

## Case Report

# Reversible Posterior Leukoencephalopathy Caused by Azathioprine in Systemic Lupus Erythematosus

Chingching Foocharoen MD\*,  
Somsak Tiamkao MD\*, Jiraporn Srinakarin MD\*\*,  
Nittaya Chamadol MD\*\*, Kittisak Sawanyawisuth MD\*

\* Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen

\*\* Department of Radiology, Faculty of Medicine, Khon Kaen University, Khon Kaen

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The authors report a case of systemic lupus erythematosus with posterior leukoencephalopathy who presented with headache, tonic-clonic seizure, loss of consciousness and bilateral loss of vision, after taking azathioprine for three weeks. The patient had hypertension with normal eye grounds. The brain CT showed a hypodensity lesion at both bilateral occipital lobes, mainly in the white matter. The symptoms and follow-up MRI were improved after the control of hypertension and discontinuation of azathioprine.

**Keywords:** Systemic lupus erythematosus, Posterior leukoencephalopathy, Azathioprine, White matter lesion, Seizure, Immunosuppressive agent

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Posterior Leuko Encephalopathy (PLE) is a brain disorder that predominantly affects the cerebral white matter. Edematous lesions particularly involve the posterior parietal and occipital lobes, and may spread to basal ganglia, brain stem, and cerebellum. Clinical signs are characterised by headache, nausea and vomiting, seizures, visual disturbances, altered sensorium, often abrupt increase in blood pressure, and occasionally focal neurological deficit<sup>(1)</sup>. PLE is not found frequently and is mostly diagnosed by a clinico-radiological correlation. It was first reported in a human immunodeficiency virus infection patient<sup>(2)</sup>. Then it was reported among patients receiving immunosuppressive drugs such as cyclosporin-A in bone marrow transplanted patient<sup>(3-5)</sup>, 5-fluorouracil for breast cancer<sup>(6)</sup>, or cyclophosphamide and prednisolone for classical polyarteritis nodosa<sup>(7)</sup>. Here, the authors report a patient who developed posterior leukoencephalopathy while on azathioprine therapy.

### Case Report

A 25-year-old woman was diagnosed with SLE

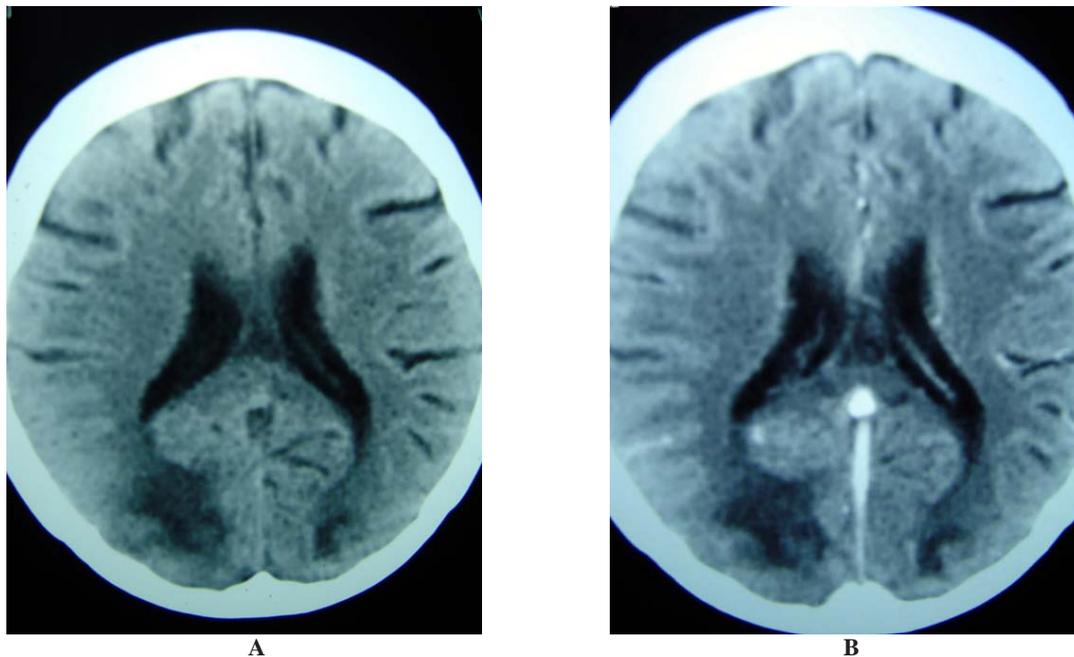
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Correspondence to : Foocharoen C, Division of Allergy-Immunology-Rheumatology, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002 Thailand. E-mail: fching@kku.ac.th

in 1990 as per criteria set by the American Rheumatism Association. Two months before admission, she experienced numbness in the right leg, weakness of ankle dorsiflexion and great toe dorsiflexion bilaterally. Nerve conduction study showed axonal involvement, bilateral demyelination of the sural and superficial peroneal nerves, and abnormal motor conduction velocity in the right common peroneal nerve. The electrodiagnosis indicated a mononeuritis multiplex pattern. The patient received 60 mg prednisolone per day, but still experienced numbness that progressed to the right hand. 50mg azathioprine per day was prescribed and stepped up to 100 mg per day. Two weeks later, she had severe headache with generalized tonic-clonic seizure. After seizure attack, she noticed bilateral loss of vision.

On physical examination, she was drowsy with tachycardia and high blood pressure (198/127 mmHg). Her visual acuity was 20/200 in both eyes with normal fundi and intact cranial nerves. Motor power of upper and lower extremities was grade IV/V and III/V bilaterally. She had decreased sensation from the tip of her toes to the knees. Deep tendon reflexes were 1+, with bilateral Babinski's sign, while other neurological examinations were within normal limits.

Peripheral blood count showed hematocrit 32.8% and normal platelet count. The prothrombin time,



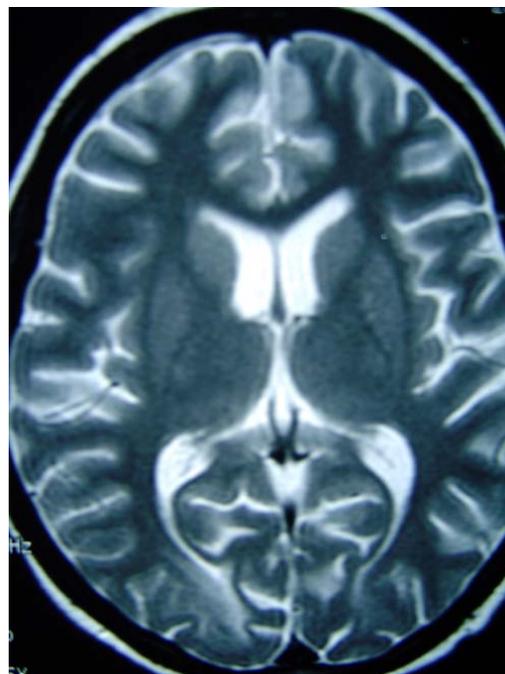
**Fig. 1** A: Pre contrast brain CT revealed bilateral hypodensity lesions at both occipital lobes, mainly in the white matter and extended to the cortex. B: Brain CT showed non-enhanced lesions after contrast injection

activated prothrombin time, blood urea nitrogen, creatinine, electrolytes, and liver function tests were normal. The 24-hrs urine collection revealed heavy proteinuria (2.2 gm).

CT brain scan revealed non-enhanced bilateral hypodensity lesions at both occipital lobes, mainly in the white matter and extended to the cortex without enhancement after contrast media (Fig. 1). Lumbar puncture showed normal opening pressure and normal cerebrospinal fluid analysis. Based on the clinico-radiological correlation, the patient was diagnosed with SLE with lupus nephritis and posterior leuko-encephalopathy. She was then treated with an anti-hypertensive agent and azathioprine was stopped. On the seventh day after admission, her vision had recovered to 20/40 and her blood pressure (before being discharged) was 123/84 mmHg. Follow-up MRI of the brain, (2 weeks later), showed hyposignal intensity in the T2-weighted, which confirmed a marked decrease in the size of the lesion at both occipital lobes (Fig. 2). Patient's visual acuity reached 20/30 and her blood pressure was stabilized at 120/70 mmHg.

### Discussion

Differential diagnosis among SLE patients experiencing headache and sudden bilateral loss of



**Fig. 2** Follow-up MRI of the brain indicated hyposignal intensity in the T2-weighted mode showed a marked decrease in the size of the lesion at both occipital lobes

vision included posterior leukoencephalopathy, anti-phospholipid syndrome with cerebral vasculitis, hypertensive encephalopathy with cerebral infarction, venous thrombosis, hypertensive occipital hemorrhage, or even cerebral vasculitis from SLE. Hypertensive encephalopathy which is a complication of malignant hypertension can make image finding on MRI as posterior leukoencephalopathy<sup>(8)</sup>. However the presented patient did not have a hypertensive encephalopathy condition, because her eye grounds had no evidence of retinal hemorrhage, exudate, or papilledema that are found in hypertensive encephalopathy patients<sup>(9)</sup>.

The most common clinical manifestations of posterior leukoencephalopathy are headache, nausea, vomiting, altered mental status, decreased alertness, cortical blindness and other visual abnormalities and transient motor deficit<sup>(8)</sup>. The most common signs and symptoms are seizures and headache<sup>(3,10)</sup>. The main finding in a neuro-imaging study was posterior white matter edema, symmetrical involvement mostly in the parietal, occipital lobes<sup>(8)</sup> and rarely bilateral thalamic lesions<sup>(6)</sup>. PLE was reported among patients receiving immunosuppressive drugs such as cyclosporin-A in bone marrow transplanted patients<sup>(3-5)</sup>, 5-fluorouracil for breast cancer<sup>(6)</sup>, or cyclophosphamide and prednisolone for classical polyarteritis nodosa<sup>(7)</sup>. Thus, the immunosuppressive drug use, such as cyclosporin A, 5-fluorouracil, cyclophosphamide, or azathioprine played important role in PLE. The mechanism is unclear but probably related to a cytotoxic effect<sup>(8,10,11)</sup>. The presented patient, developed acute hypertension with neurological symptoms, bilateral hypodensity lesion of occipital lobe especially in the white matter, and had a history of taking an immunosuppressive drug (azathioprine) for 2 weeks. Thus, PLE was diagnosed. Neuroimaging can differentiate bilateral infarction of the posterior-cerebral-artery territory and posterior leukoencephalopathy by spars of the calcarine and paramedian occipital lobe structures in the former<sup>(8)</sup>. In the presented patient, imaging study suggested posterior leukoencephalopathy rather than an infarction of the posterior-cerebral-artery. The radiologic findings of PLE can be found in hypertensive encephalopathy<sup>(12)</sup>, eclampsia patient<sup>(13)</sup>, post blood transfusion<sup>(14)</sup>, or cerebral vasculitis. The improvement of clinical symptoms and reversing of the MRI findings after treatment supported the diagnosis of PLE. If the clinical symptoms and imaging study are suggestive of PLE, hypertension should be treated with the discontinuation of the immunosuppressive agent. Most patients can recover from the symptoms so the prognosis is good.

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## References

1. Garg RK. Posterior leukoencephalopathy syndrome. *Postgrad Med J* 2001; 77: 24-8.
2. Lipton RB, Krupp L, Horoupian D, HersHKovitz S, Arezzo JC, Kurtzberg D. Progressive multifocal leukoencephalopathy of the posterior fossa in an AIDS patient: clinical, radiographic and evoked potential findings. *Eur Neurol* 1988; 28: 258-61.
3. Lamy C, Mas JL. Reversible posterior leukoencephalopathy. A new syndrome or a new name for an old syndrome? *Presse Med* 2001; 30: 915-20.
4. Gottrand F, Largilliere C, Farriaux JP. Cyclosporine neurotoxicity. *N Engl J Med* 1991; 324: 1744-5.
5. Jarosz JM, Howlett DC, Cox TC, Bingham JB. Cyclosporine-related reversible posterior leukoencephalopathy: MRI. *Neuroradiology* 1997; 39: 711-5.
6. Yasue M, Ishijima B, Sato J, Mizutani T, Morimatsu Y. A case of toxic leukoencephalopathy induced by 5FU derivatives. *No Shinkei Geka* 1985; 13: 1229-34.
7. Arai M, Shigeno K, Wada M. A reversible posterior leukoencephalopathy syndrome in a patient with classical polyarteritis nodosa. *Rinsho Shinkeigaku*. 1997; 37: 64-6.
8. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al. A reversible posterior leukoencephalopathy syndrome. *N Engl J Med* 1996; 334: 494-500.
9. Williams GH. Hypertensive vascular disease. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL, editors. *Harrison's principle of internal medicine*. Philadelphia: McGraw-Hill; 2001: 1414-29.
10. Teive HA, Brandi IV, Camargo CH, Bittencourt MA, Bonfim CM, Friedrich ML, et al. Reversible posterior leukoencephalopathy syndrome associated with bone marrow transplantation. *Arq Neuropsiquiatr* 2001; 59: 784-9.
11. Primavera A, Audenino D, Mavilio N, Cocito L. Reversible posterior leukoencephalopathy syndrome in systemic lupus and vasculitis. *Am Rheum Dis* 2001; 60: 534-7.
12. Vaughan CJ, Delanty N. Hypertensive emergencies. *Lancet* 2000; 356: 411-7.
13. Donaldson JO. The brain in eclampsia. *Hypertens*

Pregnancy 1994; 13: 115.  
14. Ito Y, Arahata Y, Goto Y, Hirayama M, Nagamutsu M, Yasuda T, et al. Post-transfusion reversible

posterior leukoencephalopathy syndrome with cerebral vasoconstriction. Neurology 1997; 49: 1174-5.

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รายงานผู้ป่วย Systemic Lupus Erythematosus ที่เกิดภาวะ Reversible Posterior Leukoencephalopathy จากยา Azathioprine

ชิงชิง พุเจริญ, สมศักดิ์ เทียมเก่า, จิราภรณ์ ศรีนครินทร์, นิตยา ฉลาด, กิตติศักดิ์ สวรรยาวิสุทธิ

ผู้ป่วยหญิง อายุ 25 ปี เป็น systemic lupus erythematosus มีอาการปวดศีรษะ ชักเกร็งทั้งตัว หมดสติ และตาสองข้างมองไม่เห็นหลังจากได้รับยา azathioprine เป็นเวลา 3 สัปดาห์ ตรวจร่างกายพบความดันโลหิตสูง จอประสาทตาปกติ ภาพรังสีคอมพิวเตอร์สมองพบความผิดปกติที่สมองส่วน occipital ทั้งสองข้างโดยเฉพาะบริเวณเนื้อสมองส่วนขาว ภายหลังจากหยุดยา azathioprine ผู้ป่วยอาการดีขึ้น ระดับความดันโลหิตปกติและผลการตรวจคลื่นแม่เหล็กของสมองอยู่ในเกณฑ์ปกติ