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CASE REPORT

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# Sentinel seizure heralding Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease

Shambaditya Das, Alak Pandit, Biman Kanti Ray and Souvik Dubey*

## Abstract

**Background** Isolated seizure as a manifestation of myelin oligodendrocyte antibody-associated disease (MOGAD) has rarely been reported previously.

**Case presentation** A 16-year-old-male presented with single episode of left focal onset motor seizure with secondary generalization and impaired awareness, without any other focal neurological deficits. There was a history of right focal onset motor seizure with secondary generalized tonic–clonic seizure and impaired awareness 4 years ago. Neurological examination showed bilateral gaze evoked nystagmus. Brain imaging revealed bilateral superficial and deep white matter lesions including the corpus callosum. Anti-MOG antibody was positive. The patient received steroids and Rituximab therapy without any further recurrence of seizure or any neuro-deficits and gradual improvement in lesion burden in brain imaging.

**Conclusions** This case of an adolescent boy with sole manifestation of episodes of focal seizures 4 years apart, finally diagnosed to be a case of MOGAD, not only boosts the evidence of establishing the possibility of MOG antibody-associated autoimmune epilepsy but also reinforces the importance of unexplained seizure as a clinical phenotype in MOGAD.

**Keywords** Myelin oligodendrocyte glycoprotein antibody, Seizure, Presenting manifestation, Primary CNS demyelination, MOG

## Background

Seizure as presenting manifestation or as an early diagnostic clue in primary demyelinating disorder like MS is rare. With the advancement of our understanding about primary demyelinating disorder of central nervous system (CNS) which also includes Myelin oligodendrocyte associated disease (MOGAD), seizure has becomes an integral part of diagnosis. MOGAD is a distinct primary CNS demyelinating disorder with seizure and encephalopathy being common manifestations. Studies have revealed that MOGAD presented with seizures or an encephalitis-like illness more commonly than patients with AQP4-positive Neuromyelitis optica spectrum disorder (NMOSD), which is another acquired primary CNS demyelinating disorder having clinical phenotype similarity with MOGAD. Recently, there are evidences to correlate the presence of such antibodies with seizures, occurring in association with CNS demyelination, or even as isolated phenomena. Pathogenesis is still unclear, though Myelin oligodendrocyte (MOG) antibody-associated autoimmune epilepsy may be one of the plausible mechanism underlying [1–3]. Authors herein intend to present a case of 16-year-old adolescent boy with sole manifestation of episodes of focal seizures 4 years apart, finally diagnosed to be a case of MOGAD, which not

*Correspondence:
Souvik Dubey
drsouvik79@gmail.com
Department of Neurology, Bangur Institute of Neurosciences, IPGMER and SSKM Hospital, 52 1/A Sambhu Nath Pandit Road, Bhowanipore, Kolkata 700025, West Bengal, India

only boosts the evidence of establishing the possibility of MOG antibody-associated autoimmune epilepsy but also reinforces the importance of unexplained seizure as a clinical phenotype in MOGAD.

## Case presentation

A 16-year-old-male,with no prior co-morbidities, presented with a single episode of sudden facial deviation to left with neck deviation followed by tonic–clonic movement of all limbs with impaired awareness lasting for 5–6 min, with up-rolling of eyeball and frothing from mouth with a post-ictal confusion for 10 min, without any focal neurological deficits (FND). There was history of one episode right focal motor seizure with secondary generalization 4 years back, after which the patient was prescribed anti-epileptic drug (AED) [Tab Oxcarbazepine 300 mg BD], however, was self-discontinued after 2 months. Neurological examination was unremarkable, apart from gaze evoked nystagmus.

Routine blood investigations were unrevealing. Cerebrospinal fluid (CSF) analysis showed 3 cells, protein— 38 mg/dL (normal: 10–50 mg/dL); glucose— 66 mg/dL (corresponding serum glucose: 90 mg/dL), negative neuroviral-panel (Zoster, Ebstein–Barr, Herpes simplex, cytomegalovirus, adenovirus, enterovirus, coxsackie B virus, and herpes virus 6, Japanese B virus). Magnetic Resonance Imaging (MRI) Brain [Machine specification—Siemens Magnetom Verio, 3 Tesla field strength, Germany] revealed extensive and scattered altered signal in bilateral superficial and deep white matters including the corpus callosum, isointense in T1-weighted image (T1WI), hyper-intense in T2-weighted image (T2WI), T2-fluid-attenuated-inverse-recovery (FLAIR), without any restricted diffusion or enhancement with contrast (Fig. 1) in stark contrast to the MRI brain that was done 4 years back which showed few indistinct scattered foci of altered signal changes in the superficial white matter of parietal lobe (Fig. 1). Further MRI imaging of spine and orbit revealed no abnormalities. Vasculitis profile, ANA, ANA profile, SS-A, SS-B and autoimmune encephalitis profile were negative. Work-up for primary CNS demyelination revealed negative results for Oligoclonal band (OCB) IgG, immunoglobulin synthesis index and serum AQP4; however, serum anti-MOG antibody came to be positive.

The patient was started on pulse intravenous (iv) methyl Prednisolone therapy (1 gm/day for 3 days) followed by oral Prednisolone (0.5 mg/kg/day). Injection Rituximab was instituted as steroid-sparing immunomodulator (two doses of 1000 mg iv, 2 weeks apart, redosing every 6 months). Oral Prednisolone was slowly tapered off starting a month following Rituximab therapy (daily dosing decreased by 5 mg per 2 weeks). The patient has been under our follow-up for 8 months and did not have seizure or any new onset neurodeficits. Repeat brain imaging revealed a decrease in signal changes in the previously affected areas (Fig. 1).

## Conclusions

MOGAD is an age-dependent distinctive disorder with a myriad of clinical presentation lending to its uniqueness among the primary CNS demyelinating disorders. While the presentations related to optic neuritis, transverse myelitis and brainstem involvement have been

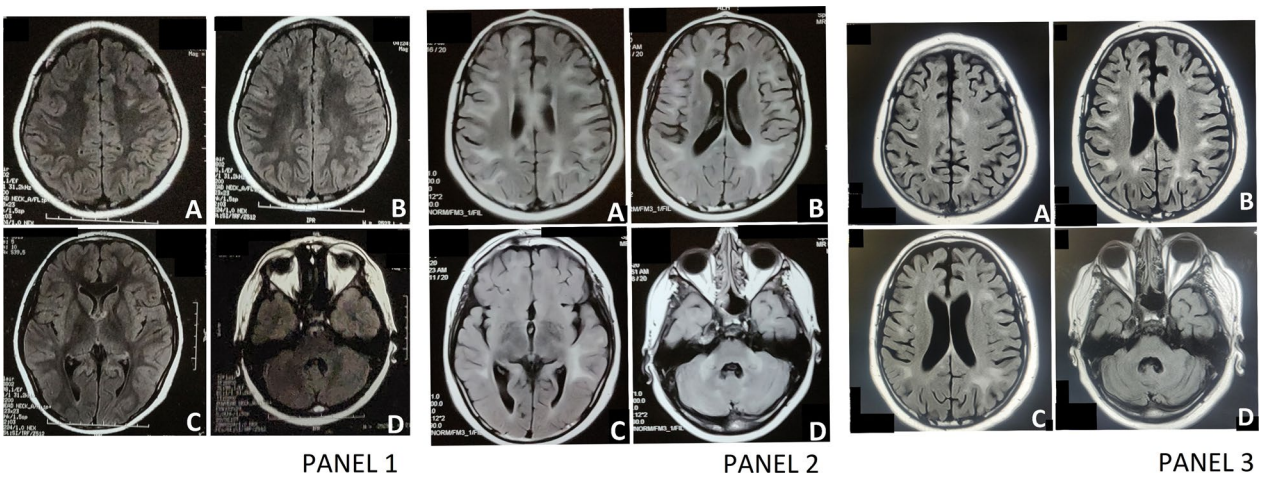


**Fig. 1** Panel 1: MRI Brain T2 FLAIR axial sections showing few indistinct scattered foci of hyperintensities in the white matters of superficial parietal lobe (**A**, **B**) without any other abnormalities (**C**, **D**). Panel 2: MRI Brain T2 FLAIR axial sections showing hyperintensities extensive superficial and deep white matter in both the cerebral hemisphere (**A**–**C**) and middle cerebellar peduncle and cerebellum (**D**). Panel 3: MRI Brain T2 FLAIR axial sections showing marked decrease in areas of hyperintensities following Rituximab therapy (**A**–**D**)

commonly documented in adult MOGAD, children and young adults have shown a tendency towards acute disseminated encephalomyelitis (ADEM) imitation, with encephalopathy. Recent reports have further expanded the horizon of clinical phenotype in MOGAD, incorporating phenotypes of cognitive and behavioral changes, ocular flutter, ADEM with complex movements and isolated seizures. There is a growing recognition of seizure as a clinical feature of MOGAD, either concurrent with or remote from demyelination, with an estimated frequency of 14.7–40%, predominantly manifesting as generalized seizure with or without encephalopathy. Seizure in MOGAD has been documented among adult patients with large unilateral cortical lesions, in children with multiphasic ADEM and optic neuritis and in both children and adults with features of NMOSD, occurring at a higher frequency than noted in AQP4-associated NMOSD or seronegative. A further rarely reported clinical phenotype of MOGAD with seizure includes a comprising of clusters of focal seizure in children as the index presentation in the absence of other typical neurological manifestation of MOGAD, subsequently developing the typical clinical and radiological manifestations of CNS demyelination by months to years [3–5]. Our case echoes with this rarely reported phenotype. Besides the rarity of such presentation, subsequent relapse comprising of only isolated seizure in the absence of the common demyelinating episodes further added to its diagnostic dilemma.

Among the acquired CNS demyelinating syndromes, seizures preferentially occur in MOGAD. However, the expression of seizure in MOGAD is highly variable. While it can be a part of demyelinating encephalopathy episode, it can also occur as an isolated event with normal brain imaging and may be absent in patients with very high MOG antibody titers. Seizure is traditionally a result of cortical insult that substantially follows neuronal cell dysfunction. The presence of isolated seizure in MOGAD, which as the name suggests, targets oligodendrocyte is thus difficult to explain. It has been hypothesized that affection of myelinated oligodendrocytes, also expressed in low density in the cortical grey matter besides its maximal presence in subcortical white matter, might lead to the cortical involvement with subsequent manifestation as autoimmune epilepsy. Although, a possibility of co-existence of yet undetected antibodies directed against neuronal cell surface targets leading to epileptogenesis cannot be ruled and could be probable future research direction [2–5].

It has been seen that clinical features of meningioencephalitis like fever, headache, nausea or vomiting, meningeal irritation, and CSF leukocytosis occurred more commonly in MOGAD with manifestations of seizures and/or encephalopathy. Furthermore, this group noted a higher chance of multiphasic course. Thus, a long-term immunomodulation therapy rather than anticonvulsant therapy in isolation might be the prudent option in the clinical management of patients of MOGAD with isolated seizure, minimizing long-term disability and probable prevention of future relapses. Besides, seizure responding to the administration of immunomodulation in all the previously reported cases further reinstates such approach [3–5]. Our case also had clinical remission without any subsequent relapse following immunomodulation therapy.

Although the experience is limited, the recurring presence of similar pattern of clinical course of initial isolated seizure as a sentinel event later followed by clinical and radiological demyelinating manifestations mandates its establishment as a distinct clinical phenotype of MOGAD, expanding its clinical spectrum further and reinforcing it as a broader disease entity. Awareness of atypical presentations of MOGAD adults on the part of treating physician-like isolated and unexplained seizures in children and young and consideration of MOG antibody testing seems to be of paramount interest, given the clinical and therapeutic implications of an accelerated and early diagnosis [2–4].

Though, AQP4 positive NMOSD and MOGAD share phenotypic similarity in clinical spectrum, the presence of seizure usually favors the later. Pathogenesis of epilepsy in MOGAD is still unclear, with probable intertwining role of autoimmunity and gray matter involvement. Isolated and unexplained seizure in childhood with no apparent clinical and radiological abnormalities must be followed up carefully and where clinically fitting, might warrant a screening of underlying MOG antibody testing.

**Abbreviations**

| | |
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| MS | Multiple Sclerosis |
| CNS | Central nervous system |
| NMOSD | Neuromyelitis optica spectrum disorder |
| MOG | Myelin oligodendrocyte |
| MOGAD | Myelin oligodendrocyte associated disease |
| AQP4 | Aquaporin 4 |
| FND | Focal neurodeficits |
| AED | Anti-epileptic drug |
| CSF | Cerebrospinal fluid |
| MRI | Magnetic resonance imaging |
| T1WI | T1-weighted image |
| T2WI | T2-weighted image |
| FLAIR | Fluid-attenuated-inverse-recovery |
| ANA | Anti-nuclear antibody |
| SS-A | Anti-Sjögren's-syndrome-related antigen A autoantibodies |
| SS-B | Anti-Sjögren's-syndrome-related antigen B autoantibodies |
| OCB | Oligoclonal band |
| ADEM | Acute disseminated encephalomyelitis |

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**Author contributions**
SD1, SD2, and BKR were involved in patient care, data entry and maintaining the Moyamoya registry. The initial concept and design of the study were generated by SD1 and SD2. Literature search was done by SD1. SD1 wrote the first draft which was subsequently improved by SD2. The statistical analysis was carried out by SD1. The draft was critically reviewed by SD2, AP and BKR from its initial stage. All the authors agreed upon the final form of the manuscript before submission. The manuscript has not been published in any pre-print format. All authors read and approved the final manuscript.

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**Availability of data and materials**
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## Declarations

**Ethics approval and consent to participate**
The approval of institutional ethics committee was waived.

**Consent for publication**
The patient's legally authorized representative consented (written) to participate in the study.

**Competing interests**
The authors declare that they have no competing interests.

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## Publisher's Note