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Case Report

Tumor-like Presentation of Cerebral Vasculitis in a Patient With Systemic Lupus Erythematosus: A Biopsy-confirmed Case

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Central nervous system (CNS) manifestations of systemic lupus erythematosus (SLE) are diverse and often difficult to distinguish from SLE-unrelated events. CNS vasculitis is a rare manifestation, which is seen in less than 10% of post-mortem studies, and lesions with multifocal cerebral cortical microinfarcts associated with small-vessel vasculitis are the predominant feature. However, CNS vasculitis presenting as a tumor-like mass lesion in SLE has rarely been reported. Herein, we report a case of cerebral vasculitis mimicking a brain tumor in a 39-year-old female with SLE. A biopsy of the brain mass revealed fibrinoid necrosis and leukocytoclastic vasculitis. The neurological deficits and systemic symptoms improved after treatment with corticosteroids and immunosuppressive agents. To the best of our knowledge, there are no reports of biopsy-proven cerebral vasculitis presenting as a brain mass in patients with SLE in Korea.

Keywords: Central nervous system vasculitis, Systemic lupus erythematosus, Tumor, Biopsy

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease with diverse clinical manifestations in multiple organ systems [1]. Neurological and psychiatric manifestations of SLE, collectively referred to as neuropsychiatric SLE (NPSLE), are occasionally observed in patients with SLE, and the cumulative incidence of NPSLE has been reported at 30%~40% [2]. The central nervous system (CNS) manifestations of NPSLE range from subtle cognitive dysfunction to acute confusional states, psychosis, seizure disorders, and stroke [3]. CNS vasculitis is a rare manifestation of NPSLE, occurring in less than 10% of post-mortem studies [1,4]. Multifocal cerebral cortical microinfarcts associated with small-vessel vasculitis are the predominant histopathologic abnormalities [5], whereas CNS vasculitis presenting as a tumor-like mass lesion has rarely been reported [6]. Diagnosing CNS vasculitis remains challenging and is based on a combination of suspicious findings from brain magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) studies, inflammatory markers, and digital subtraction angiography [7]. A brain biopsy may be imperative to distinguish cerebral vasculitis from other causes of brain lesions, such as infections or lymphoma [1]. Here, we report the case of a 39-year-old female with SLE who presented with a large mass-like lesion in the left frontal lobe on MRI. A brain biopsy demonstrated fibrinoid necrosis in the small and medium-sized arteries and leukocyto-

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clastic vasculitis.

CASE REPORT

A 39-year-old female visited the emergency department because of a fever and general weakness for two days. She did not complain of any neurological symptoms. Previously, she had been taking medication for a month due to a generalized edema. She was hospitalized in the department of nephrology for renal biopsy and discharged. She was then readmitted after two days. On admission, physical examination revealed diffuse alopecia, two oral ulcers, and pitting edema in the lower legs. Neurologic examination did not demonstrate any neurologic signs. Her blood pressure was 150/90 mmHg, and her body temperature was 38.2°C. Laboratory tests revealed a white blood cell count of 5,230/mm^3, hemoglobin level of 13.2 g/dL, platelet count of $95\times10^3/mm^3$, erythrocyte sedimentation rate of 88 mm/hr, C-reactive protein level of 0.12 mg/dL, serum albumin level of 2.0 g/dL, and creatinine level of 0.91 mg/dL. Urinalysis revealed proteinuria and microscopic hematuria. Her urine protein/creatinine ratio was 11.54 mg/mg. Several autoantibodies were detected, including antinuclear (>1:1,280, speckled), anti-double-stranded DNA (379 IU/mL; normal range <10 IU/mL), anti-Smith (480 U/mL; normal range <7 U/mL), and SS-A/Ro antibodies (50 U/mL; normal range <7 U/mL). Tests for lupus anticoagulant, anti-cardiolipin, and β2-glycoprotein 1 antibodies were negative. The levels of C3 and C4 dropped (25.5/2.6 mg/dL; normal range 90~180/10~40 mg/dL). Antineutrophilic cytoplasmic antibody was negative. Transthoracic echocardiography revealed a small pericardial effusion without vegetation. The sonographic appearance of the bilateral kidneys was normal. A kidney biopsy revealed class III lupus nephritis with inflammatory cell infiltration in the interstitium and glomeruli. No crescentic lesions were observed (Figure 1).

One day after readmission, she complained of a severe headache and lost consciousness. Speech and cognitive functions could not be assessed due to a loss of consciousness. Her pupils were equally reactive to light bilaterally. Babinski's reflex was absent. Brain computed tomography (CT) revealed a mass-like lesion measuring approximately 7 cm, with midline shifting in the left frontal lobe. Brain MRI revealed a large intra-axial heterogeneous mass with a prominent hemorrhagic component, perilesional edema in the left frontal lobe, and remote lesions in both frontoparietal lobes (Figure 2A and 2B). However, magnetic resonance angiography revealed no abnormal findings in the cerebral arteries. Considering the possibility that increased brain pressure due to large brain lesions on brain imaging modalities may cause cerebral herniation after lumbar puncture, we did not perform the CSF examination. Under the suspicion of brain tumor or CNS lupus based on the findings of brain lesions on CT and MRI images, we decided to perform a brain biopsy. After the brain biopsy, speech and cognitive impairments and paralysis of right upper and lower extremities were detected. The brain biopsy showed necrotizing vasculitis of the small- and medium-sized arteries, leading to hemorrhages and leukocytoclastic vasculitis (Figure 3).

The patient was diagnosed with SLE with cerebral vasculitis and class III lupus nephritis. Initial SLE Disease Activity Index-2000 (SLEDAI-2K) score was 40. She underwent a five-day course of corticosteroid pulse treatment (methylprednisolone, 1 g/day) and subsequent intravenous cyclophosphamide (500 mg fixed dose with two-week interval) with a high dose corticosteroid (2 mg/kg/day). She was scheduled to receive six cycles of cyclophosphamide treatments, but due to severe leukopenia, rituximab treatment was added twice after four cycles of cyclophosphamide treatments. After induction therapy with

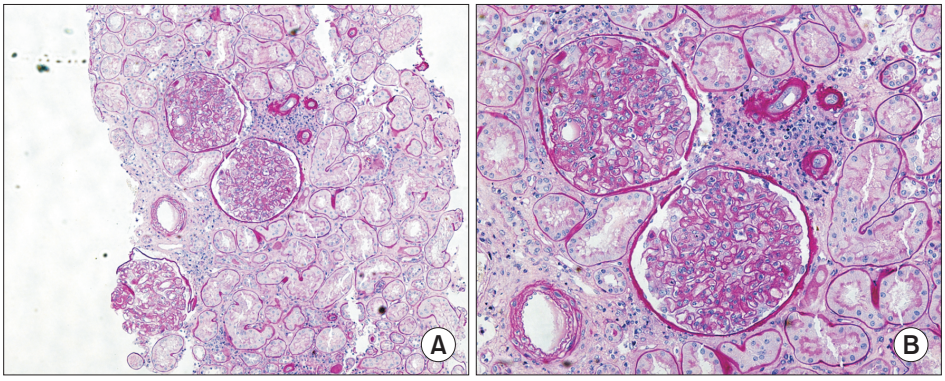

Figure 1. Light micrograph of renal specimen shows glomeruli with mesangial expansion and segmental endocapillary proliferation (PAS, A: ×100, B: ×200).

steroid pulse, cyclophosphamide, and rituximab treatments, maintenance therapy with mycophenolate mofetil (MMF) and tacrolimus was initiated. Because her leukopenia persisted despite stopping cyclophosphamide treatment, tacrolimus (2 mg/day), which is known to induce leukopenia less frequently, was added to low dose of MMF (1 g/day). After induction therapy, SLEDAI-2K score improved by up to 2. After three months of treatment, her neurological symptoms resolved without any sequelae. Four months later, follow-up brain MRI showed a reduction in the size of mass, without new lesions (Figure 2C and 2D). She has been on a follow-up in the outpatient clinic for 15 months without a flare-up. Her urine protein/creatinine ratio declined to less than 0.15 mg/mg without microscopic hematuria and anti-double-stranded DNA antibody turned negative. Corticosteroid was tapered to low dose and MMF and tacrolimus were continued.

This study was reviewed and approved by the Institutional Review Board of Daegu Fatima Hospital of Korea (approval number: FAIRB-MED-CAS-22-052).

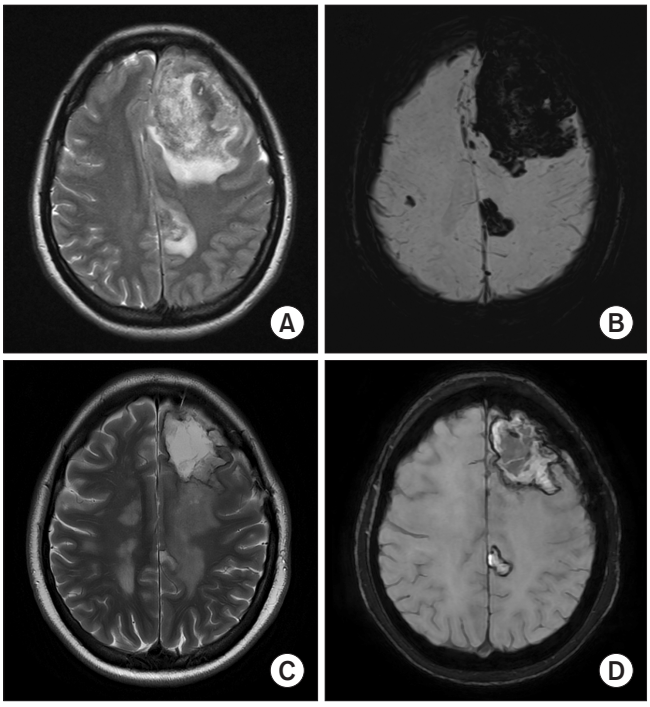

Figure 2. (A, B) Initial magnetic resonance imaging (MRI) of the brain. The axial T2-weighted image (T2WI) (A) shows a large intra-axial heterogeneous mass in the left frontal lobe with perilesional edema. Note that the prominent hemorrhagic component in the mass and other remote lesions of both frontoparietal lobes are revealed in the axial susceptibility-weighted image (SWI) (B). No significant enhancement is seen. (C, D) Follow-up MRIs after four months of immunosuppressive treatment. Axial T2WI (C) and SWI (D) demonstrate decrease in mass size, perilesional edema, and peripheral hemosiderin rim formation, even in non-operated remote lesions. No new lesions were observed.

DISCUSSION

The nervous system is one of the major organs affected in patients with SLE and focal NPSLE represents localized CNS involvement, which is generally attributable to episodes of either venous thrombosis or arterial ischemia [3]. The pathophysiological mechanisms of these events are primarily associated with thromboembolic phenomena that occur in the context of SLE-related hypercoagulable states associated with the presence of antiphospholipid antibodies, cardioembolic disease secondary to Libman-Sacks endocarditis, early and advanced arteriosclerosis in patients with SLE, and finally, CNS vasculitis, which is a very rare entity in SLE [1,3,4,7]. Cerebral vasculitis may occur by the deposition of immune complexes in the vascular path, which shows affected segments interspersed with normal areas. The presence of anti–endothelial-cell antibodies that cause cell destruction has also been observed, and the presence of these autoantibodies has been documented in 80% of patients with

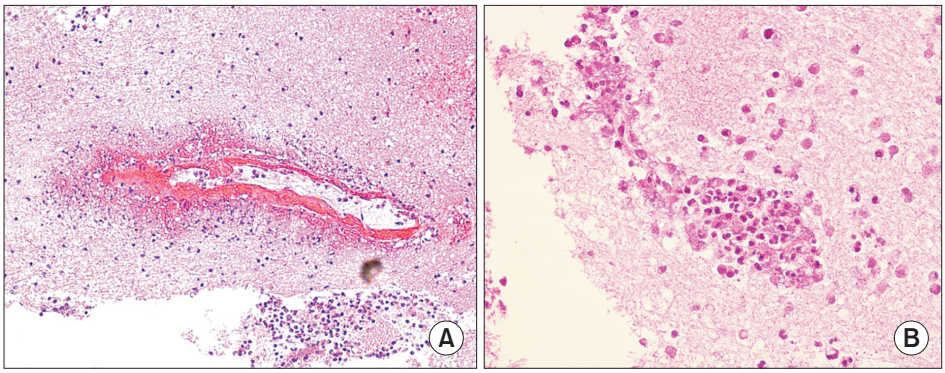

Figure 3. Histopathology from a biopsy of left frontal brain lesion shows (A) a necrotizing vasculitis with fibrinoid necrosis of vessel wall and (B) leukocytoclastic vasculitis with prominent neutrophil infiltration and adjacent nuclear debris in a perivascular area (H&E, A: ×100, B: ×400).

SLE [1].

CNS vasculitis in SLE usually affects small arterioles and capillaries in most cases [8], which induces multifocal cerebral cortical microinfarcts [5]. In contrast, CNS vasculitis presenting as a mass-like lesion in SLE is extremely rare [6]. Our case demonstrated a large intra-axial heterogeneous mass in the left frontal lobe with a prominent hemorrhagic component but no enhancement. A mass-like lesion on neuroimaging in patients with SLE should require differential diagnosis among CNS vasculitis, brain infarcts due to secondary antiphospholipid syndrome (APS), cardioemboli, atherosclerosis, brain tumors, and infectious conditions. In our case, conditions such as APS and cardioembolic diseases were ruled out based on the absence of APS antibodies, a normal platelet count, and no cardiac abnormalities on echocardiographic examination.

In CNS vasculitis, contrast enhancement is frequently observed in the walls of acutely inflamed arteries [9]. However, because our case did not show significant enhancement, a differential diagnosis of brain tumors, such as oligodendrogliomas, is essential. The majority of oligodendrogliomas are located supratentorially in the frontal lobe and occur in a younger patient population. The MRI features of oligodendroglioma are hemorrhage and no enhancement, which is consistent with those of our case. In contrast to vasculitis, oligodendrogliomas may show calcific lesions, cystic degeneration, and uncommon peritumoral edema. In addition, the arterial system is not intact in oligodendrogliomas [10]. We decided to perform a brain biopsy for an accurate diagnosis in this case and found necrotizing and leukocytoclastic vasculitis lesions in the pathological brain lesions. Although brain biopsy remains the gold standard to confirm the diagnosis of CNS vasculitis [7,11], it is usually not performed despite the low risk of complications. Early biopsy is imperative to distinguish vasculitis [1]. Even highly sensitive imaging modalities continue to be developed as imaging in CNS vasculitis is often nonspecific and some patients with NPSLE demonstrate normal MRIs [12]. The most common finding in SLE vasculitis is the presence of transmural lymphocytic infiltrates with fibrinoid necrosis and either hemorrhage or thrombosis. Biopsy case reports of clinically active leukocytoclastic vasculitis are extremely rare due to their sensitivity being limited owing to segmental involvement of the vessels [13].

Treating CNS vasculitis in SLE patients remains difficult [11]. High-dose glucocorticoids alone or in combination with cyclophosphamide or immunoglobulin have been the most frequently proposed treatment for patients with SLE with an acute or recent onset of severe neurological symptoms and active inflammation in the brain [7,11]. Plasmapheresis, azathioprine, and MMF may also warrant further consideration. Recently, several studies have reported that cyclophosphamide and rituximab are effective as the induction therapy in NPSLE as well as lupus nephritis [13,14]. In our case, early aggressive therapy with intravenous methylprednisolone pulse therapy and cyclophosphamide was a reasonable initial option because the brain lesion was acute and severe necrotizing vasculitis. NPSLE is associated with poor prognosis and has a three-fold increased risk of mortality, and focal CNS NPSLE showed nearly an eight-fold increased risk of mortality among patients with SLE [15]. In particular, active necrotizing vasculitis of the cerebral vessels is a rare complication of SLE and contributes to fatal outcomes. The neurological symptoms in our patient improved after aggressive immunosuppressive treatment.

SUMMARY

Here, we report a case of cerebral vasculitis in SLE that mimicked a brain tumor and was confirmed by a biopsy. Her neurological symptoms improved after treatment with corticosteroids and immunosuppressive drugs, including cyclophosphamide, rituximab, MMF, and tacrolimus. This is the first reported case of SLE with a biopsy-proven cerebral vasculitis in Korea.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

N.R.K. and J.W.K. analyzed and interpreted the patient data and drafted the manuscript. E.J.N. analyzed and interpreted the

patient data and reviewed and approved the final manuscript.

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