We report two cases of systemic lupus erythematosus with central nervous system involvement. Both cases presented as posterior reversible encephalopathy syndrome, which were depicted as vasogenic edema predominantly within the territories of the posterior circulation. The second patient suffered from additional subarachnoid hemorrhage a few days later. The incidence, imaging features, and mechanisms of the diseases are discussed.

**Key words:** Brain, hemorrhage; Lupus erythematosus; Posterior reversible encephalopathy

Central nervous system (CNS) involvement occurs in 14%-75% of patients with systemic lupus erythematosus (SLE) [1]. The reported CNS manifestations of SLE include brain infarctions, vasogenic edema in the posterior circulation territory caused by acute hypertension, cerebral hemorrhage caused by acute hypertension, calcinosis of the brain, and transverse myelitis [1, 2]. Recently, a few papers preferred to use the term posterior reversible encephalopathy syndrome (PRES), instead of hypertensive encephalopathy, to describe the vasogenic edema in the posterior circulation area [1, 3-5], since hypertension is not a necessary causative factor. The cause of PRES is deemed multifactorial, involving a brain capillary leak related to hypertension, fluid retention, and possibly the cytototoxic effects of immunosuppressive agents on the vascular endothelium [3, 7, 8]. The postulated mechanisms for PRES to occur in a patient with SLE include vasculopathy of small vessels [1], and increase of vasopermeability [5].

Subarachnoid hemorrhage (SAH) has a higher incidence in SLE patients than previously assumed. Many patients had active SLE and lacked an apparent cause of SAH, other than SLE [6]. We report here two cases of SLE with CNS involvement. Both cases presented as PRES. The second patient suffered additional SAH a few days later. The reported incidence, imaging features, and mechanisms of both findings are discussed.

**CASE REPORT**

Case 1: A 23-year-old female patient had 3 years history of SLE with lupus nephritis. She experienced acute, severe headache and blurred vision that forced her to rest in the bedroom for one day, before she was found unconscious with swelling and bleeding of her lips, one lower limb twitching, lying in the bed. Incoherent speech was found during her admission. Physical examination showed unremarkable findings. Her blood pressure was 126/84 mmHg on admission.
Neurological examination revealed lethargy of conscious level. Her language function could not be checked. Cranial nerves were normal. Muscle power was grade 4 in her right arm and leg while deep tendon reflexes were normal. The gait condition could not be checked. Laboratory data showed IgG 2130 mg/dL, ESR 39 mm/hr, and bleeding time >10 min. MRI with diffusion weighted image (DWI) and ADC mapping was performed. Axial T2-weighted image and FLAIR image showed multiple lesions with hyperintensity involving cortex and subcortical white matter of bilateral occipital lobes (i.e. involving predominantly the territories of the posterior circulation) (Fig. 1a). Axial DWI (diffusion sensitivity of b = 1000 s/mm$^2$) showed no evidence of diffusion restriction in the lesions (no significant hyperintensity on the DWI, and no hypointensity on the ADC maps). The findings are consistent with vasogenic edema, rather than ischemia or infarctions (Fig. 1b). She recovered well with disappearance of almost all the symptoms after regular and dose-controlled steroid treatment, which corrected the situation of poor medical noncompliance before admission. Follow-up MRI study 4 months later showed normal appearance of the brain, with complete resolution of the brain lesions (Fig. 1c). No evidence of hypertension was noted during the follow-up period.

Case 2: A 43-year-old female patient had history of SLE for 12 years with initial presentation of polyarthritis. She was sent to emergency room with the complaint of abdominal cramping pain for 2 days, associated with vomiting and watery diarrhea. Fever, lower legs edema, oral ulcer, malar rash, and signs of heart failure were also noted. Severe headache and blurred vision developed during her admission. Her blood pressure was 130/90 mmHg on admission. Neurological examination showed lethargy of her conscious level. The language function could not be checked. The cranial nerves were normal. Her muscle power was grade 4 in right arm and leg while deep tendon reflexes were normal. The gait condition could not be checked. Laboratory data showed ESR 26 mm/hr, BUN 28.9 mg/dL, and Na 127 meq/L. MRI with DWI and ADC mapping was performed. Axial T2 weighted image and FLAIR image showed symmetrical lesions with hyperintensity involving cortex and subcortical white matter of bilateral occipital lobes (Fig. 2a). Axial DWI (diffusion sensitivity of b = 1000 s/mm$^2$) showed no evidence of diffusion restriction in the lesions. These lesions showed normal or slightly high signal intensity (T2 shine through effect) on the DWI, and showed no hypointensity on the ADC maps, consistent with vasogenic edema, rather than ischemia or infarctions (Fig. 2b). She became irritable and consciousness disturbed 2 days after the MRI study. Non-contrast CT scan showed diffuse SAH, mild intraventricular hemorrhage, and obstructive hydrocephalus caused by blood filling in the 4th ventricle (Fig. 2c). Follow-up digital subtraction angiography (DSA) showed prominent intracranial vasospasm due to SAH. There were multiple segments of narrowed arteries, involving bilateral internal
carotid arteries in their supraclinoid segments, bilateral anterior cerebral arteries in their A1 segments, bilateral posterior cerebral arteries, distal part of right vertebral artery, and the vertebrobasilar junction. There was no evidence of aneurysm, arteriovenous malformation (AVM), or any other vascular malformations (Fig. 2d). The patient remained comatose on life support in the following days of admission, before she was discharged by the request of her family, who asked for transferring her to other hospital. The patient had no evidence of hypertension through the entire course of her admission.

**DISCUSSION**

Vasogenic edema, like other causes of edema, shows bright signal on the T2-weighted images. It causes no diffusion restriction effect because it is not cytotoxic edema. Diffusion-weighted image contains signal intensity caused by both diffusion coefficient and T2 relaxation. Therefore, there is a large T2 component on the diffusion-weighted images. This effect is termed “T2 shine-through” and can be associated with clinical significance, especially when the abnormalities are extremely bright on T2 weighted images. In such instances, an ADC map is helpful to distinguish T2 shine-through effect from true areas of restricted diffusion [7].

Our two cases show the findings of vasogenic edema on MR imaging in the territory of posterior circulation of the brain. This pattern of distribution and the nature of disease are consistent with the reported features of PRES, which may be the result of SLE with CNS involvement.

Before 1996, the various causes of PRES were typically listed under the category of hypertensive
encephalopathy or as separate entities [4]. While many of these patients have hypertension, some have only slight blood pressure elevation. In 1996, the term reversible posterior leukoencephalopathy syndrome was coined by Hinchey et al [3] to include hypertensive encephalopathy and its related conditions. However, as Casey et al [4] pointed out, cortical involvement was seen in 94% of the cases, hence, the term posterior reversible encephalopathy syndrome, i.e. PRES, is more appropriate to describe this cliniconeuoradiologic syndrome.

Studies have shown that vasogenic edema accounts for the changes observed in PRES. A breakdown in cerebral autoregulation results in the leakage of fluid into the cerebral interstitium, which is detected as vasogenic edema [8]. The vasogenic edema in PRES involves predominantly the posterior circulation territories, but in the most severe cases, the anterior circulation can also be involved. An atypical distribution is sometimes seen within the basal ganglia, cerebellum, brain stem, and anterior frontal lobes [10]. When promptly recognized and treated, the majority of the symptoms and radiologic abnormalities can be completely reversed. When unrecognized, the patient’s condition can progress to ischemia, infarction, and death [8]. Diseases and clinical settings associated with PRES include eclampsia, hemolytic uremic syndrome, thrombotic thromocytopenic purpura, uremia, porphyria, cryoglobulinemia, SLE, and polyarteritis nodosa. Other etiologies include antirejection therapy for organ transplantation with cyclosporin A and tacrolimus, chemotherapy for leukemia with cisplatin, interferon alpha, intrathecal methotrexate, and other drugs such as FK506 and high dose corticosteroids [8,11,12].

Aisen et al [13] first reported MR abnormalities in 2 of 8 patients with SLE that showed near-total resolution over the course of several weeks. Sibbitt et al [14] noted that up to 38% (eight of 21 cases) of CNS lesions with SLE were reversible on MR imaging. Moritani et al [1] reported the MR imaging of 20 SLE patients. Among their 9 patients who had lesions on the MR imaging, 4 showed infarction, 2 showed vasogenic edema only, 2 showed combined vasogenic edema and microinfarct, and one showed SAH. The mechanism of vasculopathy in CNS involvement of SLE was attributed to intravascular activation of complement that leads to adhesion between neutrophils and/or platelets and endothelium, resulting in leukothrombosis in the microvasculature [1,15,16]. SLE vasculopathy affects predominantly arterioles and capillaries, resulting in vessel tortuosity, vascular hyalinization, endothelial proliferation, and perivas-

ular inflammation or gliosis [1]. Despite widespread microvascular occlusion, parenchymal damage is slight and usually results only in microinfarct [1].

The preferential distribution of white matter lesions in posterior brain regions is not well understood. Sympathetic nerves from the superior cervical sympathetic ganglia supply the blood vessels of the pia. The density of sympathetic innervation is maximal in the internal carotid and anterior cerebral territories. It decreases in the posterior circulation territory and is the least in the basilar artery and its branches [17].

Our second case unfortunately suffered from SAH during her admission, just 2 days after her MRI examination. Angiography shows multiple areas of vascular narrowing consistent with vasospasm due to SAH. There is no evidence of intracranial aneurysm, AVM, or any other vascular abnormality.

Head injury is the most common cause of SAH although the mechanism and outcome are obviously different from that caused by rupture of a berry (saccular) aneurysm. Other causes of SAH include AVM, intracranial arterial dissection, bleeding diathesis and cortical venous thrombosis [18]. Mimori et al [6] found clinically defined SAH in 10 (3.9%) out of 258 SLE patients, which represented a frequency higher than previously assumed. Five of their patients had active SLE and lacked an apparent cause of SAH, other than SLE. They also reported a high mortality rate (5/5), no visible aneurysm on angiogram (3/4), and an onset during intractable SLE or after discontinued steroid therapy because of medical noncompliance (4/5). Thus, an earlier successful suppression of SLE, if possible, might have prevented their SAH.

**CONCLUSION**

It is important to know the variety of CNS manifestations in patients with SLE. MRI with DWI and ADC mapping is helpful to demonstrate PRES. Hypertension is not a necessary causative factor for either PRES or SAH in a patient with SLE. When promptly recognized and treated, the majority of the symptoms and radiologic abnormalities can be completely reversed. When unrecognized, the patient’s condition can progress to ischemia, infarction, and death [8].

**REFERENCES**

可逆性後方腦症候群與蜘蛛膜下出血，發生於紅斑性狼瘡病人

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我們報告兩例發生中樞神經病徵的紅斑性狼瘡病人。兩個病人都表現出可逆性後方腦症候群，其特徵是源自血管因子的水腫，主要發現於腦部的後循環區域。其中第二個病人還在住院中發生蜘蛛膜下出血。以上這兩種現象在紅斑性狼瘡病人的發生率、影像學特徵，以及可能的發生機轉，我們都加以討論。

關鍵詞：蜘蛛膜下出血；紅斑性狼瘡；可逆性後方腦症候群