

tremors, restlessness and altered sensorium. On examination, the Glasgow coma scale (GCS) (E4V5M6), 4/5 power in all 4 limbs, Babinski- flexor plantar response. PET CT was done which was normal. Magnetic resonance imaging (MRI) brain was done which was also normal (Figure 2).



Figure 2: MRI Brain showing no significant changes

Cerebrospinal fluid (CSF) analysis was (Figure 3) done which showed normal glucose and total leukocyte count (TLC) but elevated protein. CSF paraneoplastic and meningitis panel were negative (Fig-3). CSF autoimmune encephalitis panel was sent which came to be weak positive (Fig-3).

Test Name	Result	Unit	Ref Interval
CSF - Cell Type & Count, Glucose, Protein			
Volume	5.00	mL	
Colour	Colorless		
Visual Observation			
Appearance	Clear		
Viscosity	Normal		
Clot/Clot Web	ABSENT		
CSF Glucose	56.72	mg/dL	40 - 70
CSF Protein	83.8	mg/dL	15 - 45
CSF TLC	No cells seen	Cells/cumm	
RBC Count	NI	RBC/cumm	
Differential Cell Count			
CSF Neutrophils	NI	%	
CSF Lymphocytes	NI	%	

Test Name	Result	Unit	Ref Interval
Biofire - Encephalitis/Meningitis Panel Film Array Multiplex PCR, Cef			
Virus			
Cytomegalovirus	Not Detected		
Enterovirus	Not Detected		
Herpes Simplex Virus 1	Not Detected		
Herpes Simplex Virus 2	Not Detected		
Human Herpes Virus 6	Not Detected		
Vaccinia Zoster Virus	Not Detected		
Bacteria			
Escherichia Coli K1	Not Detected		
Haemophilus influenzae	Not Detected		
Listeria monocytogenes	Not Detected		
Neisseria meningitidis	Not Detected		
Streptococcus agalactiae	Not Detected		
Streptococcus pneumoniae	Not Detected		
Fung	Not Detected		
Cryptococcus neoformans/galli	Not Detected		

Test Name	Result	Unit	Ref Interval
Auto Immune Encephalitis Panel			
Sample Type			
NMDA (anti-glutamate receptor against NR1)	Weak Positive (1+)		
Interpretation			
AMPA (anti-glutamate) Glu-R1	Negative		
AMPA (anti-glutamate) Glu-R2	Negative		
GABA-B receptor antibody	Negative		
LGII-1 antibody (VGKC type)	Negative		
CASPR2 antibody (VGKC type)	Negative		

Figure 3: A-CSF Analysis showing CSF glucose, CSF protein and CSF TLC normal. B- Encephalitis/Meningitis panel negative. C-Auto immune encephalitis panel showing NMDA weak positive

In view of anti-NMDA, auto immune encephalitis Injection Methyl prednisolone was given and intravenous immunoglobulin (IVIG) was started in view of. Total dose of IVIG given was 110 gm. Electroencephalogram (EEG) revealed 7-8 hertz and 20-30 microvolt theta, alpha activity seen with bifrontal beta with intermittent sharp and slow activity seen from left occipital area. Patient had Oro alimentary and bimanual automatisms with behavioural arrest suggestive of complex partial seizure, patient was started on carbamazepine. Patient also developed paroxysmal kinesigenic dyskinesia which responded well with clonazepam and carbamazepine.

Intravenous immunoglobulins (IVIG: 2gm/kg + methylprednisolone 1 gm iv daily for 5 days followed by
Prednisolone 1 mg/kg/day in a tapering dose
For Agitation: Clonazepam: 0.5 mg once daily
For Abnormal movements: Carbamazepine 100mg twice daily
Additional consideration: Early physical therapy

Table 1: Therapy and dosage for anti-NMDAR encephalitis

Discussion

The protracted course of symptoms and the lack of response to conventional antimicrobial therapies prompted further investigation into autoimmune aetiologies. Weakly positive anti-NMDA receptor antibodies detected in the CSF were consistent with a diagnosis of anti-NMDA receptor encephalitis. The presence of these antibodies suggests an autoimmune mechanism underlying the patient's neurological symptoms.¹ Although the MRI brain did not show any lesions, the absence of radiological abnormalities does not exclude the diagnosis of anti-NMDA receptor encephalitis, as imaging findings can be normal or nonspecific in up to 50% of cases.² This highlights the importance of considering autoimmune encephalitis in the differential diagnosis of patients with refractory neurological

symptoms, even in the absence of characteristic imaging findings.

The patient's positive response to pulse steroids and IVIG supports the autoimmune nature of her condition, as immunomodulatory therapies are the cornerstone of treatment for anti-NMDA receptor encephalitis.³ However, the development of complex partial seizures and dyskinesias during the course of treatment underscores the heterogeneity of the disease and the need for vigilant monitoring for potential complications.⁴ The prompt initiation of antiepileptic medications, such as clonazepam and carbamazepine, resulted in symptom improvement, highlighting the importance of multidisciplinary management in optimizing patient outcomes.⁵

Differential diagnosis

The differential diagnosis often includes a primary psychiatric disorder, drug abuse, neuroleptic malignant syndrome, or infectious encephalitis.⁶ In some instances, the diagnosis of rabies has been considered due to the presence of extreme agitation, prominent sialorrhea, and abnormal movements. In contrast to anti-NMDAR encephalitis in which the brain MRI is frequently normal,⁷ the MRI of patients with rabies often shows symmetric involvement of the grey matter of dorsal brainstem,

thalamus, basal ganglia, or central region of the spinal cord.⁸ Prognosis is as follows: the recovery process from anti-NMDAR encephalitis can take many months, the symptoms may reappear in reverse order, and the patient may experience psychosis again leading many people to falsely believe the patient is not recovering. As the recovery process continues, the psychosis fades. Lastly, the person's social behaviour and executive functions begin to improve.

Conclusion

This case highlights the diagnostic challenges associated with anti-NMDA receptor encephalitis, particularly when presenting with atypical features and negative initial investigations. A high index of suspicion for autoimmune encephalitis is crucial in patients with refractory neurological symptoms, as early recognition and initiation of immunomodulatory therapies can significantly impact patient outcomes. Further research is needed to elucidate the pathophysiological mechanisms underlying the diverse clinical manifestations of anti-NMDA receptor encephalitis and to optimize treatment strategies for this debilitating condition.

Saha Monideep, Kumar Neeraj, Mehta Laveena, Budhiraja Sandeep. Unveiling a Diagnostic Conundrum: A Case of Anti-NMDA Receptor Encephalitis Mimicking Infection. MMJ. 2024, May. Vol 1 (2).

References

1. Dalmau J, Lancaster E, Martinez-Hernandez E, Rosenfeld MR, Balice-Gordon R. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. *Lancet Neurol.* 2011;10(1):63-74. doi:10.1016/S1474-4422(10)70253-2.
2. 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;12(2):157-165. doi:10.1016/S1474-4422(12)70310-1.
3. Dalmau J, Gleichman AJ, Hughes EG, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neurol.* 2008;7(12):1091-1098. doi:10.1016/S1474-4422(08)70224-2.
4. Gresa-Arribas N, Titulaer MJ, Torrents A, et al. Antibody titres at diagnosis and during follow-up of anti-NMDA receptor encephalitis: a retrospective study. *Lancet Neurol.* 2014;13(2):167-177. doi:10.1016/S1474-4422(13)70282-5.
5. Peery HE, Day GS, Dunn S, et al. Anti-NMDA receptor encephalitis. The disorder, the diagnosis and the immunobiology. *Autoimmun Rev.* 2012;11(12):863-872. doi:10.1016/j.autrev.2012.03.001.
6. Gable MS, Gavali S, Radner A et al. Anti NMDA receptor encephalitis: report of ten cases and comparison with viral encephalitis. *Eur J Clin Microbiol Infect Dis.* 2009;28:1421–1429
7. Dalmau J, Gleichman AJ, Hughes EG et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neurol.* 2008; 7:10091–10098
8. Laothamatas J, Sungkarat W, Hemachudha T. Neuroimaging in rabies. *Adv Virus Res.* 2011; 79:309–327