesions and an apparent diffusion coefficient (ADC) image revealed an increased ADC, suggesting vasogenic edema and focal central cytotoxic edema (Fig. 5). The diffuse reversible leukoencephalopathy in the pons improved in one case.

![Fig. 1](image)

**Fig. 1.** A 28-year-old male patient with multiple punctuate lesions representing small vessel vasculopathy:
An initial axial FLAIR image (A) shows multifocal punctuate lesions (arrows) at both the cerebral subcortical and left periventricular white matter. A follow-up axial FLAIR image (B) after four months showed a decrease of the size and number of lesions.

![Fig. 2](image)

**Fig. 2.** A 65-year-old female patient with acute multifocal embolic infarctions in both centrum semiovales.
Multifocal high signal intensities (arrows) at both centrum semiovales are seen on a diffusion weighted image (A). Follow-up contrast enhanced T1-weighted images after 4 months reveal rim-enhancing lesions at the cerebellar vermis and left fronto-parietal lobe representing an abscess (B, C).
month as seen on a follow-up MR examination. Both of the entire cerebral and entire corpus callosum volumes were significantly smaller in four patients with SLE as compared with the volumes in healthy control subjects. In general, symptoms of brain atrophy include cognitive impairment, mental change, and seizure, but the above four patients did not have the above symptoms. Antiphospholipid antibody was positive in five of the eleven cases (45%). The MR imaging findings of the patients with a positive antiphospholipid antibody were multiple punctate lesions in the cerebral subcortical and periventricular white matter representing small vessel vasculopathy \( (n = 2) \), multiple acute embolic infarctions \( (n = 2) \) and a normal brain \( (n = 1) \). There was no correlation between a positive antiphospholipid antibody and clinical symptoms. A follow-up MR study was performed for patients with acute territorial infarction \( (n = 3) \), reversible posterior leukoencephalopathy \( (n = 1) \), diffuse reversible leukoencephalopathy in the pons \( (n = 1) \), acute embolic infarction \( (n = 2) \), multiple punctuate subcortical and periventricular white matter lesions \( (n = 1) \) and a normal brain \( (n = 2) \). A decrease of the size and number of the multiple punctate subcortical and periventricular white matter lesions were seen on a follow-up MR study after four months. Five of fourteen cases showed occlusion or stenosis of the extracranial internal carotid and intracerebral arteries.

Fig. 3. A 26-year-old female patient with hematomas and an aneurysm. Acute and subacute hematomas at both temporal lobes are demonstrated on T1-weighted images \( \text{[A, B]} \). Right internal carotid angiography shows a 9.8×5.3 mm sized saccular aneurysm in the distal M2 segment of the right middle cerebral artery \( \text{[C]} \).

Fig. 4. A 42-year-old female patient with reversible posterior leukoencephalopathy. Both basal ganglia, both thalamuses and the brainstem show iso signal intensity on a diffusion-weighted image \( \text{[A]} \) and high signal intensity on an ADC image \( \text{[B]} \) representing vasogenic edema. There are no more abnormal signal intensities seen on a follow-up T2 weighted image \( \text{[C]} \) after 12 days. Figures of the occipital cortex and left cerebellar lesions are not shown.
Discussion

Systemic lupus erythematosus (SLE) is a prototypical multisystem disease with multiple autoantibodies involvement, and is a chronic, inflammatory, autoimmune disease of unknown etiology primarily affecting females of childbearing age. Between 30% and 70% of SLE patients have significant neuropsychiatric disturbances during the course of the disease (7). The signs and symptoms of neuropsychiatric-SLE span a wide spectrum, ranging from overt findings such as seizure, stroke, psychosis, transverse myelitis, and aseptic meningitis to more subtle abnormalities of memory, concentration, intellect, and mood (8).

Abreu et al. reported that the most frequent brain imaging findings were more prevalent in neuropsychiatric SLE; the most frequent finding in all MR examinations was focal high signal intensity in the periventricular white matter, as seen on T2-weighted and FLAIR images (9). Histopathological findings suggest that these abnormalities are caused by microinfarcts, hemorrhage, ischemic demyelination, multiple-sclerosis-like demyelination, and bland vasculopathy. The vessels affected are predominantly arterioles and capillaries (10). Jennings et al. reported on the frequency and pattern of signal abnormalities seen on conventional MRI in patients with suspected neuropsychiatric systemic lupus erythematosus; MRI was normal or nearly normal in 34% of cases. In 60% of cases, multifocal small high-signal lesions were observed on T2-weighted images, and were frequently observed in the frontal and parietal subcortical white matter (11). In our study, intracranial MR images were normal in 16 of 38 cases (42%), and periventricular and subcortical multifocal lesions were seen in five cases. Periventricular lesions detected on MRI can be impossible to differentiate from multiple sclerosis. White matter punctuate hyperintensities increase with age in

Fig. 5. An 11-year-old male patient with diffuse reversible leukencephalopathy in the pons. A T2-weighted image [A] shows diffuse high signal intensity with swelling at the pons. Iso signal intensity with focal central high signal intensity on a diffusion-weighted image [B] is noted. The ADC image [C] reveals increased intensity with a central focal decreased ADC representing vasogenic edema with central focal cytotoxic edema. There is no more abnormal signal intensity except for subtle central gliosis seen on a follow-up T2-weighted image [D] after one month.
the general population and are also associated with hypertension, and it is not possible to differentiate between SLE from other vasculopathies using conventional MRI [12]. Therefore, the different frequencies of white matter focal lesions of SLE may be caused by the inclusion of other vasculopathy-induced nonspecific findings.

Dahl et al. reported that microembolic signals on transcranial Doppler ultrasonography of 55 patients were detected in five cases (9%) and cerebral infarcts were found in nine cases (18%). These investigators reported that an embolism may be an important pathogenic factor for cerebral infarcts and cognitive dysfunction in patients with SLE [13]. Multiple small embolic infarctions on diffusion-weighted images were seen in four cases (13%) in our study. The sources of multiple acute embolic infarctions were not determined. An autopsy of a 57-year-old woman with systemic lupus erythematosus (SLE) documented the presence of multiple brain infarcts and cerebral arterial embolii that originated from the verrucae of Libman-Sacks endocarditis [14].

Magnano et al. described five cases of reversible posterior leukoencephalopathy in patients with SLE. Reversible posterior leukoencephalopathy is preceded by hypertension, renal insufficiency, and recent exposure to high doses of immunosuppressant medication [15]. A patient with reversible posterior leukoencephalopathy due to hypertension was found in our study. Both basal ganglia, both thalami, the occipital cortex, brainstem and left cerebellum showed iso signal intensity on diffusion-weighted images and high signal intensity on an ADC image representing vasogenic edema. After treatment of hypertension, there was marked improvement of the lesions on follow-up MR images after a period of 12 days.

A brain abscess in SLE is rare. SLE patients with Libman-Sacks endocarditis have mitral and aortic valve abnormalities that can lead to a septic cerebral embolism [16]. In one patient with multiple acute embolic infarctions in both centrum semiovales, abscesses in the right centrum semiovale and cerebellum developed after four months. The cause of multiple brain abscesses was not determined, but we supposed that a brain abscess developed from a septic embolic infarction.

Cerebral aneurysms associated with SLE are uncommon. There have been a few reported cases of peripherally located aneurysms associated with SLE [17–23]. The mechanism of unusual aneurysmal formation in SLE is thought to be due to transmural angiitis or fibroid necrosis producing local weakness in the walls of the small vessels [20]. A 26-year-old female presented with an aneurysm in right middle cerebral artery [M2 segment]. A follow-up study and treatment for aneurysm were not performed.

Cerebral atrophy has been described to occur in SLE with variable frequency, but its exact cause remains unclear. Appenzeller et al. reported that in an MRI analysis, cerebral atrophy was found in 8.7% of patients with SLE. Reduced cerebral and corpus callosum volumes were related to the disease duration [24]. We evaluated brain atrophy by a visual inspection method for a comparison with a normal control group of subjects that may represent a limitation of our study.

Moritani et al. reported that in four of nine patients with SLE lesions, diffusion-weighted imaging primarily showed hyperintense lesions with a decreased ADC, which indicates acute or subacute infarcts. In four other patients, diffusion-weighted imaging primarily showed iso- or slightly hyperintense lesions with an increased ADC, suggesting vasogenic edema [3]. In one patient (an 11-year-old male), diffusion-weighted images showed mild hyperintensity with a slightly increased ADC in the entire pons, which presumably represents vasogenic edema. A very hyperintense spot with ADC reduction was also seen within the lesion, indicating the presence of a microinfarct. In five cases, diffusion-weighted images showed hyperintense lesions with a decreased ADC, which indicates the presence of acute infarcts.

In conclusion, SLE may show variable MR imaging findings of the CNS. It is necessary to recognize the variable and unusual MR manifestations of the brain in neuropsychiatric systemic lupus erythematosus patients to understand the pathogenesis of the disorder and to provide accurate diagnosis and treatment.

References


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