Case Report

Autoimmune Encephalitis (Anti NMDA Receptor Antibody Encephalitis) — Our Experience

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Autoimmune Encephalitis is an immune mediated Neurological Disorder which was recognized only in the 21st century. Neuroimmunology is one arena of Neurology which is amenable to effective management if identified early. There are many types of Autoimmune Encephalitis with unique clinical manifestations. N-methyl-D-aspartate Receptor (NMDAR) encephalitis can present with subacute onset behavioral disturbances, movement disorders, cognitive decline and new onset seizures which is refractory to antiepileptic drugs. It is commonly seen in young females sometimes in association with ovarian tumors. Immunotherapy when started early in the course of the disease usually causes significant improvement of neurological symptoms. We treated two young females with NMDAR Encephalitis who improved well with Immunotherapy. Both of the patients presented with recent onset behavioral disturbances and seizures which was refractory to antiepileptic drugs.

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Key words **: Autoimmune encephalitis, New onset refractory seizures, Behavioural disturbances.**

Neuro immunology is considered to be a unique subspecialty of Neurology, wherein, timely diagnosis and appropriate treatment of the neurological syndrome leads to significant recovery. It is imperative to consider an immunological pathogenesis, when encountered with any form of acute or subacute neurological disorder. We report the following two cases of autoimmune encephalitis (Anti NMDA receptor antibody encephalitis) to emphasize the need for high index of suspicion to diagnose this rare treatable entity. Both of our patients responded exceptionally well to timely immunotherapy.

Case 1 :

A 21-year-old female with no significant past history presented with history of altered behaviour in the form of apathy and mutism of 2 weeks duration followed by multiple episodes of complex partial seizures with secondary generalisation over a period of 1 week. On examination, she was found to be in a state of post ictal confusion. Cranial nerves, motor system, sensory system, cerebellum and extrapyramidal system were normal on examination. There were no meningeal signs. Patient was started on multiple anti epileptic drugs because of recurrent episodes of seizures. She was on phenytoin 300mg, levetiracetam 1500mg, phenobarbitone 120 mg and clobazam 20 mg per day. Based on the history of recent onset behavioral disturbances and new onset seizures, the possibility of Viral Encephalitis / Autoimmune Encephalitis was made. Laboratory parameters were within normal range. Magnetic Resonance Imaging (MRI) of the brain did not show any abnormality. EEG showed (black arrow) left Temporal Intermittent Rhythmic monomorphic delta range slow waves (TIRDA)(Fig 1).

CSF analysis was done which was acellular with normal sugar and protein. Cerebrospinal Fluid (CSF) and serum viral antibody profile including Herpes Simplex Virus (HSV) was negative. CSF NMDAR antibody was positive. Patient was started on intravenous methylprednisolone 1 gm IV once daily for 5 days. She also received IV antibiotics and IV acyclovir for 14 days.

A course of intravenous immunoglobulin 20 gram per day was given for 5 days. During the course in hospital patient had disinhibited behavior, anger outbursts, inappropriate laughter and other weird behavioral disturbances. Following treatment, patient gradually improved with no further episodes of seizures. The patient's behavioural disturbances partially improved over the next few weeks. Patient was also given weekly Rituximab 500mg for 4weeks.She is on regular follow up.

Editor's Comment :

- The clinical manifestations of Autoimmune Encephalitis are diverse and are often multifocal.
- Detection of a neural specific autoantibody serves as a marker of neurologic autoimmunity.
- Timely recognition and appropriate immunotherapy ensures a better prognosis in patients with Autoimmune Encephalitis.

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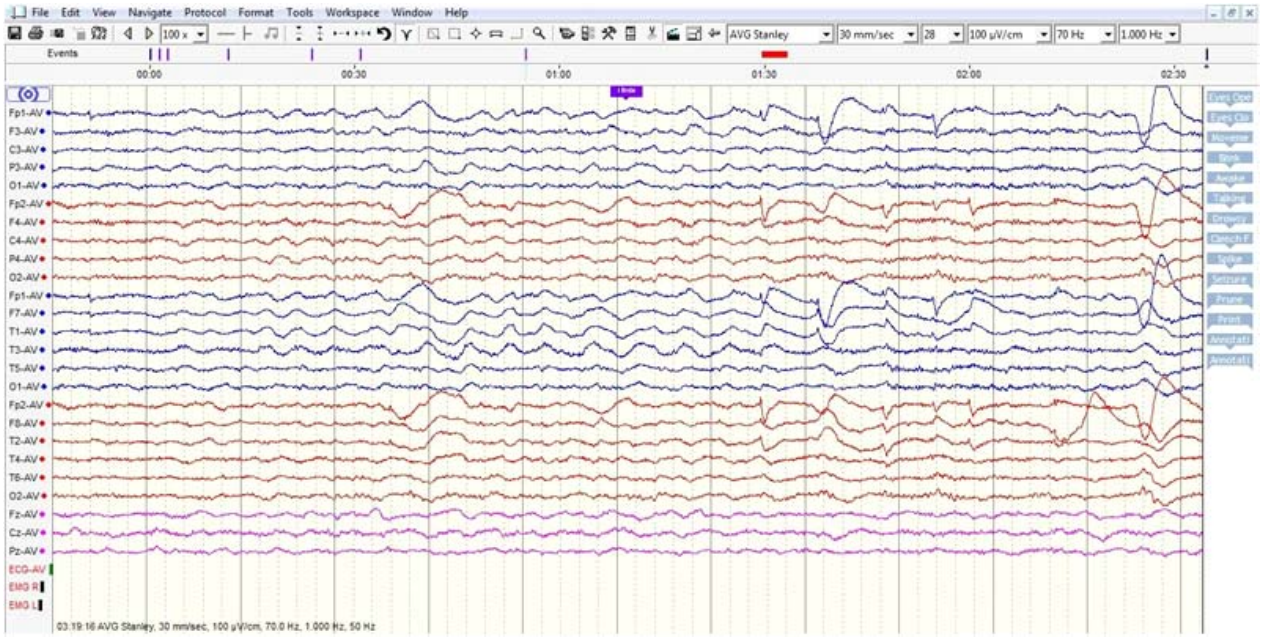

Fig 1 — EEG showed (black arrow) left temporal intermittent rhythmic monomorphic delta range slow waves (TIRDA)

Case 2 :

A 13-year-old girl presented with history of behavioral disturbances in the form of insomnia, excess shouting, anger outbursts, episodes of mutism and temper tantrums followed by fixed gaze to left side with epileptic partialis continua involving left upper limb. On examination, patient had gaze preference to left side with recurrent clonic twitching of left forefinger and left great toe with dystonic posturing of left foot. Patient was initiated on multiple Automated External Defibrillator (AED's) since she had relentlessly continuing left focal seizures. She was on Phenytoin 300mg, Levetiracetam 2000 mg, Lacosamide 200mg and Clobazam 20 mg per day with Midazolam infusions in between. Based on the clinical features of new onset uncontrolled seizures and associated behavioral/personality disturbances, a diagnosis of viral/autoimmune Encephalitis was made. Laboratory parameters were normal. MRI Brain was normal. EEG showed medium to high amplitude polymorphic slow waves in delta range over right hemisphere (Fig 2). CSF and serum viral profiles including HSV was negative. CSF NMDAR and serum NMDAR antibodies were positive. Patient was initiated on intravenous Methylprednisolone for 5 days followed by a 5 day course of intravenous immunoglobulin. We noted marked improvement of behavioral disturbances and focal seizures over a period of 2weeks following treatment. Patient was also given weekly Rituximab for 4 weeks. The patient is on regular follow up.

Discussion

We encountered two young females with NMDAR Encephalitis who had similar types of presentation in the form of new onset recurrent seizures and behavioral disturbances which responded well to immunotherapy. Autoimmune Encephalitis is a treatable disease, which has to be recognized early[1]. The clinical symptomatology of this group of diseases ranges from very subtle symptoms to severe manifestations like status epilepticus and psychosis[2]. Anti-N-Methyl-D-Aspartate Receptor Encephalitis was initially reported by Dalmau *et al* in 2007. It is commonly seen in children and young adults[2]. The Pathophysiological mechanisms by which these autoantibodies against NR1 subunit of NMDAR cause Central Nervous System (CNS) damage is being unraveled[3]. The role of complements is uncertain. The synthesis of NMDAR antibodies inside the CNS has been demonstrated in several studies[4].

A viral prodrome invariably precedes the disease. Infection with mycoplasma or other microbes is found to herald certain cases of autoimmune Encephalitis[5].

One third of patients with herpes simplex Encephalitis develop NMDAR Encephalitis, suggesting a secondary autoimmune response. The disease evolves in stages. Stage 1 is characterized by fever and headache. During stage 2, patient develop mild anxiety, irritability and anger outbursts. On reaching Stage 3, patients develop seizures, psychosis and severe disability.MRI brain is normal in the majority of patients. About one third of patients may have non specific cortical and subcortical hyperintensities. CSF analysis may show increased proteins and lymphocytosis. EEG shows focal epileptiform discharges or generalized slowing.

The sine qua non EEG feature of "delta brush" is rare. The diagnosis is made by detecting NMDAR antibodies

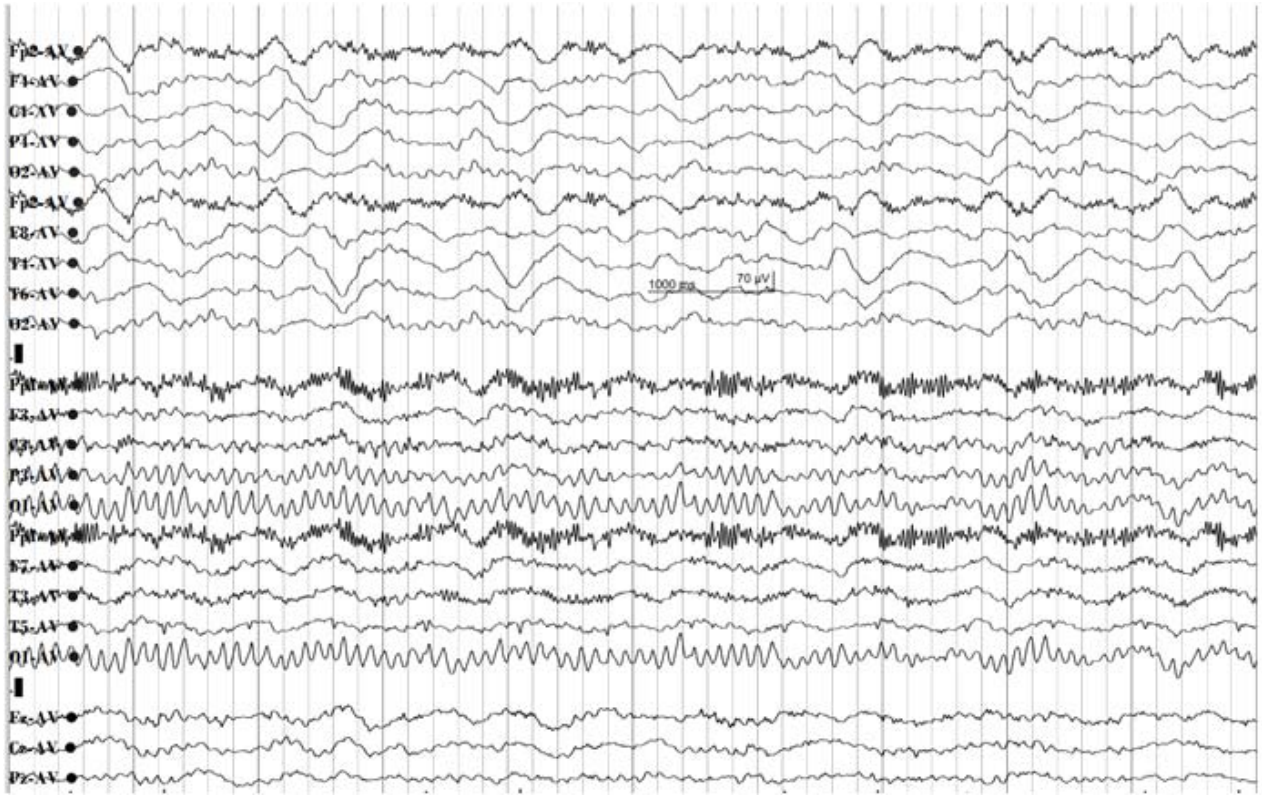

Fig 2 — EEG showed (black arrow) medium to high amplitude polymorphic slow waves in delta range over right hemisphere

in the CSF or serum. Majority of these patients recover well with immunotherapy although rare instances of death can occur[6]. Residual cognitive and psychiatric symptoms may persist in few cases. Treatment with corticosteroids, Intravenous Immune Globulin (IVIG) and Plasmapheresis forms the first line of treatment in these cases. Refractory cases are treated with Rituximab, Cyclophosphamide and other immuno-suppressants.

Conclusion :

We would like to highlight the fact that Autoimmune Etiology has to be looked for in any subacute onset Neurological Syndrome as it is highly responsive to timely immunotherapy. More research in neuroimmunology will unravel many known aspects of this entity.

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