Psychiatric Manifestation of Anti-NMDA Receptor Autoimmune Encephalitis

Maha Elamin Fatima Farid Mir Dana Mudathir Alam Ali Mazin Awad
Mohsen Mohammed Alshamy Khawla Ahmad

Dubai Health Authority, Psychiatry, Rashid Hospital, Dubai, United Arab Emirates

Keywords

Psychiatry · Autoimmune encephalitis · Emergency · Fatal condition

Abstract

Several studies have linked the presence of anti-NMDA receptor autoimmune encephalitis to the development of new-onset psychiatric symptoms. As psychiatric symptoms may predominate at the onset or over the course of the disease, the diagnosis is frequently delayed. Patient prognosis depends on the speed of disease detection, identification, and management. The case presented in this report shows a patient with psychiatric manifestation discovered to have anti-NMDA receptor encephalitis. Late diagnosis of anti-NMDA receptor encephalitis caused her condition to deteriorate. Therefore, we underline the importance of considering anti-NMDA receptor encephalitis as part of the differential diagnosis in any case presenting with first-time emotional lability or any other psychiatric finding.

© 2018 The Author(s)
Published by S. Karger AG, Basel

Introduction

First described in 1997 by Dalmau and colleagues in two isolated case reports, anti-NMDAR encephalitis is a potentially life-threatening condition with a wide spectrum of symptoms. The initial prodromal phase is a non-specific viral-like symptom disease with headache, nausea, vomiting, fever, and fatigue, which later progresses rapidly into two stages of neuropsychiatric abnormalities. The early stage symptoms include confusion, memory loss, paranoia, hallucinations, mood disturbances, anxiety, self-harming behaviors, seizures, and dyskinesia such as facial twitching and choreoathetosis. Due to the predominance of the psychiatric symptoms at this stage, the majority of these patients consult psychiatrists initially, and many of them are misdiagnosed with new-onset psychiatric disorders and are started on antipsychotics. However, these patients do not respond to these drugs and rapidly progress to late-stage symptoms of decreased responsiveness, hypoventilation, and autonomic instability manifesting as hypotension or hypertension, bradycardia or tachycardia, hyperthermia, and urinary incontinence [1].

The discovery of the correlation between autoimmune encephalitis and acute psychosis has uncovered a wide range of neurological diseases with a psychiatric disguise. Psychiatric symptoms are the most frequent initial presenting symptoms, with 77% of patients soliciting the help of a psychiatrist first [2]. Most patients reported do not have any psychiatric history; therefore, a new-onset, first psychiatric episode should be considered as an argument to test the presence of anti-NMDA receptor antibodies in the patient's cerebrospinal fluid [3].

The triggers of the disorder comprise viral infections, tumors, and other unknown factors. It is reported that herpes simplex encephalitis plays a vital role in triggering the synthesis of anti-NMDA receptor antibodies. In young adult females, the encephalitis is often accompanied with ovarian teratomas, while males and children are also affected, but the presence of a tumor is uncommon [4].

This subtype of psychosis has anatomical and immunological footprints in the brain, despite the frequent absence of structural abnormalities on conventional brain MRI. It is critical not to overlook appropriate neurological workup such as neuroimaging and EEG testing, as well as cerebrospinal fluid analysis, for cases with acute or subacute atypical onset of neuropsychiatric presentations including those dominated by acute psychotic symptoms [5]. Patient outcomes range from complete recovery to death after prolonged hospitalization [1].

Case Report

P.C., a 27-year-old previously healthy female of Filipino origin, presented to the emergency department with a 2-day history of labile mood, sleep disturbance, changes in appetite, and impulsivity with brief episodes of disorientation following a conflict. There was no history of neurological deficit. Two weeks prior to presentation, the patient was suffering from fever with chills and nonproductive cough, treated partially by an incomplete course of antibiotics. She had no recent history of travel, no personal or family history of psychiatric illness, and no previous such episode. Upon examination, the patient was noted to have several crying spells alternating with a calmer mood, a bizarre gait, visual hallucinations, irrelevant speech, and prolonged delay in answering basic personal details. Neurological and general systemic examinations were unremarkable.

Blood, urine, and spinal fluid investigations were within the normal limits at presentation. Brain CT and brain MRI with contrast were reported as normal. Medical, neurology, and infectious diseases unit teams transferred the patient to the care of the psychiatric team, as there was no evidence of an organic etiology. The patient's emotional condition persisted despite regular doses of olanzapine and escitalopram. A day later, left-sided nystagmus and jerky movements were noted, and she was reviewed by the neuro-medical team.

On the fifth day of admission, the patient's condition deteriorated as she spent the entire day lying apathetically in her bed, producing incomprehensible sounds in a low tone alternating with shouting incoherent incomplete sentences, and resisting all passive movement. The patient then developed difficulty with breathing and had an acute drop in GCS to 8/15. Management was subsequently continued under ICU, where the patient remained intubated for over 2 months. During that time, neck stiffness, nystagmus, bizarre facial movements, and tongue and upper limb dyskinesias were noted. Seizures also developed, requiring high-dose oxcarbazepine.

Repeat spinal fluid analysis revealed a final diagnosis of autoimmune anti-NMDA receptor encephalitis, which was eventually treated by intravenous immunoglobulins, methylprednisolone, and several sessions of plasma exchange under the neuromedical team. The patient's condition gradually improved enough for discharge, with no features requiring admission to the Psychiatric ward again.

Results

- Lumbar puncture: WBC 165; 97% lymphocytes; 3% polymorphs; 50 RBC; protein 34; glucose 80; glutamate receptor antibodies 1:320 +++.
- Brain MRI with contrast 1 week after admission: symmetrical bilateral posterior T2/ flair high-signal intensity with no restriction on DWI or enhancement, which was mildly increased in size compared to admission scan.
- EEG: generalized slow-wave dysrhythmia.
- Nerve conduction study: diffuse axonal motor neuropathy.
- CT chest, abdomen and pelvis with contrast: no signs of malignancy.

Discussion/Conclusion

Findings from several studies have linked the presence of anti-NMDA receptor autoimmune encephalitis to the development of new-onset psychiatric symptoms [3]. As psychiatric symptoms may predominate at the onset or over the course of these diseases, the diagnosis is frequently delayed. Patient prognosis depends on the speed of disease detection, identification, and management [6]. Retrospective studies have found that psychiatric symptoms at first presentation were reported in 80–100% of cases, and subsequent management by psychiatrists in 70–80% [5].

In 2013, Maat et al. [7] reported samples from 15 patients (13 female, 2 male, mean age 24 years, range 5–56 years) who tested anti-NMDA receptor antibody posi-

tive. Twelve of the 15 patients (80%) presented with prominent psychiatric symptoms and 8 were initially referred to a psychiatric service. The most prominent initial psychiatric symptoms were anxiety in 7 cases (47%), behavioral change (often bizarre) in 6 (40%), and agitation in 5 (33%). All patients developed psychiatric symptoms in the first 6 weeks of illness.

In 2016, Nichols reported a 19-year-old female who presented with altered mental status, seizures, and depressed affect. Upon discharge on valproic acid and paroxetine, she began exhibiting bizarre behavior (humming, dancing, laughing to self), and appeared to be responding to internal stimuli. Rehospitalization ensued, with extensive serum and spinal fluid workup which were all unremarkable. Finally, spinal fluid was sent for further antibody analysis, which revealed a diagnosis of anti-NMDA receptor encephalitis. Therapy with intravenous immunoglobulin and rituximab yielded marked cognitive and behavioral improvement [2].

The case detailed in the current report demonstrates striking similarities to those described internationally. The documentation and discussion of such cases solidifies the presence of anti-NMDA receptor encephalitis as a prominent disease entity – one which must rapidly climb up the list of differential diagnoses among all physicians encountering acutely disturbed patients.

Unfamiliarity with the diagnosis coupled with nonspecific investigations fuel progression towards decline in condition. In conclusion, we recommend testing for anti-NMDA receptor antibodies to be part of the routine workup of any patient with first-time acute onset psychosis.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors have no funding sources to declare.

Author Contributions

M.E., F.F.M., and D.M.A.A. obtained the patient's consent, and analyzed medical records, laboratory and imaging reports to write the case report. PubMed was utilized to study papers on the topic at hand, with subsequent utilization in strengthening the report. The co-authors reviewed and adjusted the report with great consideration.

References

- 1 Mitra AD, Afify A. Ovarian teratoma associated Anti-N-methyl-D-aspartate receptor encephalitis: a difficult diagnosis with a favorable prognosis. *Autops Case Rep*. 2018 Apr; 8(2):e2018019.
- 2 Nichols TA. Anti-NMDA receptor encephalitis: An emerging differential diagnosis in the psychiatric community. *Ment Health Clin*. 2016 Nov;6(6):297–303.
- 3 Bost C, Pascual O, Honnorat J. Autoimmune encephalitis in psychiatric institutions: current perspectives. *Neuropsychiatr Dis Treat*. 2016 Oct;12:2775–87.
- 4 Liu CY, Zhu J, Zheng XY, Ma C, Wang X. Anti-N-Methyl-D-aspartate Receptor Encephalitis: A Severe, Potentially Reversible Autoimmune Encephalitis. *Mediators Inflamm*. 2017;2017:6361479.
- 5 Najjar S, Steiner J, Najjar A, Bechter K. A clinical approach to new-onset psychosis associated with immune dysregulation: the concept of autoimmune psychosis. *J Neuroinflammation*. 2018 Feb;15(1):40.
- 6 Titulaer MJ, McCracken L, Gabilondo I, et al. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study. *Lancet Neurol*. 2013 Feb;12(2):157–65.
- 7 Maat P, et al. Psychiatric phenomena as initial manifestation of encephalitis by anti-NMDAR antibodies. *Acta Neuropsychiatr*. 2013 Jun;25(3):128–36.