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Case Reports on 2 Patients of Anti Nmda Receptor Encephalitis: Review

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Introduction

This review looks at the clinical manifestation of this disorder. We are going to look at the physiological processes, which make the condition develop as well as ways in which the condition can be managed.

Objective

The objective of the review is to shade more light on clinicians on how to overcome the challenges posed by this disorder and how it can be managed, as few publications give a comprehensive outlook.

Summary

The literature highlights why it is paramount to detect the initial signs and symptoms such as confusion, movement disorder, diminished mental status, seizures and hallucinations. Though cerebrospinal fluid presence confirms the diagnosis, not all have positive cerebrospinal fluid titers. Immunoserum globulin detection should make physicians carry out the test for a teratoma **[**1**]**.

This should be followed by the initial phase of treatment, which is immunosuppressant therapy. The second phase treatment with cyclophosphamide should begin if there is no improvement after ten days. Some complications such as lack of sleep, aggression and autonomic instability could arise **[**2**]**.

It takes time for a patient to be diagnosed and this can lead to severe syndromes such as coma and one has to be taken to the intensive care unit. When patients show mental issues they are medicated with antipsychotic drugs, which may cause movement disorder. If catatonia develops then the patients should be given benzodiazepine after every two hours. Physicians should also watch out for cases of malignant catatonia when patients don't respond. Its symptoms include fever, muteness and abrupt unresponsiveness **[**3**]**.

Conclusion

Clinicians of different specialties such as neurologists, immunologists and psychiatrists need to familiarize themselves with this disorder. It is only through a combined effort that a complete remission can materialize. The first progress of symptoms such as seizures altered mental status should always raise suspicions of this disorder and clinicians should come up with a rapid action plan. Patients who have also been confirmed should also be screened for tumors and if positive be placed under therapy.

Keywords: management, treatment and complication, anti-NMDA receptor

Signs and Symptoms

The clinical manifestations fluctuate and are sometimes easily misdiagnosed with viral encephalitis psychosis, thus, it is hard for psychiatrists, neurologists, and emergency physicians, as well as gynecologists and oncologists because of its close association with tumors. Identifying the characteristic features of anti-NMDAR encephalitis is crucial to diagnose exactly and to permit a more timely treatment. The signs of the disorder are graded in 8 sections.

a) Psychiatric and behavioral symptoms— nearly80% of patients start obvious psychiatric and behavioral signs such as anxiety, irritability, insomnia, paranoia, aggression, auditory or visual hallucinations, cognitive disorder, and psychosis. The frequency in younger patients is low compared to adults. The difference may be due to the situation that the behavioral symptoms are difficult to detect in young children because they are often overt with hyperactivity, irritability, or temper tantrums. The solitary symptoms are delusional thinking, mood swings, and aggression **[**4**]**.

b) Seizures—around 70% of anti-NMDAR cases present with seizures in males. Seizures are mainly partial, in females, generalized seizures occur often. Seizures are more frequent to act as the first symptom in adult male patients than in adult females. In children and adolescents, seizures are mainly

partial motor or complex seizures. Even, anti-NMDAR encephalitis causes prolonged status epilepticus, which carries a poor forecast.

c) Motor dysfunctions—a broad range of abnormal movements are frequently seen, for example, orofacial dyskinesia, chorea, ballismus, athetosis, rigidity, stereotyped movements, myorhythmia, or opisthotonus. Movement disorders are more ordinary in children and normal signs such as hemiparesis or cerebellar ataxia are predominant in this age group Orofacial dyskinesias are the most frequent, including masticatory-like movements, grimacing, and forceful jaw opening and closing. Those symptoms outcome is in lip and tongue injuries or broken teeth **[**5**]**.

d) Memory dysfunction—short-term memory loss is frequent. However, it is mainly underestimated, because language dysfunctions and psychiatric problems interfere with the evaluation.

e) Speech disorders—language dysfunctions, including less verbal output or mutism, echolalia and mumbling.

f) The decrease in the level of consciousness. Such patients when asked about issues like what is the day or month will have difficulties and may take time to answer such basic questions.

g) Autonomic dysfunctions—the most recurrent manifestations of autonomic volatility are hyperthermia, cardiac dysrhythmias (tachycardia or bradycardia) hypersalivation, hypotension, hypertension, urinary incontinence, and sexual dysfunction. Those dysfunctions occur habitually in patients with anti-NMDAR encephalitis.

h) Central hypoventilation—about 70% of patients develop hypoventilation, and also 20% of the patients need intubation due to central hypoventilation. The symptom often happens when the patient becomes comatose, but it also materializes earlier when the level of consciousness is comparatively preserved.

CSF Test, MRI, and EEG

To make an accurate diagnosis, mainly in the beginning stage of anti-NMDAR encephalitis, rational assistant analysis is necessary. The traditional analysis of CSF test, MRI and EEG are important tools, which can be used to give more information on anti-NMDAR encephalitis **[**6**]**.

Cerebrospinal fluid test

Rare alterations in CSF can be identified in more than 90% of patients by use of this test. These abnormities may include mild to severe lymphocytic pleocytosis (90%), the lenient increase of protein mix (30%), and CSF-specific oligoclonal bands (60%) **[**7**]**. The required value of white blood cells (23/mm3) is seemingly low than those in the cases of viral etiologies. The protein level with a median of

24 mg/dl is also extremely low. The glucose value is generally within the normal range the oligoclonal bands. They can easily be found even when routine CSF examinations are normal. In the early stage, fewer oligoclonal bands are seen but become more prominent as the disease progresses. The changed profile of CSF in children is similar to those of adults **[**8**]**.

Magnetic resonance imaging

MRI examinations outcome for people suffering from NMDAR encephalitis is abnormal only in 30%–50% of patients. Increased signals on fluid-attenuated inversion recovery (FLAIR) and/or on T2 sequence are observed more often in the cortical and subcortical regions and hippocampus, occasionally in the basal ganglia, posterior fossa, or medial temporal regions. The cortical-meningeal enhancement with gadolinium is less frequent and transient.

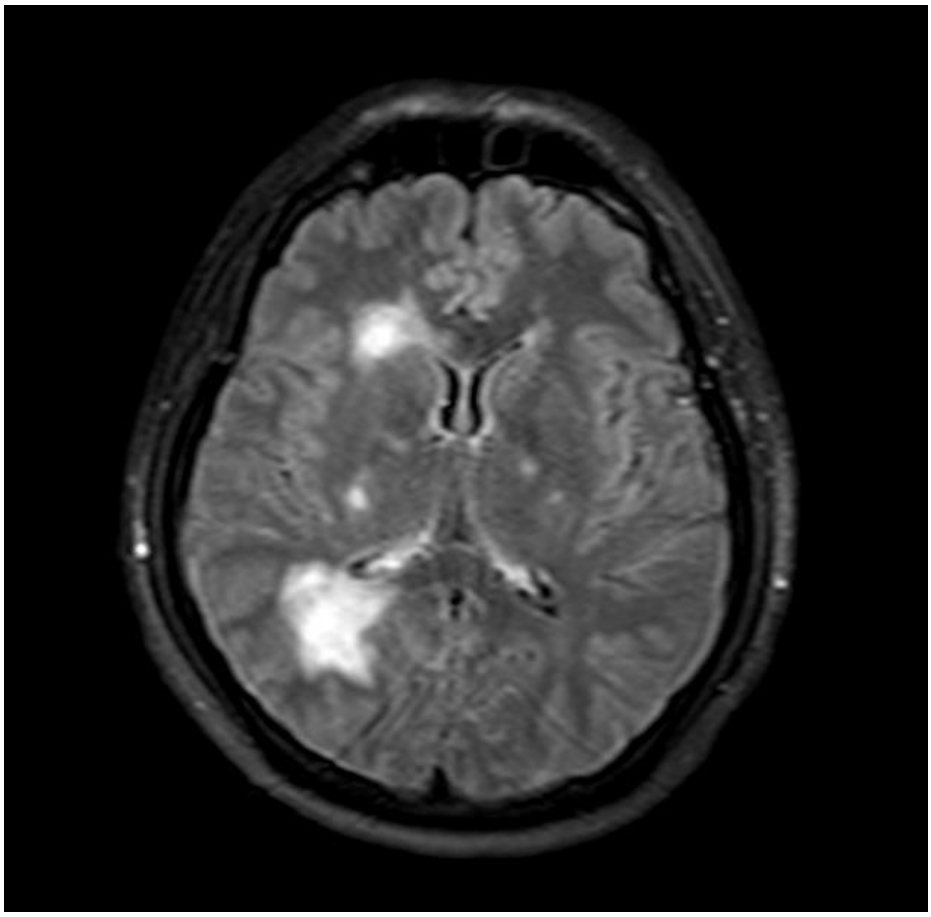

Figure 1: The MRI picture above is of a brain with acute disseminated encephalomyelitis

Most of the defects in MRI manifestations are often mild, transient, and nonspecific Multifocal or extensive demyelinating changes are also found, which suggests that anti-NMDAR encephalitis patients may develop episodes of demyelinating disorders simultaneously or separately. Despite normal manifestations in routine MRI, extensive alterations of white matter integrity and substantial changes of functional connectivity are visible in patients with anti-NMDAR encephalitis using diffusion tensor imaging and functional MRI **[**9**]**. The changes of white matter are most frequently observed in the cingulum and these changes are correlated with disease severity.

Electroencephalogram

90% or even more patients with anti-NMDAR encephalitis have an abnormal EEG. Patients develop serious EEG abnormalities manifested by focal or generalized weak activity with or without epileptic discharges. Extreme delta brush was regarded as a unique electrographic pattern for people suffering from anti-NMDAR encephalitis **[**10**]**. It was characterized by generalized rhythmic delta activity at 1–3 Hz with superimposed rhythmic 20–30 Hz beta frequency activity. This history was previously described in 30% of 23 adult patients undergoing continuous EEG monitoring **[**11**]**. The delta brush was related to a more prolonged course and should raise consideration of anti-NMDAR encephalitis **[**12**]**. The EEG abnormities are often subclinical, while some movement disorders suggestive of seizures have no EEG correlation. EEG helped distinguish between seizures and movement disorders. The picture below shows a case of extreme delta brush of a patient with NMDA receptor encephalitis**[**13**]**.

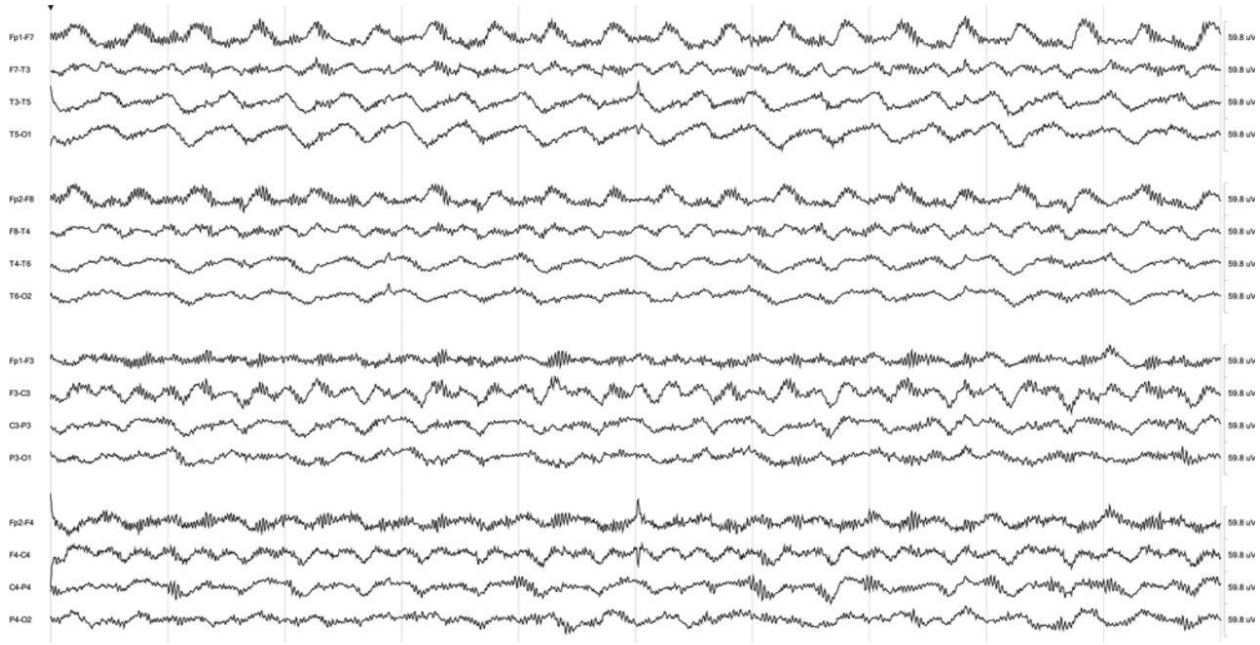

Figure 2

Conclusion

It has been suggested that the central hypoventilation condition, which is observed in patients with anti-NMDA receptor encephalitis, may be due to the disruption of Ponto-medullary respiratory reflexes, which occurs as an NMDA receptor blockade. The fact that the NMDA receptor is expressed in hippocampal, cortical and cerebellar neurons, in addition to glial cells such as oligodendrocytes and astrocytes, in varying concentrations and subunit composition may be of further pathophysiological relevance to the clinical manifestation and time course of the disease The expression changes under new pathophysiological conditions, such as ischemia. A typical trait of anti-NMDA receptor encephalitis may be explained by the increased expression of the NMDA receptor in hippocampal neurons.

Patients suspected of suffering from anti-NMDA receptor encephalitis are checked for the presence of tumors. This is done with imaging of the chest, abdomen, and pelvis. Women should also get an ultrasound of the ovaries while men receive an ultrasound of the testes. People with anti-NMDA receptor encephalitis should be checked periodically for the presence of a tumor. Many times people with anti-NMDA receptor encephalitis have been found not to have tumors. This may be because the tumor is too minute to be detected with imaging techniques, or because it has been eradicated by the defense system.

It has been demonstrated that the titer of NMDA receptor antibodies correlates with clinical outcome and that high antibody titers are more common in patients with poor outcomes or tumors in the present cases, the highest antibody titer was found in a patient with mystic teratoma who failed to be analyzed by ultrasound, CT, MRI, and PET. High antibody titers may be a sign of an underlying tumor, more so if there is no reduction following immunosuppressive treatment.

NMDA receptor antibodies are part of the overall protein mix measured in the CSF or serum. Fewer antibody titers may therefore correlate with an overall cutback in protein concentration. This is of importance for patients with anti-NMDA receptor encephalitis. Significantly decrease in the protein mix in serum and this may be avoided by calculating the antibody/protein ratio as opposed to the antibody titers alone. This also shows the significance of follow-up CSF analysis as a marker for disease actions, and forecast during this disease.

In patients with a new and not chronic onset of neuropsychiatric symptoms, the differential diagnosis of anti-NMDA receptor encephalitis should be considered and CSF analysis may aid the detection of anti-NMDA receptor antibodies. Although multistage clinical presentation is a standing out feature of the disease, the severity of symptoms is not fixed. Cranial MRI is usually paramount for differential diagnosis; however, in anti-NMDA receptor encephalitis outcomes are not certain. Depending on the signs, other diagnoses may be excluded if anti-NMDA receptor encephalitis is positive, an intensive search for tumors, more so teratomas, is needed. Immunosuppressive treatment is required

immediately, as a good clinical outcome is associated with early therapy for reducing anti-NMDA receptor antibody mix.

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