Systemic Lupus Erythematosus:

Prediction by MRI of the Subsequent Development of Brain Lesions

Koichiro Futatsuya, MD, Shingo Kakeda, MD, Yoko Kaichi, MD, Junji Moriya, MD, Norihiro Ohnari, MD, Kazuyoshi Saito, MD, Yoshiya Tanaka, MD, Yukunori Korogi, MD

Rationale and Objectives: Many patients with systemic lupus erythematosus (SLE) manifest the recurrence of new brain lesions on follow-up magnetic resonance imaging (MRI) scans. We assessed whether the initial MRI findings help to predict the subsequent development of brain lesions in patients with SLE.

Materials and Methods: We enrolled 64 patients with SLE who had undergone initial and follow-up MRI studies. Two radiologists reviewed and categorized the initial MRI findings and divided the patients into those with no lesions on the initial and follow-up MRI scans (group A, $n = 18$), those with lesions on the initial scans only (group B, $n = 32$), and those with lesions on the first and new lesions on the follow-up MRI scans (group C, $n = 14$). We then looked for independent predictors of the subsequent development of brain lesions, such as antiphospholipid syndrome (APS) and findings on the initial MRI studies.

Results: The incidence of lacunar and localized cortical infarcts was significantly greater in group C than group B (50% vs. 0%, $P < .001$ and 50% vs. 9%, $P < .05$, respectively). Multivariate logistic regression analysis indicated that lacunar or localized cortical infarcts on the initial MRI scans were independent predictors of the subsequent development of brain lesions (odds ratio [OR]: 5.412, 95% confidence interval [CI]: 1.18–24.85, $P = .03$), whereas the presence of APS was not (OR: 0.621, 95% CI: 0.18–2.19).

Conclusions: The presence of lacunar and/or localized cortical infarcts on initial MRI scans may predict the development of new brain lesions in patients with SLE.

Key Words: Systemic lupus erythematosus; neuropsychiatric systemic lupus erythematosus; antiphospholipid syndrome; prediction; brain; MRI.

Systemic lupus erythematosus (SLE) is an autoimmune disease that frequently involves the central nervous system (CNS, 1,2). Neuropsychiatric (NP) SLE has been reported in as many as 30%–56% of all patients with SLE (3,4), and the quality of life is poorer in patients with NPSLE than without NPSLE (5,6). However, the etiology of and basis for NPSLE-associated brain lesions remain uncertain (1,2,7–9).

The development of NPSLE-associated brain lesions is related to disease activity and severity; one of the most important risk factors for brain lesions is the presence of antiphospholipid syndrome (APS) and/or anticardiolipin antibodies (aPL, 10). Kaichi et al. (11) showed that abnormal magnetic resonance imaging (MRI) findings were more common in SLE patients with APS than without APS. The recognition of APS is critical for appropriate therapy. Antiplatelet and/or anticoagulation therapy is recommended for NPSLE related to aPL, especially in patients with thrombotic cerebrovascular disease (CVD, 12). SLE patients without aPL are also potentially at risk for the recurrence of CVD (13).

Earlier studies reported a wide spectrum of magnetic resonance (MR) findings in patients with SLE, for example, large, lacunar, localized cortical, and borderzone infarcts, cortical atrophy, and multifocal gray matter and/or white matter lesions (7,11,14). However, longitudinal brain changes and the progression of brain lesions that affect the prognosis of patients with SLE have not been documented. The ability to predict lesion progression on brain MRI scans obtained at the time when CNS involvement first manifests would be of clinical value, for example, for the treatment decisions and for the possible prevention of the development of brain lesions. Therefore, we looked for clinical parameters and initial MRI findings that help to predict the subsequent development of brain lesions in patients with SLE.

MATERIALS AND METHODS

Patient Selection

This retrospective study was approved by our institutional review board; patient informed consent was waived. We

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From the Department of Radiology, University of Occupational and Environmental Health, School of Medicine, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan (K.F., S.K., J.M., N.O., Y.K.); Department of Diagnostic Radiology, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan (Y.K.); and Department of Internal Medicine, University of Occupational and Environmental Health, School of Medicine, Kitakyushu, Japan (K.S., Y.T.). Received December 19, 2013; accepted February 3, 2014. **Address correspondence to:** S.K. e-mail: kakeda@med.uoeh-u.ac.jp

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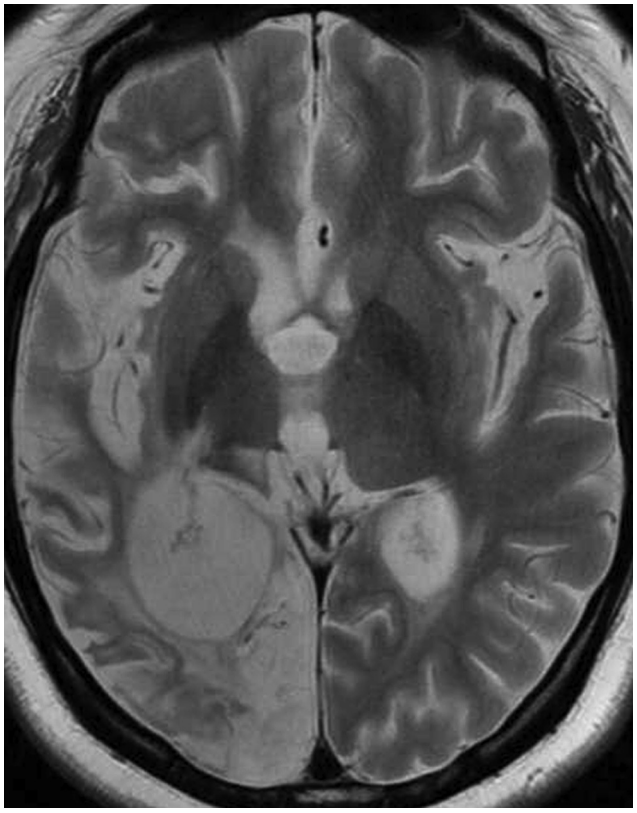

Figure 1. A 30-year-old man with systemic lupus erythematosus without antiphospholipid syndrome. The axial T2-weighted imaging scan shows a large right territorial infarct (middle cerebral artery + posterior cerebral artery).

routinely perform screening brain MRI studies to assess patients with SLE. For this study, we reviewed the database containing the medical records of patients with SLE seen between May 2004 and June 2011 and selected 256 patients diagnosed with SLE based on American Rheumatism Association criteria for the classification of SLE (15).

Among these 256 patients with SLE, we identified 91 patients who had undergone follow-up MRI studies between May 2004 and November 2011. Exclusion criteria included unsatisfactory images because of artifacts and a history of other neurologic diseases. We also excluded patients aged older than 50 years to avoid potential age-related bias posed by CVD. As we excluded two patients because of inadequate image quality, three because they had brain tumor, osmotic myelinolysis, or multiple sclerosis, and 22 patients older than 50 years, our final study population consisted of 64 patients.

Based on MRI findings, the 64 patients were divided into those with no lesions on the initial and follow-up MRI scans (group A, $n = 18$), those with lesions on the initial scans only (group B, $n = 32$), and those with lesions on the first and new lesions on the follow-up MRI scans (group C, $n = 14$).

We reviewed their demographic data for APS, vascular risk factors (diabetes mellitus, defined as a random glucose level >11.1 mmol/L, a fasting blood glucose level >7.0 mmol/L, HbA1c > 6.5%, or current use of antidiabetic drugs), hypertension (blood pressure > 140/90 mm Hg or current treatment with antihypertensive drugs), past and current smoking, dyslipidemia (low-density lipoprotein cholesterol > 3.64 mmol/L, high-density lipoprotein cholesterol < 0.91 mmol/L, triglyceride > 1.7 mmol/L, or receiving treatment), obesity (body mass index > 26 kg/m^2), and previous treatments (corticosteroids and immunomodulatory drugs). We also recorded their disease activity score (Systemic Lupus Erythematosus Disease Activity [SLEDA] Index (16) and British Isles Lupus Assessment Group [BILAG] index (17,18)) at the time of the initial brain MRI study based on parameters used for the assessment of SLE disease activity.

Image Acquisition

All studies were performed on a 1.5T or 3T MR system (Signa EXCITE, GE Healthcare, Milwaukee, WI) using a dedicated eight-channel phased-array coil (USA Instruments, Aurora, OH). The following are imaging parameters: repetition time (TR), 4000 milliseconds; echo time (TE), 85 milliseconds; number of excitations (NEX), 1; echo spacing, 13.4; and imaging time, 1 minute 50 seconds with an echo train length of 14 at 1.5T and TR, 4500 milliseconds; TE, 85 milliseconds; NEX, 1; echo spacing, 10.9; and imaging time, 2 minutes 10 seconds with an echo train length of 16 at 3T for T2-weighted fast-spin echo (FSE) imaging. For fluid attenuation inversion recovery (FLAIR) imaging, TR, 8000 milliseconds; TE, 115 milliseconds; inversion time, 2000; NEX, 2; echo spacing, 8.0; and imaging time, 2 minutes 40 seconds with an echo train length of 30 at 1.5T and TR, 12000 milliseconds; TE, 140 milliseconds; inversion time, 2600; NEX, 2; echo spacing, 9.1; and imaging time, 3 minutes 20 seconds with an echo train length of 30 at 3T. At both field strengths, T2-weighted and FLAIR images were acquired at a section thickness of 5 mm, an intersection gap of 1.0 mm, a field of view (FOV) of 22 cm, and a matrix of 256 × 192. In addition, all patients underwent our standard brain MRI protocol including T1-weighted imaging (T1WI), diffusion-weighted imaging (DWI), and three-dimensional (3D) time-of-flight (TOF) intracranial MR angiography (MRA). The following are imaging parameters at 3T: TR, 2500 milliseconds; TE, 10 milliseconds; flip angle (FA), –; section thickness, 5 mm; matrix, 320 × 224; FOV, 22 × 22; and imaging time, 1 minute 30 seconds for T1WI and TR, 6000 milliseconds; TE, minimum; FA, not available; section thickness, 5 mm; matrix, 128 × 256; FOV, 22 × 22; and imaging time, 30 seconds for DWI. For 3D TOF MRA, they were TR, 30 milliseconds; TE, 6.3 milliseconds; FA, 20; section thickness, 1 mm; FOV, 18 cm; matrix, 256 × 256; and imaging time, 4 minutes 32 seconds at 1.5T and TR, 30 milliseconds; TE, 3.3 milliseconds; FA, 20; section thickness, 1 mm; FOV, 18 cm; matrix, 384 × 224; and imaging time, 4 minutes 37 seconds at 3T. In eight of our 64 patients with SLE (12.5%), gradient echo (GRE) T2*WI scans were obtained on 1.5T or 3T systems.