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MOG positive primary autoimmune meningitis mimicking tuberculous meningitis: a case series

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ABSTRACT

Objectives Primary autoimmune meningitis presentation of myelin oligodendrocyte glycoprotein (MOG) IgG antibody positivity is infrequently reported. We aim to identify the patients with MOG IgG antibody positivity who were initially misdiagnosed and treated as tuberculous meningitis (TBM).

Methods A retrospective cross-sectional study conducted in the Neuroimmunology Laboratory and Department of Neurology of Amrita Institute of Medical Sciences, Kochi, Kerala, India between June 2018 and December 2023. MOG IgG antibody positive cases were identified from the Neuroimmunology Lab Registry, and the case sheets were screened for TBM-like presentation. Cases were included on the basis of MOG IgG positivity, an initial diagnosis of tuberculosis was suspected and antitubercular therapy was initiated with minimal response.

Results We described the clinical, microbiological, radiological and serological features of five patients with a TBM-like presentation eventually diagnosed with MOG-associated meningitis. Symptoms included headache, vomiting, visual impairment and weakness. Three patients showed normal MRIs and two patients showed MRI findings consistent with demyelination. Serum MOG antibody testing was positive only on serial testing of all five patients. The final diagnosis was MOG-associated meningitis in two patients and MOG-associated meningoencephalitis in three patients.

Discussion This case series highlights the rare presentation of MOG antibody positive patients presenting as primary autoimmune meningitis and its diagnostic challenges, especially in regions where tuberculosis is common. The study underscores the importance of considering autoimmune aetiology as a differential diagnosis when tuberculosis treatment fails or relapses occur, advocating for MOG IgG antibody testing to ensure accurate diagnosis and effective treatment.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Chronic meningitis in the tropical regions is commonly attributed to tuberculosis. Primary autoimmune meningitis has been known to present with myelin oligodendrocyte glycoprotein (MOG) and glial fibrillary acidic protein (GFAP) positivity, resulting in varied clinical and radiological presentation, and complexity in early diagnosis and management. This study was performed to add to the diverse, growing spectrum of MOG antibody disease.

WHAT THIS STUDY ADDS

⇒ We report a novel occurrence of MOG-associated primary autoimmune meningitis mimicking tuberculous meningitis, emphasising the need to include atypical presentations of MOG antibody disease in future diagnostic criteria.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Incorporating MOG antibody testing into the evaluation of patients with suspected meningitis of unknown aetiology, particularly in regions endemic to tuberculosis, may potentially help spare patients from the harmful effects of antitubercular therapy.

INTRODUCTION

Myelin oligodendrocyte glycoprotein (MOG) IgG antibodies (MOG-Abs) mediate inflammatory demyelinating diseases of the central nervous system (CNS) with diverse phenotypes including optic neuritis, myelitis, brainstem demyelination and encephalitis.[1] The spectrum of association of MOG-Abs with various conditions continues to evolve, with meningitis, an uncommon manifestation of MOG-Abs, being increasingly reported.[2]

Chronic meningitis in the tropical regions is commonly attributed to tuberculosis,[3] due to its endemicity, and has been associated with considerable morbidity and mortality over the past years. Owing to this, meningitis secondary to autoimmunity is rarely reported, despite its manifestation in a number of diseases such as systemic lupus erythematosus, Behcet's disease, sarcoidosis and rheumatoid arthritis.[4–6] Primary autoimmune meningitis has been observed in MOG positivity and glial fibrillary acidic protein (GFAP) positivity, resulting in varied clinical

and radiological presentation, and complexity in early diagnosis and management.[7]

We present a case series of five patients initially diagnosed with and treated as tuberculous meningitis (TBM), who later relapsed on steroid tapering and exhibited eventual positivity for MOG-Abs (refer to online supplemental material for case report of patient 5). This manuscript follows CAse REport (CARE) reporting guidelines.

MATERIALS AND METHODS

This is a retrospective cross-sectional study conducted at the Neuroimmunology Laboratory of a tertiary care centre between June 2018 and December 2023. MOG-Abs positive cases were identified from the Neuroimmunology Lab Registry, and the case sheets were screened for TBM-like presentation as per the diagnostic criteria proposed by Thwaites *et al*.[8] Cases were included if positive serum MOG-Abs testing was available, an initial diagnosis of tuberculosis was suspected by a team of expert clinicians, and antitubercular therapy (ATT) was initiated with minimal response. Patients lacking detailed data were excluded.

All included cases underwent comprehensive CNS infectious panel testing using the iGenetic Extended Comprehensive CNS panel.[9] In total, 20 viruses, 18 bacteria, 3 fungi, 1 parasite, *Mycobacterium tuberculosis* complex and non-tuberculous mycobacteria were examined (refer to online supplemental material 2 for detailed composition of panel).

MOG-Ab testing was performed using a commercially available fixed cell-based assay (FCBA) (Euroimmun, Lubeck, Germany)[10] that employed the use of HEK-293 transiently transfected with full-length human MOG protein and fixed with formaldehyde. Serum testing was done at a dilution of 1:10 and/or cerebrospinal fluid (CSF) without dilution as per manufacturer's instructions. A sample was considered positive if it showed typical surface staining in cells transfected with MOG, and no staining in cells transfected with a control antigen. MOG positivity was determined by visual observation of immunofluorescence staining independently by two trained observers, and the positivity was graded as per intensity of staining (+1=mild, +2=moderate, +3=strong, +4=very strong).

Patient and public involvement

No patient and public involvement.

RESULTS

We identified five patients (four female, one male; mean age: 38.2 years; range: 19–61 years) who were assigned an initial diagnosis of TBM, treated with ATT and later showed positivity for MOG-Abs (patient 5 details are included in online supplemental material 1. All patients presented with symptoms of headache, vomiting and neck stiffness, consistent with TBM. Brain MRI on presentation at our centre was normal in four patients, with one showing features consistent with MOG-Ab demyelination and TBM. One patient showed features suggestive of demyelination in their disease course, while three remained normal. *M. tuberculosis* complex was not isolated on extensive CSF culturing in any of the cases. CSF workup showed elevated cell counts with lymphocytic pleocytosis, increased opening pressure and proteins, and hypoglycorrhachia. Serum MOG-Ab testing was positive in all five cases on serial testing, with one patient showing simultaneous CSF positivity. All patients failed to show improvement with ATT (isoniazid, rifampicin, pyrazinamide and ethambutol) following the initial misdiagnosis and later showed significant improvement on immunotherapy.

Patient 1

A 19-year-old girl had complaints of headache, diplopia, and recurrent vomiting for 2 months. She had no prior similar complaints. CSF analysis performed elsewhere showed lymphocytic pleocytosis, hypoglycorrhachia and increased proteins. Suspecting meningitis, she was given acyclovir, dexamethasone and ceftriaxone and recovered completely, with normal repeat CSF workup. She presented to our hospital 20 days later with recurring similar complaints (table 1).

She grew concerned over the effect of her visual symptoms on her academic performance. There was no history or systemic symptoms suggestive of tuberculosis. She had no relevant medical, family or psychosocial history, and no indications for genetic testing. General examination revealed neck stiffness with an otherwise normal neurological examination. MRI brain and spine were normal. CSF workup showed elevated opening pressure, lymphocytic pleocytosis, elevated proteins and hypoglycorrhachia (table 2).

Infectious workup consisting of CSF gram stain, KOH mount, TB GeneXpert, cryptococcal antigen and viral PCR was negative with no organism isolated in bacterial, tuberculous and fungal culture. In view of suspected tuberculous aetiology and recurring symptoms, ATT, acyclovir, ceftriaxone and dexamethasone were initiated, leading to symptomatic improvement. Whole body positron emission tomography- computed tomography (PET CT) and serum ACE were normal. Given symptomatic improvement and absence of clinical signs of tuberculosis, an autoimmune cause was considered. Serum and CSF autoimmune workup was negative. Testing for neuromyelitis optica spectrum disorder panels containing aquaporin 4 and MOG IgG antibodies was negative (table 3).

Repeat CSF showed relative improvement (table 2). Despite being discharged in stable condition with Prednisone, she was readmitted 1 week later with bilateral lower limb pain and visual blurring for 5 days. CSF showed elevated opening pressure, lymphocytic pleocytosis, reduced proteins and hypoglycorrhachia (table 2). The patient was conservatively managed and discharged in stable condition. The patient relapsed 2 months later with a sudden drop in vision and bilateral eye pain.

Table 1 Patient characteristics and MOG antibody testing results

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age (years)	19	60	22	49	41
Duration of prior illness at presentation to our hospital	8 weeks	NA	2 years	5 days	10 weeks
Presenting symptoms	Headache, recurrent vomiting, diplopia	Headache, blurring of vision, vomiting	Recurrent neurological deficits (Quadriparesis)	Headache, generalised tonic clonic seizures	Headache, recurrent vomiting, neck pain
Recurrence on steroid tapering	Present	Present	Present	Present	Present
Response to treatment	Methylprednisolone and azathioprine	Methylprednisolone and azathioprine	Plasmapheresis	Methylprednisolone and azathioprine	Methylprednisolone and azathioprine
Serial MOG IgG antibody testing	Low positive	Low positive	Low positive	Low positive	Low positive
2023 MOGAD criteria	Fulfilled	Fulfilled	Fulfilled	Not fulfilled	Not fulfilled
Final diagnosis	MOG IgG-related meningitis and optic neuritis with supporting clinical or MRI features	MOG IgG-related meningoencephalitis with supporting clinical or MRI features	MOG IgG-related meningoencephalitis with supporting clinical or MRI features	MOG IgG-related meningoencephalitis	MOG IgG-related meningitis
Duration of ATT	3 months	2 years	2 years	3 weeks	5 weeks
Time lapse between ATT discontinuation and MOG seropositive result	--	3 months	2 years 9 months	1 week	--
Follow-up period of immunotherapy without ATT	9 months	1 year 7 months	1 year 6 months	9 months	11 months

ATT, antitubercular therapy; MOG, myelin oligodendrocyte glycoprotein; MOGAD, myelin oligodendrocyte glycoprotein-associated disease; NA, not available.

Table 2 CSF characteristics of patients throughout the course of treatment

Patient 1	Days from presentation	0	9	19	79	
	Appearance	Clear	Clear	Clear	Clear	
	CSF WCC per mm^3	67 (97% mononuclear)	14 (92% mononuclear)	5 (80% mononuclear)	5 (80% mononuclear)	
	CSF protein (mg/dL)	186	54.7	14.6	22.6	
	CSF glucose (mg/dL)	33.9	97.9	58.8	48.9	
	RBS (mg/dL)	87	180	106	104	
	Opening pressure (cm H2O)	47	27	33	15	
Patient 2	Days from presentation	0	22	67	105	197
	Appearance	Clear	Clear	Clear	Clear	Clear
	CSF WCCs per mm^3	655 (97% mononuclear)	197 (98% mononuclear)	402 (95% mononuclear)	250 (99% mononuclear)	60 (95% mononuclear)
	CSF protein (mg/dL)	92	54	79	171	67
	CSF glucose (mg/dL)	47	71	55	24	40
	RBS (mg/dL)	113	136	121	77	123
	Opening pressure (cm H2O)	NA	NA	13.5	NA	22
Patient 3	Days from presentation	0	57	165	1425	1609
	Appearance	Clear	Clear	Clear	Clear	Clear
	CSF WCC per mm^3	105 (98% mononuclear)	122 (95% mononuclear)	10 (90% mononuclear)	50 (98% mononuclear)	25 (96% mononuclear)
	CSF protein (mg/dL)	133.6	95.5	40.3	85.3	83
	CSF glucose (mg/dL)	98.6	71.2	100.5	70.5	73.6
	RBS (mg/dL)	163.8	150	NA	161	NA
	Opening pressure (cm H2O)	34	22	17.5	5	NA
Patient 4	Days from presentation	0	63	1009	1318	1555
	Appearance	Clear	Clear	Clear	Clear	Clear
	CSF WCC per mm^3	17 (94% mononuclear)	15 (93% mononuclear)	0	7 (100% predominant)	0
	CSF protein (mg/dL)	102	61.1	68.5	37	60
	CSF glucose (mg/dL)	73	65.1	54.8	61	48
	RBS (mg/dL)	130	110	NA	NA	94
	Opening pressure (cm H2O)	NA	NA	NA	22.5	9
Patient 5	Days from presentation	–	0	7	24	109
	Appearance	Clear	Clear	Clear	Clear	Clear
	CSF WCC per mm^3	245 (98% mononuclear)	52 (96% mononuclear)	55 (96% mononuclear)	62 (98% mononuclear)	10 (100% mononuclear)
	CSF protein (mg/dL)	103	39.2	70	102	40
	CSF glucose (mg/dL)	194	165.2	175	125	152
	RBS (mg/dL)	NA	NA	NA	NA	280
	Opening pressure (cm H2O)	NA	52	9	11	Normal

CSF, Cerebrospinal Fluid; NA, not available; RBS, random blood sugar; WCC, white cell count.

Ophthalmological examination revealed visual acuity of 6/12 and 6/9 on right and left eye, respectively, bilateral temporal scotomas and bilateral papilloedema. She had been stable on ATT for 2 months prior, and steroids were stopped 10 days before. Ethambutol toxicity or optic neuritis secondary to autoimmunity was considered. MRI brain and spine were normal. CSF showed reduced proteins and glucose (table 2). Visual evoked potential showed bilateral prolonged P100 latencies. Repeat MOG testing showed serum and CSF positivity (table 3). The final diagnosis was autoimmune meningitis with associated optic neuritis, evidenced by MOG positivity and relapsing symptoms on steroid tapering. ATT was stopped, and the patient showed substantial improvement with Azathioprine (50 mg two times per day) and weekly methylprednisolone (1 g for 2 months). At the latest follow-up 18

Table 3 MOG antibody testing results for the patients throughout the course of treatment

		Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Test 1	Days from presentation	5 days	6 weeks	1 month	2 days	3 days
	Serum	Negative	Negative	--	Negative	Negative
	CSF	Negative	Negative	Negative	Negative	Negative
Test 2	Days from presentation	3 months	4 years 5 months	2 years 9 months	4 weeks	2 months
	Serum	Positive	Positive	Negative	Positive	Positive
	CSF	Positive	Negative	--	Negative	Negative
Test 3	Days from presentation	--	--	4 years 3 months	--	3 months
	Serum	--	--	Positive	--	Negative
	CSF	--	--	Positive	--	--

CSF, Cerebrospinal fluid; MOG, myelin oligodendrocyte glycoprotein.

months later, the patient was asymptomatic with normal vision (visual acuity 6/6) and resolved papilloedema. The patient expressed satisfaction and gratitude for her level of care.

Patient 2

A 61-year-old female presented elsewhere with headache, blurred vision, recurrent vomiting, neck pain and mild disorientation (table 1). She had no prior similar complaints. She was conscious on examination, had mild recall deficits and no other neurological deficits. Brain and spine MRIs were normal. CSF analysis showed elevated opening pressure, lymphocytic pleocytosis, elevated proteins and no malignant cells (table 2). Infectious workup was negative. Serum ACE was normal. Whole body PET scan was normal. She was treated with ceftriaxone and acyclovir for 10 days, showed improvement in her symptoms and was discharged, but was admitted 2 weeks later to our centre with similar complaints.

There was no history or systemic symptoms indicative of tuberculosis. She had no relevant medical, family or psychosocial history, and no indications for genetic testing. MRI brain with contrast showed subtle leptomeningeal enhancement in the posterior fossa (figure 1). CSF showed increased cell count, reduced proteins and glucose as compared with before (table 2). CSF infectious workup was negative. She was started on dexamethasone and ATT due to increasing cell counts, after exclusion of alternative diagnoses. She improved over 1 week and was discharged. Three months later, she developed ATT-induced hepatitis, which was managed with modified regimen (levofloxacin and amikacin). ATT was continued for 1 year. She remained stable for 3 years but presented again with symptoms of headache and vomiting for 3 days. MRI brain and spine were normal. There were no focal neurological deficits or meningeal signs. CSF analysis showed increased opening pressure, mononuclear pleocytosis, elevated protein and hypoglycorrhachia (table 2). Considering recurrence on steroid tapering, autoimmune aetiology was suspected in spite of normal brain and spine MRI. Serum and CSF MOG testing and CSF infectious workup was negative (table 3). In view of the repeated recurrence of symptoms, the patient was initiated on monthly cyclophosphamide [750 mg/m^2 body surface area (BSA)], following which she

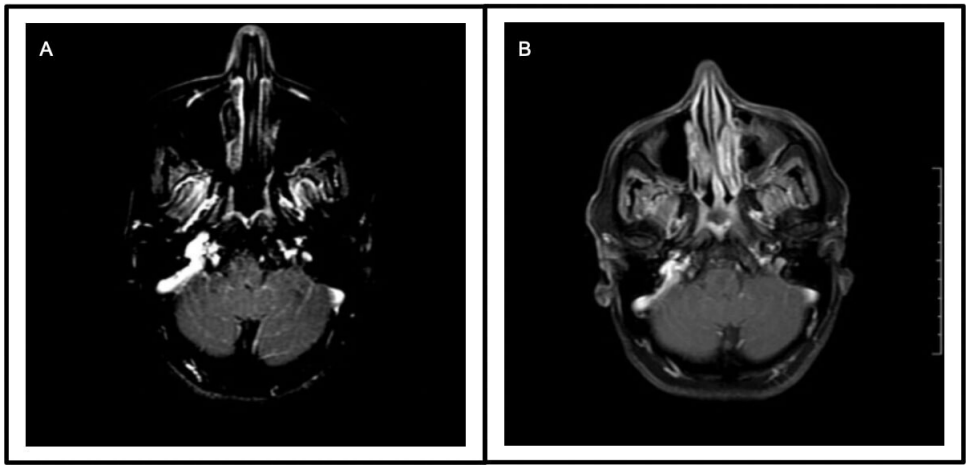

Figure 1 MRI findings of selected patients. Axial T1-weighted postcontrast MRI of patient 2 shows subtle leptomeningeal enhancement in the posterior fossa (A), which reduced on follow-up with treatment (B).

improved. When admitted for the third dose, the patient had sudden onset dull aching headache and vomiting for 3 days. MRI brain and spine were normal. CSF showed relative worsening and infectious workup was negative (table 2). MOG antibody testing was positive. The patient was discharged with a plan to continue Cyclophosphamide (every 3 weeks). On follow-up testing after the sixth dose, CSF showed increased opening pressure, with relative improvement in other parameters (table 2). The patient was initiated on Rituximab (1 g). Following two doses of rituximab and six doses of cyclophosphamide, she presented 1 month later with imbalance while walking, memory disturbances and neck pain for 1 week. MRI brain showed subtle T2 Fluid-Attenuated Inversion Recovery (FLAIR) hyperintensities. Infectious workup was negative and autoimmune workup was positive for serum MOG antibodies (table 3). She was initiated on methylprednisolone (1 g for 3 months) with azathioprine (50 mg two times per day) and showed significant improvement. She was asymptomatic on latest follow-up, 6 years from her initial presentation. The patient indicated a significant improvement in her quality of life after treatment.

Patient 3

A 22-year-old female experienced bilateral lower limb pain, paresthesias, truncal weakness. She had no similar complaints in the past. She was diagnosed with atypical Guillain-Barré syndrome elsewhere, where she received intravenous immunoglobulin therapy resulting in symptomatic improvement. A month later, she developed low backache and worsening lower limb weakness. Suspecting arachnoiditis, she was treated with ATT and prednisone. Symptoms recurred on steroid tapering, and infectious and autoimmune workup was negative (table 3), prompting increased dosage with improvement. Azathioprine was started and steroids were tapered. After 10 months, she developed severe headache, photophobia, vomiting and ataxia and was treated with methylprednisolone, cyclophosphamide and mycophenolate mofetil (MMF) alongside ATT. 7 months later, ATT-induced hepatitis led to a modified ATT regimen.

She visited our hospital after 6 months with dysarthria, bilateral proximal upper and lower limb weakness, truncal ataxia, and internuclear ophthalmoplegia (table 1). There was no history or systemic symptoms indicative of tuberculosis. She had no relevant medical, family or psychosocial history, and no indications for genetic testing. MRI brain showed T2 FLAIR hyperintensities involving both sides of centrum semiovale, focal ring-shaped enhancement in interpeduncular cistern and bilateral T1 enhancements at level of centrum semiovale (figure 2). CSF showed lymphocytic pleocytosis and elevated proteins (table 2). Infectious workup was negative, and whole body PET-CT did not show evidence of tuberculosis, leading to discontinuation of ATT. Detailed autoimmune evaluation returned negative (table 3), however, with strong clinical suspicion of autoimmunity, she received six sessions of plasmapheresis and weekly methylprednisolone for 4 weeks, and symptomatically improved. After 6 months, she was admitted with headache, vomiting and limb numbness. MRI brain showed acute lacunar infarct in the pons and features of vasculitis. CSF showed lymphocytic pleocytosis (table 2). Considering inadequate immunotherapy, rituximab was started (1 g every 6 months). She responded well and was relatively stable for 2 years on rituximab treatment. After this, she developed COVID-19 infection and immunotherapy was stopped. Following her recovery from COVID-19, she presented with dysarthria, headache, dizziness, seizures and left-sided weakness. MRI brain showed acute infarct in the right inferior frontal gyrus. CSF was notable for worsening protein (table 2). Serum MOG testing was positive (table 3), and digital subtraction angiography suggested moyamoya disease. As she was diagnosed with autoimmune meningoencephalitis with coexistent vasculitis, she received 12 sessions of plasmapheresis and cyclophosphamide (1 g/month) for immunomodulation. Weekly bortezomib was initiated after the sixth dose of cyclophosphamide. Azathioprine

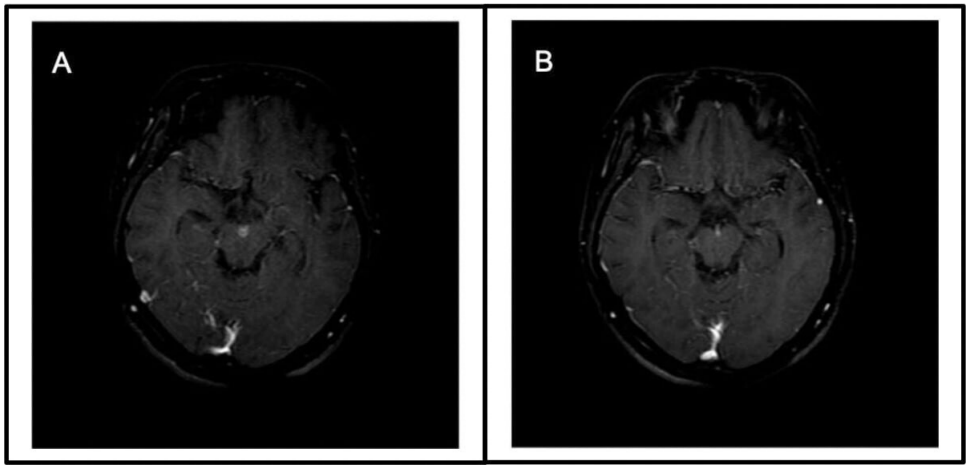

Figure 2 MRI findings of selected patients. Axial T1-weighted MRI of patient 3 that shows focal ring-shaped enhancement in the interpeduncular cistern (A), which reduced on follow-up (B).

was initiated due to MOG positivity after the ninth dose. The patient was stable for 2 years and then presented with worsening right limb power and dysphagia. MRI brain showed acute left frontal and subacute right cerebellar infarcts. CSF showed elevated proteins (table 2). She received methylprednisolone, three cycles of plasmapheresis and rituximab, and improved symptomatically. As of the latest follow-up 5 years from presentation, she is on a nasogastric tube and is continuing treatment. The patient chose not to share her perspective on treatment.

Patient 4

A 49-year-old male, who is a known case of diabetes mellitus, had headache and neck pain for 5 days, and one episode of generalised tonic clonic seizure (GTCS) (table 1). He had no prior similar complaints. He was admitted elsewhere with altered sensorium and intubated. MRI brain and venogram revealed small vessel ischaemic changes. MRI spine was normal. CSF revealed lymphocytic pleocytosis and elevated proteins (table 2). CSF gram staining showed pus cells, with chest X-ray showing left lung haziness. Bronchoscopy with bronchoalveolar lavage showed pus cells and gram-positive cocci. The provisional diagnosis was infectious meningoencephalitis with aspiration pneumonia, so ceftriaxone, acyclovir and levetiracetam were given. He was intubated and brought to our hospital for further management.

There was no history or systemic symptoms indicative of tuberculosis. He had no relevant medical, family or psychosocial history, and no indications for genetic testing. Glasgow Coma Scale score on examination was E1VTM5. Neurological examination postextubation was normal. MRI brain with contrast and MRI spine were normal. CSF showed raised opening pressure with improvement in other parameters (table 2). Infectious and autoimmune workup was negative (table 3). He was treated with levetiracetam, acyclovir, ceftriaxone, ATT and dexamethasone for 5 days and showed initial improvement followed by worsening. The patient was hence given pulse methylprednisolone (1 g for 5 days). Repeat CSF showed relatively elevated cells and proteins (table 2). Whole body PET-CT was negative for malignancy. The patient was discharged in stable condition. 2 weeks later, he presented with mild symptoms and CSF showed increased cells and proteins (table 2). Repeat autoimmune workup showed MOG antibody positivity (table 3). ATT was stopped and the patient was initiated on methylprednisolone and Azathioprine (50 mg BD). He was discharged and advised Methylprednisolone (1 g, once weekly for 11 weeks). Suspecting azathioprine-induced liver injury, azathioprine was stopped and the patient was switched to MMF (500 mg two times per day). CSF showed overall improvement (table 2) following 3 months of weekly methylprednisolone and hiking of MMF to 1 g two times per day. He was given rituximab (1 g) for maintenance immunotherapy, and at latest follow-up after 6 months, he was stable following two doses of rituximab. The patient shared that the treatment was effective and he did not experience major side effects.

DISCUSSION

Primary autoimmune meningitis is a rare form of meningitis characterised by inflammation of the meninges due to autoimmune mechanisms. Organ-specific autoimmunity is the primary pathology, as opposed to secondary autoimmune meningitis, which may be a result of underlying systemic autoimmunity.[7] This presentation, characterised by meningitis/encephalitis presentation, indicates a broader spectrum of manifestations that includes a predominantly meningoencephalitis disease, as seen in our cases.[1]

The spectrum of involvement of MOG-Abs in various disease mechanisms continues to evolve, with increasingly diverse phenotypic presentations being reported over recent years,[11 12] with meningitis also being reported.[2]

Similar to these previous cases, we were led to believe that the patients' initial presentation and diagnostic workup were in line with infectious aetiology. The initial differential diagnosis was TBM, owing to the endemicity of tuberculosis in our region. Diagnosis is of particular challenge early on, due to low bacterial load and inappropriate specimen collection reducing test sensitivity.[13] This led us to maintain a high degree of caution even after ruling out alternative diagnoses such as sarcoidosis, leading to prompt initiation of ATT in all five cases despite the inability to isolate the mycobacterium on repeated CSF culturing.

The possibility of an autoimmune aetiology was considered only later on in the course of management due to the absence of clinical or imaging manifestations of demyelination in the early stages, leading to the initial misdiagnosis and administration of ATT. Failure to show improvement with ATT strengthened evidence that the MOG autoimmunity was not induced by previous infectious insult, but rather, is the underlying primary pathology causing the meningitis/meningoencephalitis manifestations.

We aim to emphasise MOG-Ab as a differential diagnosis in patients presenting with features of chronic meningitis, who satisfy the diagnostic criteria for TBM, do not respond to ATT and relapse on steroid tapering. Previous reports of MOG-associated meningitis show comparable clinical presentations to our cases with features of limb paralysis, sensory and visual disturbances.[14] Three cases[14–16] had abnormalities related to demyelination in the brain parenchyma, optic nerve or spinal cord at the first MRI examination, while another review of 12 cases showed absent early MRI findings.[2]

Four of our patients presented with normal MRIs in the early disease stage, concordant with the findings of previous reports on MOG-associated meningitis.[17] Patient 2 showed a normal MRI brain scan at presentation but showed leptomeningeal enhancement (figure 1) as she worsened and improved with steroid therapy. Leptomeningeal enhancement has been described as an early

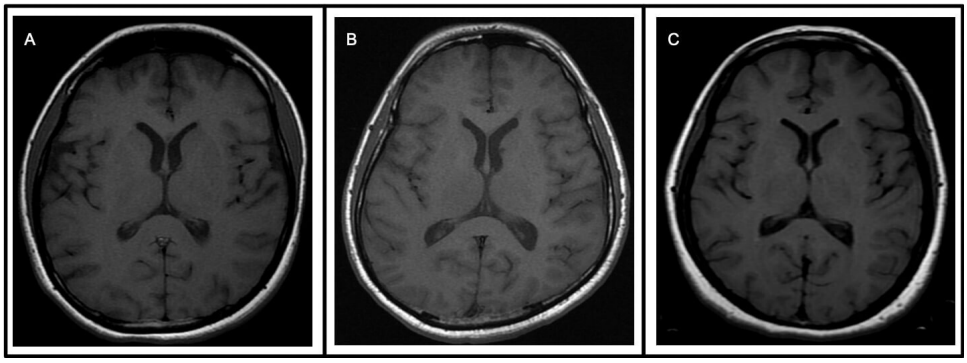

Figure 3 Normal MRI findings of patient 1 (A), patient 4 (B), patient 5 (C).

presentation of MOG-Abs positivity, with demyelinating lesions developing at a later point, as seen in our case.[17] Patient 3 presented with features suggestive of TBM (focal ring enhancements) and MOG-associated demyelination (T2 FLAIR hyperintensities in the centrum semiovale) on MRI brain (figure 2). The remaining patients continually showed unremarkable findings (figure 3). MRI Spine done in all patients was normal. On CSF analysis, our patients showed elevated cell counts, opening pressure and proteins which were comparable to other reports.[2] Hypoglycorrhachia, seen in all our cases, although an unusual presentation in typical MOG antibody disease (MOGAD), has been previously described in the literature.[18]

The 2023 International MOGAD Panel criteria were recently proposed to aid in establishing a diagnosis of MOGAD on the basis of core clinical demyelinating events, positive MOG-Abs, supportive clinical or MRI features with exclusion of better diagnoses.[19] The FCBA testing kit utilised in this study was determined to have a sensitivity and specificity of 25.3% and 98.1%, respectively, as per a previous study.[20] Another study comparing the FCBA used in this study with an 'in house' Live Cell Based Assay showed robust agreement between the two assays.[21] We, therefore, consider the positive antibody testing results obtained in all the patients to be reliable. Patients 1, 2 and 3 were diagnosed with a core clinical demyelinating event and showed supporting features, fulfilling the 2023 MOGAD criteria. Patient 1 was diagnosed with MOG-associated optic neuritis, originally thought to be ethambutol induced. This presentation underscores the importance of MOG testing in patients presenting with visual complaints undergoing ATT for TBM, to exclude possible autoimmune aetiology. This also highlights how MOG-associated primary autoimmune meningitis may progress to other MOGAD phenotypes if misdiagnosed or if immunotherapy is not administered in a timely manner.[2] Patient 3 was eventually diagnosed with cerebral cortical encephalitis and developed coexistent moyamoya disease, which has been previously reported.[22] The aetiology of moyamoya disease in this patient, however, could not be determined.

Although our patients' presentation mimicked an infectious aetiology, the potential coexistence and cross-reactivity of MOGAD with infections should be considered. To our knowledge, only one other report describes MOGAD with tuberculous meningoencephalitis.[23] Similar to our cases, poor response to ATT raised suspicion of an autoimmune aetiology, confirmed by positive MOG antibody testing. Immunotherapy alongside ATT led to significant improvement. Such presentations, however, have been rarely reported, and the emergence of a testing bias in confirmed cases of TBM must not be overlooked.

Infections reported alongside MOGAD include tuberculosis, syphilis, COVID-19 and Epstein-Barr virus among others.[24–31] This growing association suggests a possible postinfectious generation of MOG-specific antibodies via molecular mimicry, bystander activation, epitope spreading or polyclonal B cell activation.[25 32] A case of concurrent MOGAD and syphilis showed a B cell reacting to both MOG and *Treponema pallidum*, supporting molecular mimicry, though its role in MOGAD remains unproven.[25] Similarly, Miraclin *et al* diagnosed MOGAD with tuberculosis based on positive MOG antibodies and significant steroid-responsive improvement with ATT.[24]

Some may view the MOG positivity on repeated testing as secondary to tissue injury; however, we do not consider this a possibility as our patients' symptoms and clinical findings remained the same and responded only to immunotherapy. We believe the delayed seropositivity in these patients to be similar to the low yield of single testing for TB or cytology in cases of suspected malignancy.[33] Limitations of our study were the inability to test for antibody titres through further dilution and a small sample size.

In conclusion, this study seeks to highlight the importance of repeated MOG antibody testing in cases of chronic meningitis/meningoencephalitis where the organism cannot be isolated even on repeated culturing. MOG-associated primary autoimmune meningitis should be suspected as a close differential diagnosis to TBM, particularly in endemic regions, when mycobacteria is not isolated, disease relapses on steroid tapering or when the disease does not respond to ATT. Repeated testing for MOG IgG antibodies must be employed in such cases in order to identify positivity, which would otherwise go undetected, leading to complexities in disease management.

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