Case report

DOI: https://doi.org/10.4038/sljpsyc.v17i1.8671

When mania is not primary: A case report on anti-NMDA receptor encephalitis presenting during early pregnancy

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Abstract

Anti-NMDA receptor encephalitis is the most common subtype of autoimmune encephalitis, predominantly affecting young females and often presenting with psychiatric symptoms, leading to diagnostic challenges. We report a 27-year-old pregnant female presenting with first-episode mania and recurrent seizures. During hospitalisation, she developed drowsiness, orofacial dyskinesia and emerging catatonia, raising suspicion of autoimmune encephalitis. Initial EEG, MRI brain and CSF studies were normal, but CSF testing later confirmed anti-NMDA receptor antibodies. She was treated with intravenous methylprednisolone followed by mycophenolate mofetil resulting in significant recovery. This case highlights the need to consider autoimmune encephalitis in new-onset psychiatric presentations with neurological features.

Keywords: anti-NMDA receptor encephalitis, mania, pregnancy

SL J Psychiatry 2026; 17(1): 71-73

Introduction

Autoimmune encephalitis is the third most frequent cause of encephalitis, following infectious aetiologies and acute disseminated encephalomyelitis. Originally described in association with paraneoplastic neurological syndromes, the concept now includes a broader group of disorders which are mediated by antibodies directed against neuronal surface antigens. Among autoimmune encephalitis, anti-NMDA receptor encephalitis is the most frequently reported subtype with an estimated annual incidence of approximately 1.5 cases per million population (1).

It predominantly affects young females, with a female: male ratio of approximately 4:1 and a mean age of onset of around 21 years. Nearly 95% of cases occur before the age of 45, although the sex distribution becomes more equal beyond this age. An underlying ovarian teratoma is identified in a substantial proportion of affected females. Viral infections have also been described as potential triggers (1).

The clinical course often follows a recognisable sequence of stages. A viral-like prodrome lasting about one week is followed by prominent psychiatric manifestations including agitation, delusions, hallucinations, mania, speech disturbance, insomnia, disorganised thinking and catatonia. As the disease evolves, neurological features such as seizures, movement disorders, dysautonomia and hypoventilation may emerge. If untreated, patients may develop persistent cognitive and behavioural impairments including executive dysfunction, impulsivity, disinhibition and sleep disturbance (1).

Although clinical suspicion plays a pivotal role in diagnosis, confirmation is achieved through detection of IgG antibodies directed against the NMDA receptor in serum or cerebrospinal fluid. Initial immunotherapy generally involves high-dose intravenous corticosteroids together with intravenous immunoglobulin therapy or plasma exchange. Rituximab and cyclophosphamide are commonly used as second-line therapies (2). Agents such as bortezomib or tocilizumab may be considered in refractory cases (1). When an associated ovarian teratoma is identified, surgical removal is recommended (3). Maintenance immunotherapy with a steroid-sparing agent is often continued for up to two years (2).

Case history

A 27-year-old woman, eight weeks pregnant, presented with recurrent generalised tonic-clonic seizures over two weeks. She had a prior epilepsy diagnosis but had been seizure-free for five years, with antiepileptic medications tapered and discontinued one year before pregnancy.

Concurrently, her family noted behavioural changes. Psychiatric assessment revealed agitation, pressured speech, elevated mood and grandiose delusions (believing she was a famous wrestler) consistent with a manic episode with psychotic symptoms. About one week before seizures, she experienced insomnia, social withdrawal, frequent crying and vague fears regarding the pregnancy, alongside a subjective sense that "something inexplicable" was happening.

During hospitalisation, she became drowsy and developed abnormal involuntary movements (repetitive tongue protrusion, perioral dyskinesia), mutism, rigidity, stupor and abnormal hand posturing – catatonic features suggesting an organic aetiology, particularly anti-NMDA receptor encephalitis.

Ultrasound on admission showed a missed miscarriage. She later developed vaginal bleeding and completed miscarriage.

Neurological workup-including two EEGs, brain MRI and initial CSF studies – was normal. Due to high clinical suspicion, intravenous methylprednisolone was started and behavioural symptoms were managed with olanzapine. Subsequent CSF confirmed anti-NMDA receptor IgG antibodies. Abdominal ultrasonography revealed no ovarian teratoma. The patient was initiated on maintenance immunotherapy with mycophenolate mofetil and showed marked clinical recovery.

Discussion

Anti-NMDA receptor encephalitis is a treatable disorder with potential for substantial recovery when detected early. However, the diagnosis may be challenging because psychiatric symptoms often dominate the early clinical presentation leading to patients being often evaluated initially within psychiatric settings.

To facilitate earlier recognition, Graus et al. (4) proposed diagnostic criteria for probable and definite anti-NMDA receptor encephalitis. A probable diagnosis requires rapid onset of symptoms within three months together with at least four major clinical features – such as abnormal behaviour or cognitive dysfunction, speech disturbance, seizures, movement disorder, decreased level of consciousness or autonomic dysfunction – in addition to abnormal EEG or CSF findings after reasonable exclusion of alternative causes. Detection of IgG antibodies against the GluN1 subunit of the NMDA receptor confirms a definite diagnosis.

Dalmau et al. (1) proposed the mnemonic "SEARCH For NMDAR-A" to assist clinicians in identifying the condition among patients presenting with acute psychiatric symptoms. The mnemonic highlights key clinical clues including:

Sleep dysfunction

Excitement/disinhibition/manic behaviour alternating with depressive behaviour

Agitation/aggression

Rapid onset

Children and young adult predominance

History of psychiatric disease absent, Fluctuating catatonia

Negative and positive symptoms at presentation

Memory deficit

Decrease of verbal output/mutism

Antipsychotic intolerance

Rule out neuroleptic malignant syndrome

Antibodies/additional paraclinical tests.

Several clinical features in this case raised suspicion of an organic disorder. The patient developed a first episode of mania in the context of recurrent seizures after many years of well-controlled epilepsy. The age of onset and absence of a personal or family psychiatric history were atypical for primary bipolar disorder. In addition, progressive drowsiness and the emergence of neurological features, including orofacial dyskinesia and catatonia, could not be adequately explained by a primary psychiatric condition. These factors collectively supported the possibility of an organic mood disorder, which was ultimately confirmed by positive CSF antibodies.

Pregnancy has been recognised as a potential trigger for anti-NMDA receptor encephalitis, although the precise mechanisms remain unclear. Proposed explanations include hormone-mediated immune modulation, pregnancy-related immunological changes, sex chromosome-linked gene expression and interactions between genetic and environmental factors. Oestrogen is known to promote B-cell survival and antibody production while suppressing T-cell expansion, potentially facilitating autoimmune responses. In addition, the semi-allogeneic fetus may act as an immunological stimulus during pregnancy (5).

Anti-NMDA receptor encephalitis may recur in subsequent pregnancies (5). Consequently, close

monitoring would be advisable if the patient considers future pregnancies.

Conclusion

Anti-NMDA receptor encephalitis may initially present with prominent psychiatric symptoms, often leading to misdiagnosis as a primary psychiatric disorder. The co-occurrence of new onset psychiatric symptoms with neurological symptoms and signs such as seizures, catatonia or movement disorders should prompt evaluation for an underlying neurological or autoimmune cause. Normal early investigations, including MRI, EEG and routine cerebrospinal fluid studies, do not exclude anti-NMDA receptor encephalitis. Pregnancy may act as a potential trigger for autoimmune encephalitis although the underlying mechanisms are not fully understood. Early recognition and prompt initiation of immunotherapy are important, as anti-NMDA receptor encephalitis is a potentially reversible condition with favourable outcomes when treated appropriately.

Acknowledgement

We gratefully acknowledge Dr Dilum Palliyaguruge, Consultant Neurologist, Teaching Hospital Ratnapura for his expert involvement in the clinical management and guidance in the care of this patient.

Statement of contribution

Both authors managed the patient and drafted the manuscript. All authors reviewed and approved the final version.

Declaration of interest

The authors declare no conflicts of interest.

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