Psychiatric manifestations of anti-N-methyl-D-aspartate receptor encephalitis: A case report

Anti-N-methyl-D-aspartate (NMDA) receptor (NMDAR) encephalitis is a rare and relatively new type of synaptic encephalitis first described by Josep Dalmau in 2007. It is an autoimmune disorder in which antibodies attack NMDA-type glutamate receptors at central neuronal synapses. Antibodies directed toward the NR1 and NR2 heteromers of NMDARs circulate within cerebro spinal fluid (CSF). NR1 and NR2 heteromers predominate within the hippocampus, with less density in the forebrain, basal ganglia, spinal cord, and cerebellum.[1] Thus, antibodies affect areas responsible for memory, personality, movement, autonomic control, and cognition.[1] Immunologic triggers such as viral infections and neoplasms contribute to the production of NMDAR autoantibodies.[2-3]

A 16-year-old female, known case of seizure disorder, maintained on oxcarbazepine 300 mg/day was brought to the psychiatry outpatient department following an 8-day history of suspiciousness, auditory and visual hallucinations, agitation, sleeplessness, and poor self-care. Following unremarkable neurological examination and head computed tomography, the patient was diagnosed as acute schizophrenia such as psychotic disorder and admitted and started with haloperidol 10 mg/day, trihexyphenidyl 6 mg/day, and oxcarbazepine 450 mg/day. There was no improvement with antipsychotics instead she developed rigidity, intermittent facial twitching, and bladder incontinence. Five days after admission, she had three episodes of generalized tonic clonic seizure despite being on oxcarbazepine. Phenytoin loading was initiated and she was shifted to the medical intensive care unit. All routine investigations including routine CSF analysis and magnetic resonance imaging brain plain was normal. Electroencephalogram (EEG) showed background 5–6 Hz theta activity mixed with slow delta waves which was suggestive of diffuse cerebral dysfunction.

During the following days, she had falling SpO₂ levels, incomprehensible speech, bursts of shouting, and disorganized behavior and became delirious. CSF analysis for viral encephalitis was sent, and presumptive acyclovir was started. CSF and serum samples were sent for testing of anti-nuclear antibodies and anti-NMDAR antibodies, and intravenous methyl prednisolone was started. CSF serologic results demonstrated strong reactivity with the NMDARs in CSF, confirming the diagnosis of anti-NMDAR encephalitis. Following corticosteroid therapy, the patient’s mental status improved slightly over the next 3 weeks, fluctuating between communicable periods, catatonia, and extreme agitation, for which she was treated with oral risperidone and lorazepam. Over the following month, gradual improvement was observed. Antipsychotic and anxiolytic drugs were tapered down and stopped. The patient was discharged after 2 months of inpatient care. Over the next 3 months, the patient regained skills such as planning ahead, doing household chores, and attending school and monetary management. Oral prednisolone was tapered off over 6 months. She was maintained on oxcarbazepine 300 mg/day for her seizure disorder.

On a follow-up visit 6 months after recovery, the patient reported feeling happy and satisfied with her health. On examination, her affect was euthymic with a logical and coherent thought process. Although episodic memory pertaining to events before her hospitalization was preserved, she was entirely amnestic for all events that occurred during the first 3 months after hospitalization. This report illustrates the case of a female admitted following an acute-onset episode of hallucinations and suspiciousness initially treated as psychosis till she was diagnosed correctly. In a case series, 77% of the patients were evaluated by a psychiatrist before diagnosis of anti-NMDAR encephalitis.[4] Abnormal function of the NMDA-type glutamate receptors provides an alternative model to understanding the pathogenesis of schizophrenia. On screening 46 patients of first-episode psychosis, two tested positive for NMDAR antibodies. There were no clinical features to differentiate these individuals from other individuals with psychosis in the study.[5] EEG studies are not helpful in making a specific diagnosis. However, EEG is helpful in differentiating between psychiatric and encephalitic etiologies of behavioral disturbances, because most patients with encephalitis will have EEG abnormalities. In anti-NMDAR encephalitis, EEG is abnormal in 90% of patients.[6] In this case, EEG showed diffuse cerebral dysfunction.
Presence of rigidity, altered consciousness, and autonomic instability may suggest a diagnosis of NMS. Our patient developed rigidity, choreoathetosis movements, and dystonic posturing as the disease progressed causing confusion between encephalitis presentation and antipsychotic-induced extra pyramidal symptoms (EPS). Studies indicate worsened motor manifestations with antipsychotics, indicating that these patients cannot tolerate antipsychotics and are more prone to develop EPS. Future clinical work will need to examine more fully the psychiatric manifestations of the disorder and how to provide optimal care, not only during acute hospitalization but also in the prolonged recovery process.

Psychiatric diagnosis of acute psychosis should be made only after possible organic syndromes that mimic acute psychosis are eliminated. This case illustrates the pertinent need for psychiatrists, neurologists, and other physicians to become aware of anti-NMDAR encephalitis and its presentation.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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REFERENCES
1. Tüzün E, Zhou L, Baehring JM, Bannykh S, Rosenfeld MR, Dalmau J. Evidence for antibody-mediated pathogenesis in anti-NMDAR encephalitis associated with ovarian teratoma. Acta Neuropathol 2009;118:737-43.
2. Sansing LH, Tüzün E, Ko MW, Baccon J, Lynch DR, Dalmau J. A patient with encephalitis associated with NMDA receptor antibodies. Nat Clin Pract Neurol 2007;3:291-6.
3. Dalmau J, Gleichman AJ, Hughes EG, Rossi JE, Peng X, Lai M, et al. Anti-NMDA-receptor encephalitis: Case series and analysis of the effects of antibodies. Lancet Neurol 2008;7:1091-8.
4. Irani SR, Bera K, Waters P, Zuliani L, Maxwell S, Zandi MS, et al. N-methyl-D-aspartate antibody encephalitis: Temporal progression of clinical and paraclinical observations in a predominantly non-paraneoplastic disorder of both sexes. Brain 2010;133:1655-67.
5. Zandi MS, Irani SR, Lang B, Waters P, Jones PB, McKenna P, et al. Disease-relevant autoantibodies in first episode schizophrenia. J Neurol 2011;258:686-8.
6. Dalmau J, Lancaster E, Martinez-Hernandez E, Rosenfeld MR, Balice-Gordon R. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. Lancet Neurol 2011;10:63-74.
7. Chapman MR, Vause HE. Anti-NMDA receptor encephalitis: Diagnosis, psychiatric presentation, and treatment. Am J Psychiatry 2011;168:245-51.

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