CASE REPORT

Nagoya J. Med. Sci. **82**. 807–814, 2020
doi:10.18999/nagjms.82.4.807

A case of systemic lupus erythematosus associated with cerebral arteritis: a case report and case-based literature review

Akira Nishigaichi[1], Hiroshi Oiwa[1], Yohei Hosokawa[1], Masahiro Hayashi[2], Naoko Mine[2], Eiichi Nomura[2] and Takemori Yamawaki[2]

[1]*Department of Rheumatology, Hiroshima City Hiroshima Citizens Hospital, Hiroshima, Japan*
[2]*Department of Neurology, Hiroshima City Hiroshima Citizens Hospital, Hiroshima, Japan*

ABSTRACT

A 62-year-old female patient with systemic lupus erythematosus (SLE) was admitted for cerebral infarction. The magnetic resonance angiography showed focal narrowing of the cerebral arteries that was initially considered as atherosclerosis due to her cardiovascular risk factors. Ten weeks later, she was again admitted for multiple cerebral infarctions. Vessel wall magnetic resonance imaging revealed gadolinium enhancement of the arterial walls of the narrowing lesions, leading to a diagnosis of cerebral arteritis. Based on a literature review, cerebral medium-sized arteritis in SLE likely progresses insidiously during the active phase of SLE, which may later result in occlusion irrespective of disease activity.

Keywords: systemic lupus erythematosus, cerebral arteritis, cerebral medium-sized arteritis, central nervous system vasculitis, vessel wall MRI

Abbreviations:
SLE: systemic lupus erythematosus
CNS: Central nervous system
MRI: magnetic resonance imaging
MRA: magnetic resonance angiography
DWI: diffusion-weighted MRI
MCA: middle cerebral artery
ACA: anterior cerebral artery
PCA: posterior cerebral artery

INTRODUCTION

Central nervous system (CNS) involvement is a common complication in systemic lupus erythematosus (SLE). In CNS lupus, involvement of the main cerebral arteries consisting of the

Received: March 23, 2020; accepted: May 22, 2020
Corresponding Author: Hiroshi Oiwa, MD
Department of Rheumatology, Hiroshima City Hiroshima Citizens Hospital, Hiroshima, 7-33 Moto-machi, Naka-ku, Hiroshima, Japan
Tel: +81-82-221-2291, Fax: +81-82-223-1447, E-mail: hiroshioiwa@aol.com

circle of Willis is a life-threatening complication, which is reported in less than 1% of SLE cases.[1,2] A literature review in 1991 showed that 8 (67%) of 12 cases of CNS vasculitis in SLE were fatal.[3] Around that time, such cases were usually diagnosed with cerebral angiography, brain biopsy, or postmortem examination. Since the first description of the usefulness of magnetic resonance imaging (MRI) for CNS vasculitis in 1994,[4] this technique has become standard in the management of CNS vasculitis. Through magnetic resonance angiography (MRA), malformations like stenosis, ectasia, or aneurysms in the cerebral arteries could be visualized in the 2000s.[5-7] According to advances in imaging techniques, management and prognosis of cerebral arteritis in SLE may have been improved. Herein, we describe a case of SLE associated with vasculitis of anterior, middle, or posterior cerebral arteries that were diagnosed by vessel wall MRI. To clarify the clinical characteristics of cerebral medium-sized arteritis, we also performed a case-based literature review.

CASE REPORT

A 62-year-old female patient with a longstanding history of SLE was taken by ambulance to the hospital for right hemiparalysis. Three days previously, she had a fall and noticed dysarthria. Thirty years previously, she was diagnosed with SLE from malar rash, photosensitivity, arthritis, and lupus serology. Seven years previously, she had left hemiparalysis and was diagnosed as having multiple cerebral infarctions due to antiphospholipid syndrome, as transesophageal echocardiography showed an atrial thrombus at the left atrial appendage. MRI at that time showed multiple cerebral infarctions with normal cerebral arteries on MRA. She was successfully treated with warfarin and remained well for several years, while taking prednisolone (5 mg/day) and warfarin. On the present admission, she had smoked 10 cigarettes a day for 43 years until she stopped smoking 1 year before. The patient also had untreated hypertension. She denied fever but had weight loss of 20 kg within a few months. On physical examination, she was alert and blood pressure was 249/91 mmHg, heart rate 71 bpm, respiration rate 18 breaths/minute, and body temperature 36.5°C. There was no rash or arthritis, suggesting low lupus activity. Neurological examination showed muscle strength of the right upper and lower extremities to be 4 (with 5 as the maximum), right facial palsy, and dysarthria. Routine laboratory data showed C-reactive protein, 0.351 mg/dL (normal range, ≤0.14); lactase dehydrogenase, 266 U/L (124–222); and prolonged prothrombin time with international normalized ratio of 5.07, while other data including complete blood counts and biochemical tests were not remarkable. The level of anti-double-stranded DNA antibody was slightly elevated at 21 U/mL (normal range, ≤12 U/mL), and complement was normal. Anti-nuclear, anti-cardiolipin, and anti-β2 glycoprotein I antibodies and lupus anticoagulant were positive, while anti-Sm and anti-Ro/SSA were negative. The results of cerebrospinal fluid examination were normal. Diffusion-weighted MRI (DWI) showed a high-intensity lesion in the left corona radiata, compatible with cerebral infarction (Figure 1A). MRA revealed stenosis of the cerebral arteries in the distal portion of the first segment (M1) of the left middle cerebral artery (MCA), the second segment (A2) of the left anterior cerebral artery (ACA), and the second segment (P2) of the left posterior cerebral artery (PCA) (Figures 2A, B). We considered that the artery lesions may have developed due to atherosclerosis associated with the cardiovascular risk factors, but not due to antiphospholipid syndrome (because of excessive anticoagulation therapy). After therapy with edaravone and ozagrel sodium, she gradually began to walk by herself, and she was transferred to a rehabilitation hospital.

Ten weeks after the onset of stroke, the patient was again admitted for worsening of right hemiparalysis. The patient was confused and did not know what the date was. She could not

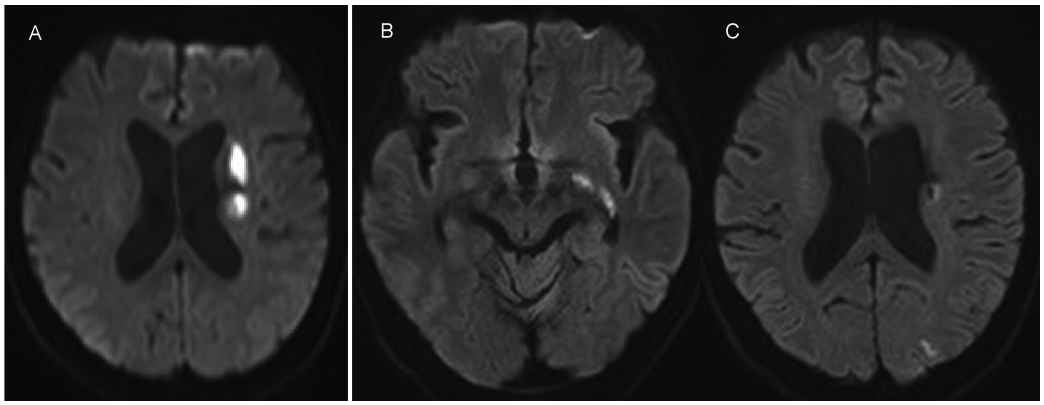

Fig. 1 Diffusion-weighted magnetic resonance imaging on the initial and the second admissions
Diffusion-weighted magnetic resonance imaging (DWI). The DWI on the initial admission (A) showed high-intensity lesions in the left corona radiata, compatible with cerebral infarction. The DWI at the second admission showed high-intensity lesions in the posterior limb of the left internal capsule, the internal region of the left temporal lobe (B), and in the left posterior lobe (C).

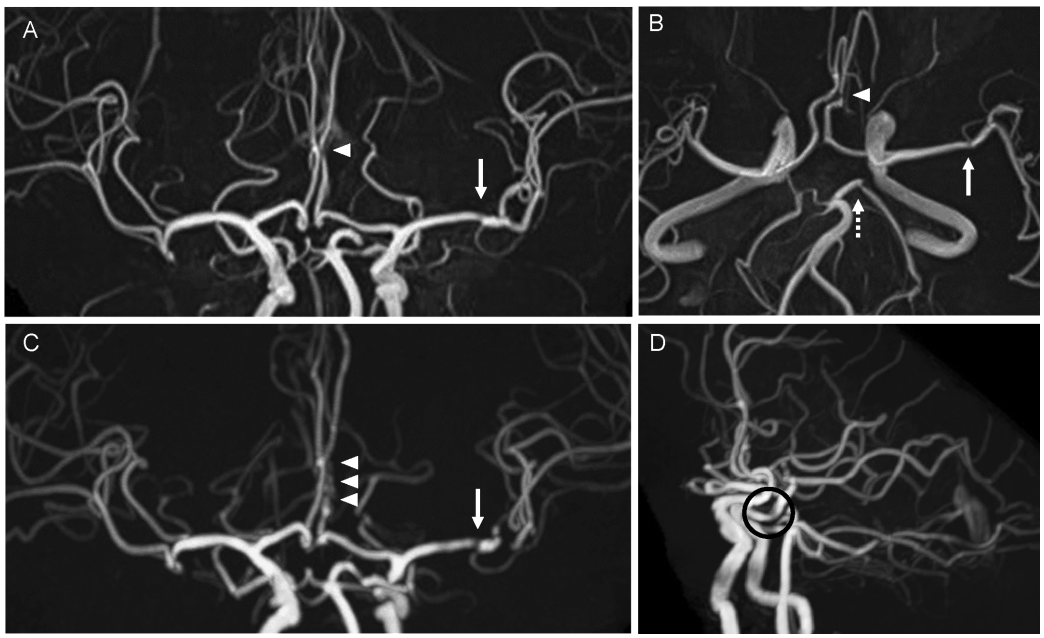

Fig. 2 Magnetic resonance angiography on the initial and the second admissions
Magnetic resonance angiography (MRA) on the initial and second admissions. The anterior-posterior view of the MRA (A) shows focal narrowing in the A2 (arrowhead) and M1 (arrow). The submentovertex view of the MRA (B) showed focal narrowing of the A2 (arrowhead), the M1 (arrow), and the P2 (dotted arrow). MRA (C) on the second admission showed beaded appearance of the A2 lesion (arrowhead) and severe narrowing of the M1 lesion (arrow). The lateral view of the MRA showed narrowing of peripheral regions (C1-2) of the left interior carotid artery (ICA; circle) (D).

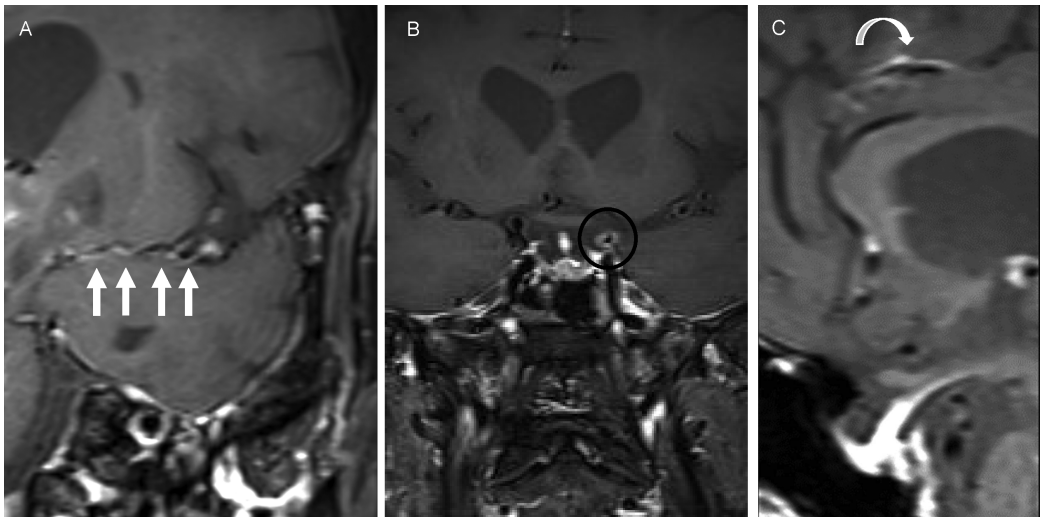

Fig. 3 Vessel wall magnetic resonance imaging on the second admission
Vessel wall magnetic resonance imaging (MRI). The coronal view (A, B) of vessel wall MRI showed gadolinium enhancement of the arterial walls of the left M1 (arrow, corresponding to the arrows in Figures 2A-C) and the left C2 lesions (circle, corresponding to the circle in Figure 2D), respectively. The sagittal view (C) showed gadolinium enhancement of the arterial wall of the anterior choroidal artery (curved arrow).

walk by herself and was severely dysarthric. Laboratory data again showed a slight elevation of anti-double-stranded DNA antibody (13 U/mL) and normal complement. The DWI showed multiple high-intensity lesions in the left cerebral hemisphere, including the left internal capsule and the temporal and posterior lobes (Figures 1B, C). MRA showed worsening of stenosis at the A2 and M1 lesions (Figure 2B) and narrowing of peripheral regions (C1-2) of the internal carotid artery (ICA) (Figure 2D). Vessel wall imaging of the arteries, performed the next day, showed gadolinium enhancement of the arterial walls of the stenotic M1 and C1-2 lesions (Figures 3A, B) and of the anterior choroidal artery (Figure 3C). She was diagnosed with recurrent stroke due to cerebral arteritis. Despite immunosuppressive therapy with a methyl-prednisolone pulse and intravenous cyclophosphamide, her paralysis worsened. A follow-up MRI, performed a month later, showed worsening of the cerebral infarctions with no changes of the cerebral arteries by MRA. Three months later, we decided to stop intravenous cyclophosphamide for cytomegalovirus pneumonia, and she was subsequently discharged to the other hospital in a bedridden state. Nine months after the initial episode, her conditions remained unchanged, and MRA showed further progression of the arterial lesions.

DISCUSSION

When a patient with SLE develops stroke, differential diagnosis should include 1) thromboembolism associated with atherosclerosis, APS, or Libman-Sacks endocarditis; 2) reversible cerebral vasoconstriction syndrome (RCVS); and 3) cerebral arteritis. Notably, RCVS cases present with multifocal arterial narrowing on MRA that is indistinguishable from cerebral arteritis.[2,8] In retrospective studies comparing the findings of vessel wall MRI between cerebral arteritis and RCVS, gadolinium enhancement of the arterial walls is highly specific for cerebral arteritis.[9,10] To

our knowledge, our case is the first case of SLE in which vessel wall MRI revealed gadolinium-enhanced vessel walls of stenotic arteries, leading to a diagnosis of cerebral arteritis.

It was surprising that cerebral arteritis developed during stable disease activity of SLE, which made it difficult to suspect cerebral arteritis in its early stage. Other manifestations of vasculitis in SLE, including mononeuropathy multiplex and lupus mesenteric vasculitis, are suggested to be related to lupus activity,[11,12] but the relationship between cerebral arteritis and lupus activity remains unknown. To clarify clinical characteristics of cerebral arteritis in SLE, we performed a case-based literature review, focusing on the timing of onset (in association with the diagnosis of SLE) and relationship with disease activity of SLE. In 1994, two cases of lupus cerebral arteritis diagnosed using MRI and angiography were the first to be described.[4] Therefore, we searched for cases of lupus cerebral arteritis reported in peer-reviewed articles published between January 1994 and January 2020 on PubMed and ICHUSHI ("Medical Central Journals") without language restrictions. Search words included "Central Nervous System", "cerebral", "brain", "cerebellar", "arteritis", "vasculitis", "angiitis", and "systemic lupus erythematosus". Inclusion criteria were 1) clinical diagnosis of SLE by the authors, if applicable, that met at least four of the ACR criteria;[13,14] 2) cases evaluated on MRI with or without MRA; and 3) definitive cases of cerebral arteritis involving branches of the internal carotid and the vertebral arteries that were diagnosed based on histologic findings, abnormal findings on angiography or MRA, or gadolinium enhancement of vessel walls on MRI. Exclusion criteria were 1) cases suspected of cerebral arteritis only on MRI findings because of its poor specificity[15,16] and 2) publications that lacked patient details. We further noticed that cerebral arteritis could be divided into two distinct groups: medium-sized arteritis based on MRA or angiography, and small vessel vasculitis based on histology. Herein, we collected and analyzed cases of cerebral medium-sized arteritis similar to our case. Although some articles described their cases as "cerebral large vessel vasculitis",[3,24,25] we used "cerebral medium-sized arteritis" in this article, because such cases did not meet the definition of large vessel vasculitis.[17]

Our case-based review of cerebral medium-sized arteritis of SLE included 15 cases (Table 1).[1,5-7,18-26] A male:female ratio was 2:13, and mean age was 38.2 years (standard deviation, 15.3). The interval between the diagnosis of SLE and onset of cerebral arteritis in 13 evaluable cases was ≤ 3 months in 6 (46%) and ≥ 5 years in 7 (54%). The mean SLEDAI (SLE Disease Activity Index) at the onset of cerebral arteritis in the 14 evaluable cases was 34.3 (9.4) with a range of 16–46. As the SLEDAI score includes several factors that can be directly related to cerebral arteritis (i.e., cerebrovascular accident), we revised the SLEDAI score by excluding points for these factors (seizure, psychosis, organic brain syndrome, visual disturbance, cranial neuropathy, headache, cerebrovascular accident, and vasculitis). The mean of the revised SLEDAI score was 5.7 (3.6). There were 11 cases (79%) with ≥ 4 points, suggesting an association of cerebral arteritis with significant lupus activity (other than findings possibly associated with cerebral arteritis), while the remaining 3 cases, including our case, had scores of ≤ 2 points.[1,18] These findings suggest that cerebral arteritis may insidiously progress during active phases of SLE, which would result in cerebral infarction after many years irrespective of lupus activity. Symptoms for cerebral arteritis included headache (n = 10, 67% of the total cases), sensory disturbance (6, 40%) , dysarthria (5, 33%), impaired consciousness (5, 33%), cognitive disorders (4, 27%), paralysis of the extremities (4, 27%), and seizure (1, 6.7%). Affected brain sites on MRI included basal nuclei (7/15, 47%), brainstem (5/15, 33%), and cerebella (4, 27%). Abnormal MRA or angiographic findings in the anterior and posterior circulation were observed in 11/14 (79%) and 12/15 (80%), respectively, while involvement of the ACA, MCA, and PCA were in 6/13 (46%), 8/13 (62%), and 5/14 (36%), respectively. Other arteries involved included vertebral (7/14, 50%), basilar (6/14, 43%), cerebellar (4/14, 29%), internal carotid (2/13, 15%),

Table 1. Clinical characteristic of the published cases of cerebral medium-sized arteritis in SLE

Age sex	Interval*	Cerebral lesions on MRI	Involved arteries on MRA or angiography	Revised SLEDAI
57F[18]	3 mos	globus pallidus, Thal, temporal lobes	ACA, MCA, PCA, VA, BA	0
16F[19]	Sim.	pons, cerebellum, midbrain, Thal	MCA, VA, BA, PCA	6
26F[19]	Sim.	medulla, cerebelum, midbrain, Thal	VA	10
41M[5]	Sim.	cerebral gray and white matter, pons	anterior/posterior circulation	6
23F[6]	Sim.	meningium	MCA & PCA	10
27F[7]	10 yrs	basal nuclei, cortex	MCA	4
32F[20]	NA	medulla, ventral pons, temporal & periventricular regions	VA, MCA, ACA	13
40F[21]	17 yrs	cerebellum	PCA, CA	6
24F[22]	Sim.	cerebellum	ACA, BA, VA, CA, ICA	NA
31F[23]	17 yrs	basal nuclei	MCA, BA, CA	5
53F[24]	12 yrs	subcortical white matter	MCA, ACA	4
39F[25]	6 yrs	pons	BA, VA, PCA	8
67F[1]	5 yrs	frontal & parietal lobes	MCA	2
35M[26]	NA	basal nuclei, internal capsule	MCA, CA, OA, posterior communicating artery	4
62F	30 yrs	corona radiata, internal capsule, temporal & posterior lobes	ACA, MCA, PCA, ICA	2

*Interval between the diagnosis of SLE and the onset of cerebral medium-sized arteritis.
Abbreviations; Thal, thalamus; ACA: anterior cerebral artery, MCA: middle cerebral artery; PCA: posterior cerebral artery, VA: vertebral artery; BA: basilar artery, Sim: simultaneous onset, NA: not available, CA: cerebellar artery, OA: optic artery, ICA: internal carotid artery.

posterior-communication, and ocular artery (1/13 each, 7.7%). Stenosis or a beaded appearance was seen in 12/15 (80%), aneurysm formation in 4/15 (27%), and occlusion in 3/15 (20%). Treatment in the 14 evaluable cases were glucocorticoid in 13 (93%), pulse steroid in 7 (50%), and intravenous cyclophosphamide in 9 (64%). Plasma exchange, immunoabsorption, intravenous immunoglobulin, tacrolimus, cyclosporine, mycophenolate mofetil, and rituximab were used in 1 case each (6.7%). Improvement of arterial stenosis after therapy was seen in 4 (29%) cases,[5,7,21,26] while disappearance of aneurysmal shadows by MRA was reported in 1 case.[7] With respect to the clinical course in the 14 cases, improvement and deterioration (or no improvement) were described in 8 (57%) and 6 (43%) cases, respectively. Two cases were fatal (14%), suggesting that prognosis in recent cases may be improved by early detection with MRI and/or MRA, compared with 67% in the previous review.[3] Several limitations of our study warrant mention. First, there were limited numbers of articles that described cerebral medium-sized arteritis in SLE, leading to selection bias. Second, we could not judge whether RCVS could be fully excluded in each case, although the authors considered the cases to be cerebral arteritis. Third, this review included many cases for which clinical data were not provided, as commonly seen in similar studies.

In conclusion, recent imaging techniques including MRI and MRA may contribute to early diagnosis of cerebral medium-sized arteritis in SLE. Based on the case-based literature review, cerebral medium-sized arteritis seemed to insidiously progress during the active phase of SLE, which may lead to occlusion irrespective of disease activity, as illustrated in our case.

ACKNOWLEDGEMENT

The authors thank Hiroko Yasutomi for assessment of the case in this study.

CONFLICT OF INTEREST

None to declare.

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