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Atypical Presentation of NMDA Receptor Encephalitis in a 4-year-old Male: A Case Report of Successful Treatment with Rituximab and Tetrabenazine

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Abstract

Background: N-methyl-D-aspartate (NMDA) receptor encephalitis is an autoimmune disorder historically associated with anti-NMDA receptor antibodies, predominantly described in young women with ovarian teratomas. This case presents a 4-year-old male with NMDA receptor encephalitis, highlights the importance of early detection and aggressive treatment of movement disorders in pediatric autoimmune encephalitis and contributes to the limited literature on the successful use of tetrabenazine for symptomatic control in children.

Case Report: A 4-year-old male presents refractory seizures, neuropsychiatric symptoms, and severe movement disorders. Initial EEG and brain MRI had unremarkable findings, the patient later exhibited focal slowing in the right parieto-occipital region, persistent buccal dystonia, athetotic hand movements, spasticity, and choreiform activity of the mouth and extremities. Additional symptoms included inattentiveness, sluggish pupillary response, and upward gaze nystagmus. Despite initial treatment with levetiracetam, the patient experienced progressive symptoms, including psychosis, aphasia, and further seizure activity. Video EEG revealed generalized slowing, focal onset seizures, and delta brushes. NMDA receptor antibodies were identified in both CSF and serum samples. Treatment with rituximab and tetrabenazine led to significant symptomatic improvement, with complete recovery achieved after two years and no subsequent relapses.

Discussion: This case underscores the diagnostic and therapeutic challenges of NMDA receptor encephalitis in pediatric populations, particularly in males with atypical presentations. It highlights the importance of early diagnosis, comprehensive management, and the potential efficacy of tetrabenazine for control of choreiform movements in children with autoimmune encephalitis. This report adds valuable insight to the limited literature on pediatric NMDA receptor encephalitis and its successful treatment outcomes.

Keywords: NMDA receptor encephalitis, Rituximab, Tetrabenazine, Neuropathology, Pediatric Neurology

Introduction

N-methyl-D-aspartate (NMDA) receptor encephalitis is a well-documented autoimmune disorder characterized by a spectrum of psychiatric, cognitive, and neurological symptoms. First described by Dalmau *et al.* in 2007, it has since been identified as one of the most common forms of autoimmune encephalitis in children and young adults [1]. Epidemiological studies suggest that NMDA receptor encephalitis accounts for up to 4% of all encephalitis cases in children, with an estimated annual incidence of 1.5 per million individuals [2]. Although the disorder predominantly affects females, with a reported female-to-male ratio of approximately 4:1, pediatric cases often display unique clinical features and a broader spectrum of presentations [3].

In pediatric populations, the clinical manifestation differs significantly from adult presentations. Symptoms such as seizures, movement disorders, and language regression are more prominent, while psychiatric symptoms are less emphasized [3]. Younger children may initially exhibit motor hyperactivity, irritability, or atypical movements, frequently

leading to diagnostic delays as the symptoms overlap with other conditions, including viral encephalitis or metabolic disorders [4]. Males, representing a minority of cases, often present with atypical clinical features, such as a predominance of movement disorders over psychiatric symptoms, further complicating early recognition and diagnosis.

This report discusses a unique pediatric case of NMDA receptor encephalitis in a 4-year-old male, distinguished by early and severe movement disorders, with minimal psychiatric manifestations. The diagnostic process was complex, given the atypical presentation, and successful treatment required the combined use of rituximab and tetrabenazine. By presenting this case, we aim to expand the existing literature on NMDA receptor encephalitis, especially in pediatric populations, and provide practical insights for clinicians encountering similar atypical presentations in young male patients.

Case Presentation

A 4-year-old male presented with an initial episode of headache and left arm shaking lasting less than 5 minutes, preceded by non-projectile emesis. During the episode, the left arm was shaking, the patient's eyes were open with a blank stare, and he did not respond to his family's directions. There were no generalized tonic-clonic seizures, tongue biting, or incontinence. Post-episode, the patient experienced limping. In the emergency department (ED), physical examination revealed up-beating nystagmus with upward gaze. Initial routine EEG and brain MRI, with and without contrast, were unremarkable.

Two days later, a similar episode prompted a return to the ED, where the patient was loaded with levetiracetam (1g) and maintained on 200 mg twice daily. Repeat EEG demonstrated possible focal slowing in the right parieto-occipital region. Shortly thereafter, the patient experienced a generalized tonic-clonic seizure lasting over 5 minutes, predominantly affecting the left side, accompanied by hypoxemia. Rescue medication was administered, and the patient was admitted for further evaluation and management. Video EEG monitoring revealed ongoing seizures despite the addition of oxcarbazepine and phenobarbital. During hospitalization, the patient developed oromotor dyskinesia, "pill-rolling" movements of the left hand, choreiform movements, encephalopathy, and severe neuropsychiatric symptoms including agitation and behavioral changes.

As the disease progressed, the patient's neurological status deteriorated, with worsening encephalopathy leading to significant bulbar dysfunction. He developed an inability to swallow and protect his airway, necessitating tracheostomy and percutaneous endoscopic gastrostomy (PEG) tube placement for respiratory and nutritional support. Long-term video EEG revealed delta brushes, a hallmark of NMDA receptor encephalitis.

CSF analysis revealed elevated white blood cell count, high-normal protein levels, and positive Lyme IgG. Initial differential diagnoses included viral encephalitis and post-infectious autoimmune encephalitis. Two doses of intravenous immunoglobulin (IVIG) were administered. Additionally, IV methylprednisolone (10 mg/kg/dose every 8 hours for 3 days) was initiated for immunosuppression, alongside IV Ativan and tetrabenazine for choreiform movements.

Subsequent CSF analysis confirmed NMDA receptor antibody positivity (titer 1:16), and serum antibodies were also positive. The patient received two additional doses of IVIG followed by rituximab therapy (375 mg/m^2 weekly for 4 weeks). MRI of the thorax and abdomen revealed no malignancies, and paraneoplastic panels were negative. Weekly antibody titers demonstrated a consistent decline. Over a 2-month PICU stay, the patient's sedation was weaned, and purposeful movements returned. Intensive physical and occupational therapy (PT/OT) supported functional recovery, and his choreiform movements gradually improved with rituximab and tetrabenazine. The patient's airway function recovered sufficiently, allowing successful decannulation of the tracheostomy after 1 year. Similarly, the PEG tube was removed after his ability to swallow was restored.

The patient was discharged after a 4-month hospitalization. Over the following months, the patient's neuropsychiatric symptoms, dystonic and choreiform movements resolved. His seizure frequency decreased significantly, and by the 12-month mark, the patient was seizure-free.

Neurological assessments at 18 and 24 months post-treatment showed normal cognitive function, normal speech, and no evidence of residual motor tics or abnormal movements.

At 2-year follow-up, the patient had fully returned to baseline with no signs of relapse. There were no significant developmental delays, and he resumed age-appropriate activities, including attending school.

Discussion

This case demonstrates an atypical presentation of NMDA receptor encephalitis in a young male who presented with chorea and seizures as an initial feature rather than the more commonly reported psychiatric symptoms and seizures. Choreiform movements, as observed in this case, are an uncommon but significant manifestation of autoimmune encephalitis, potentially resulting from autoantibody-mediated dysfunction of motor circuits, particularly involving the basal ganglia [2,4].

The diagnostic process was challenging, given the absence of fever and the initial suspicion of viral encephalitis or metabolic disorders. Pediatric cases often require differentiating from conditions such as acute disseminated encephalomyelitis

(ADEM), herpes simplex virus encephalitis, and metabolic syndromes. The presence of delta brushes on EEG, alongside confirmatory antibody testing in cerebrospinal fluid and serum, ultimately facilitated the diagnosis [1,5]. This highlights the value of comprehensive neurological and immunological workups in cases with atypical symptoms.

This case also underscores the critical role of movement disorders as diagnostic clues in autoimmune encephalitis. The use of tetrabenazine, a vesicular monoamine transporter-2 (VMAT2) inhibitor, was pivotal in managing hyperkinetic movements. Although primarily studied in Huntington's disease, tetrabenazine's efficacy in controlling movement disorders in NMDA receptor encephalitis is emerging, albeit with limited pediatric data [6].

Limitations

This case report highlights a successful treatment outcome; however, several limitations must be considered. The rarity of pediatric NMDA receptor encephalitis and the variability in its presentation constrain the generalizability of these findings. Additionally, while rituximab and tetrabenazine proved effective, their efficacy across broader patient populations and varying degrees of disease severity remains to be fully elucidated. Long-term follow-up studies are also necessary to evaluate developmental, cognitive, and neurological outcomes in similar pediatric cases.

Conclusion

This case underscores the importance of recognizing atypical presentations of NMDA receptor encephalitis in pediatric patients, especially when movement disorders dominate the clinical picture. Early diagnosis and prompt initiation of immunotherapy, combined with adjunctive therapies such as tetrabenazine, can lead to full recovery, as demonstrated here. Further research is warranted to elucidate the pathophysiological mechanisms underlying movement disorders in autoimmune encephalitis and to optimize treatment strategies for this rare but severe condition.

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