## An Unusual Case of Anti-NMDA-Receptor Encephalitis in the Psychiatry Inpatient Unit

*To the Editor:* Anti-N-methyl-D-aspartate (anti-NMDA) receptor encephalitis is a treatable paraneoplastic encephalitis that has been increasingly reported in predominantly young women harboring an ovarian teratoma. It usually presents with a combination of neuropsychiatric symptoms. This autoimmune disorder is likely mediated by antibodies against the NR1 subunit of the receptor. Since typical presentation is with acute psychotic symptomatology, these patients may initially present to the psychiatric service. Thus, a delay in diagnosis and treatment can occur unless a high index of clinical suspicion is maintained. The authors present here an unusual case of anti-NMDA-receptor encephalitis in a 52-year-old man who had a prolonged psychiatric course before seizure activity and autonomic instability was noted. Our case adds to the existing literature and emphasizes that anti-NMDA-receptor encephalitis can be seen in a wide spectrum of patients and should be included in the differential diagnosis for all patients presenting with acute onset of psychosis.

Encephalitis in healthy individuals is generally thought to be viral in origin. Anti-NMDA receptor encephalitis is now a well-documented cause of neuropsychiatric presentation, especially in young women harboring an ovarian teratoma. In male patients, frequently, a tumor may not be found in spite of a diligent search.

**Case Report**

A 52-year-old Chinese man was admitted to the inpatient psychiatric unit of an academic teaching hospital with an admitting diagnosis of major depressive disorder (MDD) with psychotic features. His chief complaint was "I do not feel happy." The patient endorsed insomnia, hopelessness, passive suicidal ideation, and increased anxiety, especially at bedtime. He was disheveled, guarded, demonstrated poor eye contact, slurred and decreased speech output, psychomotor retardation, poor cognition, flat affect, and vague auditory and visual hallucinations of seeing and hearing people. The patient had a past psychiatric history of MDD with psychotic features diagnosed when he was in his early 30s, and suicidal gestures. He had two previous inpatient admissions while in China in 2008, for psychotic features described then as robotic speech, flat affect, and minimal verbal responsiveness. At the time of his current admission, he was being followed in the psychiatry outpatient clinic. He denied past or current substance abuse. The patient's past medical history was significant for one observed tonic–clonic seizure in December 2009, which was managed with phenytoin 300 mg daily. At that time, neurologic evaluation was unrevealing, and no etiology of the seizure was identified.

After initial evaluation in the hospital, the patient was started on escitalopram 15 mg daily and paliperidone 3 mg daily, and his phenytoin 300 mg daily was continued. ECT had been considered while he was being followed as an outpatient. Upon admission, he was started on a course of ECT. Despite numerous medication trials including paliperidone, olanzapine, and clozapine, as well as a series of 12 ECT treatments, the patient's condition did not improve, and he began to show signs of cognitive decline. A neurology consult was requested for continued agitated and bizarre behavior. An EEG showed diffuse slowing, and a magnetic resonance (MRI) scan showed only small-vessel ischemic microvascular disease.

After 2 months, while still on the psychiatry inpatient unit, he developed symptoms of extreme agitation, aggressiveness, and unusual behavior, and was verbally unresponsive. His agitation was treated with lorazepam. Vital signs at that time revealed tachycardia to a heart rate of 120 bpm, a blood pressure of 90/50 mmHg, and $O_2$ saturation of 90% at room air. His temperature was 102.3°F. The patient was transferred to the medical intensive care unit (MICU) and intubated for airway protection. Laboratory data at transfer revealed a white cell count of 11.2 K/$\mu$l, BUN 32 mg/dl, Cr 1.2 mg/dl, and creatine kinase 2,361 u. Neuroleptic malignant syndrome was suspected but ruled out, as the patient's temperature and creatine kinase trended down in the subsequent days without any active intervention. After 11 days, he was extubated. He displayed echopraxia, but no focal findings were documented.

Because of his unusual course, failure to respond to standard treatments for depression and psychosis, and the presence of a documented seizure 1 month before

admission, a work-up for possible anti-NMDA receptor antibody encephalitis was started. Lumbar puncture yielded clear, colorless fluid which was acellular, with a glucose of 76 mg/dl and protein of 21 mg/dl. VDRL and oligoclonal bands were negative. CSF and serum sample was also sent for anti-NMDA receptor antibody testing. The patient had an EEG performed, which revealed bilateral independent temporal lobe discharges more prominent in the left hemisphere than the right, but no active seizures were seen. CSF and serum results confirmed the patient's diagnosis of anti-NMDA antibody encephalitis by the presence of antibodies against NRI-NR2 heteromers of the NMDA receptor. The patient was transferred to another hospital and lost to follow-up.

**Discussion**

Anti-NMDA receptor antibody encephalitis is a potentially reversible condition that typically afflicts younger women and presents with psychiatric disturbances, amnesia, seizures, autonomic features, obtundation, orofacial dyskinesias, and intermittent jerking of the limbs and trunk.[1] It often develops as a paraneoplastic syndrome. A recent study of 100 patients with this condition revealed that 59% had a tumor.[2] The most commonly described tumor with these patients is an ovarian teratoma. Patients usually have CSF pleocytosis, which is attributed to cerebral inflammation that generally occurs with this condition.[3] Many patients with anti-NMDA receptor antibody encephalitis are admitted to psychiatric inpatient units on initial presentation and subsequently develop seizures and autonomic instability within days of their admission.[4] Although there have been documented cases of anti-NMDA receptor antibody encephalitis in patients up to 76 years old, recent studies have postulated that the majority of patients with this disease are under 45 years old.[2] Kumar et al. recently reported anti-NMDAR encephalitis in three young women during pregnancy, with good outcomes for the mothers and the newborns.[5]

Our patient had several atypical findings for this disease, including the demographics of the patient (male, age 52), the lack of pleocytosis observed in the initial CSF findings, and a prolonged psychiatric course. It is important to note that it was nearly 2 months before the patient displayed any seizure activity or autonomic instability while in the hospital, although he did experience a seizure a month before admission. Anti-NMDA receptor antibody encephalitis is a diagnosis that requires a high index of clinical suspicion, as the only reliable test to diagnose this condition involves determination of antibodies to the NR1 subunit of the NMDA receptor in the patient's serum and CSF. Although this disease generally afflicts younger women with ovarian teratomas, it can be seen in a wide spectrum of patients and should be included in the differential diagnosis for all patients presenting with acute onset of psychosis.

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