**Atypical Presentation of Anti-MOG Ab Disease**
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**INTRODUCTION**
Myelin oligodendrocyte glycoprotein antibodies (MOG-IgG) associated diseases are a spectrum of central nervous system demyelinating disorders. Clinical differentiations from multiple sclerosis, neuromyelitis spectrum disorder (NMOSD) with or without Aquaporin antibody (AQP4-Ab), are very narrow. Recurrence of illness, specific antibody positivity, and response to immunotherapy favors diagnosis. NMOSD and MOG associated diseases share common involvement pattern of optic nerve and cervico-dorsal myelitis. MOG involves rhombencephalon especially pontine white matter tract, while NMOSD has predilection around the periventricular Aquaporin channels. Involvement of conus and caudal nerve roots are rare involvement in MOG antibody associated diseases. We present three cases of MOG-IgG positive patients with bilateral optic neuritis, conus cauda syndrome, and pontine demyelination mimicking Chronic Lymphocytic Inflammation with Pontine Perivascular Enhancement Responsive to Steroids (CLIPPERS).

**CASE REPORT**
Case 1. A 20-year-old male student presented with acute onset progressive painless asymmetric vision loss of five days. He had no prior comorbidities or addictions. He never experienced any focal neurological symptoms earlier. His general and neurological examinations were normal (Table 1). His intraocular pressure was normal. Maximal visual acuity in the right eye was finger counting at 1-meter; left eye was perception of light. Fundus examination revealed blurred disc margin bilaterally. Ophthalmological evaluation, including retina, anterior chamber, and posterior chamber, was unremarkable.

Routine blood parameters, including complete hemogram, liver function test, renal function test, and serum blood glucose level, were normal. Cerebrospinal fluid (CSF) examination revealed protein level (27 mg/dl) with mild lymphocytic pleocytosis (seven total cells, 86% mononuclear and 14% polymorphonuclear). HbsAg, Anti HCV Ab, and HIV Ab status were negative. Pattern visual evoked potential (VEP) was not recordable on the left eye; right eye P100 latency was prolonged 154.2 ms (amplitude 4.46 µV).

**Table 1. Clinical and laboratory findings of MOG Ab positive patients.**

| Parameters | Case 1 | Case 2 | Case 3 |
|-----------|-------|-------|-------|
| Age (in years) | 20 | 37 | 29 |
| Gender | Male | Female | Female |
| Duration of illness | 5 days | 30 days | 7 days |
| Symptoms | Bilateral vision loss | Bilateral lower limb weakness, bladder and bowel involvement | Gait ataxia, shuffled speech, horizontal diplopia (bilateral) |
| Preceding illness | Nil | Undergone caesarian section at term for fetal distress under spinal anesthesia, postoperative day one noticed paraplegia | Fever for six days one week prior to neurological deficit |
| Onset and progression | Acute, right followed by left, Nadir at five days | Acute, maximal at onset | Acute, progression for one week |
| Treatment received before admission to our Institute | Nil | IV Methyl prednisolone 500 mg x five days | Nil |
| General examinations and vitals | Normal | Normal | Normal |
| Neurological examination (abnormal findings) | VA: Right eye: finger counting from 1 meter Left eye: PL+/PR- Bilateral optic disc margin blurred | Bilateral lower limb motor power (MRC) 1/5 with weakness of lower trunk muscles, Sensation loss below umbilical level, bladder catheterized and stool incontinence | Higher mental function- normal Bilateral optic disc margin blurred, Bilateral 6th cranial nerve palsies, left L MN facial palsy, hand incoordination +, gait: ataxic |
| Biochemical parameters | Urea: 25 mg/dl Creatinine: 0.8 mg/dl LFT: Normal Na+: 134 meq/l K+: 4.5 meq/l Hb%: 14.5 gm% TLC: 8500 cumm 
N: 52%;L: 17%;T: 8% 
Urinary R/E: normal 
HIV: NR HbsAg: NR ANA: Neg Anti HCV Ab: NR ANA-TEN: CRP: Neg | Urea: 18 mg/dl Creatinine: 0.7 mg/dl LFT: Normal Na+: 136 meq/l K+: 4.3 meq/l Hb%: 12.5 gm% TLC: 75000 cumm 
N: 55%;L:4%;T: 47% 
TTP: 260000/ cumm 
Urinary R/E: normal 
HIV: NR HbsAg: NR ANA: Neg ANCA: Neg TTF: N CRP: Neg | Urea: 19 mg/dl Creatinine: 0.6 mg/dl LFT: Normal Na+: 139 meq/l K+: 4.2 meq/l Hb%: 12.9 gm% TLC: 11700 cumm 
N: 75%;L: 18%;T: 4% 
TTP: 274000/ 
cumm 
Urinary R/E: normal 
HIV: NR HbsAg: NR ANA: Neg Anti HCV Ab: NR ANA-TEN: CRP: Neg |
| CSF Examination | Total cells: 7 
85% MNC, 15% PMNC 
Glucose: 93 mg/dl Protein: 27 mg/dl | Total cells: 8 
68% MNC, 32% PMNC 
Glucose: 98 mg/dl Protein: 104 mg/dl | Total cells: 52 
88% MNC, 12% PMNC 
Glucose: 144 
mg/dl Protein: 45 mg/dl |
| Pattern VEP (P100) | Left: no wave Right: 154.2 µs Amp: 4.46 µV | Prolonged | Left: 1293 µs Amp: 4.19 µV Right: 1239 µs Amp: 3.29 µV |
| SSEP (tibial) | Bilateral prolonged CSEST | Bilateral prolonged CSEST | Bilateral prolonged CSEST |
Contrast enhanced magnetic resonance imaging (MRI) of the brain and spine were done to look for any demyelinating lesions in central nervous system which was unremarkable (Figure 1). Evaluation for underlying autoimmune pathology included serum anti-nuclear antibody, anti-neutrophilic cytoplasmic antibody; C-reactive protein (CRP) level was negative. Serum IgG anti-MOG Ab was positive by cell-based assay and simultaneous anti-aquaporin-4 antibody status was negative. CSF oligo-clonal band was negative, Tibial somato-sensory evoked potential (SSEP) showed bilaterally prolonged central sensory conduction time (CSCT), which also favored the background demyelinating pathology. Brainstem auditory evoked potential was normal bilaterally.

The patient was managed with intravenous methyl prednisolone 1 gram daily for five days followed by oral prednisolone 40 mg daily which was tapered over the next six months. At one-month follow-up, his visual acuity improved to 6/18 bilaterally.

Case 2. A 30-year-old female presented with acute onset paraplegia with bladder and bowel involvement following caesarean section under spinal anesthesia. On post-operative day one, she developed weakness of lower limb, associated truncal weakness, and sensory level below umbilicus. This patient had no prior comorbidity and did not suffer from any focal neurological symptoms earlier. General examination was unremarkable. Neurological examination revealed power (Medical Research Council scale) 1/5 in bilateral lower limbs, diminished tendon reflexes in lower limbs, and sensory impairment below D10 level. She developed urinary retention on day two of her weakness and again re-catheterized after removal during recovery from post-spinal anesthesia period. Before reaching our clinic, she received intravenous methyl prednisolone pulse therapy of 1 gm for five days, though no significant improvement was noted in form recovery of power in lower limbs and she was in bed bound state (Modified Rankin Scale - 5).

Routine blood parameters, including complete hemogram, liver function test, renal function test, thyroid function test, and serum blood glucose level, were normal (Table 1). Her HbsAg, Anti HCV Ab, and HIV Ab status were negative. Cerebrospinal fluid (CSF) examination revealed elevated protein level 104 mg/dl with mild lymphocytic pleocytosis (eight total cells, 62.8% mononuclear and 37.2% polymorphonuclear cells). MRI of the spine showed swelling of spinal cord at conus level with increased T2 signal and patchy contrast enhancement (Figure 2), the rest of spinal cord and brain was normal. Pattern VEP done was prolonged bilaterally, and tibial SSEP also was prolonged bilaterally. Serum IgG anti-MOG Ab done by cell-based assay was positive. Her brainstem auditory evoked response (BAER) was normal bilaterally. Serum anti-aquaporin-4 antibody status was negative and CSF oligo-clonal band was not detected. Routine urine examination revealed no proteinuria or hematuria. Evaluation of secondary central nervous system (CNS) demyelinating etiologies was non-contributory.

Serum IgG antibody, anti-neutrophilic antibody, and CRP were negative. CT scan of thorax and abdomen to evaluate organ involvement in background of inflammatory diseases and rule out infective etiology was non-contributory.

Table 1. Clinical and laboratory findings of MOG Ab positive patients. continued.

| Parameters                   | Case 1                      | Case 2                      | Case 3                      |
|------------------------------|-----------------------------|-----------------------------|-----------------------------|
| BAER                         | Normal                      | Normal                      | Normal                      |
| MRI Brain/spine              | Normal                      | Swelling of cord at conus, T2 hyperintense signal in most of cross section of cord up to 5 cm, patchy enhancement on post contrast. Cauda equina nerve roots are thickened and enhancement on post contrast. Brain normal |
| Serum IgG Anti-NMO Ab (cell-based assay) | Negative                  | Negative                    | Negative                    |
| Serum IgG Anti-MOG Ab (cell-based assay) | Positive                  | Positive                    | Positive                    |
| Treatment                    | IV methylprednisolone 1 gm daily for five days followed by oral prednisolone 40 mg daily | IV methylprednisolone 1 gm daily for five days followed by oral prednisolone 40 mg daily | IV methylprednisolone 1 gm daily for five days followed by oral prednisolone 30 mg daily |
| Response to treatment after two weeks | Vision improved in both eye- finger counting from 3 meters distance bilaterally | Both lower limbs having antigravity movement | Walking without support, hand incoordination improved, able to maintain daily life activities with minimal help, diplopia improved, |
| Last follow-up               | 1 month; VA 0/18            | 3 months: Walk with walker aid, urine incontinence | 3 months: Improved, mild spasticity of limbs |

VA: visual acuity, CSF: cerebrospinal fluid, VEP: visual evoked potential, SSEP: somato-sensory evoked potential, BAER: brainstem auditory response, MOG: myelin oligodendrocyte glycoprotein, NMO: neuromyelitis optica, CSCT: central sensory conduction time; LFT: liver function tests.
The patient was managed with IV methylprednisolone 1 gm daily for five days followed by oral prednisolone 40 mg daily which was tapered over the next year with overlapping therapy with azathioprine. At discharge after 15 days, her lower limb motor power improved to MRC grade 3 bilaterally. Follow-up at three months, she was ambulatory with minimal support, though urine and stool were incontinent.

**Case 3.** A 29-year-old female was admitted with acute onset gait ataxia, slurred speech, and bilateral horizontal diplopia that progressed over seven days. She had self-limiting fever one-week prior onset of neurological symptoms. General examination was normal. Neurological evaluation revealed bilateral optic disc edema, left 6th cranial nerve palsy, and left facial lower motor type palsy. Power of lower limb was grade 4/5 with brisk reflexes and positive cerebellar signs. She had no prior comorbidity and no history suggestive of any prior connective tissue disease.

Routine blood parameters, including complete hemogram, liver function test, renal function test, thyroid function test, and serum blood glucose level, were normal. Her HbsAg, anti HCV Ab, and HIV Ab status were negative. Erythrocyte sedimentation rate was 30 mm in the first hour. CSF examination revealed lymphocytic pleocytosis (52 total cells, 88% mononuclear cells and 12% polymorphonuclear cells) with normal protein 45 mg/dl and sugar level. Pattern VEP revealed prolonged P100 latency bilaterally (left: 129.9 ms; right: 123.9 ms) with preserved amplitude. Serum IgG anti-MOG Ab (done by cell-based assay) was positive and anti-NMO Ab was negative (Table 1). MRI of the brain revealed multiple discrete T2 and FLAIR hyperintense lesions in pons, medulla, middle cerebellar peduncles, and left frontal white matter showing patchy contrast enhancement. Her tibial SSEP was prolonged bilaterally though BAER was normal. CSF oligo-clonal band was not detected, and IgG Index was negative. Routine urine examination revealed no proteinuria or hematuria. Evaluation for secondary CNS demyelinating etiologies was non-contributory. Serum ANA antibody, anti-neutrophilic antibody, and CRP were negative. CT scan of the thorax and abdomen to evaluate organ involvement in background of inflammatory diseases and rule out infective etiology was normal.

The patient was managed with IV methylprednisolone 1 gram daily for five days followed by oral prednisolone 30 mg daily. At discharge after 28 days, she was able to walk independently. A repeat MRI of the brain showed significant decrease in lesion size and enhancement (Figure 3). At a three-month follow-up, mild residual spasticity in lower limbs were noted though cranial nerve features and cerebellar deficits were resolved.

**DISCUSSION**

The three cases highlighted the CNS spectrum of MOG Ab disease. Case 1 was a classic case of bilateral optic neuritis. However, cases 2 and 3 were atypical presentations of MOG disease spectrum. In adults, MOG disease usually is associated with optic neuritis and myelitis in more than 80% of cases.\(^1\) In a study, 31 (18.7%) out of 166 episodes had bilateral optic neuritis, myelitis in 32 (19.3%), and brain and stem involvement in 44 (26.5%).\(^3\) MOG Ab associated spinal cord lesions are longitudinally extensive transverse myelitis of cervico-dorsal spinal cord similar to NMOSD (AQP4-Ab+) lesions. Involvement of lower spinal cord and sacral roots are rare but pathognomonic of MOG disease.\(^4\) The second case developed paraplegia following caesarean section under spinal anesthesia, which concerns clinicians about operative and other differentials. Recovery of motor power is brisk, however, bladder and bowel control showed poor recovery, as also seen in case 2.\(^7\)

CLIPPERS are a radiological diagnosis of an inflammatory brain stem syndrome of uncertain etiology and T-cell-predominant CSF leukocytosis. CLIPPERS associated with MOG Ab are diagnosed increasingly.\(^9\) Clinically, they present with subacute onset brain stem dysfunction. Imaging revealed T2 hyperintense lesions with ill-defined margins in posterior fossa predominantly involving pons and measuring more than 2 cm. Multiple punctate and curvilinear post contrast enhancement in the pons with or without extension to cerebellum and cerebellar peduncle is characteristic of the syndrome. The lesions may extend caudally to the medulla and cervical spinal cord, cranially to the midbrain and supratentorial parenchyma. Enhancement decreases after treatment as the patients respond to corticosteroids.

CLIPPERS responds to corticosteroids both clinically and radiologically and have fair chance to relapse on stopping steroids.\(^10\) Our cases have subclinical involvement of the optic nerve and myelitis as evidenced by VEP latency prolongation and prolong central sensory conduction time in tibial SSEP. MOG Ab is expressed specifically in the central nervous system on the surface of myelin sheaths and oligodendrocyte processes.\(^8\) In humans, presence of MOG Ab are debated.
as pathogenic themselves or an epiphenomenon secondary to immune upregulation following prior demyelination or infection. In our series, cases 2 and 3 had preceding illness prior to neurological presentation.

Human MOG Ab might play a minor role in the pathophysiology of inflammatory demyelination, however, there are highly specific markers in specific clinical settings. However, recent developments have established its plausible role in human MOG Ab associated CNS demyelination and its varying clinical spectrum. The exact pathophysiological effect of human MOG Ab needs further critical evaluation in CNS and PNS demyelination.

**CONCLUSIONS**

The present case series highlighted the importance to test for anti-MOG antibodies in patients presenting with conus cauda syndrome and CLIPPERS, especially when MRI shows demyelinating features.

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