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Autoimmune Encephalopathy Presenting with Refractory Seizures and Hemiparesis in an Adolescent: A Diagnostic Challenge

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Abstract

Autoimmune encephalitis is an increasingly recognized cause of acute neurological dysfunction in children and adolescents, often presenting with a wide spectrum of clinical manifestations that can mimic infectious or structural brain disorders. Among its subtypes, anti–N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is the most common and is characterized by seizures, altered sensorium, and neuropsychiatric symptoms.

We report a case of a 15-year-old female who presented with acute onset refractory seizures, altered sensorium, and left-sided hemiparesis. Neuroimaging revealed T2/FLAIR hyperintensities in the right fronto-temporo-parietal region with mass effect. Cerebrospinal fluid analysis showed lymphocytic pleocytosis with mildly elevated protein levels. Autoimmune evaluation demonstrated strongly positive NMDA receptor antibodies, confirming the diagnosis of anti-NMDAR encephalitis.

The patient was treated with high-dose intravenous methylprednisolone, followed by plasmapheresis and rituximab, along with antiepileptic therapy. She showed significant clinical improvement, with recovery of sensorium, reduction in seizure frequency, and improvement in motor function.

This case highlights the importance of considering autoimmune encephalitis in adolescents presenting with refractory seizures and focal neurological deficits. Early diagnosis supported by antibody testing and prompt initiation of immunotherapy are crucial for favourable neurological outcomes.

Keywords: Autoimmune encephalitis, Anti-NMDA receptor encephalitis, Refractory seizures, Hemiparesis, Immunotherapy

Introduction

Autoimmune encephalitis (AE) has emerged as a major cause of non-infectious encephalitis, redefining the diagnostic landscape of acute and subacute neurological syndromes in children and adolescents[1]. Traditionally considered rare, AE is now increasingly recognized due to advances in antibody detection and growing clinical awareness, with recent epidemiological studies suggesting that its incidence is comparable to that of infectious encephalitis in developed settings[2]. Among the various subtypes, anti–N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis represents the most common and well-characterized entity, particularly affecting young individuals and accounting for a significant proportion of encephalitis cases previously labelled as idiopathic[3]. The pathogenesis of anti-NMDAR encephalitis involves IgG antibodies directed against the GluN1 subunit of the NMDA receptor, leading to receptor internalization and synaptic dysfunction without significant neuronal loss[3]. This reversible disruption of excitatory neurotransmission underlies the characteristic clinical spectrum, which includes

seizures, behavioral disturbances, movement disorders, autonomic instability, and altered consciousness[4]. Notably, the clinical presentation is often dynamic and evolves over time, frequently resulting in misdiagnosis as viral encephalitis, psychiatric illness, or acute demyelinating conditions, especially in the early stages[5].

Globally, autoimmune encephalitis has been increasingly reported across all age groups, with pediatric and adolescent populations showing distinct clinical phenotypes characterized by a higher prevalence of seizures and movement disorders compared to adults[4]. However, in low- and middle-income countries such as India, the true burden of AE remains inadequately defined. This is largely attributable to limited access to specialized diagnostic testing, particularly cerebrospinal fluid (CSF) antibody assays, and a continued emphasis on infectious etiologies in the evaluation of encephalitis[6]. Emerging evidence from Indian tertiary care centers indicates that autoimmune encephalitis constitutes a substantial proportion of paediatric encephalitis cases, often presenting with refractory seizures and focal neurological deficits, thereby posing significant diagnostic and therapeutic challenges[7].

A key issue in clinical practice is the delay in diagnosis, which arises from the overlap of clinical, radiological, and laboratory features with other neurological conditions. Magnetic resonance imaging (MRI) findings may be normal or nonspecific in a considerable number of patients, while CSF analysis typically reveals only mild inflammatory changes[5]. Consequently, reliance on conventional investigations alone may lead to underdiagnosis. The detection of neuronal autoantibodies in CSF remains the diagnostic gold standard and plays a crucial role in confirming the diagnosis, particularly in atypical presentations[2]. Importantly, autoimmune encephalitis is a potentially reversible condition, and early initiation of immunotherapy has been consistently associated with favourable neurological outcomes and reduced long-term disability[3],[4]. First-line therapies, including corticosteroids, intravenous immunoglobulin, and plasmapheresis, followed by second-line agents such as rituximab, have demonstrated significant efficacy in both adult and paediatric populations[3]. Therefore, maintaining a high index of suspicion is essential, especially in adolescents presenting with unexplained refractory seizures, altered sensorium, and focal deficits.

In this context, we report a case of anti-NMDAR encephalitis in an adolescent presenting with refractory seizures and hemiparesis—an uncommon but clinically significant presentation—highlighting the diagnostic challenges and emphasizing the importance of early recognition and prompt immunotherapy in improving clinical outcomes.

Aim and Objectives

Aim

To highlight the diagnostic approach and treatment response in autoimmune encephalitis presenting with focal deficits and seizures

Objectives

1. Outline the diagnostic pathway in suspected autoimmune encephalitis.
2. Emphasize the utility of CSF antibody panels.
3. Demonstrate positive outcomes with timely immunomodulation.

Case Presentation

A 15-year-old previously healthy female presented with acute onset of neurological symptoms. The initial complaints included multiple episodes of vomiting, followed by generalized tonic–clonic seizures and progressive alteration in sensorium. Subsequently, she developed weakness of the left side of the body. There was no history of prior neurological illness, recent trauma, or significant past medical history. Family history was non-contributory. On examination, the patient was drowsy and not following commands. Neurological examination revealed left-sided hemiparesis with increased muscle tone. Deep tendon reflexes were brisk, and ankle clonus was present. Bilateral plantar responses were mute. No meningeal signs were noted.

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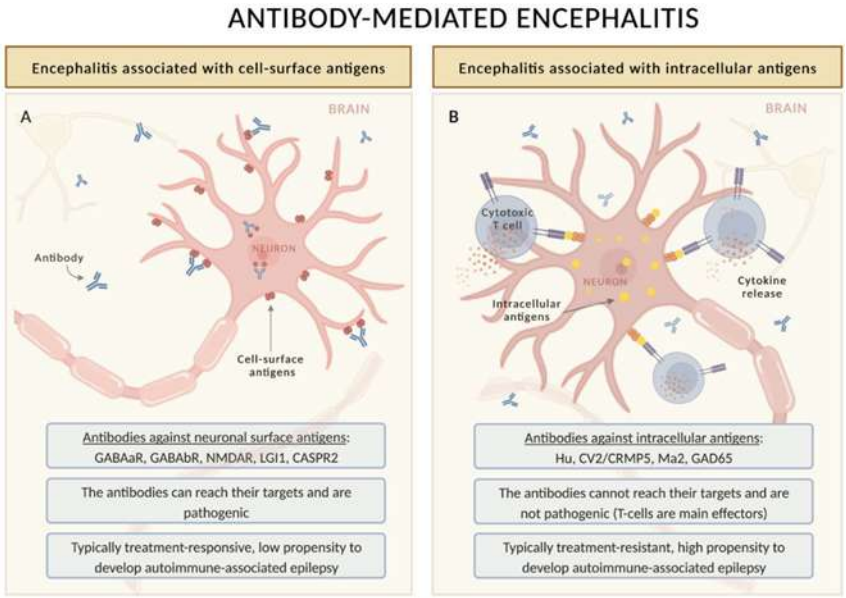

The clinical course was characterized by acute onset symptoms with rapid progression, including recurrent seizures and worsening sensorium, necessitating further evaluation.

Investigations

Magnetic Resonance Imaging (MRI Brain)

MRI of the brain showed T2/FLAIR hyperintensities involving the right fronto-temporo-parietal region, associated with mass effect and midline shift.

Electroencephalography (EEG)

EEG revealed epileptiform discharges, consistent with ongoing seizure activity.

Cerebrospinal Fluid (CSF) Analysis

CSF examination demonstrated:

1. Lymphocytic pleocytosis
2. Normal glucose levels
3. Mildly elevated protein
4. Autoimmune Encephalitis Panel

CSF autoimmune panel showed:

1. NMDA receptor antibodies: Strongly positive
2. AMPA1, AMPA2: Negative
3. CASPR2, LGI1, GABA-B: Negative

Other Laboratory Investigations

Routine laboratory investigations were performed and were within normal limits.

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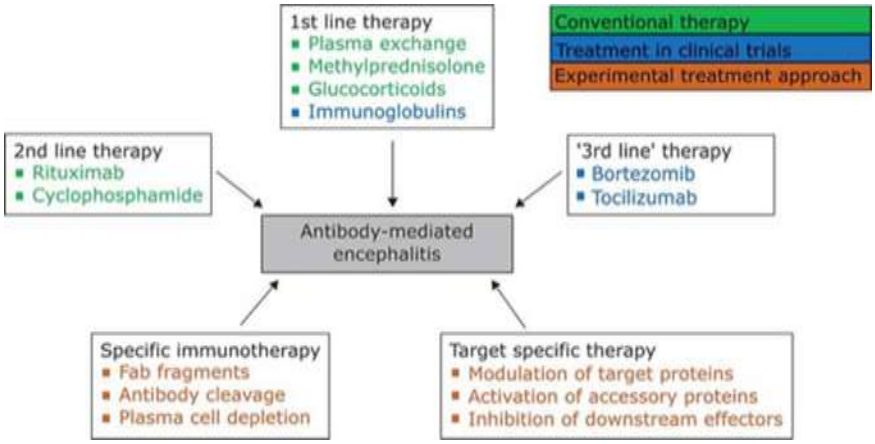
Treatment / Management



The patient was managed with a combination of immunotherapy and supportive care. Initial treatment included high-dose intravenous methylprednisolone administered for five days. Due to persistent symptoms, therapeutic plasmapheresis was initiated, and a total of five cycles were completed. Antiepileptic drugs were administered for seizure control. In view of the autoimmune etiology and to prevent relapse, rituximab was given as second-line immunotherapy. Management was carried out in a stepwise manner with close monitoring of neurological status.

Outcome and Follow-Up

During the hospital stay, the patient showed gradual clinical improvement. There was improvement in sensorium, and seizure frequency reduced significantly. Motor function also improved over time.

At follow-up, the patient was conscious, responsive, and able to ambulate with support. No further seizure episodes were reported. Overall, the patient demonstrated a favourable response to immunotherapy with significant neurological recovery.

Discussion

Autoimmune encephalitis, particularly anti–N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis, is increasingly recognized as a significant cause of acute encephalopathy in children and adolescents, often presenting with a wide spectrum of neuropsychiatric manifestations[8]. The present case highlights an atypical presentation characterized by refractory seizures and hemiparesis, which can pose a considerable diagnostic challenge, especially in the early stages of illness. While seizures are a common feature in pediatric autoimmune encephalitis, focal neurological deficits such as hemiparesis are relatively uncommon and may lead to an initial suspicion of structural brain lesions or demyelinating disorders[9].

The clinical presentation of anti-NMDAR encephalitis is often dynamic and evolves through multiple stages, beginning with prodromal symptoms followed by seizures, behavioral disturbances, and altered consciousness[10]. In pediatric populations, seizures and movement disorders tend to predominate, whereas psychiatric manifestations may be less prominent compared to adults[11]. In the present case, the early occurrence of refractory seizures along with focal neurological deficit contributed to the complexity of diagnosis, necessitating a comprehensive evaluation to exclude infectious and structural causes.

Neuroimaging findings in autoimmune encephalitis are variable and may be normal in a substantial proportion of patients. However, when present, MRI abnormalities typically involve cortical or subcortical regions, as observed in our patient, who demonstrated T2/FLAIR hyperintensities in the fronto-temporo-parietal region with associated mass effect[12]. Such findings, although nonspecific, may support the diagnosis in the appropriate clinical context. Similarly, CSF analysis often reveals mild inflammatory changes, including lymphocytic pleocytosis and elevated protein levels, but lacks diagnostic specificity[13]. Therefore, definitive diagnosis relies on the detection of neuronal autoantibodies, with CSF

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testing being more sensitive and specific than serum assays[10].

A major challenge in resource-limited settings is the delay in diagnosis due to restricted availability of autoimmune panels and a predominant focus on infectious etiologies. This delay can adversely affect outcomes, as early initiation of immunotherapy is a key determinant of prognosis[14]. In the present case, prompt recognition of autoimmune etiology and initiation of immunotherapy resulted in significant clinical improvement, including recovery of motor function and reduction in seizure frequency.

Current evidence supports a stepwise approach to treatment, with first-line therapies including corticosteroids, intravenous immunoglobulin, and plasmapheresis, followed by second-line agents such as rituximab in refractory cases[15]. Our patient demonstrated favorable response to combined immunotherapy, consistent with previous studies showing that early and aggressive treatment is associated with improved functional outcomes and reduced relapse rates.

This case underscores the importance of maintaining a high index of suspicion for autoimmune encephalitis in adolescents presenting with refractory seizures and atypical focal deficits. Early diagnosis, supported by appropriate antibody testing, and timely initiation of immunotherapy are critical in ensuring optimal neurological recovery.

Conclusion

Autoimmune encephalitis, particularly anti-NMDAR encephalitis, should be considered in adolescents presenting with acute onset refractory seizures and atypical focal neurological deficits such as hemiparesis. The heterogeneity of clinical presentation often leads to diagnostic delays, especially in settings where infectious etiologies are more commonly suspected. This case underscores the critical role of cerebrospinal fluid antibody testing in establishing the diagnosis when conventional investigations are inconclusive. Early recognition and timely initiation of immunotherapy, including corticosteroids, plasmapheresis, and second-line agents such as rituximab, are associated with significant clinical improvement and favourable functional outcomes.

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