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Case Report

PEDIATRIC ANTI-NMDA RECEPTOR ENCEPHALITIS: A CASE REPORT

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ABSTRACT

Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis is an autoimmune inflammation of the brain parenchyma mediated with autoantibodies against the NMDA receptors in the neuronal cells. It is the most common form of autoimmune encephalitides in pediatric patients. In this case report, we present the case of a child with anti-NMDAR encephalitis, refractory to the first-line therapy.

Keywords: Autoimmune encephalitis, Post-infectious encephalitis, Anti-NMDAR encephalitis, Pediatrics

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INTRODUCTION

Encephalitis is a potentially life-threatening inflammatory brain condition characterized by neurological and neuropsychiatric symptoms. It can be caused by various etiologies, including direct central nervous system infection (most frequently viral pathogens), as well as mediation by the immune system.

Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis is an autoimmune encephalitis mediated by autoantibodies against NMDA receptors. The NMDA receptors are the most well-defined subtype ionotropic glutamate receptors (GluR) found in neuronal cells [1]. They play an essential role in the establishment of proper neuronal networks, brain processes such as learning and memory as well as synaptic plasticity [1,2].

With 40% of patients under the age of 18, this condition has become a significant cause of autoimmune encephalitis in children and adolescents [3].

In this report, we present the case of a 9-year-old boy who tested positive for NMDAR antibodies and was refractory to the first-line therapy for encephalitis.

CASE PRESENTATION

In October 2022, a 9-year-old boy was admitted to our service of Pediatric Neurology with fatigue, disorientation, vertigo, ataxia, and dysarthria. He was found early that day at home unconscious on the ground, with perioral cyanosis, and contractures of the hands, with no accompanying fever.

Approximately 3 years ago, the child experienced the first episode of loss of consciousness, perioral cyanosis, jaw clenching, and pallor that lasted nearly 3 min, not accompanied by fever. A second episode occurred 1.5 years ago. No past history of recent infection and no family history of autoimmune or neurological disorders were noted.

Within 2 h of hospitalization, the child went into a comatose state; therefore, he was transferred to the pediatric intensive care unit (ICU); *encephalitis* was suspected and therapy with high-dose methylprednisolone, acyclovir, ceftazidime, IgM-enriched intravenous immunoglobulin (IgM-enriched IVIg), and valproic acid was started.

The next day, he returned to our clinic in stable condition. Despite an initial improvement, he continued to have sleeping problems, unsteady gait, ataxia, dysarthria, and myoclonic seizures; hence, levetiracetam replaced valproic acid, while intravenous phenobarbital was added to the therapy.

Complete blood count, serum biochemistry panel, and cerebrospinal liquid (CSF) findings were within normal ranges, except for low vitamin D. Serum protein electrophoresis and immunophenotyping were also normal. Electroencephalogram (EEG) presented diffuse slow waves and generalized spike-wave complexes. Brain and column magnetic resonance imaging (MRI) were unremarkable (Fig. 1). Serology tests were performed; the results are presented in Table 1.

On hospitalization day 17, deterioration of health condition was evidenced; the treatment with rituximab was started with no effect; therefore, the patient was once again transferred to the pediatric ICU with a 39° temperature, increased secretions from the lungs, breathing problems, and bradycardia. The boy was intubated, went on mechanical ventilation, and was fed with a nasogastric tube. He went on five cycles of plasmapheresis along with three other doses of Rituximab at a distance of 1 week from each other. His condition gradually improved by regained consciousness, deep tendon reflexes, and abdominal cutaneous reflex and was, therefore, extubated. The nasogastric tube was removed once he was able to deglutate and the bowel function returned.

Outcome

After 38 days of hospitalization, our 9-year-old patient was discharged in good and stable condition. His mental state was normal, but he complained of mild headache and dizziness while standing up that lasted briefly. He also had mild dysarthria and difficulty in writing due to tremors.

He is currently on physiotherapy rehabilitation and receives levetiracetam orally for secondary epilepsy as well as vitamin D for deficiency.

DISCUSSION

Several mechanisms for autoimmune encephalitis are known, including the presence of a tumor (paraneoplastic encephalitis) or a previous neurotropic infectious trigger (non-paraneoplastic and post-infectious encephalitis), such as viruses [4]. In our case, positive serology tests for

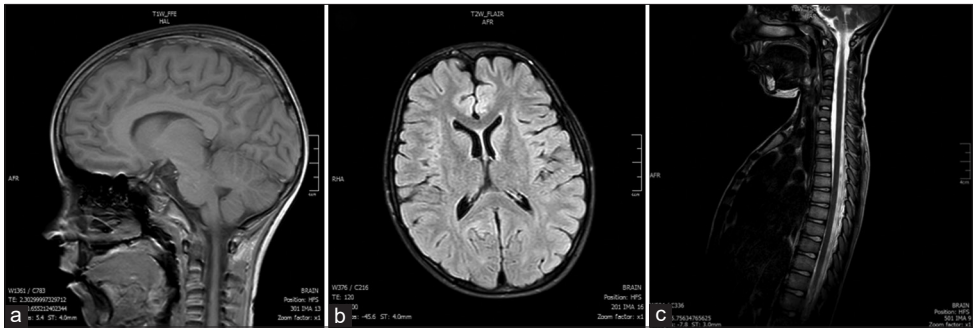

Fig. 1: Normal brain magnetic resonance imaging (MRI) (a) T1-weighted image in sagittal projection, (b) T2-FLAIR image in axial projection and normal column MRI, and (c) T2-weighted image in sagittal projection

Table 1: Serology test results

Antibodies	Results	Interpretation
ENA screen	0.37	Negative
anti-SARS-CoV-2 IgM	0.05 index	Negative
anti-SARS-CoV-2 IgG	290.50 AU/mL	Positive
anti-HSV-1 IgM	<0.500	Negative
anti-HSV-1 IgG	42.7 index	Positive
anti-NMDAR IgG	1:20 titer	Positive

ENA: Extractable nuclear antigen antibodies, HSV-1: Herpes simplex virus 1, Ig: Immunoglobuline, NMDAR: N-methyl-D-aspartate receptor, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

anti-HSV-1 IgG and anti-severe acute respiratory syndrome coronavirus 2 (anti-SARS-CoV-2) IgG displayed past infection with herpes simplex virus 1 (HSV-1) and SARS-CoV-2 virus. In the medical literature, both HSV and SARS-CoV-2 are known as triggers of autoimmune encephalitis due to their neurotropism [5-7]; therefore, we believe that either infection was an antecedent event.

Despite the clinical presentation, the brain and column MRI of our patient were unremarkable; studies show that brain MRI presents abnormalities in <50% of all pediatric patients [6].

For autoimmune encephalitis, standard immunotherapy with corticosteroids followed by or combined with IVIg is considered the first-line treatment. Plasmapheresis (plasma exchange) should also be considered in severe cases. If the condition is refractory to first-line therapy like the case of our patient, or relapses, immunotherapy with rituximab is preferred over cyclophosphamide as a second-line treatment. Despite having limited data, tocilizumab, intravenous/intrathecal methotrexate with intrathecal corticosteroids, and subcutaneous/intravenous bortezomib have been described as alternative escalation therapies [8].

CONCLUSION

Autoimmune encephalitis remains a significant challenge for health-care professionals, despite recent advances in diagnosis and treatment; therefore, it should not be underestimated. Laboratory tests and imaging examinations can provide evidence of brain inflammation; however, normal test results, computed tomography/MRI findings, and/or CSF profile do not exclude the diagnosis.

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Written informed consent was obtained from the parent of our patient for the publication of this report.

AUTHORS' CONTRIBUTIONS

All authors have contributed equally.

CONFLICT OF INTEREST

None declared.

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