Reversing the course: Tackling posterior reversible encephalopathy

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Reversing the course: Tackling posterior reversible encephalopathy

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ABSTRACT

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by damage to organs and cells mediated by tissue binding auto-antibodies and immune complexes. Tissue damage begins with deposition of auto-antibodies and/or immune complexes followed by destruction mediated by complement activation and release of cytokines and chemokines. Clinical manifestations include muco-cutaneous manifestations, non-scarring alopecia, synovitis, serositis, musculo-skeletal, renal, neurological & haematological involvement.

In this case report, we see a young woman in her reproductive age group initially presenting as pyrexia of unknown origin associated with intractable headache who is methodologically worked up and diagnosed with lupus. She was initiated on pulse steroid therapy, and lands up in accelerated hypertension & GTCS resulting in PRES with focal neurological deficits. This case also highlights how not just the symptomatic management of PRES but controlling the underlying disease flare up helps in reversing the focal deficits.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a complex autoimmune disease predominantly affecting young women, characterized by widespread inflammation and involvement of multiple organ systems. It is associated with a broad spectrum of clinical manifestations,

including constitutional symptoms, haematological abnormalities, and neurologic involvement. Central nervous system (CNS) complications in SLE, collectively referred to as neuropsychiatric SLE (NPSLE), can present with a variety of symptoms such as headaches, seizures, and cognitive disturbances. Among the rare but serious complications of NPSLE is posterior reversible encephalopathy syndrome (PRES), a neurological disorder that can manifest with seizures, altered mental status, and visual disturbances, often in association with hypertension and immunosuppressive therapy.

In addition to neurological complications, SLE patients are at risk for developing secondary macrophage activation syndrome (MAS), a potentially life-threatening hyperinflammatory state characterized by pancytopenia, hyper-ferritinemia, and multiorgan failure. MAS in SLE is often triggered by infections, medications, or disease flare-ups and poses significant diagnostic and therapeutic challenges due to its overlap with active lupus disease.

This case report describes a 26-year-old female with SLE, presenting with recurrent headache, fever, and haematological abnormalities. The complexity of the case was compounded by the onset of MAS and PRES, leading to multiple episodes of generalized tonic-clonic seizures (GTCS) and neurological deficits. Management required a multidisciplinary approach, including high-dose corticosteroids, intravenous immunoglobulin (IVIG), and immunosuppressive therapy with cyclophosphamide. This case underscores the importance of early recognition and treatment of severe SLE complications like MAS and PRES, as well as the challenges involved in managing overlapping life-threatening conditions in patients with active lupus.

CASE REPORT

A 26-year-old female P1L2 presented with complaints of severe headache and fever on & off for the last 6 months causing significant distress & sleep disturbances. On arrival patient was febrile but otherwise vitals were stable. Systemic examination was unremarkable. General examination revealed a non-scarring alopecia.

Complete hemogram revealed Hb- 8.1 g/dL, Platelet 55,000 / mm^3, TLC – 5980 / mm^3. Alb – 2g. Rest of the parameters – RFT, LFT, & Serum electrolytes were within normal range.

MRI Brain was taken which showed no significant abnormalities. Fever workup was done including viral profile, TB and other tropical profile which came out negative. Cerebro-spinal fluid was inconclusive.

In view of persistent headache & fever spikes inspite if intravenous antibiotics autoimmune workup was done & came out positive of SLE with high positivity for anti-ribosomal P antibody.

C3, C4 was low. DCT was found to be positive. Blood cultures showed no growth. Urine PCR -0.8, 24 hrs urine protein was 249.2 mg/day. Retic count was 0.3%. LDH was 372. MAS workup was done, which showed TGL-224, fibrinogen -269, OT, PT- normal, serum ferritin - 551, s/o probable MAS.

In view of high disease activity & probable MAS, patient was started on intravenous pulse steroid therapy – Injection Methylprednisolone 500mg iv once daily for 3 days.

During the course of hospital stay patient developed GTCS & accelerated hypertension.

Patient was started on anti-epileptics, anti-edema measures & other supportive measures. CT - Brain revealed **multiple, bilateral symmetrical, ill-defined hypodensities seen involving the sub-cortical and deep white matter of bilateral high frontal and high parietal region. EEG record shows nonspecific electrophysiological cerebral dysfunction involving both hemispheres** Repeat hemogram revealed worsening pancytopenia picture.

Patient then developed 4 episodes of GTCS & was intubated & put on other supportive medications.

Patient developed weakness of left upper & lower limb (Power - 0/5). Repeat brain imaging revealed **multi-focal ill-defined T2 FLAIR hyperintensities involving bilateral hemispheres- high frontal, parietal, occipital regions (PRES) with foci of blooming in SWI & phase contrast in bilateral para-sagittal high parietal region – possibly hemorrhage**.

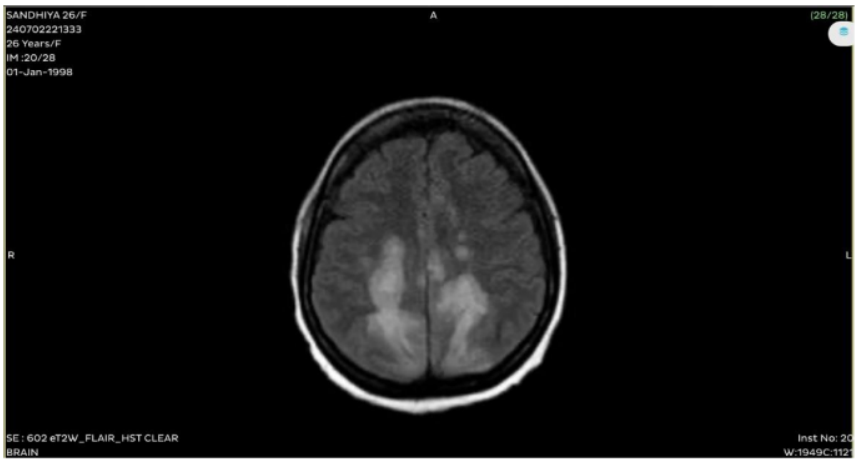


IMAGE 1 :MRI BRAIN – T2W FLAIR

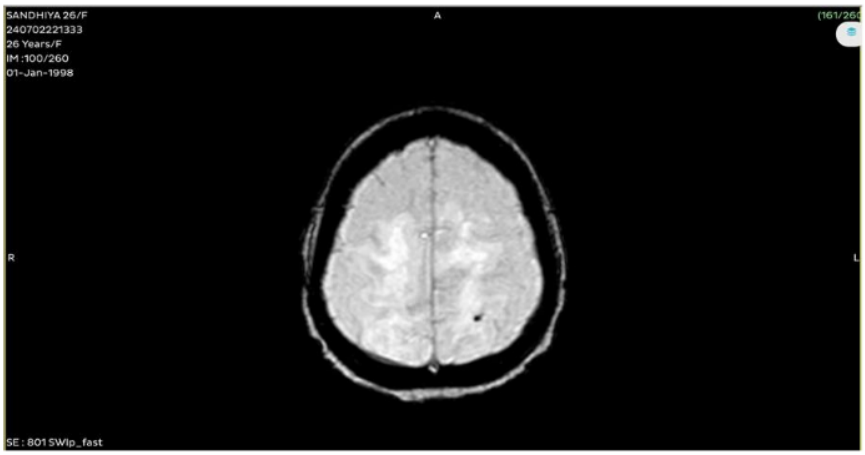


IMAGE 2 : MRI BRAIN – SWI

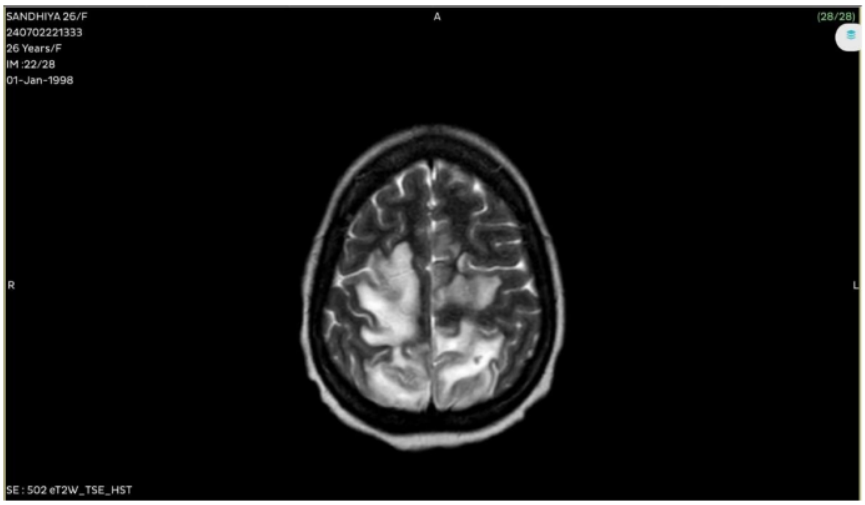


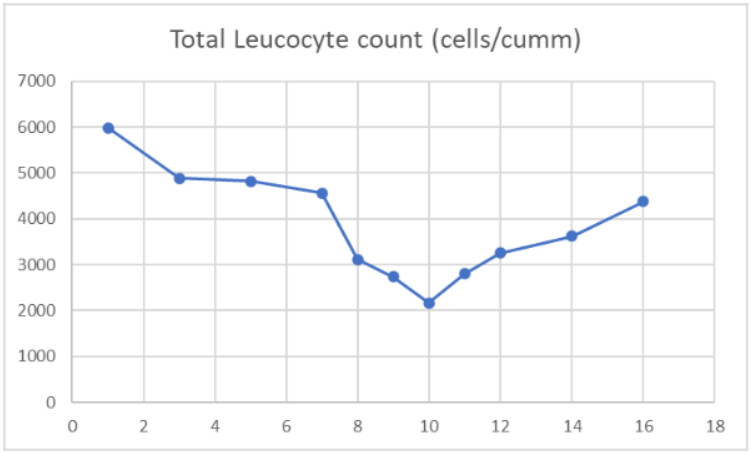
IMAGE 3 : MRI BRAIN - T2W TSE

In view of severe neurological manifestations of the disease, patient was initiated on intravenous immunoglobulin in the dose of 1 g/kg BW over 3 divided doses over 3 days (15g+15g+10g).

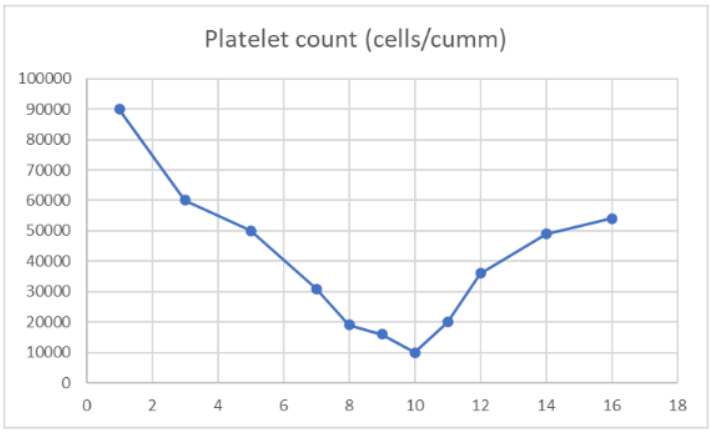
Patients power gradually improved over the next 48hrs to 4/5.

In view of probable MAS patient was planned on initiating immunomodulator therapy and hence was put on Injection Cyclophosphamide 700 mg was given (as per protocol) . Her total counts started rising following cyclophosphamide.

Patient was reviewed after 1 month during which her neurological deficits had improved and blood parameters had improved and patient was symptomatically better. Repeat MRI revealed resolving trend



GRAPH 1: Trend of total leucocyte count during the hospital stay



GRAPH 2: Trend of platelet count during the hospital stay

DISCUSSION

Posterior Reversible Encephalopathy Syndrome (PRES) is characterized by headache, confusion, seizures, and visual disturbances, often linked to hypertension, renal dysfunction, or immunosuppression. Neuroimaging typically reveals reversible subcortical edema, predominantly in the posterior cerebral hemispheres. A study conducted in New England Medical Center in Boston and Hôpital Sainte Anne in Paris evaluated from 1988 through 1994 identified 15 patients with PRES, triggered by abrupt blood pressure increases, impaired renal function, eclampsia, or immunosuppressive therapy. Management focused on controlling hypertension and reducing immunosuppressive doses, leading to complete

neurological recovery within two weeks. These findings highlight the importance of early recognition and treatment to prevent complications, with neuroimaging playing a critical role in diagnosis and monitoring disease progression [1].

A case report describes a 53-year-old patient who developed **Posterior reversible encephalopathy syndrome (PRES)** during treatment for a post-surgical chest bone infection. The patient presented with headache, blurred vision, and cortical blindness, along with left hemiparesis and severe hypertension (210/120 mmHg). Brain CT revealed parieto-occipital edema without ischemia, consistent with PRES. Despite initial antihypertensive treatment, symptoms persisted until aggressive blood pressure management with nitroglycerin and mannitol was initiated. Recovery occurred within nine days, with complete symptom resolution and normal imaging by day 15 [2].

There are primarily two mechanisms proposed to be involved in PRES namely disrupted cerebral autoregulation and toxin or immune mediated endothelial injury causing leak into occipital and parietal lobes commonly involved due to lower sympathetic innervation, making these areas more susceptible to vasodilation and edema but not restricted to only these areas [3-5].

A study conducted by Alexander McKinney expands the understanding of **posterior reversible encephalopathy syndrome (PRES)** by demonstrating that atypical imaging patterns and distributions are more frequent than previously recognized. While the parieto-occipital regions are most commonly involved (98.7%), atypical areas like the frontal lobes, temporal lobes, cerebellum, brainstem, and basal ganglia are also affected. Atypical findings, such as contrast enhancement, restricted diffusion, and hemorrhage, occurred in a significant number of cases but showed poor correlation with edema severity or blood pressure levels. Novel triggers, including contrast-related anaphylaxis and alcohol withdrawal, were identified. These findings underscore the importance of recognizing diverse manifestations of PRES [6].

Another study by Vivien H Lee conducted in Mayo Clinic provides valuable insights into Reversible Posterior Leukoencephalopathy Syndrome (RPLS), focusing on clinical presentations, associated conditions, and imaging patterns in 36 patients. Key findings include comorbid conditions such as hypertension (53%), renal disease (45%), and malignancy (32%). Most patients presented with encephalopathy (92%), seizures (87%),

headache (53%), and visual symptoms (39%), with symptoms resolving within an average of 5.3 days. Neuroimaging confirmed reversible vasogenic edema, with frequent atypical features such as frontal involvement (58%), gray matter lesions (42%), and brainstem/cerebellar involvement (58%). The study underscores that RPLS often extends beyond classic parieto-occipital regions, highlighting its clinical and radiological diversity [7].

This case highlights the diagnostic and therapeutic challenges associated with managing severe complications of systemic lupus erythematosus (SLE), such as macrophage activation syndrome (MAS) and posterior reversible encephalopathy syndrome (PRES). SLE is known for its heterogeneous presentation, affecting various organ systems, and this patient exhibited neurological, hematological, and immune-related complications that required prompt recognition and treatment.

The patient's initial presentation of recurrent headache and fever, followed by pancytopenia and neurological deterioration, raised the suspicion of neuropsychiatric lupus (NPSLE) and MAS. Neurological symptoms in SLE can range from mild headache to severe manifestations such as seizures and stroke-like symptoms [8,9]. In this case, the development of generalized tonic-clonic seizures (GTCS) and hypertensive episodes was concerning for PRES, a condition that is increasingly recognized in SLE patients, particularly when treated with immunosuppressive therapy or in the context of hypertension [10].

PRES is characterized by vasogenic edema and reversible white matter abnormalities on imaging. The MRI findings in this patient were consistent with PRES, which was likely exacerbated by underlying high disease activity and accelerated hypertension. This case emphasizes the importance of early diagnosis and management of PRES, as delayed treatment can lead to irreversible damage. The improvement in neurological function following pulse steroid therapy, anti-epileptics, and anti-edema measures indicates the potential for reversibility in PRES when managed appropriately.

The concurrent diagnosis of MAS added complexity to this case. MAS is a severe hyperinflammatory syndrome that can occur in patients with autoimmune diseases like SLE, presenting with fever, pancytopenia, and hyperferritinemia. This patient had elevated serum ferritin and triglyceride levels, consistent with MAS. Aggressive immunosuppressive therapy, including intravenous immunoglobulin (IVIG) and cyclophosphamide, was initiated to

control the hyperinflammatory state, with notable improvement in both haematological parameters and overall clinical condition.

CONCLUSION

This case illustrates the complexity of managing severe systemic lupus erythematosus (SLE) with overlapping complications of macrophage activation syndrome (MAS) and posterior reversible encephalopathy syndrome (PRES). The patient's initial symptoms of recurrent headache and fever, coupled with pancytopenia and neurological deterioration, required a comprehensive and multidisciplinary approach. Early identification of PRES, with prompt initiation of anti-edema measures and seizure management, helped prevent irreversible neurological damage. The concurrent diagnosis of MAS added to the challenge, necessitating aggressive immunosuppressive therapy with intravenous immunoglobulin (IVIG) and cyclophosphamide, leading to clinical improvement.

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