Journal of Neurology & Neuropsychiatry

Volume 1 Issue 2, Nov 2024

Short Report

Case Study of NMDA Encephalitis in an 18-Year-Old Female With No Underlying Etiology

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Abstract

Background: Anti-NMDA receptor encephalitis is a rare autoimmune disorder caused by the formation of antibodies against NMDA receptors in the brain. Symptoms can include confusion, hallucinations, seizures, memory loss, and difficulty speaking, as well as autonomic dysfunction and movement disorders. Case Presentation: The case presented is of an 18-year-old female patient who presented with altered behavior, low-grade fever, and rigidity. The patient was diagnosed with NMDA encephalitis based on elevated protein levels, lymphocytes pleocytosis, and positive NMDA antibodies in serum. The patient was treated with pulse therapy with injection Solumedrol and IVIGs, leading to significant improvement. No underlying cause for the encephalitis was identified. Conclusion: The diagnosis is typically made through a combination of clinical findings, laboratory tests, and imaging studies, and the detection of anti-NMDA receptor antibodies in the cerebrospinal fluid (CSF) and serum. Treatment typically involves immunotherapy, such as steroids or plasma exchange, and treatment of any underlying infection or tumor. Prognosis varies based on the severity of the disorder and timing of treatment, with early diagnosis and treatment leading to better outcomes. This case highlights the importance of early diagnosis and treatment of anti-NMDA receptor encephalitis for a better outcome.

Keywords: ADHD; Telemedicine; Digital Assessment

1. Introduction

Anti-N-methyl-d-aspartate (NMDA) receptor encephalitis is a rare autoimmune disorder caused by the formation of antibodies against the NMDA receptors in the brain [1]. A class of glutamate receptors called NMDA receptors is crucial for memory, learning, and brain development. These receptors, which may be found on the surface of neurons, allow specific substances, such as glutamate, to enter the cell. The development of antibodies against these receptors causes them to malfunction, which causes the encephalitis symptoms [2]. Although the precise cause for the development of these antibodies is unclear, it is considered to be connected to an underlying infection or tumor. Ovarian teratomas, which are benign tumors that can form in the ovaries, are sometimes linked to the condition [3]. Other times, no underlying reason can be identified. The symptoms of anti-NMDA receptor encephalitis typically develop over a period of several weeks and can include confusion, hallucinations, seizures, memory loss, and difficulty speaking. Additionally, patients may develop autonomic dysfunction, such as changes in heart rate

Received: 14-08-2024
Accepted: 16-09-2024
Published: 21-11-2024

or blood pressure, as well as movement disorders, such as tremors or stiffness. Because the symptoms of the ailment frequently resemble those of a psychiatric problem, diagnosing the condition can be difficult. The diagnosis is typically made based on a combination of clinical findings, laboratory tests, and imaging studies. Treatment of anti-NMDA receptor encephalitis typically involves administering immunotherapy, such as steroids or plasma exchange, to reduce inflammation and decrease the levels of antibodies [4]. In addition, any underlying infection or tumor must be treated. In some cases, a surgical procedure called a craniotomy may be required to remove a tumor that is believed to be causing the disorder [5]. Prognosis for patients with anti-NMDA receptor encephalitis varies depending on the severity of the disorder and the length of time between onset of symptoms and initiation of treatment [2,6]. Early diagnosis and treatment can lead to a better outcome, but long-term recovery can take months or even years. As the disorder is rare, the clinical signs and symptoms can be difficult to diagnose. The best way to diagnose the disorder is through the detection of anti-NMDA receptor antibodies in the cerebrospinal fluid (CSF) and serum using a laboratory test called an enzyme-linked immunosorbent assay (ELISA) [7].

2. Case Presentation

An 18-year-old female patient presented to our Neuro OPD at Services Hospital Lahore, Pakistan with a week-long history of altered behavior, low grade fever, tonic posturing and generalized rigidity. Altered behavior involved visual hallucinations, aggression, irritation, disturbed sleep cycle and crying spells. Additionally, the patient had difficulty recognizing her family members and would make gestures as if catching objects in the air. Her fever was low grade, intermittent in character and relieved on medication. She also had two episodes of tonic posturing, which lasted approximately 15 minutes to an hour respectively, along with generalized rigidity of the body. However, there were no reports of tongue biting, upward rolling of the eyes, frothing from the mouth, or urinary incontinence.

On examination, the patient's Glasgow Coma Scale score was 12/15, and there were signs of meningeal irritation. On motor examination tone was increased in all limbs and limb holding was present. There were abnormal movements of mouth suggesting orofacial dyskinesia. Rest of the neurological and systemic examination were normal.

Based on history and examination diagnosis of autoimmune encephalitis/NMDA encephalitis/ viral encephalitis were made. Laboratory test and CSF analysis revealed elevated protein levels, lymphocytes pleocytosis, and normal glucose level. Serum CPK, serum aldolase, serum calcium, serum TSH, ENA profile, ANA, ESR, CRP, viral markers and VDRL were normal. Additionally, an MRI and EEG were performed and were both unremarkable. Initially patient was treated with acyclovir for 14 days, Ceftriaxone, Dexamethasone, Levetiracetam, Baclofen, Amantadine, Kempro and fluids. However, the patient's condition did not improve, and her seizures increased in frequency. Additionally, she developed dys-autonomic signs as her blood pressure and heart rate started to fluctuate. Her repeat MRI brain revealed non-specific white matter hyper intense foci. Serum NMDA antibodies were strongly positive, confirming the diagnosis of NMDA encephalitis.

The patient was then treated with pulse therapy using injection solumedrol (1 g/day) for 5 days. Plasmapheresis was not possible due to the development of sepsis; hence intravenous immunoglobulins (IVIGs) were administered at a dose of 0.4 g/kg/day for 5 days according to ICU protocol (Figure 1).

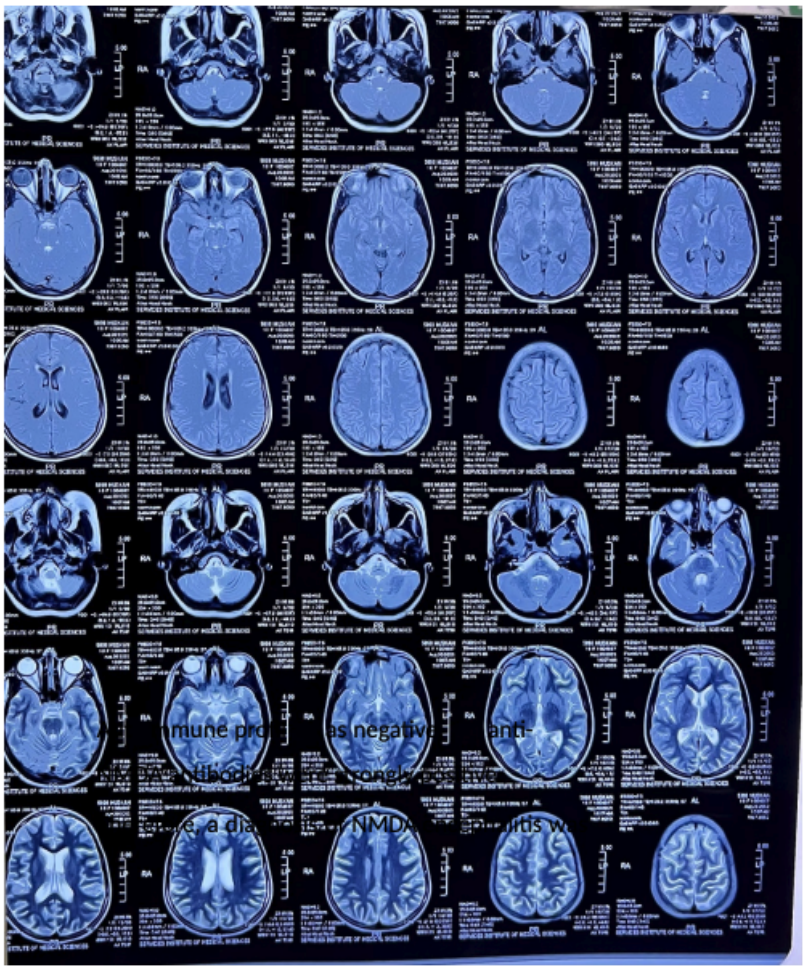

Figure 1. Aut mmune profil as negative, antiNMDA antibodies were strongly positive.

This treatment led to significant improvement in term of improve conscious level with GCS 15/15, and improvement in rigidity. The patient was discharged after a month, with a tapering course of oral tablet Deltacortil and Azathioprine. The patient is in regular follow-up and is now recovered completely. Further investigations, such as ultrasound pelvis, CA 125, and PAN CT were performed to determine the cause of encephalitis but no underlying cause was identified (Figure 2).

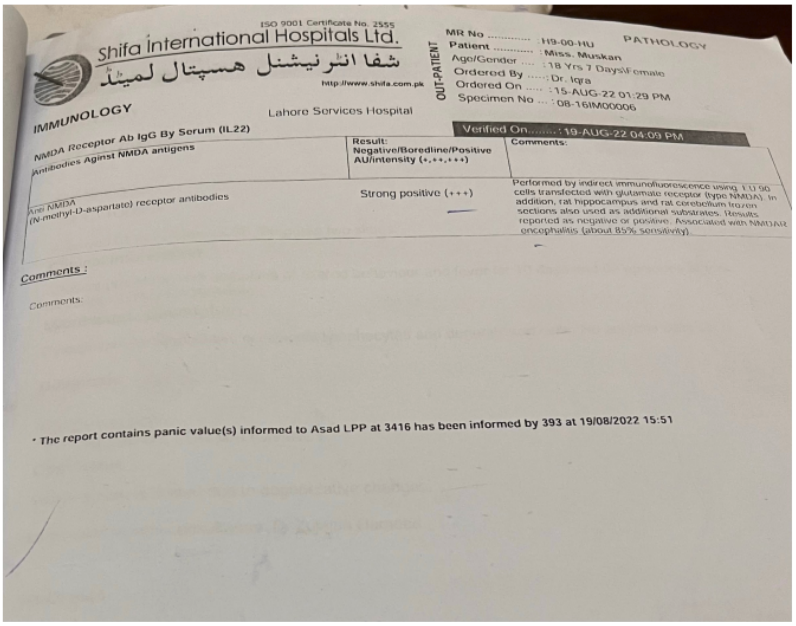

Figure 2. Serum immunology report showing strong positivity (+++) for anti-N-methyl-D-aspartate (NMDA) receptor antibodies, confirming the diagnosis of NMDA encephalitis.

3. Conclusions

Anti-NMDA receptor encephalitis is a rare neurological disorder that is characterized by inflammation of the brain and the presence of antibodies directed against the GluN1 subunits of the NMDA receptors in the serum and cerebrospinal fluid (CSF) [8]. This condition preferentially affects children and young adults, with a male to female ratio of 1:4 [9]. The origin of this disease is often paraneoplastic [10], with approximately 50% of women over 18 years and only 9% of girls under 14 years having an ovarian teratoma. In men, the presence of tumors is rare.

The diagnosis of anti-NMDA receptor encephalitis is confirmed by the detection of IgG antibodies directed against the GluN1 subunits of the NMDA receptors in serum and CSF, which is not available at the time of presentation to the emergency department. Therefore, when a patient presents to the emergency department with a suggestive clinical picture, lumbar puncture should be performed to look for CSF pleocytosis or oligo-clonal band. Electroencephalography (EEG) is useful and shows abnormal results in the majority of cases, but it is non-specific with a slow and disorganized epileptic activity. Brain magnetic resonance imaging (MRI) is often normal, with only 55% of patients having increased FLAIR or T2 signal in the cortical or subcortical areas (hippocampus, basal ganglia, white matter) in a study by Dalmau and colleagues [11].

The differential diagnosis for anti-NMDA receptor encephalitis includes acute primary psychiatric disorder, neuroleptic malignant syndrome, malignant catatonia, drug intoxications, viral encephalitis, and lethargic encephalitis. However, the diagnosis of anti-NMDA receptor encephalitis remains difficult due to the vagueness of the primary clinical picture. In a study, anti-NMDA antibodies were found in 50% of patients diagnosed with lethargic dyskinetic encephalitis. In addition, 20–30% of patients with herpes simplex virus (HSV) infection show positive seroconversion with anti-NMDA antibodies as part of a relapse not attributable to HSV relapse [12].

In the absence of reliable statistical data, there is no standard treatment for anti-NMDA receptor encephalitis. Treatment should be individualized according to age, the severity of symptoms, and the presence or absence of a tumor. Treatment can include immuno-

suppression and tumor resection when indicated. In the presence of CSF pleocytosis or oligo-clonal band at lumbar puncture and abnormal EEG or pathologic brain MRI, immunosuppressive treatment should be started. Some therapeutic variants for the initial immunosuppressive treatment are recommended, including either an intravenous infusion of methylprednisolone (1 g/day for 5 days) or intravenous treatment with immunoglobulin G (400 mg/kg/day for 5 days) or plasmapheresis [13] (Figure 3).

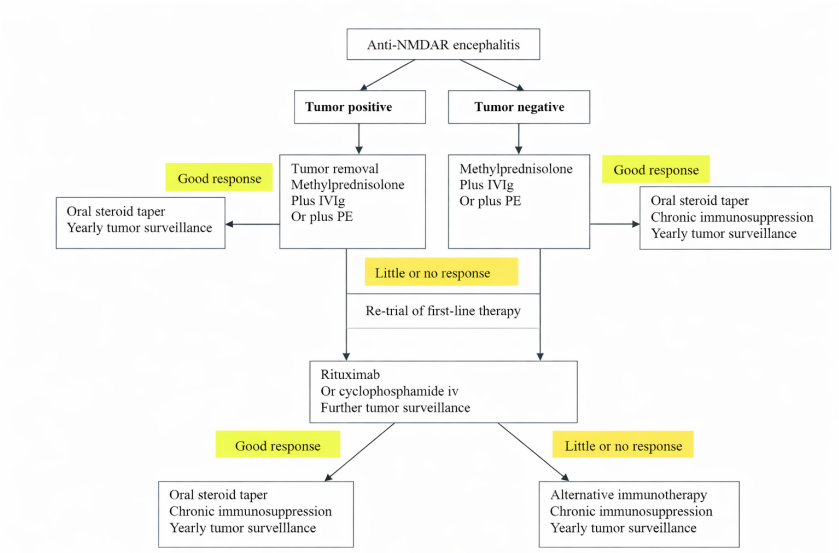

Figure 3. Treatment plan pathway for NMDA encephalitis [14].

In the absence of clinical improvement, second-line treatment with rituximab (375 mg/m^2/week for 4 weeks) or cyclophosphamide (750 mg/m^2/month for 4–6 months) or a combination of both molecules can be proposed. Mycophenolate mofetil can also be used as a second-line therapy. This drug has a selective anti-proliferative activity on lymphocytes and has shown better efficacy in inducing remission. Furthermore, it has a less side effect profile than cyclophosphamide [14].

Disclosure

No conflicts of interest.

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