CASE REPORT

Case report of a child with Myelin Oligodendrocyte Glycoprotein Associated Disease (MOG-AD)

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ABSTRACT *:* Myelin oligodendrocyte glycoprotein associated disease (MOG-AD) is an inflammatory disorder of the central nervous system characterized by immune-mediated demyelination. We present a case of a patient with subacute to chronic progressive bilateral motor weakness associated with encephalopathy, which led to the diagnosis of MOG-AD. This case highlights the importance of recognizing the diverse clinical manifestations and the need for a multidisciplinary approach in the diagnosis and management of MOG-AD. In this review, we discuss the pathophysiology, diagnostic criteria, imaging findings, treatment strategies, and prognosis of MOG-AD based on the available literature.

CASE REPORT

This case involves a 9-year-old male who presented with progressive motor weakness. The history began five weeks prior to admission with a two-day episode of cold symptoms, without cough or fever. Two weeks later, he experienced a left temporal headache that resolved after 30 minutes without medication. There were no associated symptoms such as nausea or vomiting, and no consultation was sought.

Three weeks prior to admission, weakness of the right hand was noted, affecting the patient's handwriting. He became unusually quiet, preferred to be alone, and had decreased verbal output. Although he could recognize his parents, he was unable to say their names. Two days later, there was further progression of weakness involving the right extremity such as patient can't hold objects anymore with the right hand, accompanied by facial asymmetry. A child neurologist was consulted, and a cranial MRI was ordered. The following day, the patient experienced a severe left temporal headache without vomiting, and weakness progressed to the right lower extremity. This prompted admission to a nearby hospital.

Initially, the patient was assessed for acute pediatric stroke, but the cranial MRI revealed abnormal signals in the bilateral frontal, temporal, and parietal lobes, more prominent on the left. The radiological interpretation suggested an infectious or

inflammatory process, possibly encephalitis with the beginning of abscess formation. The patient was treated as a brain abscess with ceftriaxone and metronidazole.

During the hospitalization, there was further progression of weakness involving the right upper and lower extremities, rendering him nonambulatory. Behavioral changes were also observed, including irritability, inconsistent responses to questions, and difficulty following commands. The patient experienced visual hallucinations when perceiving shadows in front of him. Urinary retention and constipation were noted as well.

A repeat cranial MRI performed on the 14th day of antibiotic treatment showed progression of the previously seen abnormal signals, with involvement of most of the left lower and capsulothalamic regions. Additionally, patchy enhancement was observed in the left frontoparietal lobe, as well as cortical ovoid foci in the bilateral frontal and left temporal lobes (Figure 1). Two days prior to admission to our institution, the patient developed an inability to eat and exhibited no verbal output, necessitating the transfer.

Pertinent findings on physical examination included stable vital signs, hypoactive bowel sounds, a distended bladder, and good sphincteric tone. On neurological examination, the patient was awake but irritable, with no verbal output or ability to follow commands. Cranial nerve examination revealed responses to visual threat and normal fundoscopic findings. The pupil size was 5-6 mm bilaterally, sluggishly reactive to light. The patient exhibited intact oculocephalic reflexes, right central facial palsy, no head turning in response to sound, and a weak gag reflex. Motor strength was assessed as 1/5 in the right upper extremity, 3/5 in the right lower extremity, and 4/5 in the left upper and lower extremities. Increased tone was noted in both the right upper and lower extremities, and the patient cried in response to pain during the prick examination. Hyperreflexia was observed in the right upper and lower extremities, as well as in the left lower extremity, accompanied by bilateral Babinski signs and clonus. Bladder retention with good sphincteric tone was also noted.

Based on the clinical presentation and investigations, the initial impression was acquired demyelinating syndrome, possibly acute disseminated encephalomyelitis (ADEM). Cerebrospinal fluid (CSF) analysis was normal, but the patient tested positive for anti-MOG antibodies. The electroencephalogram (EEG) showed continuous slowing of background activity at 0.5 to 2 Hz over the left hemisphere, predominantly in the left frontotemporal, mid-temporal, and frontocentral regions. The background activity in the right hemisphere was also slow for the patient's age. A spinal MRI revealed T2 hyperintense, non-enhancing, intramedullary signals in the center of the spinal cord at the C2-C4 and T11-T12 levels. (Figure 2)

Treatment was initiated with methylprednisolone at a dose of 30 mg/kg/day for five days, followed by a switch to prednisone at a dosage of 1 mg/kg/day. Minimal improvement was observed, leading to the decision to perform therapeutic plasma exchange (TPE) every other day for six cycles. The TPE sessions were uneventful, and the patient was discharged with a final diagnosis of MOG-IgG-associated disease, specifically acute disseminated encephalomyelitis

On follow-up, the patient showed some improvement. He was able to say "mama" and "papa," indicating some improvement in his verbal output. Motor strength in the right upper extremity also improved to 3/5, suggesting some recovery. However, the left upper and lower extremities maintained a strength of 4/5, without significant changes.

Encouragingly, there was resolution of the right central facial palsy and drooling, indicating improvement in the facial muscle weakness. No new onset neurological deficits were observed, which suggests that the disease progression may have stabilized or slowed down.

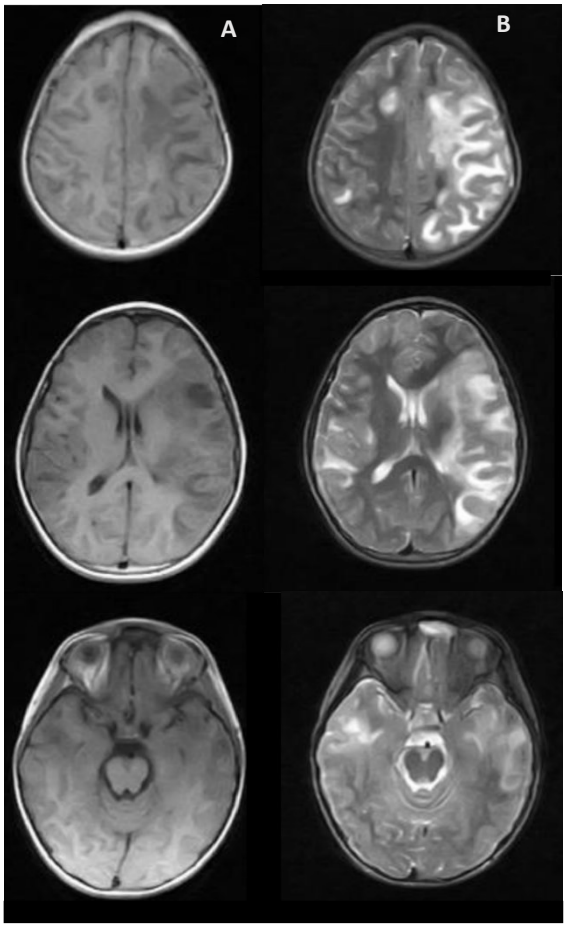

Figure 1. *Cranial MRI showing T1 hypointensity (A) and T2 hyperintensity (B) over the left frontal, parietal, temporal, thalamocapsular region and right temporal*

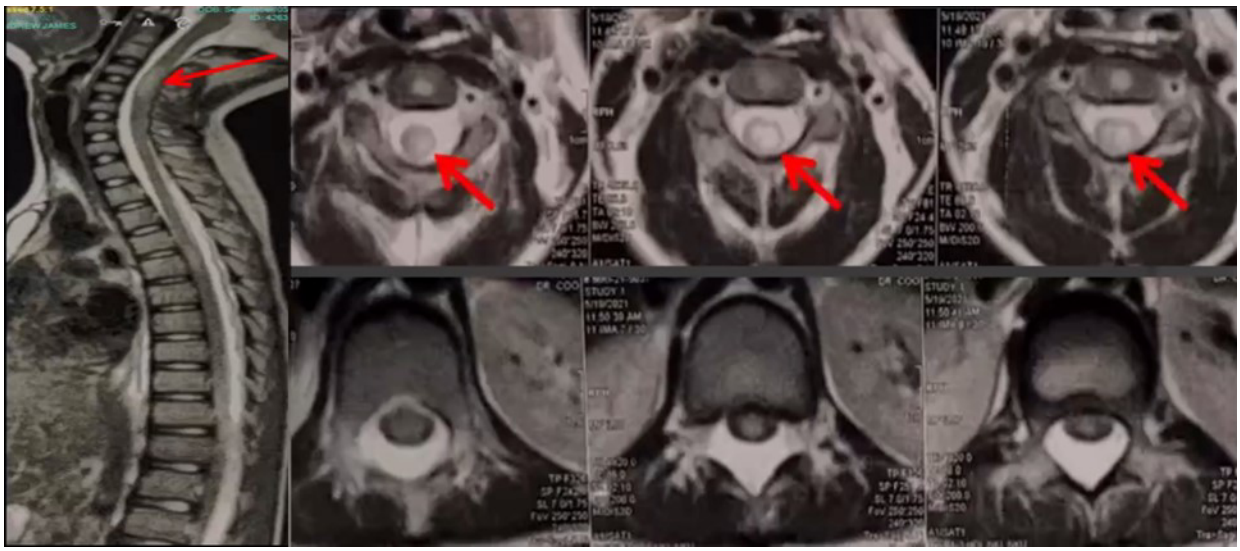

Figure 2. *Spinal MRI showing T2 hyperintensity over the levels T5, T11-T12 (red arrow)*

Discussion

MOG (myelin oligodendrocyte glycoprotein) is primarily produced by oligodendrocytes, the cells responsible for forming and maintaining the myelin sheaths in the central nervous system (CNS). MOG plays a crucial role in the development, stability, and integrity of myelin.

While MOG is found in relatively small amounts within the myelin sheaths, its structure and external location make it susceptible to interactions with the immune system. This accessibility can lead to potential antibody and T-cell responses against MOG, resulting in immune-mediated demyelination and inflammatory disorders such as MOG-associated diseases.

MOG-associated disease (MOG-AD) is an inflammatory disorder of the central nervous system (CNS) characterized by immune-mediated demyelination that primarily affects the optic nerves, brain, and spinal cord. MOG antibodies are the most common autoantibodies in acute disseminated encephalomyelitis (ADEM) and can be present in up to 68% of cases at initial presentation with MOG-AD.[1]

The coexistence of cortical and subcortical demyelinating lesions in MOG-AD is thought to be the result of an immune response involving serum IgG antibodies selectively binding to MOG. This immune response is accompanied by CD4-dominant T-cell and granulocytic inflammatory infiltrates.[2]

The suspicion of MOG-AD arises when a patient presents with optic neuritis, ADEM or ADEM-like presentations with large, poorly demarcated T2 hyperintense lesions in the brain and spinal cord, unilateral cortical encephalitis or other focal neurological findings with cortical T2 hyperintensity and swelling, or a complete spinal cord syndrome, especially with prominent bowel, bladder, or erectile dysfunction symptoms.

Cranial MRI findings in MOG-AD are typically characterized by extensive bilateral cortical encephalitis, while spinal cord MRI may reveal patterns such as extensive involvement of the spinal cord with abnormal hyperintense signals within three vertebral body segments and an H-shaped T2 hyperintensity in axial sequences. Localization of lesions over the medullary cone is highly specific for MOG-AD diagnosis. However, there are no clinical or neuroimaging findings highly specific for MOG-AD, highlighting the importance of the presence of MOG IgG antibodies for diagnosis.[3]

CSF analysis is useful in MOG-AD, showing pleocytosis in cases of myelitis and ADEM, and a potential increase in CSF protein in 50% of cases. The presence of MOG IgG antibodies in serum is crucial for diagnosis, with higher concentrations observed during acute attacks and lower concentrations during remission or the chronic phase. The specificity of MOG IgG testing ranges from 97.8% to 100%, with a positive predictive value of 72% to 94%.[4, 5, 6]

Treatment for MOG-AD involves managing acute exacerbations with high-dose intravenous methylprednisolone. Severe attacks may require therapeutic plasma exchange (TPE) or intravenous immunoglobulin (IVIG). Strategies for preventing attacks include immunomodulating and immunosuppressive therapies, such as long-term use of oral corticosteroids, steroid-sparing medications, and repeated cycles of IVIG.[5]

Studies have reported relapses in 50% of cases over a 2-year period. Gradual tapering of oral corticosteroids is used for relapse prevention, with low-dose prednisolone (10 mg daily) showing effectiveness in some studies. However, due to long-term side effects, treatment is often shifted to steroid-sparing medications.[1]

Two clinicoradiological patterns associated with poor outcomes in MOG-AD are patients who present with ADEM, frequent relapses, and progression, and those who present with non-ADEM encephalitis.

In multicenter observational studies, MOG-AD has been shown to follow a monophasic or relapsing course, with lower long-term disabilities compared to neuromyelitis optica spectrum disorder (NMOSD) or multiple sclerosis (MS). Around 4% of patients may develop MS on follow-up. MOG-AD is not associated with a primary or secondary progressive course, and mortality is low.[1]

Summary

We present a 9-year-old male with progressive hemiparesis that later progressed bilaterally and was associated with encephalopathy. Imaging studies revealed diffuse white matter lesions in the bilateral frontal, parietal, and temporal lobes, as well as the left capsulothalamic region on cranial MRI. Patchy lesions were also seen in the thoracic area (T5, T11-12) on spinal MRI. The presence of serum MOG antibodies confirmed the diagnosis of Myelin oligodendrocyte glycoprotein antibody disease.

The first-line treatment for MOG-AD typically involves intravenous corticosteroid therapy followed by oral corticosteroids. However, in this case, a poor response to initial treatment necessitated the initiation of second-line therapy. Despite the initial challenges, the patient showed improvement in motor and other cortical functions on follow-up, and no new onset focal neurological deficits were noted.

Advances in technology have facilitated the diagnosis of MOG-AD in children presenting with acute disseminated encephalomyelitis (ADEM). Due to the complexity and diversity of clinical, radiologic, and pathologic features associated with MOG-AD, a thorough history and examination of patients is crucial for accurate diagnosis.

Treatment strategies for MOG-AD aim to address acute attacks and prevent relapses. The prognosis of patients with MOG -AD varies depending on the extent of disease progression. Regular follow-up and monitoring of these patients are essential, as a small percentage may go on to develop multiple sclerosis (MS).

It is important to continue close monitoring and follow-up to assess further improvements and any potential recurrence or new symptoms. Rehabilitation therapies and supportive care may be beneficial in helping the patient regain strength and function in the affected limbs.

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