

Detection of myelin oligodendrocyte glycoprotein antibody in pediatric patient with acute disseminated encephalomyelitis: a case report



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ABSTRACT

Introduction: Acute Disseminated Encephalomyelitis (ADEM) is an immunity-mediated central nervous system demyelinating disorder. Myelin Oligodendrocyte Glycoprotein (MOG) examination provides information about a patient's ADEM development status. A positive MOG antibody can signify a first episode or incomplete recovery. This review aims to report a case of a pediatric patient with acute disseminated encephalomyelitis with positive MOG antibody.

Case Presentation: We present a 5-year-old girl with symptoms of low-grade fever, encephalopathy, blurred vision, numb and tingling sensations on hands and feet, weakness, unable to walk. Head MRI (Magnetic Resonance Imaging) examination reveals lesions in the bilateral thalamus and white matter of the left parietal lobe. There was also a bilateral thickening of the optic nerves. Blood laboratory examination was relatively normal, and the MOG antibody test was positive. The patient was then treated with corticosteroids for 1 year and had 2 recurrent episodes of attacks. MOG test evaluation was still also positive 6 months after the first attack. After Intravenous immunoglobulin (IVIG) treatment was given, resulting in excellent clinical response and no recurrent attack since then.

Conclusions: ADEM cases have a good prognosis and good recovery. IVIG administration, with the help of other supportive therapy, improves recovery in treating pediatric ADEM.

Keywords: ADEM, MOG, Myelin Oligodendrocyte Glycoprotein, Pediatric.

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INTRODUCTION

Myelin Oligodendrocyte Glycoprotein (MOG) is an antigen candidate target of the immune system in the central nervous system, demyelinating diseases. The antibody is expressed on the outer surface of myelin, which becomes an autoantibody of the damaged blood-brain barrier. MOG antibody titers may become high positive in the first episode of an ADEM attack and may then decrease to undetectable levels after recovery. Persistent MOG results can be a sign of incomplete recovery.¹ Acute disseminated encephalomyelitis (ADEM) is an auto-immune, acute non-vasculitic inflammatory demyelinating disorder of the central nervous system.² Demyelination is a myelin disorder that interferes with the transmission of the nervous system that interrupts the sensory, motor, cognitive and other nervous system functions depending on the location.^{3,4}

The incidence of ADEM in America ranges from 0.3 to 0.6 per 100,000 per year. National ADEM surveys in Germany, Canada, and Britain have reported that the incidence of ADEM in children is 0.1 – 0.3 per 100,000 children per year.^{5,6} ADEM patients range from 5-8 years old, which is more common in boys.⁶

ADEM is characterized by diffuse neurological symptoms and multifocal demyelinating lesions on neuroimaging.³ Common clinical symptoms are loss of consciousness, fever, and headache.⁷ Other symptoms include the rapid onset of multifocal neurological disorders such as seizures, mild visual disturbances, and ataxia. The percentage of complete recovery is about 50-70% of cases. About 70-90% of cases are cured but with sequelae. The average time needed for recovery is 1 to 6 months, and the mortality rate is about 5%. A poor condition that does not respond to

corticosteroid therapy usually indicates a sudden neurological attack. This review aims to report a case of a pediatric patient with acute disseminated encephalomyelitis with positive MOG antibody.

CASE PRESENTATION

A 5-year-old girl was in the emergency room with a chief complaint of weakness in the whole body, often falling asleep, and numbness in the hands and feet. Based on neurological examination, we found her to be somnolent with GCS (Glasgow Coma Scale) E3V4M5. The pupils were isochoric, with right and left diameters of 3mm, good direct and indirect light reflexes, and no pathological reflexes. She was born by caesarean section due to her mother's history of caesarean section. No one in her family suffers from the same symptoms or disease. She had received complete basic immunizations since birth.

There was no immunization given in the past month. The patient had never been hospitalized for other diseases before. CSF cytological examination was a moderate number of lymphocytes and monocytes, no cryptococcal organisms, malignant cells, or acid-fast bacilli. CSF was clear, RBC 0/mm³, WBC 15/mm³, neutrophils 0%, lymphocytes 100%, glucose 5 mmol/L, protein 25.1 mg/dl. Complete blood count, electrolytes serum, and CRP were within normal limits. Antinuclear antibody examination was negative, and C3 and C4 were within normal limits. Head MRI showed uneven hyperintensity patches on the medial thalamus bilaterally and the white matter of the left parietal lobe, contrast was not significantly increased (Figure 1). We found no acute infarction or acute hemorrhage in the brain, sellar, or suprasellar masses pressing on the optic chiasm and no retrobulbar masses in the bilateral orbital cavities. The eye muscles were within normal limits. There were bilateral thickening and enhancement of the optic nerves, from the eyeballs to the optic chiasm, most likely caused by optic neuritis. MOG antibody titer had been evaluated twice and the last one was still positive (>1:10) after 6 months of the attack. The patient was then given IVIG at 0.4g/kg/dose for 5 days. On the first day, there was no significant progress. On the second day, the patient's consciousness began to improve. On the third day, she could sit by herself and stand up on the fourth day. On the fifth day, she was finally able to walk. Her vision also gradually improved.

DISCUSSION

Acute disseminated encephalomyelitis (ADEM) is an immune-mediated central nervous system demyelinating disorder.³ Clinically characterized by the onset of acute encephalopathy associated with polyfocal neurologic deficits that are sometimes preceded by prodromal symptoms such as fever, malaise, irritability, drowsiness, headache, nausea, and vomiting. The clinical course of ADEM is usually rapidly progressive, with a maximal deficit within 2–5 days. ADEM is classically considered a monophasic disease, with the highest incidence in early childhood. Manifestations include pyramidal signs,

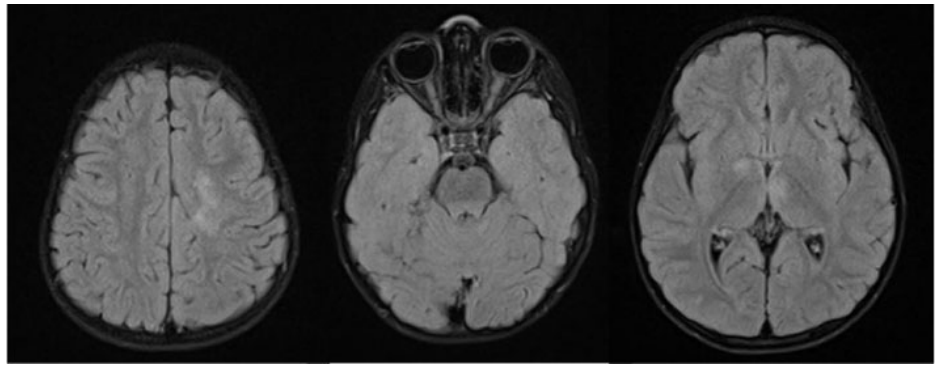


Figure 1. The head MRI showed uneven hyperintensity patches on the medial thalamus bilaterally and the white matter of the left parietal lobe.

ataxia, acute hemiparesis, optic neuritis or other cranial nerve involvement, seizures, spinal cord syndrome, and speech disturbances. Respiratory failure may occur but is rare.^{5,8} This patient had body weakness, somnolent and numbness in the hands and feet. It is important to know the biomarkers of nerve damage in infection to predict the disease's outcome and severity.⁹

Neuroimaging is very important in establishing the diagnosis of ADEM. The demyelinating lesions of ADEM were most clearly seen using MRI, T2-weighted images, and fluid-attenuated inversion recovery (FLAIR). ADEM demyelinating lesions usually do not show mass and may spread over the white matter of the posterior fossa and cerebral hemispheres. The involvement of the cerebellum and brainstem is common in children.⁶ The typical MRI image shows widespread, bilateral, asymmetrical patchy areas that are homogeneous or slightly inhomogeneous with an increased lesion density compared to the surrounding area. Abnormalities were usually found in white matter and gray matter, especially in the deep gray nuclei in the basal ganglia, thalamus, and brainstem. It can sometimes obtain a picture of a lesion that resembles a tumor.¹⁰ White matter lesions are more commonly found in the juxtacortical and deep white matter areas than the periventricular areas. Demyelination lesions in ADEM rarely involve the corpus callosum. The involvement of the corpus callosum indicates a very extensive demyelinating lesion. In ADEM, infratentorial lesions are common, including the brainstem and white matter of the cerebellum. The shape and size of the lesions vary, from small,

round lesions to amorphous, irregular, and large lesions.¹¹ In this case, bilateral thalamus and white matter lesions were found in the left parietal lobe, suitable for the common ADEM neuroimaging presentation, and gradually improved after 4 months. Based on MRI result, there were bilateral thickening and enhancement of the optic nerves from the eyeball to the optic chiasm, with the impression caused by optic neuritis.

In ADEM, there's an increase in the Myelin Oligodendrocyte Glycoprotein (MOG) antibody response as an immune-mediated CNS disorder.¹¹ Detection of MOG antibodies can help differentiate autoimmune or infectious CNS disease and provide prognostic information regarding monophasic or recurrent attack episodes. According to Brilot, 40% of children with ADEM in their study had high titers of anti-MOG IgG.¹ The pathogenesis of ADEM has not been fully understood until now. However, exposure to viral antigens can lead to the formation of autoantibodies through molecular mimicry.¹ The possible mechanism that may happen is that ADEM results from a transient autoimmune response to myelin antigens, which may result from autoreactive molecular mimicry. This happens because myelin antigens, such as basic protein, proteolipid protein, and oligodendrocyte protein, have structural similarities to the pathogen antigen components that infect the host. The host previously infected with the pathogen forms an immune response and produces antibodies that cross-react with myelin antigens that have similar structures and produce an autoimmune response. These antibodies can cross the blood-brain barrier to enter the central

nervous system and cause demyelination and inflammation of the central nervous system.

Formalin fixation was used for immunofluorescence anti-MOG IgG assay, and the standard value was < 1:10. Positive titer (1: 100) persisted as long as the patient was in remission.¹² MOG antibodies were positive but did not decrease to undetectable levels. Some studies stated that MOG antibodies can still be positive at 4-69 months. Patients with ADEM who have not fully recovered tend to remain positive with low titers on MOG examination. It is advisable to check for MOG antibodies in children with ADEM cases. This patient has not had a recurrent attack after the IVIG treatment. Persistent MOG antibody results lead to early treatment for patients with ADEM. They are at risk of recurrence or incomplete recovery of ADEM, especially to ascertain quickly whether the cause of the case is infectious or autoimmune.

There is no standard therapy for the management of ADEM. All ADEM treatments are based primarily on insights obtained from clinical experience, descriptive research, or reports from the expert community. Standard therapy for ADEM has not yet been confirmed using randomized control trials (RCTs).¹³ Supportive therapy in patients with ADEM includes airway protection in patients with impaired consciousness, mechanical ventilation in patients with cervical lesions, anticonvulsant drugs in patients with seizures, or correction of electrolyte disturbances.^{14,15} Intravenous (IV) methylprednisolone is the first choice drug for managing ADEM as immunomodulatory therapy, with a success rate of 80%. The IV dose of methylprednisolone is 10–30 mg/kg/day, a maximum of 1g/day for 3–5 days. Corticosteroids will be continued orally and tapered off for 6 weeks to prevent relapse.¹⁴ Administration of IVIG had been reported in case reports, mostly given as combination therapy with corticosteroids or as second-line therapy in ADEM unresponsive to corticosteroids. In our case, the patient received IVIG therapy alone without a combination of steroids with good results.

Recovery can occur within a few days, and complete resolution may occur

within a few days but is more common in weeks or months. During this recovery period, a relapse of neurologic deficits may also occur. In general, ADEM has a good prognosis. Almost 50% to 75% of reported cases show complete recovery, and between 70% to 90% of recovered cases still have sequelae. The average time required for recovery is from 1 to 6 months. Serious complications (including death) are rare in the pediatric population. The mortality rate is up to 5%.¹⁵ This patient had no sequelae from the last attack after IVIG administration. The motor of all extremities was within normal limits.

CONCLUSION

ADEM cases have a good prognosis and good recovery. IVIG administration, with the help of other supportive therapy, improves recovery in treating pediatric ADEM.

AUTHOR CONTRIBUTION

All authors contribute in all areas to prepare this study.

CONSENT FOR PUBLICATION

The patient's parents approve for publication of this study, and the patient's identity remains confidential.

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DISCLOSURE

The author reports no conflicts of interest in this work.

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