

# Posterior reversible encephalopathy syndrome: the importance of its recognition in patients with systemic lupus erythematosus

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## ABSTRACT

The posterior reversible encephalopathy syndrome (PRES) is a clinical-radiological entity characterized by the association of clinical neurological signs (headache, confusion, vision changes, vomiting and seizures) and the typical changes in magnetic resonance imaging of the brain. Its pathogenesis is still poorly defined but seems to imply a vascular and endothelial dysfunction. It occurs more frequently in patients with hypertensive encephalopathy, eclampsia, renal failure and has also been associated with the use of immunosuppressive drugs. The authors present a case of PRES in a young woman with systemic lupus erythematosus with active and severe manifestations of the disease.

**Keywords:** PRES; Posterior reversible encephalopathy syndrome; Systemic lupus erythematosus

## INTRODUCTION

In 1996, Hinchey *et al.* described 15 patients with sudden onset of neurological symptoms associated with abnormalities in neuroimaging, predominantly affecting the posterior lobes; this clinical entity was designated as Reversible Posterior Leukoencephalopathy Syndrome<sup>1</sup>. In 2000, while verifying that it could also affect the gray matter, Casey *et al.* proposed the term Posterior Reversible Encephalopathy Syndrome<sup>2</sup>.

Currently, the controversy concerning the correct term remains, because PRES is not always reversible, and not necessarily confined to the posterior regions of the brain<sup>3,4</sup>.

PRES is characterized by sudden onset of headache, cognitive dysfunction, visual disturbances, vomiting or seizures associated with signal changes in brain magnetic resonance imaging (MRI)<sup>5</sup>.

Its pathogenesis is still poorly defined. It appears to be a development of cerebral oedema with diffusion of plasma proteins and other cells into the extracellular space. Nevertheless, the mechanisms of this process remain unclear<sup>3</sup>.

It is often associated with an abrupt increase in blood pressure and it can be seen in transplanted patients, in eclampsia, renal failure and / or patients under immunosuppressive treatment<sup>6</sup>. However, there are some reports and case series in the literature of PRES associated with other clinical conditions, namely systemic lupus erythematosus (SLE).

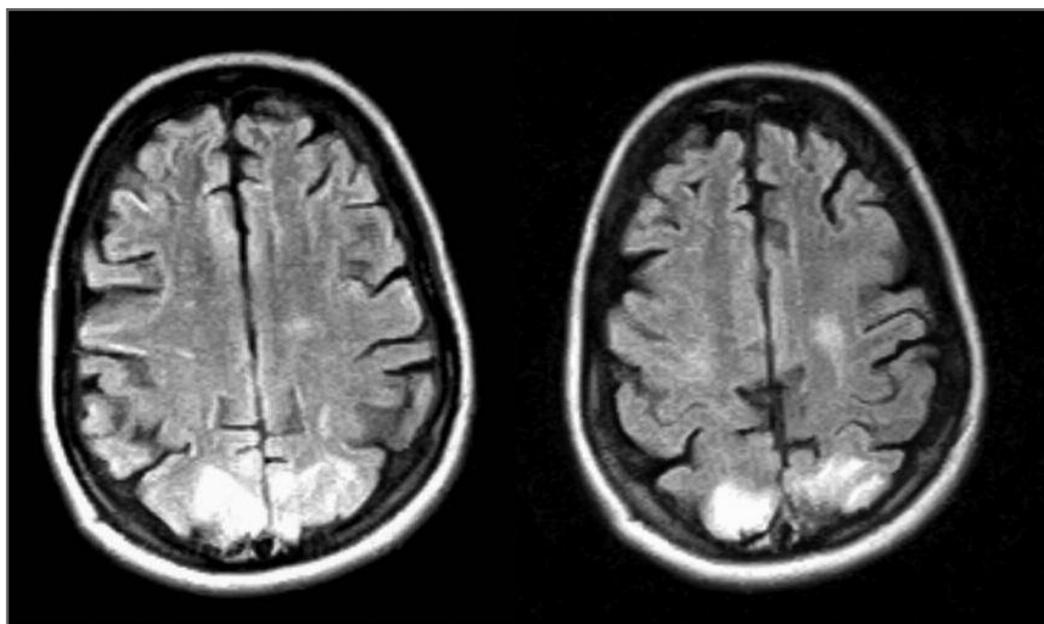
## CLINICAL CASE

A 25-year-old woman, previously diagnosed with SLE 8 years before, currently with hematologic and central nervous system (CNS) involvement, and recurrence of proliferative glomerulonephritis (class IV).

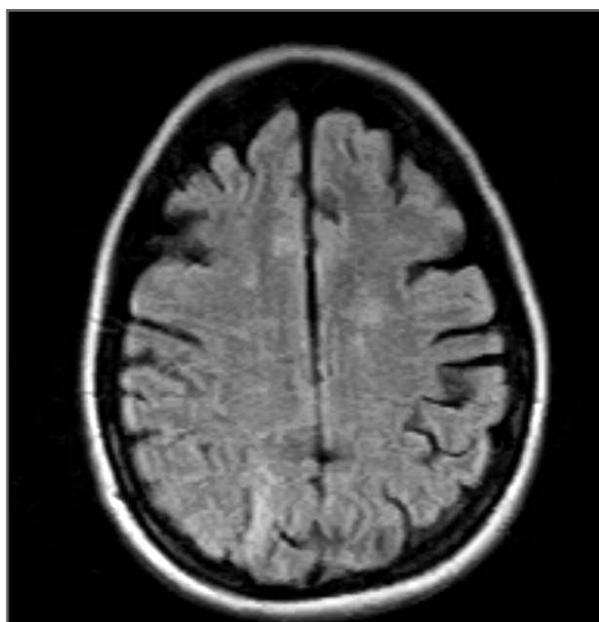
Recently she started periods of confusion and incoherent speech. The brain MRI showed multiple small foci of bright fluid attenuated inversion recovery (FLAIR) signal in the subcortical white matter of both frontal lobes and the cerebrospinal fluid examination revealed no abnormality, including the study of oligoclonal bands.

Laboratorial tests revealed hemolytic anemia (hemoglobin 8.2 g/dl), renal insufficiency (serum creatinine 1.33 mg/dl) and nephritic syndrome (active urinary sediment and 24 hours proteinuria of 2.2g). In the immunological study she presented positive antinuclear antibody (ANA 1/640), positive anti-dsDNA and hypocomplementemia, with C3 of 41 mg/dl (normal

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**FIGURE 1.** Cranial T2 FLAIR-weighted MRI: bilateral parietal and occipital white matter hyperintensities



**FIGURE 2.** Cranial MRI (after 1 week): complete resolution of previously reported changes

range 90-180 mg/dl) and C4 of 7 mg/dl (normal range 12-40mg/dl).

We conclude that in addition to hematologic and renal involvement, she also had CNS vasculitis. She was hospitalized to perform intravenous methyl-

prednisolone pulses (500 mg daily for 3 days) and then rituximab. The decision of this therapy was based on the involvement of organs (in particular kidney and CNS), as well as for being a woman of childbearing age, previously treated as cyclophosphamide, with a high cumulative dose.

During the administration of the third pulse, she started worsening headache and tonic-clonic seizures. There were no reports of hypertension in the monitoring of treatment. Cranial T2 FLAIR-weighted MRI revealed bilateral parietal and occipital white matter hyperintensities, and the diffusion weighted imaging scans showed increased apparent diffusion coefficient, suggestive of vasogenic oedema (Figure 1).

Treatment with intravenous phenytoin controlled the seizures and the remaining immunosuppressive therapy was delayed. Repeated brain MRI showed near complete resolution of previously reported changes at 1 week (Figure 2) and she had no lasting neurologic sequelae.

## DISCUSSION

The differential diagnosis for a patient with SLE who develops headache and seizures includes cerebrovascular disease, hypertensive encephalopathy, uremic encephalopathy, neuropsychiatric lupus and PRES<sup>7,8</sup>.

In our patient, with a previous diagnosis of CNS vasculitis, the onset of new neurological symptoms addressed us to a brain MRI, which showed changes consistent with a diagnosis of PRES. Total remission of symptoms and radiological lesions after one week reinforced this diagnosis.

Although classically PRES can be attributed to loss of autoregulation of cerebral blood flow induced by hypertension, in this patient there was no register of an hypertensive peak. However, some cases of PRES associated with normal blood pressure levels have been described, and its appearance has been associated with treatment with cyclophosphamide or high doses of corticosteroids<sup>1,9,10</sup>. Corticosteroids are implicated in the occurrence of PRES by predisposing to hypertension and fluid overload. The manner in which cyclophosphamide predisposes to PRES is not clearly known<sup>4</sup>.

Recently, Varaprasad and colleagues published a case series of patients with SLE and PRES. The authors assessed 13 adolescents and young adults and found that the majority of patients had severe disease activity, particularly with active lupus nephritis. This suggests that systemic inflammation and endothelial dysfunction may play a central role in the pathophysiology of PRES in patients with SLE<sup>4</sup>.

Previous studies also documented renal insufficiency in over 70% of patients with SLE and PRES<sup>8,11</sup>. However, in this recent series of cases, only one patient had renal failure, suggesting that disease activity, rather than fluid overload secondary to renal insufficiency, is a critical factor in the pathogenesis of PRES<sup>4,7</sup>. Even though PRES has been described as a rare complication in patients with SLE, the increasing number of cases reported in the literature, emphasizes the necessity to consider this diagnosis in a patient with new neurological symptoms. Although reversible by definition, a delay in diagnosis and treatment can result in significant sequelae such as epilepsy, cerebral ischemia, subarachnoid hemorrhage, coma or even death<sup>12,13,14</sup>.

#### CORRESPONDENCE TO

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