

Case Reports of Transient Loss of Vision and Systemic Lupus Erythematosus

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Abstract

Introduction: Neuropsychiatric manifestations can occur in up to two-thirds of patients with systemic lupus erythematosus (SLE). The presentations as well as the underlying immunopathogenic mechanisms can be heterogeneous and therefore have an enormous impact on therapeutic options. **Clinical Picture:** We describe 2 patients who presented similarly with acute onset binocular reversible visual loss. The first patient had anti-phospholipid syndrome and optic neuritis, while the second patient suffered from posterior reversible leukoencephalopathy syndrome. **Treatment:** Patient one was treated with anti-coagulation and immunosuppression while the second patient required the withdrawal of immunosuppression and supportive therapy. **Outcome:** Both patients responded favourably and had complete visual recovery. **Conclusions:** Different management strategies have to be employed for similar presentations having different aetiologies, underscoring the need for constant clinical vigilance.

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Introduction

In 1999, the American College of Rheumatology (ACR) research committee defined 19 specific neuropsychiatric systemic lupus erythematosus (SLE) syndromes to achieve a consensus in defining this broad disease spectrum which accounts for 4% to 16% of SLE mortality and may affect as many as 90% of SLE patients.¹ They can occur singly or in combination, and may co-exist with non-SLE-related neurological complications.

The immunopathogenic mechanisms responsible for neurologic symptoms in SLE can be classified as primary (resulting directly from immune mediated injury to the nervous system) or secondary (related to SLE complications or treatment). However, a specific neurological feature can often be attributed to a combination of both mechanisms.

Acute onset transient visual loss in SLE patients illustrates the complex and multifactorial nature of SLE. Acute reversible visual loss in association with the anti-phospholipid syndrome is well known.^{2,3} More recently, this phenomenon has been described in association with posterior reversible leukoencephalopathy (PRES), a clinicoradiologic entity characterised by altered mental

status, seizures and visual deficits associated with reversible changes on magnetic resonance imaging (MRI) of the brain.⁴

We describe 2 SLE patients presenting to our institution in the last 4 months with acute onset transient binocular visual loss, the first associated with secondary anti-phospholipid syndrome (APS) and optic neuritis, the other associated with PRES. Different management strategies were employed for these similar neurologic features which had differing aetiology; both responded favourably and had complete visual recovery.

Case 1

A 26-year-old Filipino female presented in June 2006 with acute onset bilateral visual loss while doing housework. She reported being unwell for 1 week with fever and sore throat. Her past medical history was significant with recurrent fever, arthralgia, rash, weight loss and amenorrhoea for 6 months since coming to Singapore to work as a domestic helper.

At presentation she was confused, lethargic, febrile, had a temperature of 38.8°C, was tachycardic with a heart rate

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Fig. 1. Retinal photograph showing optic disc swelling and multiple cotton wool spots.

of 130 beats/min and hypotensive with blood pressure of 100/60 mm Hg. She had a malar rash and post-inflammatory pigmentation of the small joints of both hands. Her neck was supple. Although her pupils were reactive to light, visual acuity was zero and she was unable to perceive light. She had enlarged tonsils with extensive cervical lymphadenopathy. Respiratory, cardiovascular and abdominal examination was unremarkable.

Investigations revealed a total white blood cell count of $3.67 \times 10^9/L$ (3.3-9.6) with relative lymphopaenia (lymphocytes 5.6%), platelets $126 \times 10^9/L$ (162-427) and haemoglobin 11.1 g/dL (10.7-14.9). Serum sodium was 117 mmol/L (135-150), potassium 4.7 mmol/L (3.5-5.0) and chloride 89 mmol/L (98-107). Erythrocyte sedimentation rate was raised at 77 mm/h (3-9), C-reactive protein (CRP) was normal <5 mg/L, serum albumin 30 g/L (38-48) and prothrombin time (PT) was normal 13.2 s (12-14.8). Liver enzymes were raised and were more than twice the limit of the upper range of normal.

She was dehydrated and intravenous fluids were administered. Computed tomography (CT) scan of her brain was normal as was cerebrospinal fluid analysis. Ophthalmologic evaluation showed evidence of retinal vasculitis, multiple cotton wool spots and optic disc swelling (Fig. 1). She was treated as a lupus flare likely precipitated by infection.

Her confusion improved as did her fever, and her vision reverted to normal within 12 hours of initiation of intravenous steroids and antibiotics. Blood cultures grew *Salmonella enteritidis*, confirming the earlier impression of infection precipitating the flare. Further investigations showed positive anti-double-stranded DNA (anti-dsDNA) antibodies, hypocomplementaemia and the presence of lupus anti-coagulant and raised anti-cardiolipin IgG antibodies. She was anti-coagulated and hydroxychloroquine was added.

MRI and magnetic resonance angiography (MRA) were normal with no evidence of ischaemia or vasculitis. There was no recurrence of symptoms and a repeat ophthalmological examination 3 days later showed significant resolution of disc swelling. The dose of warfarin was adjusted to

achieve a target International Normalised Ratio (INR) of 2 to 2.5 in view of secondary anti-phospholipid syndrome (presence of ischaemic retinopathy and positive anti-cardiolipin antibodies and lupus anti-coagulant). She was discharged completely well and returned to the Philippines for further treatment.

Case 2

A 27-year-old Indonesian female, recently diagnosed with SLE, presented in September 2006 with acute onset bilateral visual loss while doing housework. She had been admitted 6 months earlier with severe anaemia secondary to autoimmune haemolytic anaemia which responded completely to steroids but recurred within a month of the discontinuation of steroids. A rheumatological opinion was sought when she reported new onset photosensitivity and arthralgia and anti-nuclear antibodies were strongly positive. The diagnosis of SLE was confirmed by low complement levels, high titre anti-dsDNA, anti-RNP, anti-Sm and anti-cardiolipin antibodies. Azathioprine was started in addition to steroids.

Three weeks later she presented to the emergency department with acute onset bilateral visual loss. Her medications included prednisolone 30 mg daily and azathioprine 50 mg daily. She was alert and well oriented, but blind and unable to perceive light. She was afebrile, her blood pressure was 165/105 mm Hg and pulse rate was 72 beats/min. She had 3 episodes of generalised tonic clonic seizures followed by post-ictal left-sided hemiparesis and gaze preference. Clinical examination revealed equal and reactive pupils with normal fundoscopy. Cardiovascular and respiratory examination was unremarkable, but she had extensive lymphadenopathy and hepatosplenomegaly.

Blood investigations revealed a white blood cell count of $10.54 \times 10^9/L$ (3.3-9.6) with predominant neutrophilia (neutrophils 89%), haemoglobin 11.2 g/dL (10.7-14.9) and platelets $306 \times 10^9/L$ (162-427). Serum electrolytes, liver function tests and coagulation profile were normal. CT scan of the brain showed 2 ill-defined hypodense lesions in the left occipital lobe.

The working diagnosis was secondary anti-phospholipid

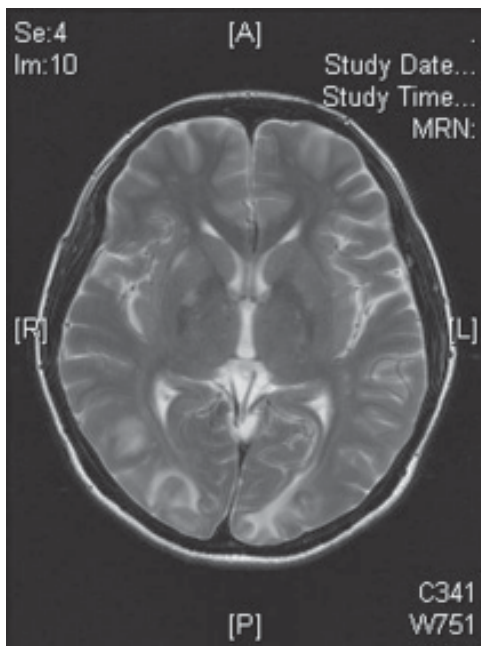


Fig. 2. Axial magnetic resonance imaging (MRI), T2-weighted image of brain at presentation, showing multiple hyperintense lesions, predominantly in occipital cortex.

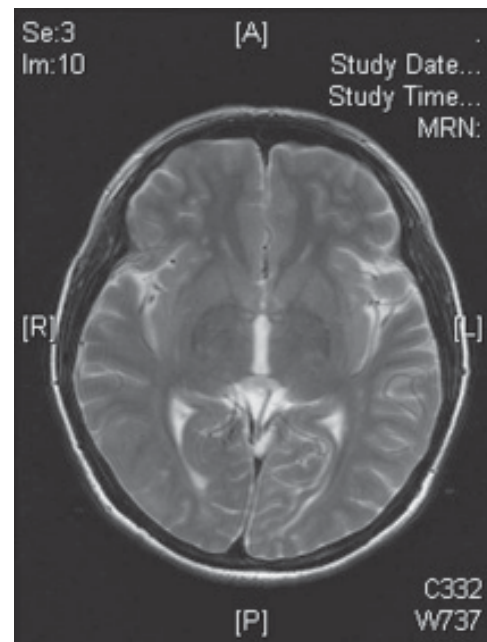


Fig. 3. Axial magnetic resonance imaging (MRI), T2-weighted image of brain, repeated after 1 week, showed resolution of hyperintense lesions.

syndrome causing occipital infarcts and neuropsychiatric lupus. She received intravenous pulse methylprednisolone for 3 days, pulsed cyclophosphamide, low molecular weight heparin and intravenous phenytoin. She had no recurrence of seizures and within 12 hours her vision was normal and hemiparesis resolved completely. Her blood pressure remained high requiring anti-hypertensive treatment. 24-hour urine collection revealed proteinuria of 2.02 gm/day with creatinine clearance of 114 mL/min. Urine microscopy was normal.

An MRI of her brain showed multiple hyperintense lesions in the cortical and subcortical areas of both hemispheres with surrounding oedema (Fig. 2). In view of the atypical MRI findings, a repeat MRI of her brain 1 week later showed significant resolution of the lesions noted earlier (Fig. 3). The diagnosis was revised to PRES; warfarin was discontinued and azathioprine withheld. She was discharged with tapering doses of prednisolone, aspirin, hydroxychloroquine and enalapril. She has since returned to Indonesia.

Discussion

SLE, in association with APS, has been associated with several distinct ocular and visual disorders, occurring in 15% to 88% of patients.² These include a variety of transient visual disturbances termed transient visual symptoms (TVS), ranging from blurring of vision to complete visual loss. A literature review by Giorgi et al³ established that unilateral visual loss is the most common TVS with a

frequency of 53%, followed by blurring of vision in 20.6%, with the least common being bilateral visual loss at a frequency of 5.9%. The pathophysiology of TVS in this review has been attributed to ischaemia secondary to thromboembolism, hence the recommendation for anticoagulation along with immunosuppressive therapy.

Retinal involvement is the second most common (after keratoconjunctivitis sicca) ophthalmological manifestation in SLE.⁵ Visual impairment is usually secondary to ischaemic retinopathy and higher incidences are reported in association with APS. Immune complex mediated retinal vasculitis, ischaemic optic neuropathy, papillitis and retrobulbar neuritis are also rarely reported causes of visual loss. Frohman et al⁶ have described a case of reversible visual loss secondary to isolated optic chiasmitis.

Our first patient highlights the complex and inter-related pathophysiological mechanisms that may be seen in SLE. Although she had no evidence of ischaemia on brain imaging, she had serological evidence of secondary APS. Retinal ischaemia was probably due to APS; however, she also had optic neuritis coupled with retinal vasculitis, secondary to active SLE contributing to her visual symptoms.

Our second patient is a classic example of PRES. This clinicoradiologic entity was first described as a distinct syndrome in 1996 by Hinchey et al⁴ and since then it has been increasingly recognised with expanding associations. Known causes of PRES include hypertensive encephalopathy, eclampsia, renal failure, post-transplant state,

immunosuppressive therapy and rheumatologic diseases. The clinical presentation encompasses headache, altered mental function, seizures (usually generalised) and visual disturbances (ranging from blurred vision and hemianopia to cortical blindness). In addition to the clinical features, the diagnosis is supported by hyperintensity in T2-weighted MR images of the parieto-occipital white matter. Diffusion weighted imaging (DWI) scans show increased diffusion in PRES, consistent with vasogenic oedema. The aetiology of PRES is believed to be dysregulation of brain perfusion by sympathetic innervation in the setting of severe hypertension. The predominantly posterior distribution of white matter changes has been attributed to differences in cerebral autoregulation with an antero-posterior gradient of sympathetic cerebral arterial innervation.^{4,7-9} The mechanism by which immunosuppressive drugs cause PRES is less clear; direct cytotoxicity on vascular endothelium leading to endothelial dysfunction, vasospasm, reduced tissue perfusion, activation of the coagulation cascade and fluid extravasation has been postulated. Metabolic derangements and sepsis are also speculated to be contributory factors.⁹

The causes of PRES may be diverse, but the most common precipitants are acute elevations in blood pressure, renal decompensation and treatment with immunomodulatory drugs. The pathogenesis of PRES in rheumatic diseases is thought to be multifactorial. Hypertension, nephritis, disease activity and medications have all been implicated. In SLE, PRES can be a manifestation of lupus disease activity or a consequence of immunomodulatory therapy and management is dependent on the aetiology.⁷ In the setting of a possible manifestation of disease activity, with or without active nephritis, PRES is usually treated with immunosuppression, most commonly with intravenous methyl prednisolone and cyclophosphamide.⁷ If the cause is thought to be drug induced, prompt cessation of the offending drug is necessary together with rapid control of seizures and management of hypertension. Although initially described in association with cyclosporine and tacrolimus, azathioprine, which was started in our second patient 3 weeks earlier, has also been implicated.¹⁰

These 2 cases emphasise the diagnostic and therapeutic challenges in the management of SLE. Although our 2 patients presented with bilateral visual loss, these manifestations had different underlying immunopathogenic mechanisms. Immunosuppressant therapy was necessary in our first patient but azathioprine was withdrawn in our second patient. Anti-coagulation was necessary in our first patient but not in our second patient. These cases underscore the need for constant clinical vigilance in the care of patients with rheumatic diseases.

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