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Case Report

NEUROPSYCHIATRIC MANIFESTATION ON ANTI-NMDAR ENCEPHALITIS: A CASE REPORT

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ABSTRACT

Introduction: Anti-NMDA (N-methyl-D-aspartate) receptor encephalitis (Anti-NMDAR Encephalitis) is a rare autoimmune disorder that primarily affects the central nervous system, which is characterized by complex neuropsychiatric disorders and the presence of Immunoglobulin G (IgG) against the NR1 subunit of the NMDA-receptor in the central nervous system. This disease is one of the most commonly diagnosed autoimmune encephalitis. Frequently misdiagnosed, an accurate examination is required.
Case Report: A 24-year-old female presented with continuous seizures and psychiatric disorders such as hallucinations and behavioral changes. Physical examination revealed loss of consciousness, fever, positive meningeal sign, and involuntary movement in the mouth and left hand. Immunofluorescence test revealed positive anti-NMDA antibodies, lumbar puncture revealed pleocytosis, head contrast enhanced CT-scan suggests meningoencephalitis, and electroencephalography revealed ictal and interictal epileptiform discharges. The patient is diagnosed with the Anti-NMDAR Encephalitis.
Discussion: Anti-NMDAR Encephalitis is a rare autoimmune encephalitis that affects the central nervous system because the body's immune system mistakenly attacks the NMDA receptor in the brain. The main symptoms consist of a combination of neurologic and psychiatric symptoms. Treatment of this disease could include corticosteroids, Intravenous Immunoglobulin (IVIG), and plasma exchange if necessary, followed by supportive care to treat the symptoms.
Conclusion: Anti-NMDAR Encephalitis is a rare form of autoimmune encephalitis that should be included in the differential diagnosis when facing a patient with neuropsychiatric disorder, especially in patients who have never experienced psychiatric symptoms before.
Keywords: anti-NMDAR encephalitis; neuropsychiatric manifestation; behavioral changes; autoimmune disease

INTRODUCTION

Anti-NMDAR (N-Methyl-D-Aspartate Receptor) encephalitis is a form of paraneoplastic encephalitis, characterized by an acute or subacute psychiatric syndrome which often manifests as a combination of hallucinations, panic, delusions, and incoherent speech, along with seizures, memory disturbances, and

hypoventilation.[1] Although it is one of the most common forms of autoimmune encephalitis, the incidence of this disease is still quite rare, ranging from 0.173 per 100,000 people in 2018 according to Nissen et al[2], According to Dalmau et al., the incidence of anti-NMDAR encephalitis is extremely rare, affecting only 1 in 1,500,000 people.[3]

Autoimmune encephalitis is characterized by IgG antibodies targeting the GluN1 subunit of the NMDA receptor in the brain.[4] An autopsy study revealed that patients with anti-NMDAR encephalitis experience moderate inflammation, plasma cell infiltration, IgG accumulation, and microglial proliferation in the brain, without evidence of T-cell-mediated neuronal loss.[5] This condition is classified under paraneoplastic encephalitis, which is further subdivided into encephalitis with antibodies targeting cell surface or synaptic antigens, and those with antibodies targeting intracellular antigens. Anti-NMDAR encephalitis belongs to the former group, where antibodies target cell surface or synaptic antigens, with ovarian teratoma being the most common associated complication.[6]

Anti-NMDAR encephalitis is one of the most common forms of autoimmune encephalitis, though its incidence remains rare to very rare. This highlights the importance of enhancing our knowledge and ability to differentiate the differential diagnosis of this condition, particularly in diseases presenting with a combination of neurological and psychiatric symptoms, regardless of disease onset. We report the case of a 24-year-old female patient diagnosed with anti-NMDAR encephalitis.

CASE REPORT

A 24-year-old woman presented with complaints of continuous seizures upon admission to the hospital. The symptoms began two months prior, initially manifesting as psychiatric disturbances, including hallucinations and behavioral changes, for which she consulted a mental health specialist. One month later, she developed seizures, characterized by sudden generalized convulsions accompanied by a loss of consciousness. Each episode lasted

1-2 minutes, involving stiffening of both limbs followed by jerking movements, with the head and eyes deviating to the left. There was no history of tongue biting, incontinence, or fever. Postictally, the patient would fall asleep for approximately 5-10 minutes before regaining consciousness, after which she exhibited involuntary oral movements resembling chewing. The seizures became more frequent and persistent, prompting hospital admission for further evaluation.

On general physical examination, the patient was found to have a fever. Neurological examination revealed decreased consciousness (GCS 9), isochoric round pupils, positive meningeal signs, involuntary movements in the mouth area, and no evidence of hemiparesis or cranial nerve palsy. During hospitalization, the patient also experienced tonic-clonic seizures, starting in the left arm and followed by the right arm, which occurred while the patient was unconscious (Figure 1).

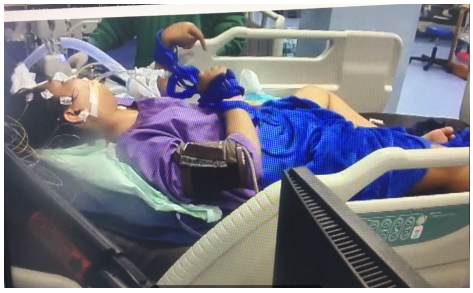

Figure 1. The patient experienced tonic clonic seizures of both hands while in an unconscious state.

Cerebrospinal fluid analysis via lumbar puncture revealed positive results for anti-NMDA antibodies and pleocytosis. The chest X-ray examination appeared normal. A contrast-enhanced CT scan of the head indicated findings suggestive of meningoencephalitis accompanied by mild hydrocephalus (Figure 2). Both BTA and GeneXpert tests returned negative results. Electroencephalography revealed ictal and interictal epileptiform bursts, as well as fast activity in the right frontotemporal lobe that became bilaterally synchronous (Figure 3).

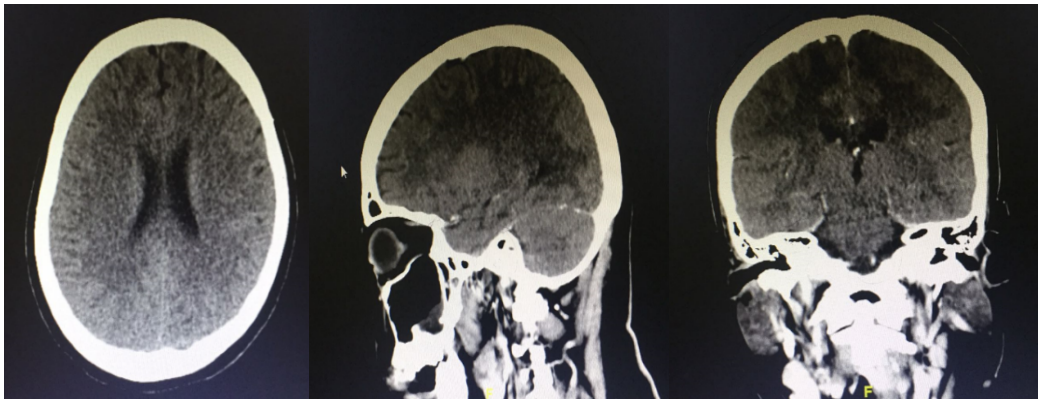

Figure 2. CT scan of the head with contrast shows the impression of meningoencephalitis with mild hydrocephalus.

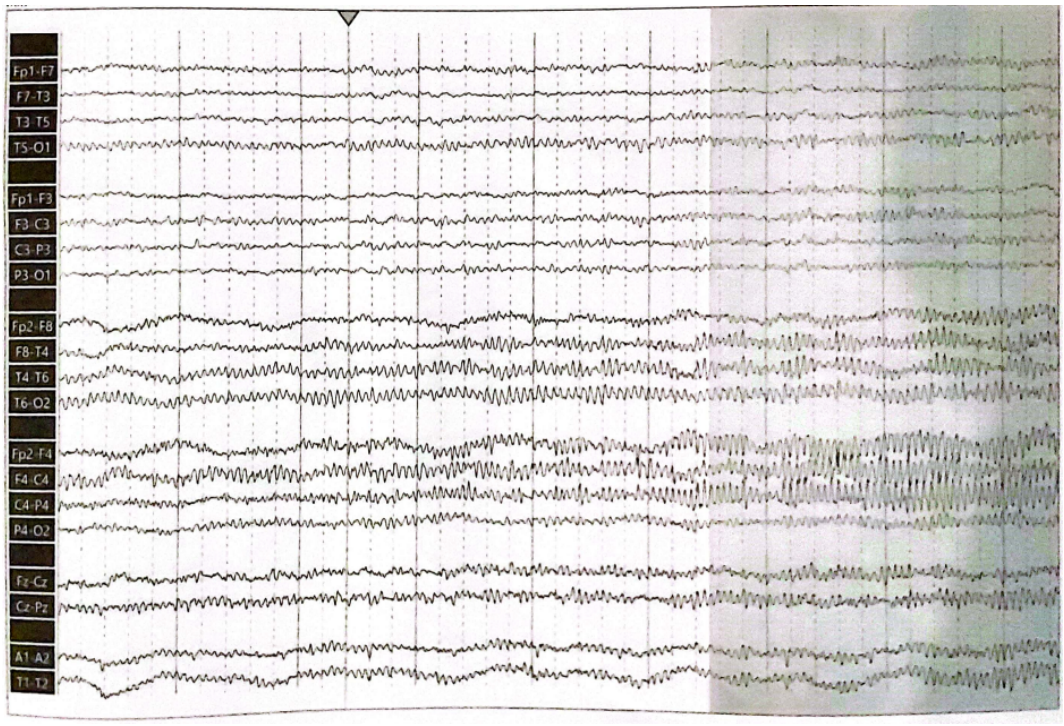

Figure 3. EEG results show that there is Fast Activity in the right front temporal lobe which is bilaterally synchronous.

The treatment management included a loading dose of Levetiracetam and Methylprednisolone at a dosage of 1000 mg/day for 5 days. By the second week of treatment, the patient exhibited clinical improvement, although residual symptoms of cognitive impairment persisted.

DISCUSSION

Anti-NMDAR encephalitis can be diagnosed with certainty when positive anti-GluN1 IgG antibodies are detected, along with the

presence of one or more of the six main symptoms that have an onset of less than three months: (1) abnormal behavior or cognitive disorders, (2) speech disturbances, (3) seizures, (4) movement disorders, including dyskinesia, rigidity, or abnormal posture, (5) altered consciousness, and (6) autonomic dysfunction or central hypoventilation.

Prodromal symptoms in some patients with anti-NMDAR encephalitis resemble those of viral encephalitis, making initial differentiation challenging. Shortly after the prodromal phase, acute or subacute psychiatric symptoms emerge, including anxiety, personality changes, hallucinations, paranoia, mild psychosis, and social withdrawal, along with cognitive and speech disturbances.[4,7,8] Subsequently, movement disorders may present as dyskinesia (typically affecting the orofacial region or extremities), dystonia, and choreoathetosis, along with seizures. In the final phase of the disease, symptoms may include impaired consciousness, autonomic dysregulation (manifesting as hyperthermia, tachyarrhythmia, fluctuations in blood pressure, and central hypoventilation), as well as an increased frequency of seizures.[7,8] "The entire course of the disease exhibited an acute to subacute onset, lasting a total of less than three months.[4] Furthermore, Laboratory findings and supporting examinations revealed MRI of the head demonstrating FLAIR/T2 hyperintensities in 30% of the mesial hippocampus, cerebrospinal fluid (CSF) examination positive for NMDA receptor antibodies with lymphocytic pleocytosis, and electroencephalography (EEG) results indicating partial or generalized epilepsy, which may present with positive or negative extreme delta waves.[7,8]

In this case, the clinical and supporting findings indicate a distinct neuropsychiatric disorder characterized by the initial appearance of psychiatric symptoms, followed by neurological symptoms, with an onset of approximately two months. The results of the MRI of the head with contrast, the cerebrospinal fluid examination revealing positive

anti-NMDA antibodies and pleocytosis, along with the EEG findings, collectively support the definitive diagnosis of anti-NMDAR encephalitis.

According to established guidelines, the management of anti-NMDAR encephalitis is categorized into two phases: first-line management, which includes the administration of corticosteroids, intravenous immunoglobulin (IVIG), and plasmapheresis, and second-line management, which involves the intravenous administration of rituximab and cyclophosphamide.[9,10] In this patient, the management provided was appropriate, aligning with first-line treatment protocols and symptomatic management to address the seizures. Notably, the patient's clinical condition improved during the second week of hospitalization.

Long-term evaluation and careful monitoring are essential for this patient. As she is a woman, it is necessary to conduct cancer screening tests, specifically for ovarian teratoma, which have not yet been performed. Furthermore, an assessment of higher cognitive functions is required to evaluate the integration and performance of the brain regions underlying behavior and neurobehavior. This is particularly important because anti-NMDAR encephalitis involves a complex interplay of both neurological and psychiatric disorders.

CONCLUSION

Establishing a diagnosis and providing therapy for anti-NMDAR encephalitis—a condition that remains relatively rare in clinical practice—presents a significant challenge for physicians today. The combination of neuropsychiatric disorders can lead to clinical manifestations and supporting symptoms that may resemble those of other diseases. Therefore, it is crucial for healthcare professionals to pay close attention to patients presenting with neuropsychiatric disorders, particularly those with no prior history of psychiatric illness. This vigilance can help prevent misdiagnosis or underdiagnosis, ensuring that patients receive optimal treatment and improving their prognosis.

ACKNOWLEDGEMENT

The patient and her family have consented to the publication of this case report to enhance knowledge and awareness of neuropsychiatric disorders associated with anti-NMDAR encephalitis, a condition that remains quite rare.

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