ABSTRACT

We report a rare case of systemic lupus erythematosus (SLE) presenting with posterior reversible encephalopathy syndrome (PRES). A 31-year-old female presented with six episodes of generalized tonic-clonic convulsions. She recovered very well with corticosteroids and immunosuppressive therapy. SLE is a heterogenous, inflammatory, multisystem autoimmune disease of multiorgan involvement in which antinuclear antibodies appear in serum often years before clinical symptoms. Posterior reversible encephalopathy syndrome (PRES) is a clinicoradiological entity that can be missed by many clinicians. A high index of suspicion should alarm a clinician to think of PRES when patients present with seizures, altered mental status, headaches and visual disturbances. Prompt diagnosis and treatment are therefore mandatory for full recovery of abnormalities.

KEYWORDS: Posterior Reversible Encephalopathy Syndrome (PRES), Systemic Lupus Erythematosus (SLE).
INTRODUCTION
Posterior reversible encephalopathy syndrome (PRES) has been reported in association with hypertension, renal failure, transplantation and immunosuppressives.[1] However, reports of PRES in conjunction with SLE are sparse.[2] Majority of these patients had lupus nephritis and hypertension.[3] Recent reports have shown a stringent association of PRES with hypertension in SLE patients and response to cyclophosphamide-methylprednisolone pulse therapy.[4] Here, we report a rare case of a SLE presenting with PRES. The patient was treated and her neurologic impairment and overall disease activity improved following treatment with pulse therapy and immunosuppressive combination.

CASE REPORT
A 31-year-old women was admitted with history of generalized seizures for last twelve hours. There were six episodes in total, each of them being tonic-clonic in nature, as per her parents’ description. Patient had history of headache & altered sensorium since one day. There was no prior history of seizures, fever, head trauma. The patient was drowsy, disoriented and confused. Her vitals were: pulse 130/min, regular, blood pressure 170/110 mm Hg, respiration rate 22/min and temperature 98° F. She had pallor and bilateral pedal edema. However, there were no focal neurodeficit.

The patient’s seizures were controlled with intravenous phenytoin (15mg/ kg) and midazolam. Her haematological and biochemical parameters were within normal limits. (haemoglobin 9.8g/dl; white cell count of 9400/mm³ ; platelet count 236,000/ mm³ ; blood glucose 101mg/dl; serum sodium 141mmol/L; potassium 4.3mmol/L; serum creatinine 1.9 mg/dl). Computed tomography of brain was normal and there was no evidence of left ventricular hypertrophy on electrocardiography. Cerebrospinal fluid study revealed a cell count of 20/ high power field (HPF), 90% lymphocytes, protein 60 mg/dl, glucose 40 mg/dl. MRI of brain (fig:1 A&B) showed bilateral diffusion restricted hyperintense lesions in T2 and T2FLAIR sequences affecting cortical and subcortical white matter of fronto-parietal and occipital regions, suggestive of acute demyelination which indicates PRES.

To investigate the cause of edema, routine examination of urine was done, which revealed 3+ albuminuria, 2-3 RBCs/HPF and RBC casts. Ultrasonography of abdomen showed increased cortical echogenicity of both the kidneys with mild ascites and minimal bilateral pleural effusion. Antinuclear antibody by indirect immunofluorescence was positive (1:160) and anti-ds DNA antibody was also positive (1:320).
Considering all these evidence, the patient was diagnosed as a case of SLE with PRES. The pattern of demyelination was suggestive of PRES. The patient was treated as hypertensive emergency with intravenous nitrate followed by labetolol. Her blood pressure was eventually controlled to approximately systolic of 120-140 mm of Hg and diastolic of 60-90 mm of Hg. The patient was started on immunosuppressive therapy consisting of methylprednisolone (1gm) and cyclophosphamide (500 mg/m² of body surface area). The patient remained asymptomatic after the first pulse.

She was discharged and asked to follow up after 3 weeks with a repeat MRI of brain. The repeat scan (fig:1 : C&D) showed complete resolution of previous lesions, confirming the diagnosis of PRES. Repeat estimation of anti-ds DNA antibody revealed a titer of less than 1:80. She was scheduled for six pulses at one month interval. Till date the patient remains free of further neurological symptoms or signs.

A&B : extensive demyelinating lesions (arrows) at presentation.
C&D : completely resolved after pulse of immunosuppresants therapy.

Figure 1: MRI of brain (T2) showing
DISCUSSION

PRES has been related to presence of hypertension and nephritis in SLE patients. Though PRES has been reported early in the course of SLE, a patient presenting with PRES is unusual. Hincley et al. first described reversible posterior leukoencephalopathy in 1996, now most commonly known as posterior reversible encephalopathy syndrome. It can be a manifestation of a variety of disorders with neuroimaging changes suggestive of white matter edema, predominantly in the posterior regions of the brain. The common presentations are headache and altered conscious level, as well as visual problems including cortical blindness and seizures. This condition has been reported in hypertensive encephalopathy, pre-eclamptic toxemia, renal failure, immunosuppressant such as cyclosporine or high dose steroid, cytotoxic drugs and connective tissue diseases.

The first description of PRES in SLE patients is as recent as 2006. The pathogenesis of PRES in patients with SLE is probably multifactorial: hypertension, nephritis, disease activity and immunosuppressive drugs have all been implicated. The distinctive role of immune mechanisms in the physiopathology of PRES can be clouded by these concurrent conditions. Abnormal endothelial activation, dysfunction and leukocyte tracking have recently been reported to cause cerebral and systemic hypoperfusion, which may be causative factors for PRES in SLE.

The pathophysiology of PRES involves cerebral edema with diffusion of plasma proteins and cells into the extracellular space. However, the actual mechanism remains unclear. Two distinct theories have been proposed: the vasogenic and the cytotoxic theories. PRES has been well described in patients with established diagnosis of SLE with lupus nephritis. In SLE, patients are more prone to endothelial dysfunction, mainly due to its autoimmune or ischemic complications (vasculitis and thrombosis). In addition, the use of cytotoxic or immunosuppressants in these group of patients may worsen the vasogenic edema. Fluid retention and high blood pressure in lupus nephritis may also worsen the vasogenic edema. Both cytotoxic and vasogenic theories could explain the susceptibility of PRES amongst SLE patients.

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. 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. 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.\cite{12}

Central nervous system (CNS) involvement occurs in 14%-75% of patients with systemic lupus erythematosus.\cite{13} The postulated mechanisms for PRES to occur in a patient with SLE include vasculopathy of small vessels, and increase of vasopermeability.\cite{14}

The posterior aspect of the brain is commonly affected due to the differences in autonomic innervations between the anterior and posterior circulations.

The posterior column has lesser sympathetic chain, and hence diminishes the ability to autoregulate well in the setting of sudden change in blood pressure, bodily fluid or biochemical components. Typically, imaging shows T2-weighted and FLAIR bilateral subcortical and cortical hyperintensities of the white and grey matter with a predominantly posterior distribution. However, the involvement of other areas such as the frontal lobes, basal ganglia, thalamus and brainstem have also been reported. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) analysis reveal vasogenic cerebral edema in the majority of cases.\cite{15}

The main differential diagnosis is bilateral ischemic stroke of the posterior cerebral artery territory. It would be crucial to distinguish PRES from a stroke as the latter does not involve rapid control of blood pressure. If hypertension complicates PRES, controlling the blood pressure with intravenous agent, to avoid permanent damage is warranted. In acute ischemic infarction however, blood pressure control is only mandatory when there is end organ damage such as hypertensive encephalopathy or acute pulmonary edema. PRES can also be mistaken for central venous sinus thrombosis, demyelinating disorders, lupus encephalitis, cerebral vasculitis and infectious or metabolic encephalopathy.\cite{15}

There is no international guideline regarding treatment of PRES. Reports mention use of different regimens including cyclophosphamide alone, or in combination with plasmapheresis.\cite{7} Those who developed PRES while on immunosuppressant discontinued the
drug. In presence of major organ involvement, high dose immunosuppressants are needed and they do not adversely affect the outcome of PRES.

Treatment must be instituted immediately. Parenteral antihypertensive treatment should be started with close blood pressure control, avoiding hypoperfusion as this could worsen the cerebral edema. Other supportive treatments such as hemodialysis are needed for fluid overloaded patients. If appropriate, the patients may need anticonvulsants and nursed in the intensive care unit.

Looking at the recent literature, PRES manifested by seizures and loss of vision was reported in a case of SLE in 2007.\(^{[16]}\) In 2008, four new cases of PRES were described in adults with SLE\(^3\). A woman with lupus nephritis and PRES developed intraparenchymal and subarachnoid hemorrhage, according to a 2010 report.\(^{[17]}\) Recently, Balint syndrome (a disorder of inaccurate visually guided saccades, optic ataxia, and simultanagnosia) presented as PRES in a SLE Patient.\(^{[18]}\) Of note, two reports accounted for the occurrence of PRES in juvenile SLE.\(^{[19,20]}\)

Varaprasad et al.\(^{[4]}\) reviewed the features of 13 patients with SLE and PRES from 2006–2010: all had active disease and hypertension. Six patients had PRES as part of their initial presentation of SLE, and nine had nephritis. Four patients were on cyclophosphamide therapy when they developed PRES. Of interest, an association of PRES with lupus activity had already been postulated.\(^{[21]}\)

PRES has been claimed as a particular form of neurological manifestation of SLE with characteristic MRI findings and a usual good outcome. Antihypertensive, antiepileptic, and supportive care are the mainstay of treatment.\(^{[22]}\)

**CONCLUSION**

We report a case of SLE who presented with PRES and recovered with a regimen of methylprednisolone - cyclophosphamide combination therapy. MP Pulse therapy, disease activity, hypertension, and infection were possible triggers. It highlights the need for a high index of suspicion and a good outcome related to early recognition and appropriate intervention.
REFERENCES


