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Systemic lupus erythematosus complicated with reversible posterior encephalopathy syndrome: a case report

Dong-Lin Hao[1,*], Yan-Li Yang[2,*], La-Mei Zhou[3], Qiu-Hong Liu[1], Rui Liu[1], Ke Xu[2], Gai-Lian Zhang[2] and Li-Yun Zhang[2]

Abstract

A 28-year-old female patient was hospitalized primarily because of "intermittent fever for 28 days aggravated by systemic rashes, oral ulcer, and edema in both eyelids for 5 days." During treatment, convulsions and loss of consciousness occurred. Magnetic resonance imaging (MRI) of the head revealed an abnormal signal with shadows in the bilateral frontal, parietal, temporal, and occipital lobes; cerebellar hemispheres; and basal nodes, with high signal intensity on T2 weighted imaging (T2WI), on fluid-attenuated inversion-recovery, and of the apparent diffusion coefficient and low signal intensity on T1WI and diffusion weighted imaging. Therefore, the patient was diagnosed with systemic lupus erythematosus (SLE) with reversible posterior encephalopathy syndrome (RPES). Intravenous high-dose methylprednisolone and cyclophosphamide were administered for blood pressure control, which effectively controlled the disease. Therefore, when patients with SLE and hypertension or renal insufficiency or those receiving high-dose methylprednisolone or immunosuppressants suddenly present with neurologic abnormalities, a diagnosis of RPES must be considered, and head MRI is the first choice for diagnosis of this disease. In terms of treatment, the blood pressure should be quickly controlled, and the primary disease should be aggressively treated.

[1]Department of Rheumatism and Clinical Immunology, Suzhou TCM Hospital Affiliated to Nanjing University of Chinese Medicine, Suzhou, China
[2]Department of Rheumatology and Clinical Immunology, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Third Hospital of Shanxi Medical University, Taiyuan, China
[3]Department of Rheumatology and Immunology, Wuxi Hospital of Traditional Chinese Medicine, Wuxi, China

*These authors contributed equally to this study.

Corresponding author:
Li-Yun Zhang, Department of Rheumatology and Clinical Immunology, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Third Hospital of Shanxi Medical University, No. 99 of Longcheng Street, Xiaodian District, Taiyuan 030032, China.
Email: zly1184_drzhang@163.com

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Introduction

Neuropsychiatric systemic lupus erythematosus (SLE) refers to symptoms involving the central, peripheral, and autonomic nervous systems as well as mental symptoms caused by SLE, but other causes need to be excluded.[1–3] Neuropsychiatric SLE can occur in the early, active, and resting stages of lupus. However, the exact pathogenesis of nervous system damage caused by SLE remains unclear. Antibody-mediated direct injury to the nerve cells and antibody-induced abnormal blood dynamics may comprise the two main types of pathogenesis. Reversible posterior encephalopathy syndrome (RPES) is a neurological disease that primarily involves the posterior white matter of the cerebral hemisphere and exhibits clinical and imaging abnormalities. It is possible to completely recover from RPES in a short time.[4–6] The present study reports a case of SLE complicated by RPES. The results of this study will provide guidance for the management of SLE with RPES in clinical practice. The reporting of this study conforms to the CAse REports (CARE) guidelines.[7]

Case presentation

A 28-year-old female patient was admitted to the hospital on 8 June 2014, primarily because of "intermittent fever for 28 days aggravated by systemic rashes, oral ulcer, and edema in both eyelids for 5 days." The patient developed an intermittent fever on the fourth day after delivery in May 2014, with a highest body temperature of 39.0°C, but had no chills, cough, expectoration, fatigue, or night sweating. The patient visited a local hospital for treatment, where she received antibiotic treatment (details unknown), but the outcome was poor. Five days before admission, the patient was suffering from an intermittent fever; a cough that produced sticky white phlegm; a red rash without itching that was distributed over her face, the front of her neck, and all four limbs; an oral ulcer that caused obvious pain and restricted her ability to open her mouth; and edema in both eyelids, with no edema in the lower extremities. The patient was treated at another hospital for suspected SLE and was admitted to the Department of Rheumatism and Immunology at our hospital for further diagnosis and treatment. A physical examination at admission showed the following: body temperature, 36.8°C; pulse, 110 beats per minute (bpm); respiration, 18 bpm; blood pressure, 107/79 mmHg; and oxygen saturation, 97%. The patient was conscious but exhibited slow responses and limited speech. A red rash was observed on her face, the front of her neck, and all four of her limbs. Dermohemia was observed in the extremities of both hands and feet, which did not fade under pressure. Both eyelids were swollen. Breathing sounds were weak in both lower lungs, with no dry or wet rales. Her heart rate was 110 bpm with a regular cardiac rhythm. There was no tenderness in the abdomen; sifting dullness, joint

tenderness, and neck rigidity were negative (−); and the bilateral Babinski signs were positive on one side and negative on the other side. In addition, pitting edema was found in the four extremities and the lower legs.

Auxiliary examination

Routine blood tests showed the following: white blood cell (WBC) count, 1.4×10^9/L; hemoglobin, 89.9 g/L; and platelet (PLT) count, 88.5×10^9/L. Routine urine tests showed the following: pH, 1.015; blood in urine, 3+; urine protein, 3+; erythrocyte sedimentation rate, 70 mm/hour; and C-reactive protein, 3.06 mg/L. Kidney function tests showed the following: blood urea nitrogen, 12.4 mmol/L; serum creatinine, 124.6 μmol/L; serum albumin, 20.9 g/L; immunoglobulin A, 1.34 g/L; immunoglobulin G, 19.10 g/L; immunoglobulin M, 1.29 g/L; compliment C3, 0.18 g/L; and compliment C4, 0.13 g/L. Antibody tests showed the following: antinuclear antibody: (+) 1:1280, homogeneous type; anti-ds-DNA antibody: (+) 1:160; anti-histone antibody: 183.64 relative units (RU)/mL; anti-nucleosome antibody: 339.34 RU/mL; perinuclear anti-neutrophil cytoplasmic antibodies: (+) 1:40; extractable nuclear antigen antibodies: anti-Smith antibody (+); and anti-histones, anti-SSA/Ro60, and anti-ds-DNA antibodies were weakly positive. Computed tomography of the head revealed suspected low-density foci in the right parietal lobe.

Course of diagnosis and treatment

Methylprednisolone was given after admission at a dose of 80 mg two times a day for 5 days and 80 mg once per day for 1 day; meropenem was given for anti-infection treatment, and r-globulin was given at 20 g/day for 5 days. The patient's temperature returned to normal, and the rash faded. However, the cough and expectoration continued to occur intermittently, and the WBC and PLT counts increased. Six days after admission, the patient experienced sudden systemic convulsions, loss of consciousness, cyanosis, upturned eyes, trismus, foaming at the mouth, and urinary incontinence. She was sedated, treated for dehydration, and given antiepileptic medication and corticosteroids (methylprednisolone, 160 mg/day). The patient experienced a fever and rapid heart rate. These symptoms were not reduced after symptomatic treatment, and seizure recurred. The patient was transferred to the intensive care unit, given corticosteroids (methylprednisolone, 160 mg/day) for inflammation, sedated, and given antiepileptic, antipyretic, and acid suppression medications, and her electrolyte disorder was corrected. After the patient regained consciousness, she was returned to our department for treatment of the primary disease.

Twelve days after admission, the patient again presented with a loss of consciousness. Magnetic resonance imaging (MRI) of the head revealed the following: abnormal signal with shadows in the bilateral frontal, parietal, temporal, and occipital lobes; cerebellar hemispheres; and basal ganglia (Figure 1). The cerebrospinal fluid showed elevated protein levels. Therefore, epilepsy and posterior cerebral encephalopathy syndrome were considered. The following medications were given: methylprednisolone, 1000 mg once per day for 3 days; dexamethasone, 20 mg and 10 mg (intrathecal injection); and prednisone tablets, 60 mg in the morning. Immunosuppressive agents were given, including hydroxychloroquine sulfate, 0.2 g two times a day; cyclophosphamide, 0.4 g per week as needed; and r-globulin, 20 g once per day for 5 days. Symptomatic and supportive therapies were also given, including treatment for dehydration, antiepileptic medication, therapies to protect

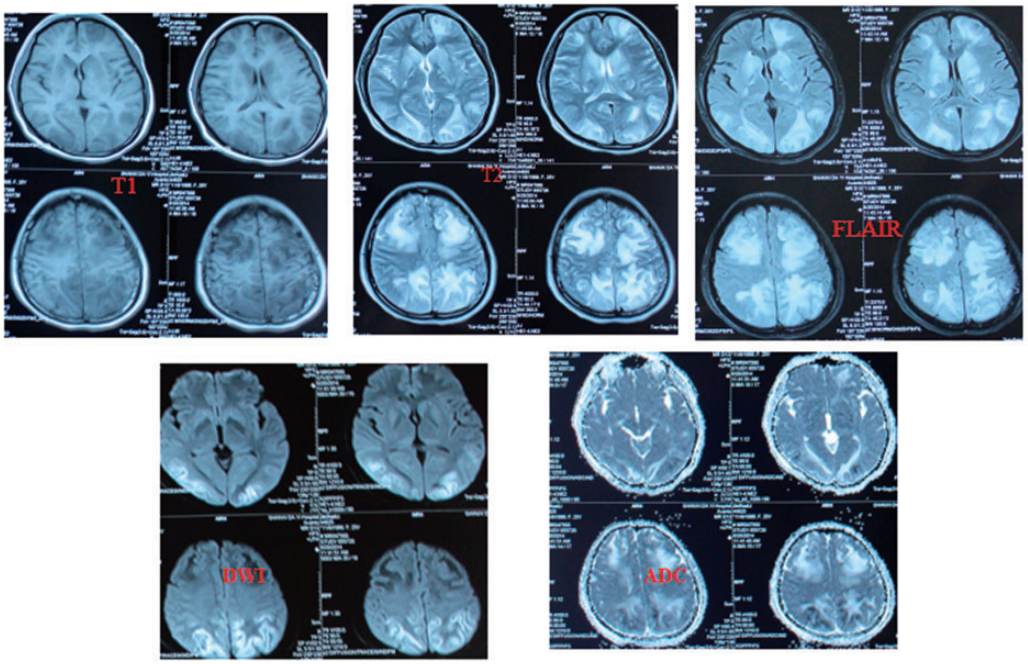

Figure 1. Magnetic resonance imaging results obtained on 20 June 2014. a. T1-weighted image. b. T2-weighted image. c. fluid-attenuated inversion recovery image. d. diffusion-weighted image. e. apparent diffusion coefficient

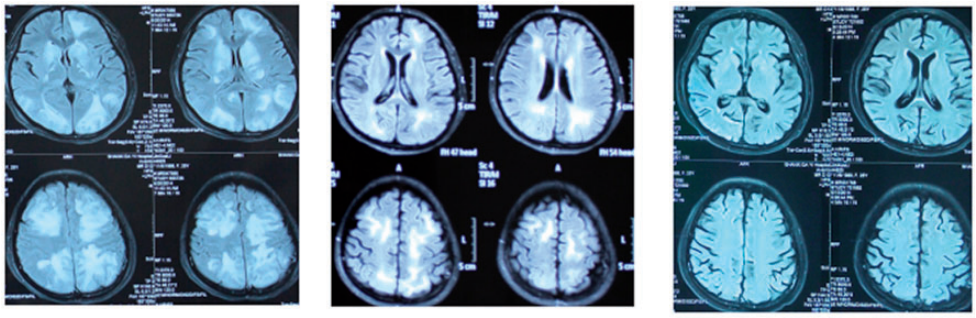

Figure 2. Comparison of magnetic resonance imaging results before and after treatment. a. fluid-attenuated inversion recovery (FLAIR) image obtained on 20 June 2014. b. FLAIR image obtained on 2 July 2014. c. FLAIR image obtained on 15 August 2014

brain cells, blood pressure-lowering medications, potassium and sodium supplements, and diuretics. The patient regained consciousness, and her condition improved. The patient was then discharged from the hospital. On 15 August, MRI of the head revealed that the lesions had mostly been absorbed (Figure 2).

The patient has been monitored until the present day. She is currently taking prednisone tablets (5 mg orally), hydroxychloroquine (0.3 g once per day), and mycophenolate mofetil (0.75 g once per day). Her condition is stable.

Discussion

The present study reports a case of SLE complicated by RPES. During treatment, intravenous high-dose methylprednisolone and cyclophosphamide were used for blood pressure control, which effectively controlled the disease.

The American College of Rheumatology classification of neuropsychiatric SLE identifies 12 types of central nervous system SLE including aseptic meningitis, cerebrovascular disease, demyelinating syndrome, headache (migraine and high benign intracranial pressure), dyskinesia (chorea), myeleterosis, epileptic seizure, acute confusional, anxiety, cognitive impairment, emotional disorder, and psychoses.

The patient was a young female with a 30-day medical history, multiple system involvement, and various positive autoantibodies. On the basis of the disease characteristics and the auxiliary examination, a diagnosis of SLE was clear, and the disease primarily involved the blood, kidneys, skin, and mucous membranes. The SLE disease activity index score was 15, and the disease was in the highly active stage. The treatments administered after admission included methylprednisolone, 160 mg/day; cyclophosphamide, two doses of 400 mg (12 and 16 days after admission); and r-globulin, 20 g for 5 days. The rash faded, the leukocyte and PLT counts increased to normal levels, and the patient's condition improved. However, the patient experienced nervous system symptoms during the treatment, and it was considered that the lupus encephalopathy may not be consistent with the disease activity. Twelve days after admission, a head MRI revealed abnormal signal with shadows in the bilateral frontal, parietal, temporal, and occipital lobes; cerebellar hemispheres; and basal ganglia (irreversible). Therefore, lupus encephalopathy, epilepsy, and cerebral posterior encephalopathy syndrome were considered.

RPES is a type of neurological disease that primarily involves the posterior white matter of the cerebral hemisphere, with clinical and imaging abnormalities, and patients can completely recover within a short time.[8,9] Patients presenting with RPES generally present with serious basic diseases, and most exhibit nervous system symptoms during the course of treatment of these basic diseases. If a timely diagnosis is made and treatment is started immediately, patients quickly return to normal status.[10,11] However, delayed diagnosis and treatment may lead to permanent brain function damage. The common causes of RPES are thought to include hypertension, eclampsia or preeclampsia, immunosuppressive agents, cytotoxic drugs (e.g., cyclosporine A and tacrolimus FK506), and chronic renal failure.[12,13] Rare causes include connective tissue disease, thrombocytopenic purpura, and organ transplantation. Because the symptoms, signs, and neurological imaging changes of RPES are similar to those of probable posterior encephalopathy, RPES does not specifically refer to an independent disease. The clinical manifestations of RPES are usually acute or exhibit subacute onset. The most common neurological symptoms include headache, epileptic seizures, disturbance of consciousness, and visual abnormalities (vision loss is the most common symptom). Seizures are usually the first clinical symptom, and attacks often consist of systemic tonic-clonic episodes. In addition, visual precursors or visual hallucinations often occur before seizures, which are consistent with occipital

lobe seizures. Most patients experience repeated seizures but rarely develop status epilepticus and exhibit acute elevated blood pressure, hypomagnesemia, hypocholesterolemia, and metabolic disorders. The fundus examination and pupillary light reflex are usually normal. The cerebrospinal fluid examination is most often normal but may present with a slight increase in protein.

The imaging findings of RPES are particularly characteristic, and MRI is the first choice for diagnosing this disease. In typical cases, diffuse brain edema can be observed in the subcortex of the posterior parietal and occipital lobes of both cerebral hemispheres, showing symmetrical or asymmetrical high signals on T2 weighted imaging (T2WI) and low signals on T1WI; the fluid-attenuated inversion recovery (FLAIR) sequence also reveals obviously high signals; diffusion-weighted imaging (DWI) reveals an equal signal or low signal changes; the apparent diffusion coefficient (ADC) value is higher than that of normal white matter; the lesions primarily involve the white matter but may also affect the gray matter; the gray matter can sometimes be extensively involved; and the frontal and temporal lobes, brain stem, cerebellum, and basal ganglia can be involved in atypical cases. However, the occipital lobe adjacent to the midline and cortex of the calcarine fissure is generally not involved. The most significant feature of RPES is that the symptoms, signs, and imaging abnormalities can rapidly be reversed if patients are diagnosed quickly and immediately receive treatment, allowing most patients to fully recover. The brain MRI of the patient (Figure 1) showed multiple patchy low signals on T1WI, high signals on T2WI, FLAIR, and DWI images, and low signal on ADC images of the bilateral parietal lobe and basal ganglia, which are consistent with the brain MRI findings of a patient with RPES.

Patients with SLE-RPES often exhibit a sharp increase in blood pressure, renal insufficiency, and humoral retention, especially when high-dose methylprednisolone or immunosuppressants are used during the treatment of serious conditions. Therefore, some scholars have considered that the interaction of the above factors comprises the pathogenic process of SLE-RPES.[12] However, the autoimmune inflammation or ischemic changes caused by SLE (e.g., vasculitis, thrombus, embolism, and vasospasm) may lead to vascular endothelial dysfunction and cause RPES. Other scholars have proposed that RPES should be interpreted as a secondary complication of SLE during treatment rather than being directly caused by the underlying lesion of SLE itself.[13] In the present case, autoimmune-mediated vascular injury secondary to lupus activity may also have caused RPES, but immunosuppressive agents were not associated with the onset of RPES because high doses of methylprednisolone or cyclophosphamide and mycophenolate mofetil were not used at the time of onset. Although removal of the immunosuppressant was beneficial to the recovery from RPES, intravenous methylprednisolone and cyclophosphamide were administered, which effectively controlled the condition because lupus activity was present in the patient. This finding is consistent with the results reported by Mak et al.,[14] which revealed that when RPES is caused by the use of corticosteroids and immunosuppressive agents, their administration needs to be stopped immediately. However, intravenous methylprednisolone and cyclophosphamide are still the most commonly used treatments for patients with lupus activity, and RPES may be a sign of lupus activity.

In summary, RPES cannot be excluded in clinical practice when patients with SLE exhibit hypertension or renal insufficiency or receive high-dose methylprednisolone or immunosuppressants and exhibit sudden nervous system abnormalities.

Head MRI is the first choice for the diagnosis of this disease. In terms of treatment, the blood pressure should be quickly controlled, and the primary disease should be aggressively treated. When necessary, a large dose of corticosteroid and r-globulin should be given to prevent the development of the disease and improve the prognosis.

Ethics statement

This study was approved by the Ethics Committee of Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences. Written informed consent was obtained from the patient.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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ORCID iD

Li-Yun Zhang https://orcid.org/0000-0001-5882-2179

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