


# Intravenous thrombolysis in SLE-related stroke: a case report and literature review

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Received: 11 May 2017 / Accepted: 12 October 2017  
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**Abstract** Patients with systemic lupus erythematosus (SLE) bear an increased risk of ischemic stroke. However, evidences for treating acute stroke due to artery thrombosis in SLE patients are extremely limited. A 45-year-old woman experienced sudden left hemiplegia. She was transported to the emergency department of our hospital 2 hours after the initial symptom. According to the medical records, the patient was diagnosed with SLE at the age of 28. CT scanned 150 min after the initial symptom showed no evidence of acute changes or hemorrhage. Magnetic resonance angiography (MRA) revealed occlusion of the right proximal middle cerebral artery (MCA). Ischemic stroke was diagnosed and NIHSS scored 11. The occluded MCA was successfully recanalized with intravenous rtPA. Sequent vascular imaging and serological results indicated that the etiology of the occlusion in right MCA was SLE vasculitis. The patient attained a mRS of 3 at the 3-month follow-up. The case is the first one in the literature that acute ischemic stroke related to SLE vasculitis was treated successfully with intravenous rtPA thrombolysis. The feasibility of intravenous thrombolysis for stroke related to SLE warrant further study.

**Keywords** Thrombolysis · Stroke · Systemic lupus erythematosus · Vasculitis

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Systemic lupus erythematosus (SLE) is an important etiology of ischemic stroke, especially in young patients [1]. Inflammation-induced endothelial injury and subsequent thrombosis have been regarded as the remaining pathogenesis for SLE-related stroke [2]. However, experiences for treating acute stroke due to artery thrombosis in SLE patients are very limited. To our knowledge, only three cases of SLE-related stroke being treated with intravenous rtPA have been reported [3–5]. Here, we present a case of acute ischemic stroke due to right middle cerebral artery (MCA) occlusion in a 45-year-old woman with previous history of SLE. The occluded right MCA was successfully recanalized after intravenous administration of rtPA. We then reviewed the literatures concerning the intravenous thrombolysis and endovascular treatment of ischemic stroke related to SLE.

## Case report

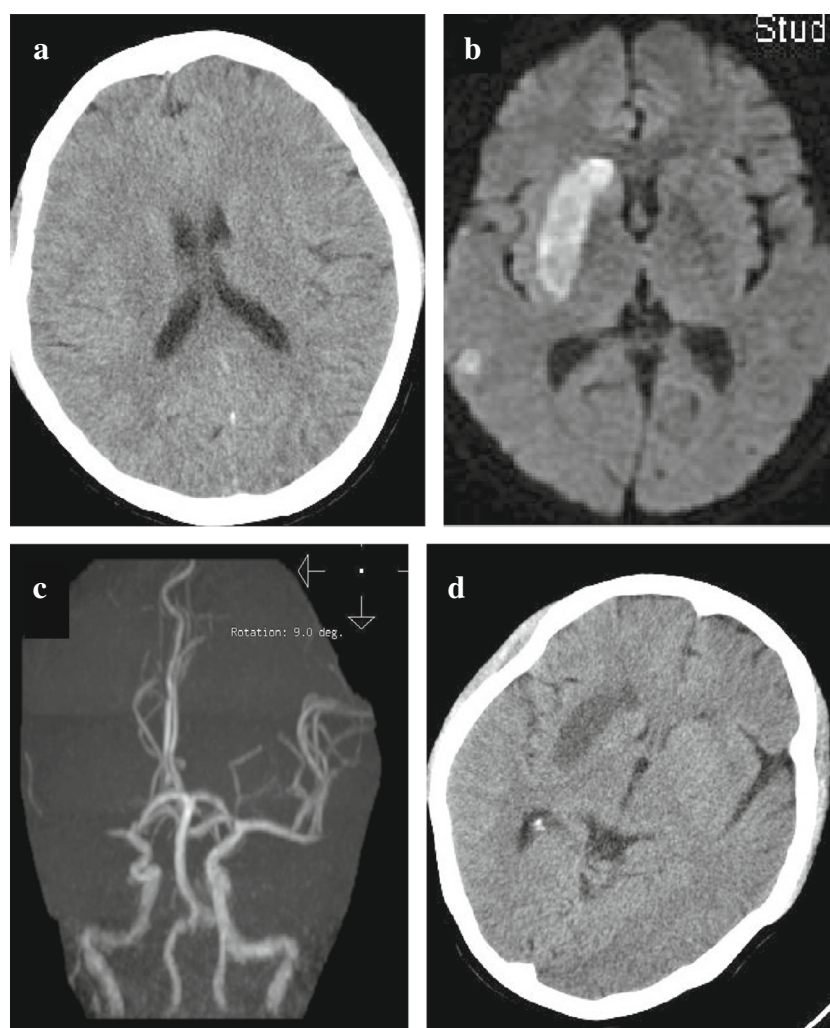
A 45-year-old female experienced sudden left hemiplegia. She was transported to the emergency department of our hospital 2 hours after the initial symptom. According to the medical records, the patient was diagnosed with SLE at the age of 28. She had experienced mild to moderate fever for 12 days. She was currently on prednisone 10 mg/day and azathioprine 50 mg/day. She had no history of seizure, illicit drug use, or oral contraceptive use. On admission, the patient was alert and oriented. The axillary temperature was 37.4 °C. The blood pressure was 154/94 mmHg, and pulse 111 beats per minute. Overt left central facial palsy and left hemiplegia were observed during physical examination. National Institute of Health Stroke Scale (NIHSS) scored 11. Routine blood test revealed that the white blood cell count was  $15.3 \times 10^9/L$ , with 76% as neutrophils. There was mild hypoferric anemia (hemoglobin as 95.2 g/L). Serum CRP level ( $> 120.0$  mg/L)

increased remarkably. Serum fibrinogen (4.16 g/L) and D-dimer levels (2.0 mg/L) also increased. Both platelet count and routine coagulation parameters were normal. The capillary blood glucose level was 6.83 mmol/L. The renal function was normal, as were blood levels of other electrolytes, calcium, magnesium, and cholesterol, and results of hepatic function tests.

Non-contrast computed tomography (CT) scanned 150 min after the initial symptom showed no evidence of acute changes or hemorrhage (Fig. 1a). Acute ischemic stroke was then diagnosed. Intravenous rtPA (0.9 mg/kg, 5.5 mg as bolus followed by 49.5 mg as infusion) was initiated 195 min after the stroke onset. Magnetic resonance imaging (MRI), scanned 200 min after the stroke

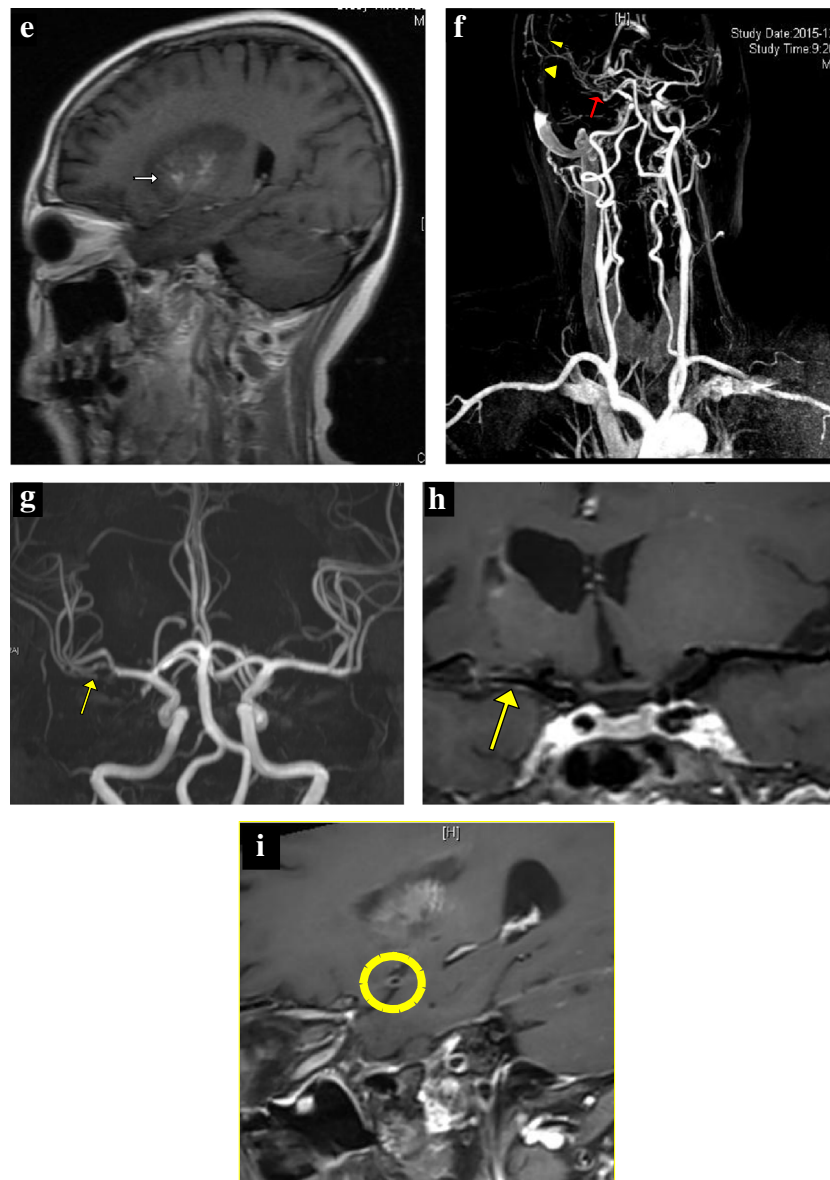
onset, revealed abnormal signals in right basal ganglia and temporal lobe. Magnetic resonance angiography (MRA) revealed occlusion of the right proximal MCA, (Fig. 1b, c). The volume of the diffusion abnormality was less than 25 mL, and therefore the patient was likely to benefit from endovascular thrombectomy, but the patient refused it after receiving adequate information.

Sixty minutes after the bolus of rtPA, the strength of left extremities improved gradually. Twenty-four hours later, her NIHSS score was 7. She did not have any complications post thrombolysis. A repeated CT, scanned 24 h after rtPA thrombolysis, showed acute infarction in right basal ganglia (Fig. 1d). Contrast-enhanced MR (CE-MR) showed partial enhancement in the infarction core (Fig. 1e). CE-MRA revealed



**Fig. 1** **a** Axial CT image before thrombolysis showed no evidence of early changes or hemorrhage; **b** and **c** MRI after the bolus of rtPA, DWI showed acute infarction in the territory of right MCA; MRA revealed occlusion of proximal right MCA; **d** Axial CT scanned 24 h after thrombolysis shows acute infarction; **e** and **f** Contrast-enhanced MR 24 h after thrombolysis revealed partial reinforcement in the infarction area (white arrow); MRA shows an abrupt drop off of signal in the right

MCA (red arrow) with an inhomogenous distribution of blood distally (yellow arrowheads), which indicated vasculitis as the etiology of the stroke; **g**, **h**, and **i** High-resolution, black-blood MRI after gadolinium injection scanned at 3-month follow-up demonstrating a strong, smooth, and concentric vessel wall enhancement in right MCA (yellow arrow and yellow circle)



**Fig. 1** continued.

recanalization of right MCA and partially recovered distal blood flow (Fig. 1f). The stenosis in right MCA as shown in MRA suggested that the etiology of the occlusion was vasculitis.

After intravenous rtPA treatment, the patient underwent further examinations to determine the etiology of the stroke. The results of carotid and vertebral ultrasound scan, transesophageal ECHO, ECG Holter were unremarkable. Blood test showed normal levels of serum protein C, protein S, factor V Leiden, antithrombin III, homocysteine, and antiphospholipid antibodies. Of noted, ANA, anti-SSA levels increased in both serum and cerebrospinal fluid (CSF), but serum C1q (102 mg/L), C3 (0.83 g/L), C4 (0.06 g/L), and immunoglobulin M (0.31 g/L) levels decreased. Erythrocyte sedimentation rate (ESR)

increased remarkably (83 mm/h). CSF was colorless, with a total protein level of 670 mg/L, and elevated immunoglobulin G (0.1 g/L). According to criteria by the American College of Rheumatology [6], stroke related to SLE was diagnosed. We consulted the immunologist. Thereafter, the patient started a treatment with intravenous 1 g methylprednisolone daily for 3 days followed by 60 mg prednisone daily, cyclophosphamide (1 g/day), and lifelong oral warfarin anticoagulation with regular INR monitoring (target 2–3).

At the 3-month follow-up, strength in left extremities further improved. She could walk independently and move her left arm freely, but she could not take articles with her left hand. mRS scored 3, and there were no further stroke during 90 days after the index stroke.

## Discussion and review of literature

Stroke and transient ischemic attacks (TIA) occurred in 0.5 to 15% of patients with SLE [7]. The related stroke can be attributed to several factors, such as Libman Sacks endocarditis, inflammatory-mediated atherosclerosis, hypercoagulation secondary to anticardiolipin antibodies, and vasculitis [8, 9].

In the present case, ischemic stroke due to right MCA occlusion was evidenced by CT, MRI, and MRA results. A diagnosis of SLE was indicated by elevated serum inflammatory markers, positive lupus serologic results, CSF changes, and abnormal signal of right MCA in CE-MRA images. This diagnosis was further supported by the gradual improvement of the patient after being treated with high-dose glucocorticoid.

The first case of stroke related to SLE-treated with intravenous thrombolysis was reported in 2015 by Loharia and colleagues [3]. A 37-year-old female with acute MCA stroke attained excellent outcome after rtPA thrombolysis (10 mg as IV bolus followed by 80 mg as IV infusion, treatment initiated at 4 h after stroke onset). The patient was subsequently diagnosed with antiphospholipid syndrome (APS) [3]. Recently, Lemarroy et al. [4] reported a case of acute ischemic stroke involving a large territory of the right MCA. This 22-year-old woman also attained good clinical outcome after intravenous rtPA treatment (0.6 mg/kg, treatment started at 150 min after stroke onset), despite concomitant thrombocytopenia and prolonged prothrombin times due to SLE and APS. Successful treatments of these two cases emphasized the need for further evaluating the feasibility of intravenous thrombolysis in stroke patients with SLE, especially in those with secondary APS and/or thrombocytopenia.

Recently, Stadler et al. [10] reported a case of acute ischemic stroke with concomitant APS and thrombocytopenia. This 48-year-old woman was treated successfully with mechanical thrombectomy. The occluded MCA was recanalized using stent-like clot retriever 150 min after symptom onset. She attained favorable outcome after the endovascular procedure.

There is only one case reported in literature concerning the use of rtPA for treating stroke related to SLE vasculitis [5]. A 40-year-old woman with acute ischemic stroke was treated with rtPA (0.9 mg/kg, treatment initiated at 90 min after symptom onset). She had a previous history of SLE with secondary APS. Although there was no hemorrhagic transformation, the patient attained no significant improvement after thrombolysis. Subsequent MRI scan revealed a large infarction in right hemisphere, and the MRA revealed signs of vasculitis [5].

In non-SLE patients, both definite and possible vasculitis can increase the risk of intracranial hemorrhage after intravenous rtPA thrombolysis [11, 12]. CNS vasculitis can result in intracranial hemorrhage by damaging vessel

wall and promoting aneurysm formation. In rare cases, SLE has been associated with changed blood coagulation factors and necrotized vasculitis in cerebral vessels, both of which might be devastating in the presence of rtPA [13].

Given the potential risk of intracranial hemorrhage, the use of thrombolysis in stroke patients with history of CNS vasculitis should be considered with extra caution. In the management of acute ischemic stroke, the benefit of intravenous thrombolysis is crucially time-dependent. On the other hand, early hemorrhagic transformation, either due to reperfusion injury or damage of the blood-brain barrier, is also time-dependent. Time, therefore, should be considered preferentially when making the treatment decisions for these patients. Considering the successful experiences from this case and others reported previously, the feasibility of intravenous thrombolysis for stroke related to SLE warrant further study.

### Compliance with ethical standards

**Conflict of interest** The authors declare that there are no conflicts of interests.

## References

1. Wiseman SJ, Ralston SH, Wardlaw JM (2016) Cerebrovascular disease in rheumatic diseases: a systematic review and meta-analysis. *Stroke* 47:943–950
2. Dhillon PK, Adams MJ (2013) Thrombosis in systemic lupus erythematosus: role of impaired fibrinolysis. *Semin Thromb Hemost* 39:434–440
3. Loharia JJ, Alam JM, Abdelhadi HA et al (2015) Thrombolytic therapy at systemic lupus onset with secondary antiphospholipid syndrome. a rare stroke experience. *Neurosciences (Riyadh)* 20: 55–60
4. Camara-Lemarroy CR, Infante-Valenzuela A, Andrade-Vazquez CJ et al (2016) Successful intravenous thrombolysis in a patient with antiphospholipid syndrome, acute ischemic stroke and severe thrombocytopenia. *Blood Coagul Fibrinolysis* 27:354–356
5. Majdak MR, Vuletić V (2016) Thrombolysis for acute stroke in patient with systemic lupus erythematosus: a case report. *J Neurol Sci* 15:7–8
6. Ad Hoc ACR (1999) Committee on neuropsychiatric lupus nomenclature. The American College of Rheumatology nomenclature and care definitions for neuropsychiatric lupus syndromes. *Arthritis Rheum* 42:599–608
7. Fernández-Nebro A, Rúa-Figueroa Í, López-Longo FJ et al (2015) Cardiovascular events in systemic lupus erythematosus: a nationwide study in Spain from the RELESSER registry. *Medicine (Baltimore)* 94(29):e1183
8. Wick G, Schett G, Amberger A et al (1995) Is atherosclerosis an immunologically mediated disease? *Immunol Today* 16:27–33
9. Kabakov AE, Tertov VV, Saenko VA et al (1992) The atherogenic effect of lupus sera: systemic lupus erythematosus-derived immune complexes stimulate the accumulation of cholesterol in cultured smooth muscle cells from human aorta. *Clin Immunol Immunopathol* 63:214–220

10. Stadler K, Mutzenbach JS, Kalss G et al (2015) Therapeutic challenges after successful thrombectomy in a patient with an antiphospholipid syndrome associated M1-occlusion: a case report. *Interv Neuroradiol* 21:598–602
11. Fattahi P, Sheriff F, Narayanan NS et al (2013) Thrombolysis for acute stroke in patients with vasculitis: case report and literature discussion. *Clin Neurol Neurosurg* 115:351–353
12. Gopalakrishnan S, Cynthia B, Roth Sanford I et al (1997) Unsuspected vasculitis and intracranial hemorrhage following thrombolysis. *Clin Cardiol* 20:84–86
13. Goel D, Reddy SR, Sundaram C et al (2007) Active necrotizing cerebral vasculitis in systemic lupus erythematosus. *Neuropathology* 27: 561–565