

Anti-NMDA Receptor Autoimmune Encephalitis- A Case Report

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ABSTRACT

One of the most popular autoimmune encephalitis is the Anti-N-methyl D-aspartate (NMDA) receptor (anti-NMDAR) encephalitis. N-methyl-D-aspartate receptor (NMDAR) antibody encephalitis is a potentially fatal autoimmune syndrome that generates antibodies against NMDAR causing severe dysregulation of neurotransmission. Auto immune encephalitis is a growing category of clinical syndromes that may occur at any age. Such conditions are associated with antibodies to proteins from the surface of neuronal cells and synaptic receptors involved in synaptic transmission, plasticity, or neuronal excitation. A 38 year old female patient was admitted in ICU presented with seizure on 2 days (1st episode and next day 2nd episode) and altered sensorium. The patient has severe, prolonged and potentially fatal pathological bilateral ovarian dermoid. Patients most often present with a constellation of neuropsychiatric signs and symptoms, including memory loss, hallucinations, and decreased level of consciousness. This patient has also the same neuropsychiatric signs and symptoms. This condition is lethal if left untreated. Immunomodulation, high dose of steroids and surgical resection of the culprit malignancy often results in the rapid resolution of symptoms with an excellent prognosis.

Key Words: Anti-N-methyl D- aspartate, Autoimmune encephalitis, Neurotransmission, Seizure, Altered sensorium

INTRODUCTION

Anti-N-methyl D-aspartate receptor (NMDAR) encephalitis is a rare autoimmune condition characterised by serious neurological and psychological symptoms. Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is a recently described disorder with a well defined set of clinical features.¹ Autoimmune encephalitis is an acute secondary autoimmune inflammation of the brain that presents as seizures, cognitive dysfunction, and neuropsychiatric symptoms². In 2005, high levels of antibodies were detected against an antigen in the hippocampus of four women with ovarian teratomas who presented with prominent psychiatric symptoms, memory loss, and a decreased level of consciousness.³ The target antigen was identified as NMDAR in 2007,¹ since when research into this disease has expanded rapidly. Its pathogenesis involves the development of an autoantibody to the NMDA-type glutamate receptor, involved in synaptic transmission that helps to modulate human memory, cognition, and plasticity, known to play a role in neuropsychiatric disorders⁴. NMDAR function is not only impaired by many exogenous drugs, including PCP, ketamine, and ethanol, but also endogenous brain immune interactions that can have significant clinical implications.

Autoimmune encephalitis is classified in the past as paraneoplastic or non-paraneoplastic, depending on whether there are any identifiable tumor-associated antibodies. These paraneoplastic antibodies include anti-neuronal nuclear antibody type 1 (anti-Hu), anti-Ri, or Yo, etc. With a better understanding of the pathophysiology of different auto-immune encephalitis, the better way of classification is pathophysiologically based. The modern-day classification is to classify the immune encephalitis according to the targets of the antibodies. The classical paraneoplastic encephalitis, as named above, is mediated through a predominant T-cell mediated mechanism with cytotoxic T cells demonstrated in the pathological specimens. These immune responses are the result of molecular mimicry between the neuronal tissue antigen and tumor antigens. The antibodies themselves are not pathogenic. These antibodies direct their activity towards intracellular constituents. The other class of autoimmune encephalitis consists of antibodies directed against synaptic or cell-surface antigens such as anti-NMDAR, anti-GAD, anti-VGKC antibody-mediated encephalitis. These are real antibody or B-cell mediated autoimmune encephalitis with real pathogenic antibodies. Anti-NMDAR antibody immune encephalitis is a B-cell mediated autoimmune encephalitis with an actual pathogenic antibody that can be removed by plasma exchange resulting in improvement of the underlying pathology.

Immunomodulation and neoplasm removal targeting both symptomatic and causal factors are mainstays of treatment. Immunotherapy such as with steroids, plasmapheresis and IVIG helps reduce antibody titers. Tumor removal in those with identifiable lesions leads to rapid clinical improvement. Second-line therapy consists of Rituximab or cyclophosphamide. Benzodiazepines and antipsychotics round out the pharmacotherapies employed in the

treatment of seizures, psychosis and behavioral dysfunction.

CASE REPORT

A 38 year old Female patient with significant past medical history of headache presented to the ICU complaining of headache and tiredness for past 4 days, seizure- for 2days with altered sensorium. On examination patient is disoriented and hallucinated. On day 1 of admission patient had cardiac arrest, was intubated and started on mechanical ventilation. Patient started with ACYCLOVIR 500mg IV Q8H and ceftriaxone 2g IV Q8H. Auto immune panel was positive for NMDA Auto immune encephalitis. Acyclovir was stopped in view of AKI and started on pulse steroid therapy with Inj. Dexamethasone 8MG IV Q8H, Inj. Methyl Prednisolone IV BD, T. Prednisolone RT (Rice tube) 40 mg OD. After completing methylprednisolone course, oral prednisolone (4mg) was initiated. Tracheostomy tube ventilation started to the patient. Hemodialysis (HD) catheter inserted and underwent 5 cycles of PLEX (Plasma exchange).

On investigation: Ultra sonogram of abdomen shows Left ovarian hyperechoic lesion possibility of ovarian dermoid to be considered. Small right kidney. MRI brain with MR venogram shows Scattered sulcal space hyperintensity with minimal subcortical changes likely meningoencephalitis. MRI brain shows Follow up case of autoimmune encephalitis. Patient developed ventilator associated pneumonia (VAP)- right lower lobe pneumonia and patient underwent culture follow up.

Patient started with inj. Meropenem 1gm IV Q8H and inj. Colistin 3MU Q8H. and T. Fluconazole 100mg in view of perineal fungal infection. And patient has on and off seizures and on triple antiepileptic therapy inj. Levetiracetam 500mg IV Q8H Inj. Fosphenytoin 150mg IV Q8H. Inj. Lacosamide 100mg IV BD. Patient become hemodynamically stable and improved sensorium and shifted to HDU.

TABLE:1 CULTURE REPORT

| SPECIMEN | ORGANISM |
|----------------------|---|
| BAL | STENOTROPHOMONAS MALTOPHILIA KLEBSILA |
| URINE | ESBL E COLI |
| BAL | GRAM -VE ACINETOBACTER BAUMANNI |
| BLOOD | STERILE |
| BAL | PSEUDOMONAS AEUROGINOSA |
| BROTH MICRO DILUTION | PSEUDOMONAS AEUROGINOSA COLISTIN sensitive |

DISCUSSION

Anti-NMDAR encephalitis is an autoimmune disorder caused by autoantibodies inactivity of the extracellular portion of NR1 subunits of NMDARs this protein includes memory function and synaptic plasticity, resulting in the characteristic neuropsychiatric symptomatology⁷. Anti-NMDAR encephalitis leads to encephalitis of up to 21%. Although the exact cause remains unclear, in this case patient was initially treated with antiviral drugs, most studies postulated a virus induced aetiology.⁸

The clinical presentation is variable and may be mild with only a few symptoms or mimics a psychiatric disorder with delayed diagnosis of encephalitis. More complex symptomatology may be present and it can also have a fulminant course with a fatal outcome⁹. Anti-N-Methyl-D-Aspartate Receptor Encephalitis is a type of autoimmune encephalitis, first described by Joseph Dalmau et al (2007), characterized by antibodies targeting the NR1 subunit of NMDA receptor. It is considered to be the second most common cause of autoimmune encephalitis. Differential diagnosis represents a major challenge because symptoms may overlap with other disorders and initial laboratory tests may not provide directive findings. As in this case, clinical presentation could have led to the diagnosis of epilepsy, or viral encephalitis and started antiviral therapy. Then later patient was diagnosed with autoimmune encephalitis¹⁰. Although anti-NMDAR encephalitis has a mortality rate of 7%, 80% of cases have substantial or full recovery. Recovery is usually slow and may take upto 2 years. The last symptoms to improve are social

interactions, language and executive functions. Relapses occur in 24% of cases.

Immunomodulation and neoplasm removal targeting both symptomatic and causal factors are mainstays of treatment¹¹. corticosteroids, IVIG or plasmapheresis are first-line therapy. Second-line therapy, like rituximab, cyclophosphamide and mycophenolate is also needed. They should be reserved for those who are refractory or have relapses with first-line immunotherapy¹². Prompt recognition and early use of high-dose steroid treatment can shorten the duration of the disease and possibly prevent complications; however, there are still gaps in knowledge, specifically, when to add disease-modifying therapy and how long to remain immunotherapy in patients who have returned to their baseline.⁸ In our patient, we continued immunotherapy for 2 more months, after our patient has returned to her neurological baseline.

CONCLUSION

Anti-NMDAR autoimmune encephalitis is one of the most common causes of autoimmune encephalitis. Early identification, immunotherapy, and malignancy work-up are the mainstays of management. With early detection and immunotherapy, 80% of patients show full recovery.

REFERENCES

1. Dalmau J, Tuzun E, Wu HY, et al. Paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. *Ann Neurol* 2007; 61: 25–36
2. Najjar S, Pearlman D, Devinsky O, Najjar A, Nadkarni S, Butler T, Zagzag D. Neuropsychiatric autoimmune encephalitis

- without VGKC-complex, NMDAR, and GAD autoantibodies: case report and literature review. *Cogn Behav Neurol*. 2013; 26(1):36-49
3. Vitaliani R, Mason W, Ances B, Zwerdling T, Jiang Z, Dalmau J. Paraneoplastic encephalitis, psychiatric symptoms, and hypoventilation in ovarian teratoma. *Ann Neurol* 2005;58:594–604.
 4. Irani SR, Bera K, Waters P, Zuliani L, Maxwell S, Zandi MS, et al. N-methyl-D-aspartate antibody encephalitis: temporal progression of clinical and paraclinical observations in a predominantly non-paraneoplastic disorder of both sexes. *Brain* 2010;133(Pt 6):1655–1667.
 5. Venkatesan A, Tunkel AR, Bloch KC et al (2013) Case definitions, diagnostic algorithms, and priorities in encephalitis: consensus statement of the international encephalitis consortium. *Clin Infect Dis* 57: 1114–1128.
 6. Venkatesan A, Michael BD, Probasco JC et al (2019) Acute encephalitis in immunocompetent adults. *Lancet* 393:702–716
 7. Salvucci A, Devine IM, Hammond D, Sheth RD. Pediatric anti-NMDA (N-methyl D-aspartate) receptor encephalitis. *Pediatric Neurology*. 2014 May 1;50(5):507-10.
 8. Leypoldt F, Armangué T, Dalmau J. Autoimmune encephalopathies. *Annals Of The New York Academy Of Sciences*. 2015 Mar;1338(1):94.
 9. John ST, Salam KA. Autoimmune Encephalitis: A Case Report. *BMH Medical Journal-ISSN 2348–392X*. 2017 Jan 1;4(1): 38-40.
 10. Hallowell S, Tebedge E, Oates M, Hand E. Rituximab for treatment of refractory anti-NMDA receptor encephalitis in a pediatric patient. *The Journal Of Pediatric Pharmacology And Therapeutics*. 2017; 22(2):118-23.
 11. Barry H, Byrne S, Barrett E, Murphy KC, Cotter DR. Anti-N-methyl-d-aspartate receptor encephalitis: review of clinical presentation, diagnosis and treatment. *Bjpsych Bulletin*. 2015 Feb;39(1):19-23
 12. Titulaer MJ, McCracken L, Gabilondo I, Armangué T, Glaser C, Iizuka T, Honig LS, Benseler SM, Kawachi I, Martinez-Hernandez E, Aguilar E. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study. *The Lancet Neurology*. 2013 Feb 1;12(2): 157-65.

How to cite this article: Syam Prakash KR, Maheshwari.V, Anto A et. al. Anti-NMDA receptor autoimmune encephalitis- a case report. *International Journal of Research and Review*. 2020; 7(9): 322-325.
