Posterior reversible encephalopathy syndrome: an acute manifestation of systemic lupus erythematous

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ABSTRACT Stroke mimickers are common, and they represent a diagnostic dilemma for clinicians. Many, like posterior reversible encephalopathy syndrome (PRES), are easily reversible. The manifestation of PRES is characterised by headaches, convulsions, altered mental functioning and blindness. In most cases, computed tomography of the brain will show hypodense lesions in the parieto-occipital lobe, which only further confounds the physician. Although this syndrome is uncommon, prompt and accurate recognition allows early treatment, which has been shown to produce favourable outcomes. Herein, we report the case of a 54-year-old woman, who presented with PRES, as an acute manifestation of systemic lupus erythematous (SLE) and lupus nephritis. The patient was initially thought to be experiencing an ischaemic stroke, but the diagnosis was later changed. On management of her underlying condition, her symptoms resolved. PRES should be recognised as an acute emergency manifestation of SLE. It should not be mistaken for an ischaemic stroke as inappropriate treatment could have adverse outcomes.

Keywords: hypertension, management, posterior reversible encephalopathy syndrome, systemic lupus erythematous

INTRODUCTION
Posterior reversible encephalopathy syndrome (PRES), also known as reversible posterior leucoencephalopathy syndrome, was first described by Hinchey et al in 1996. (1) It is increasingly recognised as a neurological condition that manifests clinically as headaches, convulsions, altered mental functioning and blindness. It also presents with the classical neuroradiological finding of oedema in the parieto-occipital lobes of the brain on computed tomography (CT) and magnetic resonance (MR) imaging. (1) The causes of PRES are varied and have been largely attributed to hypertension, renal decompensation and the use of immunosuppressants. (2) This report highlights the case of a 54-year-old woman who presented with PRES on a background of hypertension and recently diagnosed systemic lupus erythematous (SLE) complicated with lupus nephritis. The patient was initially thought to have an ischaemic stroke, but her signs resolved with symptomatic control and treatment of the underlying cause of PRES.

CASE REPORT
A 54-year-old woman with a known history of SLE, Raynaud's syndrome, hypertension, herpes zoster and poor compliance to medications, presented to our institute following sudden bilateral visual loss and a 2-min episode of generalised tonic-clonic seizure in the ambulance. This was preceded by a three-day history of headaches and confusion. On presentation, the patient had a Glasgow Coma Scale score of 13 (E3, V5, M5) and an initial blood pressure of 173/100 mmHg, which rose steadily to 206/110 mmHg. The patient then developed another episode of generalised tonic-clonic seizure, which lasted for 2 mins and was resolved with diazepam and a phenytoin infusion. Her temperature remained at about 37.2°C and her pulse was 90 bpm in sinus rhythm. On physical examination, the patient’s visual acuity was reduced to only bilateral light detection. Fundal examination did not show hypertensive retinopathy or retinal vasculitis. All other neurological, cardiovascular and respiratory examinations were unremarkable. Electrocardiography showed that the patient’s sinus rhythm and dynamic cardiac enzymes were normal.

An urgent CT of the patient’s brain was performed and ill-defined, irregular hypodensities were found in the bilateral parietal and occipital cortex, the subcortical white matter, and to a lesser extent, the right frontal region (Fig. 1). As these findings were more suggestive of PRES than ischaemic stroke,
the patient was admitted to the intensive care unit and started on phenytoin and intravenous labetalol. However, she became bradycardic and hypotensive, requiring treatment with adrenaline and dobutamine. Further tests included an echocardiography and a lumbar puncture, which were both unremarkable. Blood tests, however, showed the following: haemoglobin 5.1 g/dL, white blood cell count 3.0 × 10^9/L, lymphocytes 0.3 × 10^9/L and platelets 2.0 × 10^9/L. She had low levels of haptoglobin, and complement components 3 and 4. The patient’s serum creatinine level and creatinine clearance were 357 μmol/L and 5 mL/min, respectively, and she had elevated levels of red blood cells in her urine, as well as a total protein of 2.5 g. Although the findings were suggestive of lupus nephritis, this could not be confirmed as the patient refused a renal biopsy. She was started on intravenous methylprednisolone, but her hypertension was refractory and her renal function deteriorated. This time, the patient tolerated treatment with labetolol (oral instead of intravenous). She did, however, develop bilateral pleural effusion and experienced weight gain. The patient subsequently refused any further procedures, tests and intravenous medications, but agreed to take oral medications and was discharged against medical advice. Repeat CT performed one week before her discharge showed resolution of the hypodensities. Her visual deficits had also resolved prior to discharge.

**DISCUSSION**

As its name suggests, PRES is an easily treated condition, resolving with appropriate management. In order to prevent progression to permanent neurological damage and death, the underlying cause should be addressed, and treatment should be initiated as soon as possible. Although the neurological symptoms usually resolve together with the radiological signs, the duration of symptom resolution is not well defined and may range from days to weeks. It is important that this condition is not mistaken for other conditions such as an ischaemic stroke, as thrombolysis could have severe consequences in PRES patients.

PRES has been largely associated with hypertension, pre-eclampsia, eclampsia, autoimmune diseases, renal failure, post-organ transplantation and the use of immunosuppressants. Its pathophysiology has been attributed to a loss of cerebral vascular autoregulation, hypertension and hyperperfusion. An increase in blood pressure results in the blood-brain barrier breaking down and subsequent fluid transudation into the cerebral white matter, which then causes vasogenic oedema. Another contributing factor is increased cerebral vasculature endothelial permeability secondary to fluid overload, a common feature in a number of causes of PRES. Other postulated mechanisms include endothelial dysfunction and vasospasm resulting in transient cerebral ischaemia. Although severe hypertension seems to be a common factor in most cases of PRES, as also evidenced in our patient, other reports have shown that PRES is also possible in normotensive or only mildly hypertensive patients.

The susceptibility of the posterior regions of the brain, including the cerebellum and brainstem, to the physiological changes that occur during severe hypertension is largely unknown. However, its reduced ability to cope with changes in blood pressure and perfusion could possibly be explained by the lack of sympathetic innervation in the posterior regions of the brain. The posterior regions of the brain are less readily able to regulate endothelial function and luminal diameter when blood pressure is increased, resulting in hyperperfusion of the subcortical white matter. It has been widely reported that the frontoparietal regions of the brain could also be affected. In fact, atypical distribution of oedema is more common than previously thought. The brain regions affected might point to the cause of PRES; for example, cerebellar involvement is more frequently associated with autoimmunity, although this was not seen in our patient.

Radiological findings in PRES include bilateral symmetrical hypodensities localised to the subcortical white matter areas on CT, and hypointense and hyperintense areas on T1- and T2-weighted MR images. The grey matter of the brain is usually spared. With treatment, most of these radiological signs resolve on subsequent scans. The presence of hypodensities on CT supports the hypothesis of fluid accumulation overwhelming cerebrovascular autoregulation, resulting in oedema. MR imaging is superior to CT and believed to be best for diagnosing PRES. The various sequences available on MR imaging, such as fluid-attenuated inversion recovery (FLAIR) and diffusion weighted imaging, enable better enhancement of the oedema, and thus, an earlier diagnosis. Certain radiological patterns on FLAIR MR imaging, including holohemispheric watershed pattern, superior frontal sulcus pattern and dominant parietal-occipital pattern, are associated with the diagnosis of PRES. McKinney et al classified the severity of oedema on FLAIR MR imaging into mild, moderate and severe, but the association between the severity of oedema and the clinical manifestation of PRES has been shown to be poor.

The role of SLE in the pathophysiology of PRES is multifactorial. The disease process of SLE, hypertension, glomerulonephritis and the use of immunosuppressants are all implicated in PRES. It was unknown whether our patient had elevated blood pressure days before her presentation. It was, however, known that the patient had poor compliance with medications and was not on any immunosuppressants at the time of presentation. PRES is not widely mentioned as an acute manifestation of SLE, but there have been a number of reports of such incidents. In our patient, a flare-up of her SLE manifested as an episode of PRES, which resolved once her blood pressure was controlled and her SLE treated with prednisolone. Furthermore, the patient experienced an episode of acute chronic renal failure, which could have caused a sudden increase in her blood pressure, overwhelming the...
autoregulatory mechanism of the cerebral vasculature, resulting in vasogenic oedema.

In conclusion, the causes of PRES are diverse and the condition should be recognised as an acute emergency manifestation of SLE. The syndrome can be readily identified using its clinical and radiological features. Prompt reduction of blood pressure and treatment of the underlying cause in an emergency setting would reverse any clinical signs and prevent end-organ failure. It is important that the radiological features are not mistaken for ischaemic stroke as inappropriate treatment could have adverse outcomes.

REFERENCES