Black-blood magnetic resonance imaging suggesting central nervous system vasculitis in moyamoya syndrome associated with systemic lupus erythematosus

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1. Introduction
Systemic lupus erythematosus (SLE) is a systemic autoimmune disorder characterized by a wide range of organ manifestations and autoantibody production. The central and peripheral nervous system involvements of SLE are called neuropsychiatric SLE (NPSLE). Central nervous system (CNS) vasculitis is a rare but potentially devastating manifestation of NPSLE.

Moyamoya disease (MMD) is an idiopathic disorder characterized by progressive stenosis and occlusion of the distal internal carotid arteries and their major intracerebral branches. The vascular stenosis/occlusion is accompanied by the growth of small collateral vessels in the cerebral perforating vessels, hence the name came ‘moyamoya’ (which describes the angiographic view of collateral vessels as a puff of smoke in Japanese). The etiology of moyamoya disease is unknown. However, these angiographic findings are not specific to the disease. Moyamoya-like vasculopathy might develop in patients with other well-characterized diseases or syndromes, including SLE. In these patients, the condition is called moyamoya syndrome (MMS) rather than MMD. Both conditions predispose patients to brain ischemia (i.e., stroke, transient ischemic attacks, and seizures) [1,2].

Black-blood magnetic resonance imaging (BB-MRI) is an established tool for vessel wall imaging. It is useful for the characterization of arteriosclerotic plaques and the evaluation of inflammatory changes. Concentric wall thickening and circumferential contrast enhancement of the affected arterial wall segments indicate vasculitis [3].

Here, we present a case of SLE complicated by MMS in which BB-MRI suggested CNS vasculitis as the etiology of vascular occlusion.

2. Case presentation
A 45-year-old woman was admitted for recurrent ischemic strokes.

At the age of 33 years, she was diagnosed with SLE (lupus nephritis, pancytopenia, arthralgia, and positive antinuclear antibody and anti-dsDNA antibody). She achieved remission after induction therapy and was in sustained remission with low-dose glucocorticoid and mizoribine therapies. At the age of 43 years, she visited the emergency department with temporary weakness of her right arm. Brain MRI revealed acute multiple infarcts in the left
corona radiata and stenosis of the left middle cerebral artery (MCA; Figure 1(A)). She was prescribed aspirin for the prevention of stroke.

At the age of 45 years, she suffered temporary weakness of the left arm and dysarthria. Brain MRI revealed acute multiple infarcts in the right frontal and parietal lobes and old multiple infarcts in the left corona radiata, which were stable after the first ischemic event. MR angiography revealed new-onset stenosis of the right MCA and persistent left MCA stenosis. At this time, she was diagnosed with MMS and underwent left superficial temporal artery (STA)-MCA bypass (Figure 1(B): MR angiography after the bypass surgery). However, she suffered weakness and paresthesia of the right arm two weeks after the bypass surgery. Brain MRI revealed acute multiple infarcts in the left caudate nucleus and the watershed areas of bilateral hemispheres. Old multiple infarcts in bilateral hemispheres were stable after the second ischemic event, and so was the bilateral MCA stenoses on MR angiography. She was referred to our department under the suspicion of NPSLE.

Physical examination results, including the neurological findings, were normal. Laboratory investigation revealed pancytopenia (hemoglobin level, 9.3 g/dL; white blood cell count, 2800/μL; platelet count, 14 × 10^4/μL). The complement levels were normal. Her serum anti-nuclear antibody test results were positive (80-folds, homogeneous pattern); anti-RNP, anti-SS-A, and anti-centromere antibody tests were also positive, although she had not experienced clinical manifestations related to mixed connective tissue disease, systemic sclerosis, or Sjögren’s syndrome, such as Raynaud’s phenomenon, nail fold changes, skin thickening, digital ulcers, and sicca symptoms. Anti-DNA antibody, anti-Smith antibody, lupus anticoagulant, IgG and IgM anti-cardiolipin, anti-cardiolipin/β2-glycoprotein I, and anti-phosphatidylserine/prothrombin antibody were negative. The protein C, protein S, and antithrombin-3 levels were within the normal limits. Her urinalysis and cerebrospinal fluid analysis results were normal. The results of the whole-body computed tomography (CT), echocardiography, ultrasonography of the lower extremity veins, and single-photon emission CT of the brain were all unremarkable. To investigate the etiology of the moyamoya syndrome, BB-MRI (three-dimensional T1-weighted fat and blood-suppressed sequences with and without contrast injection using a 3-Tesla MR scanner) was performed. A 3-Tesla MR scanner (Ingenia; Philips Medical Systems. Best, Netherlands) was used to obtain T1 weighted black blood images by high-resolution three-dimensional sequence (Volume Isotropic Turbo spin echo Acquisition; VISTA). Post-contrast BB-MRI images demonstrated strong concentric enhancement along the stenotic portions of the MCAs, bilaterally (Figure 2). Contrast enhancement was stronger in the M1 segment of the right MCA, where the stenosis had developed more recently. Based on the imaging findings, the etiology of MMS, in this case, was considered as vasculitis in both MCAs secondary to SLE.

During hospitalization, she developed left hemiparesis and acute-onset cognitive dysfunction (Mini-Mental State Examination, 24 points; revised Hasegawa’s dementia scale, 20 points) with profound impairment of frontal lobe function such as attention and execution (Frontal Assessment Battery 9 points). Brain MRI revealed acute multiple infarcts in bilateral frontal and parietal lobes and the left
caudate nucleus. Treatment with high-dose glucocorticoid therapy was immediately initiated, and intravenous cyclophosphamide was added as an adjunct therapy. She did not develop new neurological symptoms thereafter, and follow-up MRIs did not reveal new infarcts. Her hemiparesis and cognitive dysfunction gradually improved. The glucocorticoid dose was subsequently tapered. She was treated in the outpatient office with low-dose prednisolone, azathioprine, hydroxychloroquine, and warfarin, and had had no relapse since then.

Written informed consent was obtained from the patient for this case report.

3. Discussion

This is the first reported case of MMS associated with SLE, evaluated by BB-MRI to reveal its inflammatory etiology.

MMS is a rare but critical manifestation of SLE, which can cause significant mortality and morbidity in the affected patients. There have been several reported cases of MMS associated with SLE, but the etiology of MMS associated with SLE has rarely been described in previous reports [4,5].

Zhou et al. reported a case of SLE complicated by MMS, in a female patient, whose brain biopsy showed lymphocytic infiltration of the vessel wall suggestive of vasculitis [6]. Although histological evaluation is the diagnostic gold standard for intracranial vasculitis, brain biopsy is an invasive and time-consuming procedure and might reveal false-negative findings. Digital subtraction angiography can detect intracranial vasculitis with good sensitivity in large and medium-sized intracranial vasculitis, but it misses most of the changes in the small vessels or non-stenotic vasculitic lesions and might not differentiate between vasculitis and reversible cerebral vasoconstriction syndrome (RCVS) [7].

BB-MRI has emerged as a non-invasive tool to measure wall thickness and identify the pathological features of extracranial vessels. Recently, its application has been extended to intracranial vessels to recognize atherosclerosis, RCVS, and vasculitis [8,9], and it has shown promising results in primary angiitis of the central nervous system (PACNS) [10]. Vasculitic stenosis is characterized by concentric vessel wall stenosis with contrast uptake [9]. Atherosclerotic stenosis presents as a focal, eccentric vessel wall thickening with a mixture of enhanced fibrous layer and non-enhancing lipid-rich necrotic core or calcification. RCVS can be distinguished from vasculitis by the presence of diffuse, uniform wall thickening without enhancement. In our case, the strong, concentric contrast enhancement with vessel wall thickening in both MCAs on BB-MRI suggested intracranial vasculitis. BB-MRI allowed prompt identification of the inflammatory etiology of MMS in our case and might have contributed to the favorable outcome of this rapidly progressive and potentially devastating manifestation.

We have no way of knowing when CNS vasculitis started in our case, but it seems reasonable to suppose that CNS vasculitis had developed at the first ischemic event. Ideally, BB-MRI should have been performed at the first ischemic event. If BB-MRI had revealed findings suggestive of vasculitis in the left MCA at that time, immunosuppressive treatment should have been considered to protect her from subsequent vascular stenoses and ischemic events.

Interestingly, our case suggests that the intensity of contrast enhancement on BB-MRI indicates active vessel wall inflammation. In our case, the M1 segment of the right MCA that had developed stenosis more recently than the left MCA showed stronger contrast enhancement. Although follow-up BB-MRI was not performed in our case, contrast enhancement on BB-MRI might provide information about the chronological changes in vessel wall inflammation.

Our report has some limitations. First, we did not perform a brain biopsy, and thus CNS vasculitis was not confirmed histologically in our case. Second, follow-up BB-MRI was not obtained in our case, and therefore usefulness of contrast enhancement on BB-MRI in monitoring therapeutic response is outside the scope of our report. Third, electroencephalography (EEG) was not performed in our case. EEG might have provided additional
information on altered brain function underlying the cognitive dysfunction in our case.

In conclusion, this was a case of MMS associated with SLE evaluated by BB-MRI. The BB-MRI finding suggested CNS vasculitis as the etiology of the asynchronous bilateral MCA stenoses and justified the intensive immunosuppressive treatment. When CNS vasculitis is suspected in patients with SLE, BB-MRI can be a non-invasive and prompt imaging modality to guide the treatment strategy.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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References

[1] Scott RM, Smith ER. Moyamoya disease and moyamoya syndrome. N Engl J Med. 2009;360(12):1226–1237.
[2] Phi JH, Wang KC, Lee JY, et al. Moyamoya syndrome: a window of moyamoya disease. J Korean Neurosurg Soc. 2015;57(6):408–414.
[3] Treitl KM, Maurus S, Sommer NN, et al. 3D-black-blood 3T-MRI for the diagnosis of thoracic large vessel vasculitis: a feasibility study. Eur Radiol. 2017;27(5):2119–2128.
[4] Wang R, Xu Y, Lv R, et al. Systemic lupus erythematosus associated with Moyamoya syndrome: a case report and literature review. Lupus. 2013;22(6):629–633.
[5] Tanaka R, Shimojima Y, Ueno KI, et al. Moyamoya syndrome related to systemic lupus erythematosus developing during pregnancy: a case-based review. Clin Rheumatol. 2020;39(12):3861–3867.
[6] Zhou G, An Z, Gokhale S. Moyamoya syndrome as an unusual presenting manifestation of systemic lupus erythematosus in a young woman. Med Princ Pract. 2014;23(3):279–281.
[7] Eiden S, Beck C, Venhoff N, et al. High-resolution contrast-enhanced vessel wall imaging in patients with suspected cerebral vasculitis: prospective comparison of whole-brain 3D T1 SPACE versus 2D T1 black blood MRI at 3 Tesla. Plos One. 2019;14(3):e0213514.
[8] Qiao Y, Steinman DA, Qin Q, et al. Intracranial arterial wall imaging using three-dimensional high isotropic resolution black blood MRI at 3.0 Tesla. J Magn Reson Imaging. 2011;34(1):22–30.
[9] Perren F, Vargas MI, Kargiotis O. Etiology of intracranial arterial stenosis: are transcranial color-coded duplex ultrasound and 3T black blood MR imaging complementary? J Neuroimaging. 2016;26(4):426–430.
[10] Pfefferkorn T, Linn J, Habs M, et al. Black blood MRI in suspected large artery primary angiitis of the central nervous system. J Neuroimaging. 2013;23(3):379–383.