https://doi.org/10.46389/rjd-2024-698
www.jrdiabet.ro
Rom J Diabetes Nutr Metab Dis
2024; Volume 31, Issue 1, pages 698-704

A CASE OF MONOCLONAL ANTIBODY (RITUXIMAB) INDUCED POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES) IN A PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Dr. Abinaya Srinivasa Rangan[1] , Dr. Dhanush Balaji. S[2], Dr. Saranya. C[3] & Dr. Prasanna Karthik. S[4]

[1]Postgraduate, Department of General Medicine, Saveetha medical college and hospital, Thandalam, Chennai, Tamilnadu, India.
abinayarangan97@gmail.com

[2]Postgraduate, Department of General Medicine, Saveetha medical college and hospital, Thandalam, Chennai, Tamilnadu, India.
dhanushbalajis@gmail.com

[3]Professor, Department of Rheumatology, Saveetha medical college and hospital, Thandalam, Chennai, Tamilnadu, India.
drcsaranya1987@gmail.com

[4]Professor, Department of General Medicine, Saveetha medical college and hospital, Thandalam, Chennai, Tamilnadu, India.
kartpress@gmail.com

ABSTRACT

Background: This case report aims to present a rare occurrence of systemic lupus erythematosus (SLE) with posterior reversible encephalopathy syndrome (PRES) following rituximab therapy. We describe the clinical features, diagnostic evaluation, treatment, and outcomes of a patient diagnosed with SLE who developed PRES after receiving rituximab.

Case - The patient, a 23-year-old female known case of SLE, presented with sudden-onset neurological symptoms, including seizures and altered mental status, after receiving rituximab for management of lupus nephritis class IV not responding to mycophenolate mofetil. Brain imaging revealed characteristic findings consistent with PRES. Prompt intervention and discontinuation of rituximab were initiated, along with the administration of appropriate supportive care and immunosuppressive therapy. The patient demonstrated gradual improvement of neurological symptoms.

Conclusion: This case highlights the importance of recognizing the potential neurological complications, such as PRES, associated with rituximab therapy in patients with SLE. Early diagnosis and prompt management are crucial for achieving favorable outcomes.

Keywords: systemic lupus erythematosus, posterior reversible encephalopathy syndrome, PRES, rituximab, MRI

INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is a rare clinical-radiological entity characterized by seizures, severe headache, mental status instability and visual disturbances.[1] The

syndrome is most commonly encountered with chronic hypertension, acute kidney injury, chronic kidney disease, eclampsia, pre-eclampsia, sepsis, immunosuppressive drugs, illicit drugs (cocaine), organ transplantation, collagen vascular disease, autoimmune disorders, and other conditions.[2]

Systemic Lupus Erythematosus (SLE) is a chronic multisystem inflammatory disease that follows a relapsing and remitting course. It is characterized by an auto-antibody response to nuclear and cytoplasmic antigens. SLE can affect any organ system, but mainly involves the skin, joints, kidneys, blood cells, and nervous system.[3]

Posterior reversible encephalopathy syndrome (PRES) as an manifestation of SLE is not widely reported in the literature. A case control study reported prevalence of PRES in SLE as much as 0.43%.[4] This case report aims to present a rare occurrence of systemic lupus erythematosus (SLE) with posterior reversible encephalopathy syndrome (PRES) following rituximab therapy.

CASE REPORT

A 23 year old female, known case of SLE since 8 years on medication and diagnosed with lupus nephritis class IV in 2022 and started on T.mycophenolate mofetil, T.Hydroxychloroquine and Steroids. In view of unresponsiveness to mycophenolate mofetil and steroids for more than 6mg than of therapy and persistent renal failure rebiopsy of kidney was done and showed lupus nephritis grade IV-V with activity score of 12/24 and she was started on full dose steroids and in view of her reproductive age Inj. Rituximab 500mg was started instead of cyclophosphamide -dose 1 on 23/05/23 and 2nd dose on 02/06/2023 came with complaints of diffuse type of headache associated with retro orbital pain 2 days following Rituximab therapy and blurring of vision and facial puffiness and 1 episode of vomiting in the morning non projectile and had 2 episodes of generalized tonic clinic seizures associated with up rolling of eyes and tongue bite lasting 1 minute each and she regained consciousness between the episodes 4 days following Rituximab therapy.On examination patient was conscious, restless, afebrile. Bilateral pitting pedal edema present, bilateral pupil 2 mm reacting to light. Her GCS was 13/15. Her vitals were, pulse rate 137/min, blood pressure 180/120 mmHg, SpO_2 96% on room air. On CNS examination, bilateral plantar were extensor, no neck rigidity & dolls eye present. Her CBG was 102mg/dl.

On admission CBC findings were hemoglobin 7.1 gm/dl, total leucocyte count 14170, RFT findings were elevated urea (87.8 mg/dl), elevated creatinine (2 mg/dl), raised CRP (54.7), normal ESR (19) & serum electrolytes were normal. Urine PCR-7.6. Other investigations suggestive of low C3-67mg/dl (88-165 mg/dl) & normal C4-24.6mg/dl (14-44mg/dl). EEG done showed nonspecific electrophysiological cerebral dysfunction. CSF analysis was done and found to be normal.

MRI brain with CT screening was done and showed posterior reversible encephalopathy syndrome (likely etiology- drugs or SLE) in bilateral cerebral hemispheres (bilateral gangliocapsular region, bilateral thalami, bilateral frontal temporal parietal occipital lobes,

bilateral corona radiata and centrum semiovale- predominantly in bilateral occipital lobes), bilateral cerebella's hemispheres, dorsal and ventral aspects of bilateral hemipons and bilateral middle cerebella's peduncles with features of intracranial hypertension.

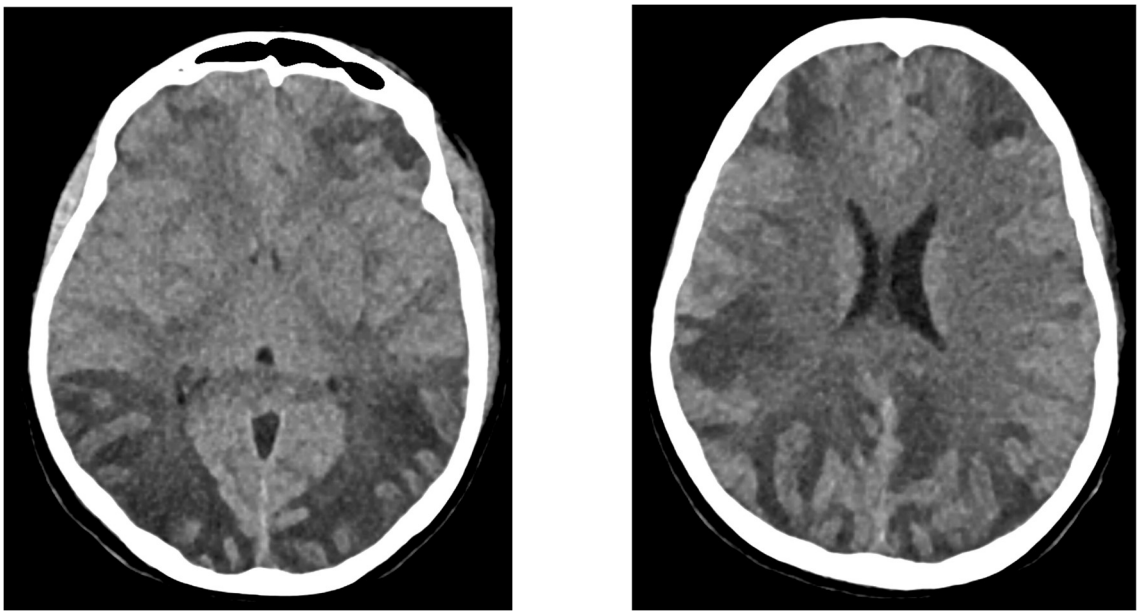

FIGURE-1(A&B)-CT Brain*:* Axial plane shows Intra axial ill defined diffuse multi-focal hypo dense areas in the bilateral cerebral hemispheres predominantly in bilateral occipital lobes, Bilateral corona radiata, centrum semiovale, gangliocapsular region, with perifocal sub-cortical mild edema with effacement of adjacent sulcal spaces

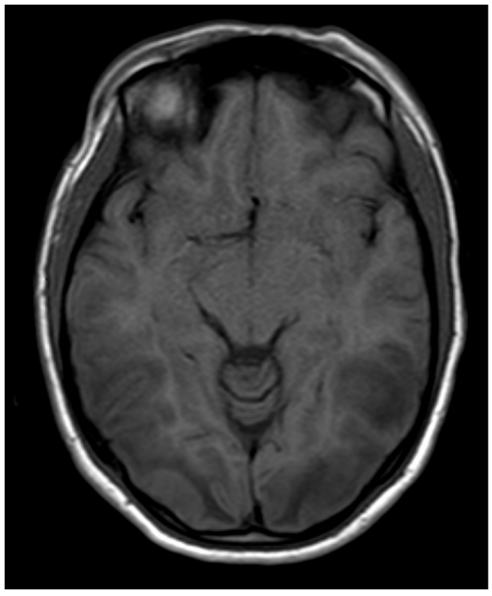

FIGURE-2-MRI BRAIN T1 AXIAL

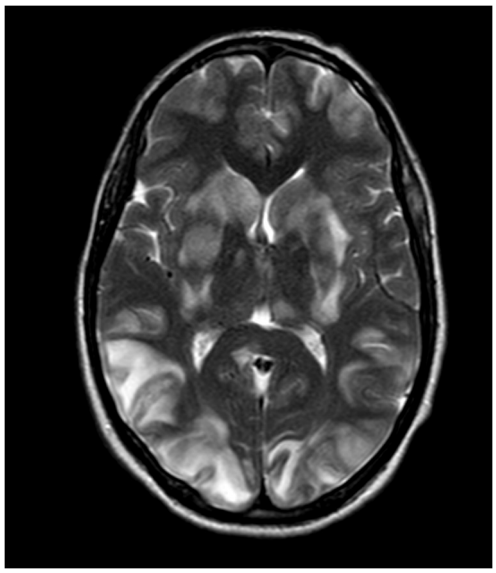

FIGURE-3-MRI BRAIN- T2 AXIAL

FIGURE 2&3-MRI - Brain: T1 Axial images shows Multi-focal / Multi-centric asymmetrical hypointensities areas of deep grey matter, deep white matter, sub-cortical white matter / U-fibers and cortical white matter in the bilateral cerebral hemispheres (bilateral ganglio-capsular region, bilateral thalami, bilateral frontal, parietal, temporal, occipital lobes, bilateral corona radiata, bilateral centrum semiovale)(predominantly in bilateral occipital lobes), bilateral cerebellar hemispheres and T2/FLAIR Axial shows corresponding hyperintensities

TREATMENT:

She was started on anti-epileptics, anti-hypertensives, anti-edema measures and continued on T.MMF, and T.HCQ and other supportive measures. Rheumatology opinion was obtained and suggested to continue T.HCQ and T.MMF and initiated on dexa in view of CNS involvement.After 2 days she had a drop in GCS- responding only to pain stimulus and was intubated and CT brain was done and no new changes were found. Patient was symptomatically managed on ventilatory support for 7 days and ET culture showed growth of Klebsiella pneumoniae and started on appropriate antibiotics. In view of persistently elevated urea levels hemodialysis was initiated and RFT monitored. Adequate hypertension control was done and she has no further episodes of seizures , patient demonstrated gradual improvement of neurological symptoms hence extubated and tracheostomy done. Currently patient is conscious oriented, off ventilator support and continued tracheostomy care given along with other supportive measures.

DISCUSSION

Posterior reversible encephalopathy syndrome (PRES) is a clinicoradiological entity that was first described by Hinchey et al. in 1996.[5] It is characterized predominantly by white matter edema affecting the occipital and posterior parietal lobes of the brain. The pathophysiology of PRES remains elusive. However, it has been suggested that compromised cerebrovascular autoregulation due to acute hypertension may play a pivotal role. Accordingly, impaired cerebrovascular regulation may lead to arteriole leakage and cerebral vasogenic oedema.[6]

The extensive use of immunosuppressive therapy (methylprednisolone, dexamethasone, cyclosporine and cyclophosphamide)[6] and the autoimmune nature of rheumatological diseases including SLE may render patients more vulnerable to developing PRES over the course of the disease.[7]

Rituximab is a murine/human-chimeric monoclonal antibody that depletes CD20+ B cells through both cell-mediated and complement-mediated cytotoxic effects with resultant apoptosis.[8] Rituximab, a monoclonal antibody against CD20, is widely used in various hematological malignancies, systemic lupus erythematosus, neuromyelitis optica and sarcoidosis, and because of the expression of CD20 in activated endothelial cells, it may cause direct cell damage and endothelin mediated vasospasm.[9] PRES has been described as an uncommon neurological manifestation in SLE, mainly associated with hypertension, renal insufficiency and use of immunosuppressive drugs.[10]

Mustafa KN et al.,[11] described a case report of 36-year-old woman with SLE and class IV lupus nephritis treated with pulse corticosteroids, cyclophosphamide and rituximab; her course was complicated by the development of signs and symptoms of PRES several days after receiving rituximab, and was successfully treated with full recovery.

The term posterior reversible encephalopathy syndrome may be a misnomer as the syndrome can involve or extend beyond the posterior cerebrum. Furthermore, although most cases involve a resolution of changes with the treatment of the precipitating cause and clinical recovery, some patients can progress to develop permanent cerebral injury and be left with residual neurological defects.

Secondary complications such as status epilepticus (SE), intracranial haemorrhage, and ischemic infarction can cause substantial morbidity and mortality.[12] The prognosis of PRES is often benign provided that early diagnosis is made and management is accurate and in time. In these cases restoration is usually seen several days or weeks after the onset of symptoms.[13] However, delayed diagnosis and improper management may result in permanent brain insult, even death.[14]

SLE is a multisystem disease affecting nearly every organ system of the body, making its diagnosis difficult, especially when the patient presents with rare manifestations. Although PRES is not common in SLE, it should be considered among differential diagnoses in patients presenting with seizures, altered mentation, and blurry vision consistent with brain imaging. This case

highlights the high index of suspicion, imperative assessment, early diagnosis, and treatment of PRES in SLE as PRES is reversible once the underlying precipitating cause is treated.

CONCLUSION

This case highlights the importance of recognizing the potential neurological complications, such as PRES, associated with rituximab therapy in patients with SLE. Early diagnosis and prompt management are crucial for achieving favorable outcomes. Healthcare professionals should maintain a high index of suspicion for PRES in SLE patients receiving rituximab and consider appropriate monitoring and intervention strategies.

REFERENCES

1. Casey SO, Sampaio RC, Michel E, Truwit CL. Posterior reversible encephalopathy syndrome: utility of fluid-attenuated inversion recovery MR imaging in the detection of cortical and subcortical lesions. AJNR Am J Neuroradiol 2000;21:1199-206.
2. Hobson E, Craven I, Blank S. Posterior reversible encephalopathy syndrome: a truly treatable neurologic illness. Perit Dial Int. 2012;32(6):590-594.
3. Rahman A, Isenberg DA (2008) Systemic lupus erythematosus. N Engl J Med 358: 929-939.
4. Merayo-Chalico, J., et al. Clinical outcomes and risk factors for posterior reversible encephalopathy syndrome in systemic lupus erythematosus: a multicentric case control study. J Neurol Neurosurg Psychiatry. 87(2016):287-94.
5. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al. A reversible posterior leukoencephalopathy syndrome. N Engl J Med 1996;334:494-500.
6. Bartynski WS. Posterior reversible encephalopathy syndrome, part 2: controversies surrounding pathophysiology of vasogenic oedema. AJNR Am J Neuroradiol 2008;29:1043–1049.
7. Rahmanzadeh R, Rahmanzade R, Zabihiyeganeh M. Posterior reversible encephalopathy syndrome in a patient with mixed connective tissue disease: a case report. J Med Case Rep 2016;10:145.
8. Reff ME, Carner K, Chambers KS, et al. Depletion of B cells in vivo by a chimeric mouse human monoclonal antibody to CD20. Blood. 1994;83(2):435-445.
9. Sa´nchez-Carteyron A, Alarcia R, Ara JR, Martı´n J. Posterior reversible encephalopathy syndrome after rituximab infusion in neuromyelitis optica. Neurology 2010; 74: 1471–1473.
10. Bartynski WS. Posterior reversible encephalopathy syndrome, part 2: controversies surrounding pathophysiology of vasogenic edema. AJNR Am J Neuroradiol 2008; 29: 1043-1049.
11. Mustafa KN, Qasem U, Al-Ryalat NT, Bsisu IK. Rituximab-associated posterior reversible encephalopathy syndrome. Int J Rheum Dis. 2019 Jan;22(1):160-165.

12. Kwon J, Kim S, Kim K, et al. A case of gemcitabine and cisplatin associated posterior reversible encephalopathy syndrome. Cancer Treat Res. 2009 March;41(1): 53–55.
13. Lee VH, Wijdicks EF, Manno EM, Rabinstein AA. Clinical spectrum of reversible posterior leukoencephalopathy syndrome. Arch Neurol 2008;65:205-10.
14. Grossbach AJ, Abel TJ, Hodis B, Wassef SN, Greenlee JD. Hypertensive posterior reversible encephalopathy syndrome causing posterior fossa edema and hydrocephalus. J Clin Neurosci 2014;21:207-11.
15. Kur, Jason K., and John M. Esdaile. "Posterior reversible encephalopathy syndrome--an underrecognized manifestation of systemic lupus erythematosus." *The Journal of rheumatology* 33.11 (2006): 2178-2183.
16. Siddiqi, Ahmed Imran. "Rituximab as a possible cause of posterior reversible encephalopathy syndrome." *The Australasian Medical Journal* 4.9 (2011): 513.

