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CASE REPORT

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Neuropsychiatric manifestations of anti-N-methyl-D-aspartate receptor encephalitis in a 14-year-old female: A case report

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Key Clinical Message

This case underscores the critical importance of timely recognition and management of NMDAR encephalitis in adolescents to mitigate potential long-term sequelae. If a pediatric patient presents with suspected viral encephalitis, autoimmune etiology must be excluded via cerebrospinal fluid antibody assay to guide appropriate immunosuppressive therapy, and improve patient outcomes.

Abstract

Autoimmune encephalitis particularly involving the n-methyl-d-aspartate receptor (NMDAR) is recognized as a rare cause of acute encephalopathy in pediatric patients. The following case is of a 14-year-old female diagnosed with anti-NMDAR encephalitis who initially presented with fever, episodic convulsions, and loss of consciousness. She subsequently developed right-sided body weakness, expressive aphasia, and visual hallucinations. Clinical examination revealed prominent neuropsychiatric manifestations such as altered sensorium, motor deficits, hallucinations, and visual disturbances. Cerebello-bulbar signs were not appreciable in this particular case. She was treated for viral encephalitis but showed no improvement. Laboratory investigations revealed the presence of NMDAR antibodies in the cerebrospinal fluid confirming the diagnosis of autoimmune etiology. The patient demonstrated notable improvement following immunosuppressive treatment.

KEYWORDS

anti-N-methyl-D-aspartate receptor encephalitis, autoantibodies, hallucinations, immunosuppressive therapy, limbic system

1 | INTRODUCTION

Anti-n-methyl-d-aspartate receptor (NMDAR) encephalitis is a rare autoimmune disorder characterized by the presence of antibodies against NMDAR in the central nervous system.[1] It often presents with a spectrum of neurological and psychiatric symptoms.[2,3] We present a case of anti-NMDAR encephalitis in an adolescent patient emphasizing its clinical manifestations, diagnostic approach, and therapeutic management.

2 | CASE HISTORY

A 14-year-old female presented with an altered level of consciousness, right-sided body weakness, and an inability to speak. She had a history of sudden-onset fever, repetition of tasks, and visual hallucinations. No significant past medical history or recent travel history was reported. Table 1 shows the clinical events of the patient from the day of admission along with interventions done in the hospital.

3 | DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS, AND TREATMENT

Differential diagnoses included viral, autoimmune and postinfectious encephalitis and psychiatric illness. CBC and CT scans of the brain were unremarkable. EEG showed no changes. CSF analysis revealed mild elevation of proteins with lymphocytic predominance. Table 2 shows the result for CSF antibodies assay. The presence of anti-NMDAR antibodies in the CSF is highly specific and confirmed the diagnosis of anti-NMDAR encephalitis. MRI of the brain (Figure 1) demonstrated bilateral temporal lobe enhancement, a characteristic finding in anti-NMDAR encephalitis.[4]

The patient was treated with intravenous corticosteroid (methylprednisolone 1 g IV OD for 5 days), antibiotic (ceftriaxone 2 g IV BD), and supportive medications (i.e., intravenous fluids and proton pump inhibitors).

TABLE 1 Summary of clinical events.

Time (from the day of admission to the hospital)	Clinical event(s)
Day 1	The patient presented with sudden-onset fever and altered consciousness
Day 2–5	She was treated empirically for viral encephalitis
Day 6	She developed right-sided weakness, inability to speak, repetition of tasks, and visual hallucinations
Day 7	CSF tests diagnosed anti-NMDAR encephalitis in the patient
Day 8–12	Initiated treatment with intravenous corticosteroids and antibiotics
Day 13–20	The patient showed gradual improvement in symptoms with therapy

TABLE 2 Autoimmune encephalitis antibodies profile by CSF test.

Antibodies	Result
NMDAR	Positive
Anti-contactin-associated protein-like 2	Negative
Glutamate Receptor (type AMPA1/2)	Negative
Leucine-rich glioma inactivated protein 1 (LGI1)	Negative
GABA-b receptor	Negative
Dipeptidyl-aminopeptidase-like protein 6	Negative

4 | OUTCOME AND FOLLOW-UP

Following treatment, the patient showed a significant improvement in motor function, expressive aphasia, and visual hallucinations within 10 days. The symptoms regressed at varying rates, with motor function improving first, followed by speech and visual symptoms. The treatment was well-tolerated without significant adverse effects. During follow-up visits, the patient showed gradual improvement in symptoms with strict adherence to the prescribed intravenous corticosteroid regimen. No additional long-term medications were required beyond the initial immunosuppressive treatment.

5 | DISCUSSION

The pathogenesis of anti-NMDAR encephalitis involves the production of antibodies targeting the NR1 subunit of the NMDAR.[5] These autoantibodies disrupt the normal functioning of NMDAR which leads to dysregulation of glutamatergic neurotransmission. Ultimately, this dysregulation in neurotransmission causes neuronal dysfunction and inflammation in the CNS. The resulting neurological and psychiatric manifestations vary widely but commonly include altered consciousness, seizures, movement disorders, and psychiatric symptoms such as hallucinations and behavioral changes.[3] The bitemporal enhancement seen on MRI of the brain, while characteristic, is only observed in about 55% of patients with

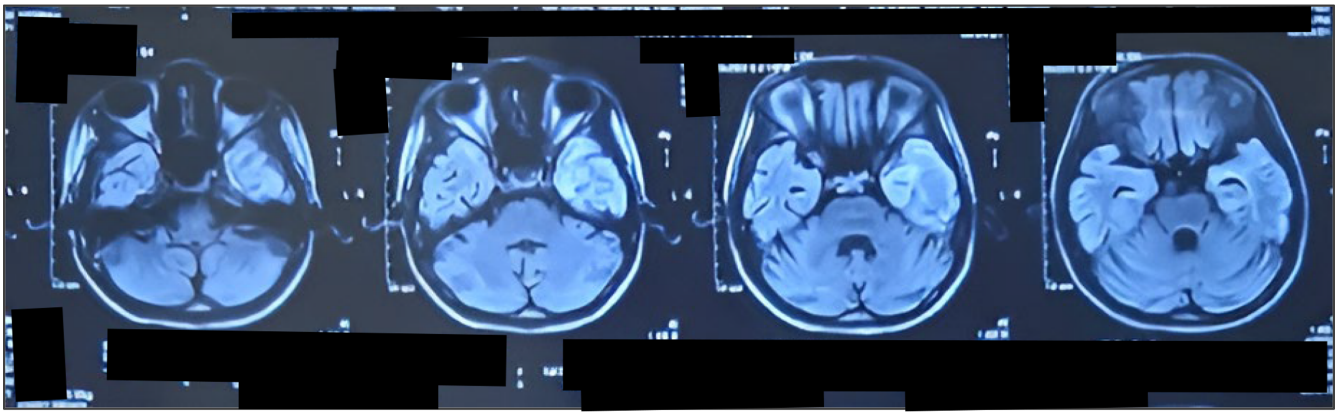

FIGURE 1 MRI of the brain showing bilateral temporal enhancement.

anti-NMDAR encephalitis.[6] This pattern of enhancement reflects the inflammatory process affecting the limbic system.[4] The limbic system is involved in various cognitive and emotional functions, which may explain the diverse psychiatric manifestations observed in this patient. It is important to consider viral infections, such as herpes simplex virus (HSV) and COVID-19, as potential triggers of anti-NMDAR encephalitis, emphasizing the need for thorough diagnostic evaluations in suspected cases of autoimmune encephalitis.[7,8]

Different autoantibodies correlate with varied clinical outcomes and treatment response. For example, anti-LGI1 antibodies associated with limbic encephalitis often exhibit a more favorable response to immunotherapy compared to GABA-b receptor antibodies.[9] Consequently, identifying the autoantibodies (Table 2) in autoimmune encephalitis is crucial for effective clinical management.[9]

Management of anti-NMDAR encephalitis typically involves immunosuppressive agents,[10] supportive care, and treatment of associated complications. In this case, the patient was given intravenous corticosteroids and antibiotics to target the underlying autoimmune process and manage potential infectious etiologies. Supportive measures including intravenous fluids and proton pump inhibitors were also administered to maintain hydration and prevent complications such as gastrointestinal bleeding. The association between anti-NMDAR antibodies and underlying malignancies, particularly ovarian teratoma in young women, is well-documented.[11] Hence, we recommend screening for malignancy in this patient.

Despite the efficacy of immunosuppressive therapy in mitigating autoimmune-mediated neuronal damage, there are certain limitations and challenges in the management of this disease. Delayed diagnosis and initiation of treatment can lead to prolonged neurological deficits and poorer outcomes. Additionally, some patients may experience relapses or refractory disease requiring escalation of immunosuppressive therapy or alternative treatment modalities such as plasma exchange or immunomodulatory agents.[4] We should maintain a high index of suspicion for anti-NMDAR encephalitis, especially in young patients with acute neurological and psychiatric symptoms.[7]

6 | CONCLUSION

This case highlights the importance of considering anti-NMDAR encephalitis as a differential diagnosis in a pediatric patient presenting with acute neuropsychiatric symptoms. Understanding the patho-physiology and mechanism of autoimmune-mediated neurological injury is crucial for reaching diagnosis and developing a therapeutic regimen.[10]

AUTHOR CONTRIBUTIONS

Masab Ali: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; supervision; validation; visualization; writing – original draft; writing – review and editing. **Haris Naveed:** Conceptualization; project administration; resources; supervision; validation; visualization; writing – review and editing. **Ateeq Ur Rehman Sheikh:** Conceptualization; project administration; resources; supervision; validation; visualization; writing – review and editing. **Muhammad Husnain Ahmad:** Project administration; supervision; visualization; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors have no competing interests to declare.

DATA AVAILABILITY STATEMENT

Data and materials available upon request from corresponding author.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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