NMDA Receptor Encephalitis with Significant Autonomic Instability and PRES Like MR Images

Anti N-methyl D-aspartate (NMDA) receptor encephalitis is the most common autoimmune encephalitis affecting young adults (median age of 21 years, range 1-85 years) and females (8:2 ratio).[1] The patients present with sleep disturbances, neuropsychiatric disorders, seizures or status epilepticus, abnormal movements, memory disturbances, and behavioral disturbances. Autonomic disturbances like tachycardia, bradycardia, bradyarrhythmia, cardiac asystole, tachyarrhythmia, hypothermia, hyperhidrosis, and hypertension are commonly associated with autoimmune encephalitis.[2-6]

Admission to intensive care unit, treatment delay for >4 weeks after disease onset, no improvement after four weeks of treatment initiation, abnormal Cerebro Spinal Fluid (CSF) and Magnetic Resonance (MR) imaging are independent for functional outcome after one year, hence delay in initiation of treatment may predict poor outcome.[1] Here, we describe a case of NMDAR encephalitis complicated with significant autonomic disturbances and paroxysmal episodes of hypertension with MR imaging of posterior reversible encephalopathy syndrome (PRES).

A 29-year-old female, with no co-morbidities, was treated for psychiatric disturbances for 15 days, later she presented with status epilepticus to the emergency department, where she was intubated and shifted to the intensive care unit. She has behavioral disturbances, memory disturbances, and perioral dyskinesias. The MR brain imaging showed hyperintensity in the right anteromedial temporal cortex indicating autoimmune encephalitis. CSF and serum anti-NMDA antibody titers were raised (Serum Anti-NMDA positive titer 1:10, CSF Anti-NMDA positive 1:10), and computed tomography of the abdomen revealed left ovarian cystic lesion with enhancing solid components, thin septation, fat, and calcification, suggestive of left ovarian teratoma. The EEG was suggestive of generalized slowing and extreme delta brush pattern. CSF infections were ruled out with a negative CSF meningo encephalitis panel. She was diagnosed to have NMDAR encephalitis and was treated with pulse doses of intravenous methylprednisolone and intravenous immunoglobulin which was started on the 16th day of disease onset. She underwent laparoscopic resection of the left ovarian mass, and histopathological examination confirmed immature ovarian teratoma grade 3. On day 40 after symptom onset, she developed intermittent paroxysmal episodes of malignant hypertension associated with severe dyskinesia of the perioral region leading to lip mutilation and worsening sensorium. Repeat MR brain imaging showed heterogenous hyperintensities involving bilateral parietooccipital white matter with hemorrhagic foci suggestive of PRES. MR images are shown in Figure 1. She received intravenous labetalol, furosemide, and oral clonidine for control of malignant hypertension. Electrocardiograph (ECG) and Echocardiogram (ECHO) were normal. Her hospital course was complicated with systemic infection, sepsis, and multiple organ failure requiring dialysis. She received 1st dose of rituximab (375 mg/ms/dose) on day 45 of disease onset. She had minimal improvement in her sensorium with second-line immunotherapy and was shifted to the nearby nursing center for further management.

NMDAR encephalitis is associated with autoantibodies against Glu1 NMDA antigen.[1] Generally followed by a viral prodrome, a patient presents with behavioral disturbances, seizures, memory disturbances, movement abnormality, catatonia, and sleep disturbances. The dysautonomia, seizures, and worsening memory disturbances are the neurological complications associated with later stages of NMDAR encephalitis.[1] Early treatment and no intensive care admission, leads to better functional outcome after one year. Dysautonomia is usually present in the later stages of NMDAR encephalitis, which includes tachyarrhythmia, bradyarrhythmia, cardiac asystole, hyperhidrosis, hypothermia, hyperthermia, hypoventilation, and variation in heart rate are described in the literature. We encountered a case with malignant hypertension and MR imaging of PRES complicating the management of NMDAR encephalitis.

PRES is an acute neurological disorder presenting with a history of headache, encephalopathy, visual disturbances, and seizures, which is usually associated with altered cerebral autoregulation leading to accelerated hypertension and endothelial injury, cerebral hyperperfusion, and cytokines and T lymphocyte aggregation.[7] Other causes of PRES are renal failure, preeclampsia/eclampsia, cytotoxic drugs, post-transplant, and autoimmune disorder. MR imaging of the brain is suggestive of vasogenic oedema in subcortical white matter predominantly involving parietooccipital lobe, and less frequently frontal lobe, holo-hemispheric watershed pattern, brainstem, and spinal cord.[7]

The autoimmune disorders like systemic lupus erythematosus (SLE), hypothyroidism, scleroderma, Crohn's disease, ulcerative colitis, primary sclerosing cholangitis, rheumatoid arthritis, Sjogren syndrome, Neuromyelitis Optica, granulomatosis with polyangiitis, and thrombotic thrombocytopenic purpura are frequently associated with PRES.[7-13] The autoimmune disorders lead to endothelial injury, T lymphocyte, and monocyte activation and aggregations, cytokine activation leading to Vascular Endothelial Growth factor (VEGF) activation, and an increase in permeability and endothelial injury. PRES can present as initial manifestations of autoimmune disorders like LGI1 encephalitis.[9] The association between Autoimmune Encephalitis (AE) and PRES is not well described, however, interleukin 6 and VEGF is increased in immune-mediated disorder which leads to endothelial injury, and precipitates PRES; alternatively, PRES can lead to endothelial injury and disruption of the blood-brain

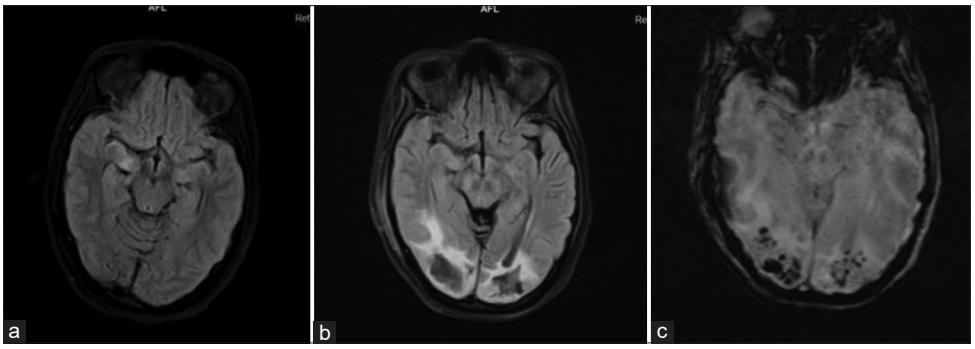

Figure 1: (a) T2 FLAIR suggestive of bilateral medial temporal pole (right > left) hyperintensity. (b) T2 flair shows bilateral medial occipital white matter heterogenous hyperintensity without mass effect. (c) SWI image shows punctate hemorhagic foci in bilateral occipital lobe

barrier, exposing the brain epitope. Whether an immune injury is primary or secondary to underlying endothelial injury and lymphocyte activation is yet not clear, however, there is evidence of immune-mediated injury in a certain biopsy report.

NMDAR encephalitis can be complicated with autonomic disturbances; requiring Intensive Care Unit (ICU) care and mechanical ventilation; hence, predicting a poor functional outcome.[7,14,15] Autonomic disturbances can independently predict poor functional outcomes.[14,15] PRES is well described in patients with malignant hypertension, here we describe a case with autonomic disturbances, malignant hypertension, and PRES like MR image. Recognizing autonomic disturbances, MR imaging of PRES, and early treatment can improve functional outcomes. To the best of our knowledge, we describe the first case associating PRES and NMDAR encephalitis elaborating the complications of NMDAR encephalitis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

Nil.

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Submitted: 19-May-2022 **Revised:** 03-Aug-2022 **Accepted:** 04-Aug-2022
Published: 03-Dec-2022

DOI: 10.4103/aian.aian_449_22