SYSTEMIC LUPUS ERYTHEMATOSUS WITH RECURRENT CEREBRAL INFARCTION AS THE FIRST SYMPTOM: A CASE REPORT

Yu Shen, Qian Cao, Lijun Xu*
Department of Neurology, The Second Affiliated Hospital of Nanchang University, Nanchang, Jiangxi, China, 3 30006

ABSTRACT

Introduction*: Systemic lupus erythematosus(SLE) with recurrent cerebral infarction is rarely reported. It is difficult to diagnose of SLE according to the initial symptoms.*

Material and method*: We admitted a 70-year-old woman who first symptom was muscle strength diminished and inarticulation. Imaging suggests cerebral infarction.Besides,she had a cerebral infarction again during the hospitalization,just found several tumour indicators abnormally elevated and Lupus-related antibody positive. Underwent exclusivity laboratory and diagnostic tests,neuropsychiatric syndromes of SLE was considered.The patient had discharged from the Division of Rheumatology with improvement of the health condition.and regular follow-up visits in long-term outpatient clinics.*

Result and conclusion*: The purpose of this report is to draw the attention of clinicians to patients with recurrent cerebral infarction as the first symptom. At the same time, a reference case is given in treatment. Systemic lupus erythematosus encephalopathy is difficult to diagnose based on the first manifestation. The role of abnormal tumor indicators in SLE needs to be further explored.*

Keywords: *neuropsychiatric syndromes of SLE (NPSLE), r ecurrent cerebral infarction, case report.*

DOI: 10.19193/0393-6384_2021_4_340

Received *October 15, 2020;* ***Accepted*** *March 20, 2021*

Introduction

Systemic lupus erythematosus(SLE), an autoimmune disease involving the whole body system, is more common in young and middle-aged women[1]. Women account for 90% of patients with SLE, and 50% of them have the first symptoms between 15 and 20 years old, and most patients show the disease between 15 and 44 years old[2]. Other symptoms include systemic manifestations such as fatigue, weakness, fever, and weight loss. Some patients may have symptoms such as photosensitivity, Raynaud's phenomenon, livelihood reticula, and arthralgia[3]. The cumulative nervous system is called neuropsychiatric systemic lupus erythematosus (NPSLE). All 19 syndromes have been found, including neurological syndromes of the central, peripheral, and autonomic nervous systems, and psychotic syndromes observed in patients with SLE[4]. According to previous reports, 5%-10% of patients with SLE may have cerebrovascular accidents throughout the course of the disease, and only a few patients have stroke as the initial symptom[5]. During the period of hospitalization with standard treatment, SLE with recurrent cerebral infarction is extremely rare.

As far as we know, this is the first case report and literature review of an elderly female patient with multiple cerebral infarction as the first symptom

of SLE. Recurrence of cerebral infarction during standard treatment during hospitalization, with two cerebral infarctions the period is less than one month apart. This patient also has features such as increased tumour markers, so it is more meaningful for reporting.

Case report

A 70-year-old Chinese woman was admitted to our hospital after her right upper limb weakness accompanied by inarticulation for 10 days. She was in good health before, and she did not even have cerebrovascular risk factors, such as high blood pressure, diabetes and other risk factors for cerebral infarction. On admission, neurological examination revealed the muscle strength of both lower limbs was normal, the muscle strength of the right upper limb was 4-grade, and the muscle strength of the left upper limb was normal. No common manifestations of SLE, such as butterfly erythema, were observed. Moreover, it was found that the patient had a decline in cognitive function, and the MMSE score was 3. After asking family members, it was discovered that it appeared after this illness. On day after admission, the patient underwent brain CT and MRI examination. There were multiple bead-like high signals on diffusion-weighted imaging (DWI) and the same area on T2 also had high signals (figure 1).

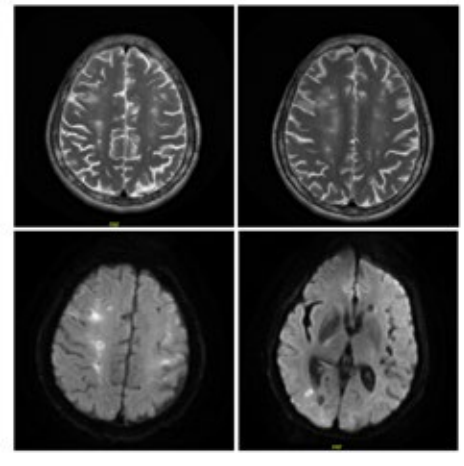

Figure 1: The patient's brain magnetic resonance image, Axial T2-weighted images showed multiple dot-like or patchy hyperintense lesions in the bilateral cerebral hemispheres. Axial DWI demonstrated restricted diffusion areas in the same location.

CT angiography (CTA) showed that the cerebral blood vessels were normal, hypoperfusion in the corresponding cerebral infarction area (figure 2). Routine and perfect related laboratory examinations, Contrast-enhanced trans-cranial Doppler (c-TCD) revealed no evidence of intracardiac Shunt. No abnormal heart rhythm was found in 24-hour Holter. Transesophageal echocardiography found no evidence of mural thrombosis and abnormal cardiac structure. Chest CT scans found no evidence of lung infection or tumor. Tests for hereditary hypercoagulability and blood disorders were also normal. Subsequent digital subtraction angiography was also performed, revealing beaded changes in the blood vessels in the brain's anterior and posterior circulation (figure 3). Some of the meaningful test results and reference ranges are shown in Table 1, No obvious abnormalities in other examination.

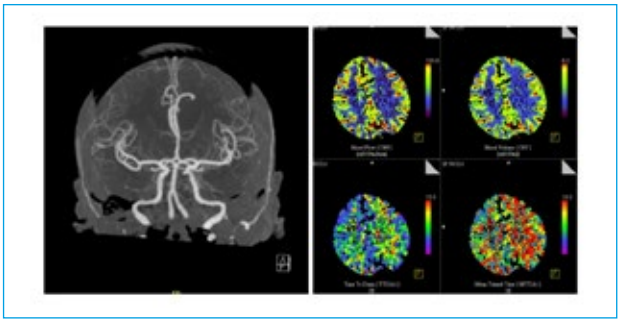

Figure 2: CTA showed cerebral blood vessels were normal, hypoperfusion in the corresponding cerebral infarction area.

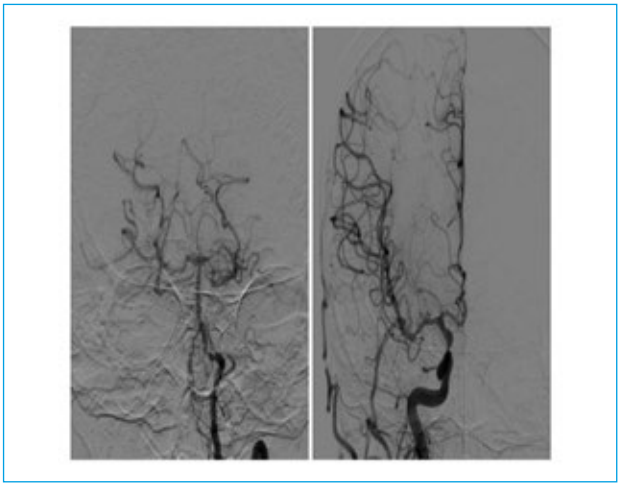

Figure 3: Beaded changes in the blood vessels in the brain's anterior and posterior circulation.

The patients was administrated with aspirin, statin and Circulating drugs. However, the mechanism of cerebral infarction is not well understood, the cause of cerebral infarction needs further consideration. The patient's blood vessels are in good condition and have multiple foci. So atherosclerotic cerebral infarction is ruled out. It may be a cerebral infarction caused by SLE, a tumour-related hypercoagulable state, or a

combination of both. So I invited a rheumatology and immunology specialist for assistance, transferred to the rheumatology and immunology department after a week of neurology treatment. Standard dose of hormones and immunosuppressive therapy were given. After several days of treatment, the patient developed weakness of the left upper limb and 2+ muscle strength of the left upper limb. Re-examination of the cranial magnetic resonance revealed new multiple cerebral infarction on DWI (figure 4).

Index	Inspection result	Reference value
carbohydrate antigen-125(U/mL)	36.6	0~35
carbohydrate antigen-153(U/mL)	111.8	0~32.4
carbohydrate antigen-199(U/mL)	57.61	0~37
anti-nuclear antibody s-type (ANA)	1:3200	negative
anti-ds-DNA(IU/ml)	60.75	0~18
dsDNA(U/ml)	256	0~30
anti-Smith antigen antibodies	+	-
anti-ribonucleoprotein antibodies	+	-
Urine protein concentration(mg/L)	1384.15	0~100
D-Dimer(ug/ml)	2.4	0~0.9

Table 1: Some of the meaningful test results and reference ranges..

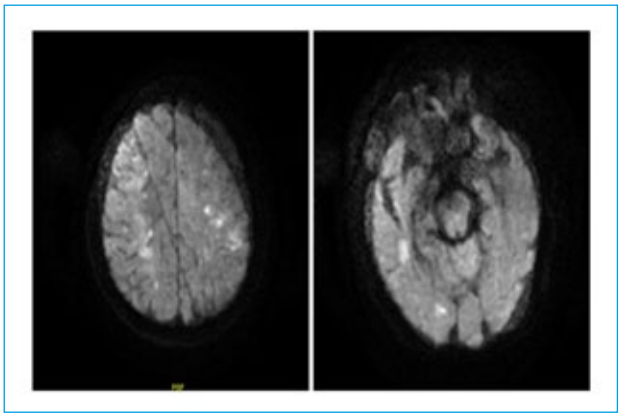

Figure 4: The patient's brain magnetic resonance showed multiple high signals. Because the patient did not cooperate during the examination, the image was unclear..

Later, he was transferred to the Neurology Intensive Care Unit. It was believed that the number of tumour indicators and D-dimer were increased, CA-153 was more than three times higher. It was necessary to rule out the hypercoagulable state caused by the tumour (Trousseau's syndrome). So we performed CT scans of the whole abdomen and PET-CT of the whole body. Both tests did not find any evidence of a tumor. Based on the 2019EULAR/ACR diagnostic criteria for SLE, SLE can be diagnosed based on proteinuria and specific antibodies. It is also considered that cerebral infarction is caused by SLE. After systemic treatment, the patient's limb weakness improved, both lower limb muscle strength was normal, the right upper limb muscle strength was grade 5, and the left upper limb muscle strength was 4-, but the symptoms of cognitive decline still remained.

Discussion

The exact evidence for the pathophysiology of NPSLE has not been established, but the current research shows that NPSLE is damage caused by blood vessels or immune complexes between blood vessels, blood vessel or neuron damage caused by autoantibodies,and locally produced cytokines and subsequent occurrences. Blood vessel or neuron damage caused by cellular immune-mediated response[6]. The possible mechanisms of ischemic stroke in SLE patients include atherosclerosis and arterial-to-arterial embolism, small vasculitis, antiphospholipid antibody syndrome, and renal hypertension[7]. There are also studies suggesting that the increase of anti-dsDNA and other antibodies and the presence of lupus anticoagulants are related to the damage of the patient's central nervous system. It was found that this large class of antibodies is directly related to the blood hypercoagulability state and thrombosis[8]. This patient's antibody level is increased, and the blood vessels are normal, after removing the blood clot from the heart, which seems to support cerebral infarction caused by the hypercoagulable state caused by the antibody and small vascular lesion due to SLE.

SLE patients accumulate the central nervous system, and patients with mild symptoms generally only have migraines and changes in consciousness. Critically ill patients in the later stages of the disease may have critical symptoms such as unconsciousness and persistent seizures[9]. Different symptoms can also occur because of different parts of the cerebrovascular accidental damage[10]. The first symptom of this patient is cerebral infarction, which is rare, and cognitive decline appears immediately. However, a new cerebral infarction reappears in the course of standardized hormone and immunosuppressant therapy, and the interval is less than one month. As far as we know, no relevant cases have been reported. Cerebral infarction generally occurs during maintenance therapy with low-dose prednisolone[11]. But this patient did not use low-dose prednisolone maintenance therapy.According to our existing research,in several connective tissue diseases, the incidence of malignant tumors may

increase[12]. In addition, chronic inflammation may lead to tumour development[13.14]. Autoimmune diseases related to chronic B cell stimulation, such as SLE and Sjogren's syndrome, are all related to B cell lymphoma[15]. Therefore, SLE systemic immune system diseases,we should worry about the occurrence of tumors. Moreover, the number of tumor indicators were increased in this patient, and we are more suspicious of whether it has tumors. Therefore, we conducted a whole-body examination of the patient, including whole-abdominal CT and whole-body PET-CT. No cancer was found. After reviewing the literature, we found that SLE patients may be associated with the increase of a variety of tumour indicators, and SLE may be associated with CEA, CA19-9, CA125 and CA72-4. It is expected that such substances can be used to assess the disease activity of SLE patients[16]. Although the existing research only elaborates on this clinical phenomenon,it also informs our clinicians that the increase in tumor indicators in SLE patients does not necessarily mean that they have associated tumors. However, it is also necessary to carefully investigate the occurrence of tumors in clinical work. Especially in patients with cerebral infarction, it is necessary to rule out hypercoagulable state caused by tumour.

The treatment of SLE is mainly based on hormone therapy. The effect of hormone therapy for patients with cerebral infarction in SLE is not good. Short-term high-dose hormone shock combined with immunosuppressive therapy, has achieved good results in many cases. Antiphospholipid antibody positive brain Anticoagulants such as aspirin, heparin or warfarin should be added to the treatment of patients with infarction[17].

In summary, SLE patients with multiple cerebral infarctions as the first episode are rare, and this patient has elevated tumour indicators, which arouse our thinking. Our purpose in reporting this case is to recommend that patients with cerebral infarction need to exclude SLE, tumour-related hypercoagulability and other causes, to find the cause early and treat it symptomatically.

References

1) Denburg JA, Denburg SD, Carbotte RM, Long AA, Hanly JG. Nervous system involvement in systemic lupus erythematosus. Isr J Med Sci. 1988;2 4(12): 754-758.
2) Park SH. Systemic lupus erythematosus. J Korean Med Assoc 2009; 52: 645-56.
3) Fortuna G, Brennan MT. Systemic lupus erythematosus: epidemiology, pathophysiology, manifestations, and management. Dent Clin North Am. 2013 Oct; 57(4): 631-55.
4) Kim SY, Yoon TS, Suh JH. Concomitant occurrence of cervical myelopathy, cerebral infarction, and peripheral neuropathy in systemic lupus erythematosus: a case report. Ann Rehabil Med. 2014 Apr; 38(2): 263-8.
5) Brey RL, Holliday SL, Saklad AR, et al. Neuropsychiatric syndromes in lupus: prevalence using standardized definitions. Neurology. 2002; 58(8): 1214-1220.
6) Stahl HD, Ettlin TH, Plohmann A, et al. Central nervous system lupus: concomitant occurrence of myelopathy and cognitive dysfunction. Clin Rheumatol. 1994; 13(2): 273-279.
7) Mikdashi J, Handwerger B, Langenberg P, Miller M, Kittner S. Baseline disease activity, hyperlipidemia, and hypertension are predictive factors for ischemic stroke and stroke severity in systemic lupus erythematosus. Stroke. 2007; 38(2): 281-285.
8) van Dam AP. Diagnosis and pathogenesis of CNS lupus. Rheumatol Int. 1991; 11(1): 1-11.
9) Szmyrka M. (Central nervous system involvement in systemic lupus erythematosus - diagnosis and therapy). Wiad Lek. 2017; 70(4): 790-797. Polish.
10) de Amorim LC, Maia FM, Rodrigues CE. Stroke in systemic lupus erythematosus and antiphospholipid syndrome: risk factors, clinical manifestations, neuroimaging, and treatment. Lupus. 2017; 26(5): 529-536.
11) Petri M, Perez-Gutthann S, Spence D, Hochberg MC. Risk factors for coronary artery disease in patients with systemic lupus erythematosus. Am J Med. 1992;93(5):513-519.
12) Szekanecz E, András C, Sándor Z, et al. Malignancies and soluble tumor antigens in rheumatic diseases. Autoimmun Rev. 2006; 6(1): 42-47.
13) Eisenlohr LC, Rothstein JL. Oncogenic inflammation and autoimmune disease. Autoimmun Rev. 2006; 6(2): 107-114.
14) Ghia P, Scielzo C, Frenquelli M, Muzio M, Caligaris-Cappio F. From normal to clonal B cells: Chronic lymphocytic leukemia (CLL) at the crossroad between neoplasia and autoimmunity. Autoimmun Rev. 2007; 7(2): 127-131.
15) Szekanecz E, Szamosi S, Gergely L, Keszthelyi P, Szekanecz Z, Szucs G. Incidence of lymphoma in systemic sclerosis: a retrospective analysis of 218 Hungarian patients with systemic sclerosis. Clin Rheumatol. 2008; 27(9): 1163-1166.
16) Szekanecz E, Szucs G, Szekanecz Z, et al. Tumor-associated antigens in systemic sclerosis and systemic lupus erythematosus: associations with organ manifestations, immunolaboratory markers and disease activity indices. J Autoimmun. 2008; 31(4): 372-376.
17) Sanna G, Bertolaccini ML, Mathieu A. Central nervous system lupus: a clinical approach to therapy. Lupus. 2003;1 2(12): 935-942.

Author contributions
Conceptualization:
Yu Shen (YS), Lijun Xu (Lj X)
Supervision:
Lijun Xu
Writing-original draft:
Yu Shen
Writing-review & editing:
Yu Shen ,Qian Cao (QC), Lijun Xu

Corresponding Author:
Professor Lijun Xu
Department of Neurology, The Second Affiliated Hospital of Nanchang University, No.1, Minde Road
Nanchang, Jiangxi, China
Email:xulijun20050901@sina.com
(China)