Myelin oligodendrocyte glycoprotein (MOG) antibody positive disease presenting as acute disseminated encephalomyelitis and unilateral optic neuritis

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Abstract

The autoantibody against myelin oligodendrocyte glycoprotein (MOG-abs) is a recognized biomarker in acquired demyelinating syndromes. The diversity in clinical and neuroimaging phenotypes is still being understood in the paediatric population. The presenting clinical phenotype strongly depends on the age at onset. Acute disseminated encephalomyelitis (ADEM) and ADEM-like phenotypes are common in younger children, but optic neuritis (ON), often bilateral, is predominantly seen in females and older children and or adults.

We present a 6.5-year-old boy with a rapid onset encephalopathy due to ADEM and a unilateral longitudinally affected optic neuritis detected on neuroimaging. His serum was positive for MOG-abs but negative for Aquaporin-4 antibodies. His cerebrospinal fluid was negative for oligoclonal bands. He gradually improved following treatment with intravenous high-dose methylprednisolone and five cycles of plasma exchange. Complete clinical recovery was achieved within twelve weeks of admission.

Conclusion: Contrary to the usual older age of MOG-ON, and the bilateral involvement, this case illustrates a unilateral ON in a six-year-old boy occurring in conjunction with a MOG-ab positive encephalomyelitis.

KEYWORDS

Demyelination, ADEM, optic neuritis, MOG

BACKGROUND

The myelin oligodendrocyte glycoprotein antibodies (MOG-abs) have been identified in an expanding spectrum of demyelinating syndromes, predominantly in the paediatric age group.¹ ² The typical MOG-abs-associated disease (MOGAD) presentations consist of acute disseminated encephalomyelitis (ADEM), optic neuritis (ON), longitudinally extensive transverse myelitis, and neuromyelitis optica spectrum disorder (NMOSD)-like phenotype. The relapsing phenotypes are multiphasic disseminated encephalomyelitis, relapsing ON, ADEM-ON, and relapsing NMOSD-like phenotype. The emerging and atypical phenotypes are encephalitis, overlapping syndrome and seizures, leukodystrophy-like phenotype, combined central and peripheral demyelination in MOGAD, and non-classifiable clinical phenotypes.³ The classical spectrum of specific phenotypes at initial presentation varies according to age. ADEM is the dominant phenotype in
young children while optic neuritis (ON) and/or transverse myelitis (TM) is seen mainly in older children and adults. The transition of this bimodal distribution of the dominant phenotype occurs around the age of nine.1,2 The difference in clinical expression in different age groups suggests that regional expression of MOG is age-dependent.

CASE PRESENTATION

A previously well 6.5-year-old boy presented with progressive drowsiness of four days duration. He had one episode of vomiting, arthralgia and myalgia, mild headache, and urinary incontinence during the last two days before admission. His parents were unaware of any visual symptoms. There was no preceding history of fever or respiratory tract infection. His past medical history had been uneventful.

On initial examination, he was drowsy and afebrile with a Glasgow Coma Scale (GCS) of 10/15 (E-3, V-2, M-5). The pupil sizes were unequal but were responding to light. A positive relative afferent pupillary defect of the left eye was noted. Fundal examination showed no evidence of disc oedema or papillitis. Visual acuity and color vision were difficult to assess due to the drowsiness. Upper and lower limb examination revealed bilateral hypertonia with muscle power of 3/5 both distally and proximally. He had bilateral exaggerated reflexes and extensor plantar responses. His cardiovascular system revealed a resting tachycardia with an elevated blood pressure above 95th percentile for his estimated height, a normal apex beat, and dual rhythm without murmurs. His respiratory system and abdominal system examination were normal.

His clinical condition deteriorated rapidly over the ensuing hours. The drowsiness and unresponsiveness progressed, followed by the development of decorticate posturing. The dysautonomia worsened with an increasing heart rate with further blood pressure elevation. Within 12 hours of admission, he required ventilatory support due to progressively deteriorating breathing.

Investigations on admission revealed a normal peripheral blood count (white blood cells: 10.4×10⁹/L(4.4-12.3×10⁹/L); neutrophils: 84% (32-71%), lymphocytes: 13% (20-59%). His haemoglobin was 11.8 g/dl (11-14 g/dl); platelets: 345×10⁹/L (200-450×10⁹/L). The C-reactive protein was < 5 mg/L (0-5 mg/L) and erythrocyte sedimentation was 20 mm/first hour. The random blood glucose, serum electrolytes, renal function, and liver function tests were within normal limits. The cerebrospinal fluid (CSF) analysis showed a clear and colourless appearance with a single lymphocyte and no polymorphs or red blood cells; the gram stain revealed no organisms. The protein and glucose levels in the CSF were normal. Oligoclonal bands were not detected and the CSF-IgG index was high 1.11 (0.3-0.7).

An electroencephalogram (EEG) soon after admission showed only mild changes with mixed slower rhythms of theta in the temporo-parietal region. The posterior basal background activity was slower consisting of 6 Hz activity noted bilaterally (Figure 1a). This rapidly changed to a more diffusely slower background mixed with 0.75-4 Hz delta activity during the continuous EEG monitoring performed in the intensive care unit. There was no significant asymmetry in the background or record of electrographic seizures (Figure 1b).

**FIGURE 1** (a) The EEG performed within the first three hours of admission showed mild changes with slower basal posterior rhythm bilaterally. (b) Worsening of the background slowing with mixed theta and delta activity in the continuous EEG, done 24 hours after admission.
The non-contrast computerized tomography (CT) done on admission revealed an area of focal hypodensity in the right frontal region with no cerebral oedema (Figure 2a). The magnetic resonance imaging (MRI) revealed multiple areas of T2/FLAIR high signal intensity in the juxta cortical regions in both cerebral hemispheres (Figure 2b), both thalami and basal ganglia (Figure 2c) and diffuse brain stem involvement (Figure 2d). The left optic nerve showed signal changes longitudinally with swelling, suggestive of left-sided optic neuritis (Figure 2e). The spinal images were unremarkable (Figure 2f).

His serum on the sixth day after admission was found to be positive for MOG antibodies at a dilution of 1:10 but no further dilutions had been performed. Serum was negative for Aquaporin-4 antibodies.

In conclusion, he presented with ADEM as the core clinical demyelinating event with supporting clinical and MRI evidence of a brain stem and cerebral syndrome with left optic neuritis. He had a low positive MOG-IgG titre. The diagnosis of MOGAD was made according to International MOGAD Panel proposed criteria 2023.3

**FIGURE 2** (a) CT scan showing a focal white matter hypodensity in the right frontal region. (b) T2-weighted MRI brain demonstrating high signal intensity areas involving the gray-white junction of both cerebral hemispheres, thalami, and right basal ganglia. (c) T2-FLAIR axial brain image showing changes in the grey-white junction of both cerebral hemispheres, thalami, and right basal ganglia. (d) T2 weighted coronal MRI demonstrating high signal intensities in the pons and cerebral peduncle. (e) There is a thickening and increased T2 signal in the left optic nerve (white arrow). The right optic nerve and chiasm appear normal (f) T2-FLAIR spine demonstrating no abnormalities.
The patient was initially treated with intravenous cefotaxime 50 mg/kg six-hourly and intravenous acyclovir 350 mg eight-hourly. Following negative microbiology in the CSF and the above MRI findings, his treatment was changed to three days of intravenous methylprednisolone at a dose of 30 mg/kg followed by five cycles of total plasma exchange. He was extubated within 14 days after a marked improvement in his conscious status. He recovered with gestural communication noted around the 20th day since admission. With intensive physiotherapy and supportive medications, he could self-ambulate by the fourth week. A complete visual assessment including acuity and color vision was performed when he was able to understand and respond appropriately at the end of the third week of admission. No clinically identifiable abnormality was found in the left eye at that time.

At the one-month review post-discharge, he had recovered his mobility completely. He had no residual neurological deficits or abnormalities. The EEG performed at this review was normal. He was placed on a protracted course of oral prednisolone. At six months after discharge from the hospital, he remains free of any motor disability.

DISCUSSION

The clinical phenotype of MOGAD is dependent on the age at onset of illness. Predominant brain involvement (including ADEM and ADEM-like phenotypes) is seen more commonly in younger children while optico-spinal phenotypes (including ON and/or TM or brainstem involvement) are often seen in older children and adults.

The phenotypes of MOGAD include ADEM in 53% (range: 33-65), ON in 40% (range: 10-67), and TM in 18% (range: 0-35). The clinical syndrome of ADEM is the most common MOGAD in children. In paediatric cases of ADEM, up to 50% of affected children are MOG-ab positive. Few clinical and radiological features differ between ADEM with and without MOG-ab. However, distinguishing between these two groups based on these features at disease onset is difficult. One of the key differences between the two groups is the greater spinal involvement (93%) seen in MOG-ab-positive patients compared to 33% in ab-negative patients. This was however not the case in our patient.

ON is the second most frequent presentation in MOGAD presenting with unilateral or bilateral visual symptoms. It typically results in significant visual loss, central scotoma, reduced visual fields, and impaired colour vision, often accompanied by painful eye movements. Paediatric MOG-ab-positive ON (MOG-ON) is seen predominantly in adolescents between the ages of 13 and 18 years. Studies exclusively analyzing paediatric patients with MOG-ON are limited. In one European and two large Asian cohorts, most paediatric MOG-ON patients had severe visual loss at onset, with visual acuity of 0.1 at its nadir. However, at six months the MOG-ab-positive patients made a good recovery with a functional visual acuity of 0.5 in 98% of patients, and 0.8 in 89% of patients; significantly better than that reported in AQP4-ab-positive ON.

In contrast to the finding in our patient, simultaneous bilateral optic nerve involvement is the more frequent presentation, seen even in up to 73% of paediatric MOG-ab positive patients. The percentage of radiologically identified bilateral ON can be even higher.

A substantial proportion of paediatric MOG-ON patients present with prominent optic disc oedema (60-90%), due to anterior involvement of the optic nerve. Unlike in adults, disc oedema does not distinguish MOG-ab-positive ON from AQP4-ab-positive and double seronegative paediatric ON patients. Besides the anterior optic nerve inflammation, MRI images of MOG-ON showed high rates of longitudinal involvement of the optic nerve in mixed paediatric and adult cohorts (90%), with relative sparing of the chiasm and optic tracts.

Most children with bilateral ON appear to have a monophasic disease course. However, a small subgroup of children with bilateral ON and MOG-ab continue to have further relapses. MOG-ab are frequently present in chronic relapsing inflammatory optic neuropathy (CRION), which is predominantly seen in adults. The ADEM-ON phenotype is rare and the majority of them are MOG-ab positive. The number of relapses and interval between relapses are heterogeneous in this group.

ADEM patients generally have a favourable long-term prognosis with more often a full recovery in paediatric patients and patients presenting with ON and ADEM/ADEM-like phenotypes. This is mainly based on the recovery of motor function. However, there is a risk of long-term cognitive impairment and a higher risk of post-ADEM epilepsy in MOG-ab-positive children when compared to MOG-ab-negative patients. While ADEM patients typically have a monophasic disease course, relapses can occur in MOG-ab-positive ADEM patients. The longitudinal serologic evaluation of MOG-IgG1 could help predict the disease course and consideration of immunotherapy.

In 2012, a study reported that a proportion of MOG-ab-positive children with ON will experience further relapse(s) and suggested that these patients represent a separate subgroup distinct from MS or NMOSD. Our patient is maintained on long-term immunomodulation, due to this potential for greater relapses. In paediatric MOG-ab-positive ADEM-ON patients, a high proportion (60-70%) of residual visual deficits are reported. Memory impairment, attentional problems, poor concentration, and learning or academic difficulties are residual cognitive deficits reported following MOGAD, affecting 10 to 50% of paediatric MOG-ab-positive patients. Irreversible deficits in motor function are reported in 6-15% of all MOGAD.
patients. Our patient did not have any residual visual or motor deficits.

The CSF findings were normal in our patient. An abnormal CSF with pleocytosis and absence of oligoclonal bands (OCBs) is typical of MOGAD, but its frequency depends on the clinical and radiologic phenotype, and corticosteroid treatment before the lumbar puncture may reduce the likelihood of abnormal CSF findings. The Paediatric European Collaborative Consensus have provided recommendations for acute and maintenance therapy for MOGADs based on clinical experience and evidence limited to those mainly from retrospective studies. The acute attack treated with intravenous methylprednisolone (IVMP) as first-line followed by oral steroids up to a maximum of three months had favourable outcomes in the majority of patients. Intravenous immunoglobulins and plasmapheresis constitute second-line therapies in case of insufficient response to IVMP.

**Learning points**

This case of MOG-Ab positive ADEM-ON is reported due to its occurrence in a young male child and its associated complete recovery. MOGAD-ON is generally seen in older age groups and is often associated with residual visual deficits.

**REFERENCES**