Case Series

Uncommon Phenotypes of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease : A Case Series

Rajarshi Chakraborty[1], Rajesh Verma[2], Harish Nigam[3], Ankit Khetan[3]

Abstract

Background : Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) is a primary demyelinating autoimmune disorder of the Central Nervous System targeting the myelin. In recent time, the incidence and diversity of MOGAD cases are increasing. This may open-up further clinical presentations of MOGAD and there is requirement for enhancing its awareness for further detection. In this case series, we discuss seven distinct uncommon clinical phenotypes with radiological interpretation observed in MOGAD.

Key words : MOGAD, Phenotype, Uncommon.

Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease(MOGAD) is an autoimmune primary demyelinating disorder of the Central Nervous System (CNS). Forty five years from its inception in experimental encephalomyelitis, dating back to 1980s, it has shown a variety of clinico-radiological presentations worldwide[1]. Nonetheless, its incidence and importance is increasing in the Asian population. Neuromyelitis Optica Spectrum Disease (NMOSD), Multiple Sclerosis (MS), Vasculitis and infections of the CNS are important differentials. A multitude of case studies and case reports have been documented in MOGAD. This case series tries to explore the uncommon phenotypes of MOGAD along with discussing such phenomena (Table 1, Figs 1 and 2 as per case description). This case-series comprises of 7 MOGAD cases selected out of 25 MOGAD cases, being admitted in neurology department over a-2-years-period.

Editor's Comment :

- Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) is a newer demyelinating entity of the central nervous system.
- The spectrum of clinical and imaging features are expanding with time.
- Clinicians should have a broader approach in suspecting MOGAD in different clinical phenotypes.

Case 1 :

A 25-year-old-male presented with complaints of bilateral vision loss for 4 days followed by paraplegia with bowel/bladder involvement. He was conscious and oriented to time, place and person. Pupil were bilateral sluggishly reactive to light. His visual acuity was Finger Counting (FC) at ½ metre bilaterally with normal extra-ocular movements. He had Upper Motor Neuron (UMN) paraparesis. Magnetic Resonance Imaging (MRI) showed cerebritis, bilateral Optic Neuritis (ON) with chiasmal lesions and Longitudinally Extensive Transverse Myelitis (LETM). His serum Anti-MOG Antibody (Ab) was positive, while Anti-AQP4 (aquaporin-4) Ab and Cerebrospinal Fluid (CSF) Oligoclonal Band (OCB) were negative. He was managed with pulse-dose methyl-prednisolone, followed by prednisolone. At 3-months, complete recovery occurred in vision and lower-limb power.

Case 2 :

A 17-year-old-male presented with fever followed by weakness of all four limbs with bowel/bladder incontinence, dysphagia and dysarthria for 5 days. He was conscious and oriented. His ophthalmic examination were normal. He had UMN quadriparesis with bulbar palsy. His MRI showed cervico-dorsal LETM(C3-D5), features of Acute Disseminated Encephalomyelitis (ADEM), corpus callosal and brainstem lesions. His Anti-MOG-Ab was positive, Anti-AQP4 and CSF-OCB were negative. He was managed with steroids (pulse-dose methyl-prednisolone, followed by prednisolone) and showed complete recovery at 3 months.

Department of Neurology, King George's Medical University, Lucknow, Uttar Pradesh 226003
[1]DM, Assistant Professor and Corresponding Author
[2]DM, DNB, Professor
[3]DM, Assistant Professor
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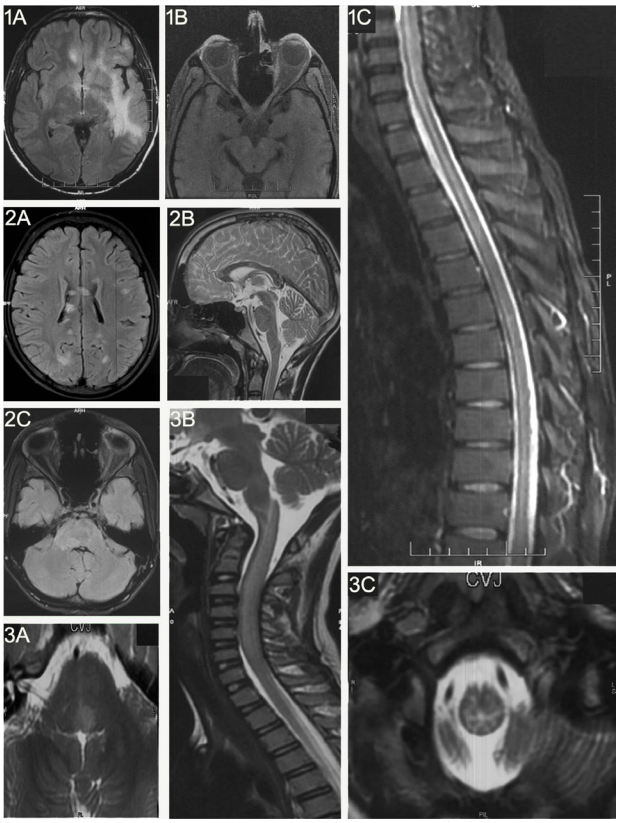

Fig 1 — Brain Magnetic Resonance Imaging(MRI) showing asymmetric left-temporal cerebritis (1A); longitudinally extensive optic neuritis(LEON) with chiasmal lesion(1B); longitudinally extensive transverse myelitis(LETM)(1C); pericallosal and juxtacortical hyperintensity (2A); multiple ovoid callosal T2 hyperintensities(2B); Middle Cerebellar Peduncle (MCP) sign (2C) and dorsal-medullary hyperintensity (area postrema involvement) (3A); LETM extending upto medulla (3B); moth-eaten appearance of cervical cord (3C).

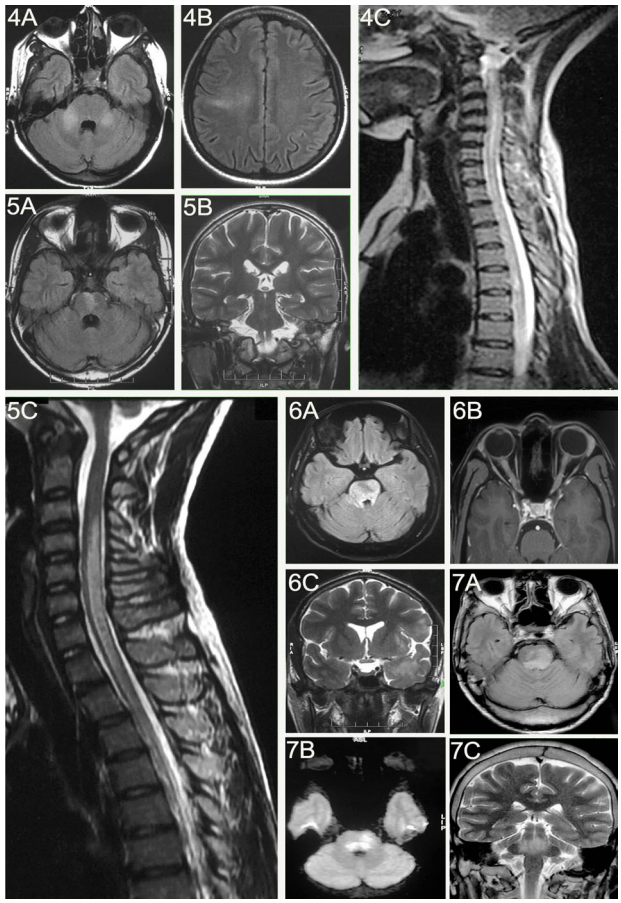

Fig 2 — MRI-brain showing bilateral MCP sign(4A) and right fronto-parietal cerebritis (4B); LETM (4C); medial longitudinal fasciculus hyperintensity (5A); central pontine hyperintensity (5B); LETM (5C); pontine hyperintensity with bilateral MCP sign(6A); contrast-enhancement of bilateral optic nerves (6B); optic chiasmal hyperintensity (6C); pontine hyperintensities(7A), with diffusion restriction (7B) and coronal-T2 ponto-cerebellar hyperintensity (rhombencephalitis)(7C).

Case 3 :

A 10-year-old-male presented with intractable vomiting for 4 days followed by bilateral lower limb weakness with bowel/bladder incontinence for 2 days. His vision was normal. He had UMN paraparesis with normal eye examination. MRI showed area postrema lesion, with LETM (cervico-medullary junction/CMJ to C7) showing moth-eaten appearance. His Anti-AQP4-Ab and CSF-OCB were negative, but Anti-MOG-Ab was positive. He was managed with steroids (pulse-dose methyl-prednisolone, followed by prednisolone) and showed complete recovery at 3-months.

Case 4 :

A 35-year-old-female presented with acute-onset weakness of all four limbs with bowel/bladder incontinence. Her examination showed UMN quadriplegia Her MRI showed LETM (cervico-medullary junction to conus medullaris), bilateral Middle Cerebellar Peduncle (MCP) sign and cerebritis. Her Anti-MOG Ab was positive, while His Anti-AQP4 Ab and CSF-OCB were negative. She was started on pulse methylprednisolone, followed by Intravenous Immunoglobulin (IVIg), without improvement. Rituximab therapy was also tried, but there was poor recovery at 3-months.

Case 5 :

A 17-year-old-male presented with high-grade fever 3 days back, followed by weakness of all four limbs, along with bladder/bowel involvement. His ophthalmic examination was normal except for having adduction lag in left eye and abducting eye nystagmus in right

Table 1 — *Uncommon phenotypes of MOGAD patients*

Age (Y), Sex	Clinical presentation	Magnetic resonance imaging			Treatment	Follow-up
		Brain	Orbit	Spine		
25, M	Bilateral vision loss and paraparesis for 4 days	Cerebritis	B/L ON and chiasmal lesion	D6-D12 LETM	MPS, f/b prednisolone	At 3 months, complete recovery in vision and lower limb power.
17, M	Quadriparesis and bulbar palsy for 5 days	ADEM with corpus callosum and brainstem lesions	Normal	C3-D5 LETM	MPS, f/b prednisolone	At 3 months, complete recovery
10, M	Intractable vomiting, paraparesis for 4 days	Area postrema lesion	Normal	Cervico-medullary Junction to C7 LETM, moth-eaten appearance	MPS, f/b prednisolone	At 3 months, complete recovery
35, F	Quadriparesis for 2 days	B/L MCP sign, cerebritis	Normal	Cervico-medullary Junction to conus medullaris	MPS, IVIg, RTX	Poor recovery at 3 months
17, M	Quadriparesis, INO for 3 days	MLF lesion	Normal	C3-D11 LETM	MPS, f/b prednisolone	At 3 months, complete recovery
30, F	B/L vision loss, ataxia, right-sided hemiparesis for 10 days	B/L MCP sign and pontine lesion	B/L ON and chiasmal lesion	Normal	MPS, IVIg, RTX	Poor recovery, remained blind at 3 months
36, M	Fever, tinnitus, right-sided hemiparesis, dysphagia, dysarthria, horizontal gaze palsy	Flluffy pontine lesion	Normal	Normal	MPS, f/b prednisolone	At 1 month, complete recovery

Note : Y=Years; M=Male; F=Female; B/L=Bilateral; On=Optic Neuritis; D=Dorsal, C=Cervical; Letm=Longitudinally Extensive Transverse Myelitis; MPS=Methyl Prednisolone; ADEM=Acute Disseminated Encephalomyelitis; f/b=followed by; MCP=Middle Cerebellar Peduncle Sign; IVIg=Intravenous Immunoglobulin, RTX=Rituximab; INO=Internuclear Ophthalmoplegia; MLF=Medial Longitudinal Fasciculus

eye on right gaze. He has UMN quadriplegia. His MRI showed LETM(C3-D11) along-with Medial Longitudinal Fasciculus (MLF) lesion. His Anti-AQP4 Ab and CSF-OCB were negative, but Anti-MOG Ab was positive. He was managed with steroids (pulse-dose methyl-prednisolone, followed by prednisolone) and showed complete recovery at 3-months

Case 6 :

A 30-year-female presented with acute-onset bilateral vision loss, headache, painful ocular movements, ataxia and right-sided weakness over 10 days. She had history of vision loss in left eye 1 year back which recovered completely with treatment. At present, her visual acuity was FC at 1 metre in right eye and 6/60 in left eye. Pupils were mid-dilated and sluggishly reactive to light. She had ataxia, cerebellar signs along with UMN right-sided hemiplegia. MRI showed bilateral ON with chiasmal lesion, pontine lesions and Bilateral MCP sign. Anti-AQP4-Ab and CSF-OCB were negative, while Anti-MOG-Ab was positive. She was treated with pulse methyl-prednisolone, IVIg and Rituximab therapy. Her ataxia and hemiplegia improved but her vision didn't show any improvement.

Case 7 :

A 36-year-old-male presented with fever of 3 days duration followed by tinnitus in the right ear, right-sided weakness of body including face. It was followed by diplopia, dysarthria and dysphagia. Examination revealed right-sided UMN type complete hemiplegia, horizontal gaze palsy with bulbar palsy. Patient also had reduced sensation over right half of face with reduced movements of sight side of palate. MRI revealed fluffy hyperintense pontine signals. A diagnosis of acute rhombencephalitis was made on the basis of clinical and radiological findings and patient was managed with intravenous pulse steroid therapy. Patient improved drastically over 1-month.

Discussion

MOGAD is an antibody-mediated inflammatory disorder of CNS myelin at the outermost myelin sheath layers and oligodendrocyte cell surface myelin, and hence can have features common to NMOSD and MS[2]. MOGAD usually affects the anterior part of optic nerves, lobes, deep gray matter, and spinal cord. In this case series, we tried to describe the different

aspects of MOGAD manifestation with review of literature.

Chiasmal involvement has been observed in only 5-12% MOGAD cases in a study by Ramanathan et al. and Chen, *et al*[3,4]. Asymptomatic Corpus Callosal (CC) involvement is observed in18-33% of MOGAD[5]. In a study by Chia, *et al*, CC lesions were variable, often large and involving the sagittal midline, with frequent extra-callosal extension to bilateral sagittal frontoparietal cortices in MOGAD[6]. Area Postrema Syndrome is characterized by Intractable Nausea, Vomiting and Hiccups (INVH) for ≥48 hours and can occur in isolation with discrete T2/FLAIR and T1-gadolinium-enhancing lesions involving the area postrema[7]. Till date, APS is recognized in only one MOGAD patient, with isolated INVH in a study with an incidence of 0.6%[8]. It may be due to disruption of the "emesis circuit" between the area postrema, nucleus tractus solitarius, and the central pattern generator. INO is rarely described in MOGAD with isolated anecdotal cases observed Globally[9]. In a case report, new-onset INO was observed in the background of recurrent LETM due to MOGAD despite on immune therapy[10]. Bulbar palsy is another rare entity observed in MOGAD with anecdotal case reports[11,12]. Patients with brainstem involvement account for 30% MOGAD-associated encephalomyelitis cases and isolated brainstem encephalitis that occurs without ON or myelitis is much rarer, accounting for only 1.8%[13].

In this case series, we highlight the atypical clinico-radiological presentations of MOGAD. This is the first case series of MOGAD targeted to uncommon patterns of Central Nervous System involvement.

Conclusion

MOGAD can have a plethora of neurological manifestation, similar to MS and NMOSD requiring clinical acumen. There is an inevitable requirement for enhancing the awareness about such atypical case presentations.

Declaration of patient consent :

The authors certify that they have obtained all appropriate patient consent forms for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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