Anti-NMDA receptor encephalitis with phenytoin toxicity: A diagnostic dilemma and management challenge

Sir,

Anti-N-methyl D-aspartate receptor (NMDAR) encephalitis is an immune-mediated disease characterised by a complex neuropsychiatric syndrome and the presence of antibodies against NMDAR in cerebrospinal fluid (CSF). The disease is rare, with an estimated incidence of 1.5 per million populations per year with female to male ratio of 8:2.[1] Here, we report a case that presented with seizures after phenytoin overdose and later on diagnosed as anti-NMDAR encephalitis.

A 23-year-old male presented to the emergency department with the Glasgow Coma Scale score of E_2V_T M_2 on mechanical ventilation with a history of phenytoin overdose and seizure episodes. History from the relatives revealed that he allegedly took 30 tablets of 100 mg phenytoin after which he became unconscious with abnormal movement of the head, trunk and body. He was taken to a local hospital where he was intubated and referred to our hospital. He was a known case of seizure disorder for 2 months and was taking phenytoin and phenobarbitone for the same.

On examination, vitals were stable, pupils were sluggishly reactive to light, and the patient was having persistent head-nodding and dyskinesia of limbs. Routine investigations were within normal limits. Serum phenytoin levels were 29.66 μg/dL. The patient was put on levetiracetam and midazolam infusion along with other supportive treatment. However, the symptoms were not resolved, and the patient was put on other drugs like lacosamide, oxcarbazepine and haloperidol. Computed tomography (CT) brain, magnetic resonance imaging (MRI) brain, electroencephalography (EEG) and CSF examination were within normal limits. With due course of treatment, abnormal movement of limbs decreased and the patient was weaned from the ventilator and extubated on the 10th day of admission; however, unresponsiveness and head-nodding were still persistent. To detect the cause of unexplained persistent abnormal movements, repeat CSF was sent for autoimmune epilepsy evaluation tests, which came out to be positive for NMDAR antibodies and a diagnosis of anti-NMDAR encephalitis was made. The patient was then started on 1 gm methylprednisolone/day for 5 days. The patient was not having any significant improvement and head-nodding continued. Plasmapheresis was then started on alternate days for 5 cycles after which the patient became responsive and head-nodding subsided, however, slight facial dyskinesis was persistent. The patient was discharged and was asymptomatic after a follow-up of 2 months.

NMDAR encephalitis is considered a multistage disease, characterised by nonspecific prodromal flu-like symptoms, followed by psychiatric symptoms in the initial phase and later neurological alterations like abnormal movements, seizures, dysautonomia or coma. Movement disorders and seizure are seen in about 70% of adults.[2]

Diagnosis in this patient was difficult as the patient presented with overlapping symptoms of phenytoin overdose and was in critical condition. Phenytoin has both cardiac and neurological effects. It blocks the sodium channels in the cardiac tissue and causes junctional bradycardia and sinus arrest.[3] The neurological effects of phenytoin overdose are concentration-dependent and can range from mild nystagmus to ataxia, slurred speech, vomiting, lethargy, and eventually seizures, coma, and death.[4] The symptoms like dyskinesia, seizure and coma are common manifestations of both phenytoin toxicity and anti-NMDAR encephalitis. These non-specific symptoms along with normal EEG and radio imaging studies lead to a diagnostic dilemma. Delayed diagnosis and complications associated with intensive care unit (ICU) stay was a management challenge. To date, there has been no prospective open-label treatment trial to evaluate the efficacy of treatments available, and all existing evidence is graded as Class IV.[5] The treatment approach involves first-line therapies with steroids, intravenous immunoglobulins (IVIg), or plasma exchange (PE) and second-line therapies with rituximab or cyclophosphamide if needed.[2] Some of the clinicians prefer comprehensive immunotherapy with rituximab, IVIg or PE, and methylprednisolone upfront all at the same time and some prefer a stepwise approach. We followed a stepwise approach with corticosteroids initially followed by plasmapheresis after non-response, which successfully aborted the symptoms.

Careful consideration of the syndrome and determination of IgG antibodies in CSF is crucial to prevent misdiagnosis. It is still not clear as to whether one should use a comprehensive immunotherapy approach or a stepwise approach for its management. The debate is still open and more scientific evidence is awaited.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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REFERENCES

1. Dalmau J, Armangue T, Planaguma J, Radosevic M, Mannara F, Leypoldt F, *et al*. An update on anti-NMDA receptor encephalitis for neurologists and psychiatrists: Mechanisms and models. Lancet Neurol 2019;11:1045-57.
2. Titulaer MJ, McCracken L, Gabilondo I, Armangué T, Glaser C, Iizuka T, *et al*. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: An observational cohort study. Lancet Neurol 2013;12:157-65.
3. Mathew RR, Raju K, Nair BR, Mariappan R. An observational case-control study comparing the recovery profile in patients receiving additional dose of anticonvulsant vs. regular dose during supratentorial craniotomy. Indian J Anaesth 2020;64:222-9.
4. Iorga A, Horowitz BZ. Phenytoin toxicity. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2020 Jan. Available from https://www.ncbi.nlm.nih.gov/books/NBK482444/. [Last accessed on 2021 Feb 03].
5. Bartolini L. Practice current: How do you treat anti-NMDA receptor encephalitis? Neurol Clin Pract 2016;6:69-72.

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