HIDING IN PLAIN SIGHT: ANTI-NMDAR- ENCEPHALITIS IN A 30-YEAR-OLD MALE- A CASE REPORT

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ABSTRACT

The most common type of autoimmune encephalitis is anti-NMDAR-encephalitis. It is characterized by IgG antibodies against the GluN1 subunit of the NMDA receptor, leading to marked neuropsychiatric and behavioural symptoms that progress in a subacute manner to seizures, speech abnormalities, and a depressed level of consciousness. In this case report, the clinical course of a 30-year-old man who first received treatment for viral encephalitis after exhibiting normal symptoms is described. CSF showed lymphocytic pleocytosis with normal brain imaging. The EEG demonstrated diffuse slowing and encephalopathy. An autoimmunity encephalitis workup was done after exhaustive investigations for metabolic and infectious causes came back negative. A diagnosis of anti-NMDAR encephalitis was made after antibodies were found in the CSF.

Keywords: Anti-NMDAR encephalitis; Autoantibodies; Immunotherapy; Psychiatric manifestations.

INTRODUCTION

Contrary to its increasing recognition in the developed world, with incidences comparable to those of infectious encephalitis.[1] Autoimmune encephalitis is still underdiagnosed in the developing world.[2] A literature review reveals that the first two cases of autoimmune encephalitis in Pakistan were reported by Memon et al. in 2015 and Zubair et al. in 2018.[3] Sheikh et al. published a case series in 2019 that described seven cases and their outcomes.[4] This case was reported to highlight the need for a differential diagnosis that includes autoimmune encephalitis in cases of sudden onset of neurobehavioral symptoms. We present the case of a young guy who exhibited these symptoms before being identified as having anti-NMDAR encephalitis.

Case Report

Generalized tonic-clonic seizures and impaired mentation were evident when a 30-year-old previously healthy man arrived at the emergency department of a local hospital. Two weeks before the presentation, he had experienced an episode of a severe, throbbing headache followed by a seizure, necessitating a visit to the local ED. He was treated symptomatically and sent home. Over an ensuing couple of weeks, the frequency of his seizures increased along with the development of aggressive behaviour and irrelevant talk. He was seen by a psychiatrist, who prescribed treatment for seizures and psychosis. Worsening seizures and unconsciousness finally led to his admission to the local hospital, where he was intubated for airway protection and shifted to the medical ICU. The workup revealed CT brain CT-brain and lymphocytic pleocytosis in the CSF. Despite treatment, his conscious state did not improve, and a tracheostomy was done on day ten of mechanical ventilation. The patient was then transferred to our hospital for further management. On arrival, a conscious state corresponded to a GCS score of 6/15. Eye-opening was spontaneous; there were no purposeful or tracking movements. Brainstem reflexes were intact. Plantars were bilaterally down. He exhibited twitching movements of his facial muscles and automatisms in the form of tongue protrusions and chewing movements. CSF showed lymphocytic pleocytosis with normal protein and glucose. A CT of the brain was reported as normal. Liver function, renal function, electrolytes, and thyroid functions were normal. The MRI brain did not reveal any abnormalities, and the HSV PCR was subsequently reported as negative. The EEG showed diffuse encephalopathy. Considering the persistent catatonic state, the subacute onset of his neurobehavioral symptoms, and the lack of any other plausible explanation, autoimmune encephalitis was considered, and CSF was sent for antibodies. Anti-NMDAR antibodies were positive. First-line treatment was initiated in the form of pulsed steroids and plasmapheresis, albeit without benefit. Rituximab was given as a second-line treatment. Unfortunately, our patient succumbed to the complications of immuno-

suppressive treatment by developing hospital-acquired pneumonia and, subsequently, septic shock and multi-organ failure.

DISCUSSION

Anti-NMDAR-encephalitis is one of the many types of autoimmune encephalitis that have been recognized in the past two decades. The seminal paper on anti-NMDAR-encephalitis described four young women with ovarian teratomas and encephalitis referred to as teratoma-associated encephalitis.[5] Two years later, their work identified the target antigen as NMDA receptors.[6] The pathogenic antibodies cause crosslinking and subsequent internalization of the NMDA receptors leading to downstream disruption of glutamatergic synaptic transmission and function.[7] Anti-NMDAR-encephalitis affects younger individuals (95% < age 45 years) with a female preponderance of 4:1. 58% of patients will have an underlying neoplasm usually teratomas.

The clinical manifestations of anti-NMDAR-encephalitis can be divided into eight categories as described by the largest case series to date of 577 patients.[8] These are behavior and cognition, memory, seizures, central hypoventilation, movement disorder, loss of consciousness, and autonomic dysfunction. The typical patient with this disorder will present with a subacute onset of neurobehavioral disturbance such as agitation, psychosis, and irritability. Catatonia has been described in 42% of patients.[9] A psychiatric institute or practitioner may be the first point of contact with the healthcare system for these patients. As the illness progresses, they develop orofacial, limb, and trunk dyskinesias and seizures, either generalized or focal with impaired awareness. A depressed or altered level of consciousness may then follow. Memory impairments may be present at this point but are difficult to elicit instead of the other neuropsychiatric symptoms making memory evaluation suboptimal.

This indicates that patients with autoimmune encephalitis may hover around the healthcare system before finally landing in a hospital where they may or may not be ultimately diagnosed. The diagnosis becomes even more difficult in developing countries with limited resources and physician awareness. Considering this and the observation that early treatment portends a better chance at recovery, clinical guidelines for the diagnosis of anti-NMDAR-encephalitis were published in 2016.[10] Patients with 4 of 6 primary groups of symptoms, an abnormal EEG or CSF, and a good exclusion of other disorders, particularly HSV encephalitis, can be given a probable diagnosis of anti-NMDAR-encephalitis. IgG anti-GluN1 antibodies found in the CSF lead to a certain diagnosis.[10] Half of the patients with this disorder will have a normal MRI, while the other half may show fleeting T2/FLAIR hyperintensities.[11]

Treatment for anti-NMDAR-encephalitis centers on immunomodulation and management of the tumor where applicable. If a diagnosis is made without a known tumor, imaging is advised to look for one. First-line treatments include steroids, IVIG, and plasma exchange. Tumor detection and removal where applicable significantly increase the chances of response to treatment.[11] Second-linee treatments include Rituximab and Cyclophosphamide. Half of these patients will respond favorably to first-line treatments. Of the remaining half, 57% would respond to second-line treatments.[8] Prognostic factors for functional outcomes in these patients have been incorporated into a NEOS score (anti-NMDAR-Encephalitis One-year functional Status). The score uses a five-point system to predict outcomes. 69% of patients with NEOS scores of 4 or more will have poor functional outcomes at one year.[12]

CONCLUSION

Anti-NMDAR-encephalitis is an exceedingly debilitating, potentially fatal but reasonably treatable disorder. Its propensity for young people represents a significant loss of functional years and an increased burden of care highlighting the significance of a swift diagnosis and urgent management. Lastly, along with infectious etiologies, autoimmune encephalitis should be considered in the differential diagnosis of young patients presenting with the above-mentioned constellation of symptoms.

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Author's Contribution

MLS conceived the idea and wrote the manuscript. AR, AN, and FN contributed in wite up of the manuscript. Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

Authors declared no conflict of interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.