Psychosis associated with anti-N-methyl-d-aspartate receptor encephalitis

Udayan Bhaumik¹, Hemendra Singh²

¹Department of Psychiatry, Pramukhsamvi Medical College, Karamsad, Gujarat, India,
²Department of Psychiatry, MS Ramaiah Medical College and Hospital, Bengaluru, Karnataka, India

Correspondence: Dr. Hemendra Singh, MBBS, MD, Assistant Professor, Department of Psychiatry, MS Ramaiah Medical College and Hospital, Bangalore-560054, Karnataka, India. hemendradoc2010@gmail.com

Received: 20 March 2018
Revised: 21 November 2019
Accepted: 25 November 2019
Epub: 28 November 2019
DOI: 10.5958/2394-2061.2020.00007.5

INTRODUCTION

Various psychiatric presentations are known in patients with synaptic autoimmune neurological disorders. Anti-N-methyl D-aspartate (NMDA) receptor encephalitis is one such novel entity. First reported in 2007,[1] there has been a rapid accumulation of literature on neuropsychiatric manifestations of anti-NMDA receptor encephalitis. It is characterised by prominent psychotic symptoms and behavioural disturbances along with neurological presentations such as catatonia, seizures, dyskinesias, autonomic dysfunction, and impaired consciousness.[2] It commonly occurs in women (80%) and is associated with neoplasms, mainly ovarian teratomas in about half of those cases.[3] Retrospective studies have found that approximately one per cent of all intensive care unit (ICU) admissions in patients between the ages 18-35 years had this autoimmune synaptic encephalitis.[4] The typical age of presentation is young adulthood (<30 years), in whom it is nearly as common as viral encephalitis.[5] Viral illnesses have been implicated as a trigger for this autoimmune activation.[6] Psychotic symptoms are usually the first to draw attention, with patients often getting admitted to psychiatric setups initially.[7] Purely psychiatric presentation is known to four per cent of those who are affected.[8] In this case report, we describe a 22-year-old woman presenting with this disorder and how recovery was managed in this case.

CASE SUMMARY

A 22-year-old woman was admitted under neurology in ICU of MS Ramaiah Medical College and Hospital, Bengaluru, Karnataka, India with history of three episodes of generalised tonic-clonic convulsions, fever, and psychotic symptoms for one week. She had delusion of persecution and symptoms of catatonia prior to admission. She was treated with intravenous levetiracetam 500 mg and phenytoin 100 mg twice daily. Her complete blood count, thyroid function test, urine examination, serum electrolytes, creatinine phosphokinase, renal function tests, and fundus examination were normal. Cerebrospinal fluid (CSF) examination showed 100% lymphocytes with normal serum adenosine deaminase. DNA assay for herpes simplex viruses 1 and 2, varicella zoster virus, and acid-fast bacilli, cryptococcal antigen detection test, blood and urine cultures were negative. Electroencephalography (EEG) and ultrasonography (USG) of abdomen and pelvis were unremarkable. Acyclovir 500 mg thrice a day was empirically started. Magnetic Resonance Imaging (MRI) showed multiple scattered foci of high signal intensity in supratentorial white matter regions of brain corresponding to the limbic cortex (Figure 1). Patient was then found positive for NMDA and thyroid peroxidase receptor antibodies in CSF whereas voltage-gated potassium channel antibodies (LGI1 and CASPR2) were negative. She was diagnosed with anti-NMDA receptor encephalitis. She was treated with quetiapine 50 mg and clonazepam 0.5 mg for the psychiatric symptoms. She was also started on intravenous immunoglobulins (Ig) for five days and thereafter with methylprednisolone infused in normal saline four times daily for another five days before being started on prednisolone 50 mg daily in three divided doses. It had to be discontinued.

Abstract

Aim: Anti-N-methyl D-aspartate (NMDA) receptor encephalitis is commonly seen in women with various neuropsychiatric symptoms. Here we report a case of psychosis associated with anti-NMDA receptor encephalitis. Case description: A 22-year-old woman was admitted with acute onset fever, generalised tonic-clonic seizures, reduced speech output, and delusion of persecution for one week. She was found positive for anti-NMDA receptor antibodies and anti-thyroid peroxidase antibodies. Her psychotic symptoms improved with antipsychotics, immuno-modulators, and steroids within two months. Conclusion: A possibility of anti-NMDA receptor encephalitis should be kept in mind in young women presenting with psychotic symptoms. It is ideal to liaise with neurologist to screen all such cases with suspicion of autoimmune encephalitis visiting a psychiatry clinic.

Keywords: Neuropsychiatry. Delusion. Antipsychotics.

CASE STUDY

A 22-year-old woman was admitted under neurology in ICU of MS Ramaiah Medical College and Hospital, Bangalore-560054, Karnataka, India.
due to worsening of psychotic symptoms. She was discharged on tablet levetiracetam 750 mg and mycophenolate mofetil 500 mg twice daily. She lost to follow-up in psychiatry but was readmitted in neurology after two months with another relapse having reduced responsiveness, irrelevant talk, and overfamiliarity of one week, and improved in two weeks with mycophenolate mofetil 500 mg thrice daily.

**DISCUSSION**

Our patient, presenting in the same age group as observed in most studies,[6,7,9,10] had history of fever, confused behaviour, and psychiatric manifestations. Although not clearly demarcated, the stages of anti-NMDA encephalitis were observed in our case. Similar to previously reported cases, CSF examination was also normal in our case apart from lymphocytosis. MRI brain showed non-specific scattered foci of high intensity and EEG also was normal as other cases described.[6,7,9-13] As in other cases, our patient also improved rapidly once immuno-modulator therapy was given [9,12-14] However, recovery was slow with an indolent course characterised by relapses, as seen in other case reports.[3-6]

We have not found any associated tumour on USG examination. However, the illness may precede the underlying neoplasm; hence, periodic surveillance for at least two years using MRI USG of the abdomen and pelvis in females of all ages is recommended.[8] NMDA receptors are ligand-gated cation channels which bind glycine and glutamate, and play crucial role in synaptic transmission and plasticity.[15] Anti-NMDA receptor encephalitis is associated with antibodies against NR1-NR2 heteromers expressed mainly in hippocampus and forebrain. The mechanism for evolution of psychiatric symptoms in this condition is believed to be secondary to rapid and reversible loss of surface NMDA receptor by antibody-mediated capping and internalisation emergence of a state of NMDA receptor hypofunction.[16] It thus gives impetus to the NMDA receptor hypofunction theory and phencyclidine model of psychosis.[11] It usually affects young women with a mean age of 23 years (range: five to 76 years). Rapid removal of the neoplasm is associated with good prognosis with reduced risk of relapse in future.[12] The clinical course of this highly characteristic syndrome is known to follow five stages: prodrome phase, psychotic phase, unresponsive phase, hyperkinetic phase, and gradual recovery phase.[9] Supportive findings include lymphocytic pleocytosis or oligoclonal bands in CSF. EEG may show infrequent spikes, frequent slow, disorganised, and sometimes rhythmic activity; but, these are not specific. In one third of patients, a unique EEG pattern of ‘delta brush’, consisting of 1-3-Hz rhythmic activity with superimposed 20-30 Hz rhythmic activity has been reported,[10] MRI is normal in half of the cases or may show transient FLAIR or contrast-enhancing abnormalities. Autopsy changes reveal IgG deposits over the hippocampus, microgliosis, and neuron degeneration in hippocampal area,[13] Treatment data suggest that over half of patients respond to first-line immunotherapy (steroids, intravenous Ig, and plasmapheresis, alone or in combination) within four weeks. Second-line treatment (rituximab and/or cyclophosphamide) is usually effective and can be considered when first-line therapies fail.[14] In a case series of 100 patients,[14] 25 had severe deficits and died later. Despite immuno-modulator treatment, all the patients continued to remain anti-NMDA receptor antibody positive and correlation of psychotic symptoms also has been found to the antibody levels.

**Conclusion**

Prompt recognition of anti-NMDA receptor encephalitis is important as it is treatable and can be diagnosed serologically. Our case highlights the importance of high index of suspicion in diagnosing anti-NMDA receptor encephalitis, particularly in young women presenting with neuropsychiatric manifestations, especially in absence of previous psychiatric history. Necessary investigations must be undertaken to identify an underlying neoplastic disorder, although the absence of an underlying neoplasm does not reduce the likelihood of the illness as in our case. Recovery in our case might be due to early diagnosis and treatment; hence, multidisciplinary treatment should be done in all cases where it is suspected.

**REFERENCES**

7. Kayser MS, Titulaer MJ, Gress-Arribas N, Dalmau J. Frequency and characteristics of isolated psychiatric episodes in...

Source of support: Nil. Declaration of interest: None.