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REVIEW ARTICLE

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The neuro-ophthalmological manifestations of NMOSD and MOGAD—a comprehensive review

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Optic neuritis (ON) is one of the most frequently seen neuro-ophthalmic causes of vision loss worldwide. Typical ON is often idiopathic or seen in patients with multiple sclerosis, which is well described in the landmark clinical trial, the Optic Neuritis Treatment Trial (ONTT). However, since the completion of the ONTT, there has been the discovery of aquaporin-4 (AQP4) and myelin oligodendrocyte glycoprotein (MOG) antibodies, which are biomarkers for neuromyelitis optica spectrum disorder (NMOSD) and MOG antibody-associated disease (MOGAD), respectively. These disorders are associated with atypical ON that was not well characterised in the ONTT. The severity, rate of recurrence and overall outcome differs in these two entities requiring prompt and accurate diagnosis and management. This review will summarise the characteristic neuro-ophthalmological signs in NMOSD and MOGAD, serological markers and radiographic findings, as well as acute and long-term therapies used for these disorders.

Eye (2023) 37:2391–2398; https://doi.org/10.1038/s41433-023-02477-0

INTRODUCTION

Optic neuritis (ON) is one of the most common neuro-ophthalmological conditions worldwide leading to visual morbidity, especially in younger patients. Multiple sclerosis (MS) is the most recognised underlying aetiology of ON. Much of what we know about typical optic neuritis characteristics comes from the landmark Optic Neuritis Treatment Trial (ONTT) that was published in 1992 [1, 2]. The ONTT was designed to evaluate acute unilateral ON in patients with or without a history of MS and the influence of corticosteroid treatment on outcomes. Ultimately, it found that roughly 50% of ON is caused by MS and that high-dose intravenous methylprednisolone (IVMP) leads to faster recovery, but did not change the ultimate outcome [1, 3]. The ONTT found that typical ON usually presents as subacute monocular vision loss in a young adult, associated with eye pain worsened with eye movements, decreased contrast and colour vision, and evidence of relative afferent pupillary defect (RAPD) on examination. The degree of visual acuity loss and visual field defect can be variable. There is optic disc oedema on presentation in about a third of cases, which is typically mild because the lesions are often predominantly retrobulbar [1, 4].

Our understanding of other diseases associated with ON as part of their clinical presentation has tremendously grown in the past two decades with advances in serological antibody testing and imaging protocols. Since the completion of the ONTT, there has been the discovery of biomarkers of atypical ON, namely aquaporin-4 (AQP4) and myelin oligodendrocyte glycoprotein (MOG) antibodies, which are associated with neuromyelitis optica spectrum disorder (NMOSD) and MOG antibody-associated disease (MOGAD) respectively, that have different characteristics, prognoses, and treatment [5, 6]. A recent study found that among a third of blood samples remaining from the ONTT, none were positive for AQP4 antibodies and only 1.7% were found to have MOG antibodies [7]. These results indicate that the ONTT provides excellent details of typical ON, but not for the atypical ON seen in NMOSD or MOGAD. Our understanding of NMOSD and MOGAD has greatly expanded over the past decade, which extends our knowledge of ON beyond what was found in the ONTT.

In this review, we will summarise the neuro-ophthalmological findings, diagnostic measures, and acute and long-term therapeutics in NMOSD and MOGAD.

NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD)

Historical overview and epidemiology

In 1894, Eugene Devic and his student Fernand Gault introduced the term 'neuromyelitis optica acuta' after describing a case of bilateral blindness and paraplegia with post-mortem pathology revealing demyelination of the optic nerves and demyelination and necrosis of a long portion of the spinal cord [8]. Over the years, the phenotypical differences, such as recurrence and severity of ON, as well as improvement in imaging techniques, led to many appreciating there was a difference between neuromyelitis optica (NMO) and MS. The first diagnostic criteria for NMO was devised in 1999 and required both ON and transverse myelitis for the diagnosis supported by imaging and CSF findings [9]. Despite phenotypic differences, it was initially unclear if NMO was a separate entity of MS or a more severe variant [10]. In 2004, AQP4-IgG was discovered [5], which is an antibody against a transmembrane water channel protein in the central nervous system (CNS) expressed on astrocytic end-feet that was found to be both a biomarker and pathologic cause of NMO. This discovery led to NMO becoming recognised as an independent clinical entity. Because of the availability of a specific biomarker of NMO, the spectrum of potential phenotypes has expanded. In 2015, the NMO diagnostic criteria was revised

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Received: 30 December 2022 Revised: 7 January 2023 Accepted: 28 February 2023
Published online: 16 March 2023

Table 1. Diagnostic criteria for neuromyelitis optica spectrum disorder (adapted from Wingerchuk et al. [13]).

Core clinical characteristics	AQP4-IgG positive	AQP4-IgG negative or unknown AQP4-IgG status	Additional MRI requirements in AQP4-IgG negative or unknown AQP4-IgG status
1. Optic neuritis 2. Acute myelitis 3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting 4. Acute brainstem syndrome 5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions 6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions	1. At least 1 core clinical characteristic 2. Exclusion of alternative diagnoses	1. At least 2 core clinical characteristics occurring as a result of 1 or more clinical attacks and meeting all the following requirements: a. At least 1 core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome b. Dissemination in space (2 or more different core clinical characteristics) c. Fulfilment of additional MRI requirements, as applicable 2. Negative tests for AQP4-IgG3. Exclusion of alternative diagnoses	1. Acute optic neuritis: a brain MRI showing normal findings (or only non-specific white matter lesions), or an optic nerve MRI with a T2-hyperintense lesion or a T1-weighted gadolinium-enhanced lesion extending over more than one-half the optic nerve length or involving the optic chiasm 2. Acute myelitis: an associated intramedullary MRI lesion extending over either ≥3 contiguous segments (LETM) or ≥3 contiguous segments of focal spinal cord atrophy in patients with a history compatible with acute myelitis 3. Area postrema syndrome: associated dorsal medulla/area postrema lesions 4. Acute brainstem syndrome: associated periependymal brainstem lesions

AQP4 aquaporin 4, *IgG* immunoglobulin G, *LETM* longitudinally extensive transverse myelitis, *MRI* magnetic resonance imaging, *NMOSD* neuromyelitis optica spectrum disorder.

allowing for the molecular and clinical diagnosis of neuromyelitis optica spectrum disorder (NMOSD) [11–13], which is now known to represent a spectrum of clinical symptoms and MRI findings in addition to the seropositivity to AQP4-IgG. About 30% of NMOSD is seronegative for AQP4-IgG (Table 1).

AQP4-IgG positive NMOSD (AQP4-IgG + NMOSD) is a rare immune astrocytopathy with an incidence of 0.04–0.25 per 100,000 and prevalence of 0.70–1.91 per 100,000 in White populations and an incidence of 0.34–1.31 per 100,000 and prevalence of 0.86–4.25 per 100,000 in non-white populations [14]. Unlike MS, NMOSD is more prevalent in Asians and Blacks [15, 16]. The median age of onset is 39 years, about a decade later than MS, with a strong female preference (70–90%) [17]. It is generally a sporadic disorder, however, rare familial cases have been reported [18].

Clinical presentation

Based on International Panel for NMO Diagnosis criteria, one core clinical characteristic of NMOSD with positive serum AQP4-IgG is sufficient to make a diagnosis of AQP4-IgG + NMOSD. Core clinical characteristics include: (1) Acute ON; (2) Acute transverse myelitis; (3) Area postrema syndrome presenting with intractable nausea, vomiting, and/or hiccups; (4) Acute brainstem syndrome; (5) Acute diencephalic clinical syndrome or symptomatic narcolepsy; (6) Symptomatic cerebral syndrome [13]. A diagnosis of AQP4-IgG seronegative NMOSD can be made with the presence of 2 core clinical characteristics with at least one of them being ON, transverse myelitis, or area postrema syndrome (Table 1). It was initially thought that NMOSD was a monophasic disorder, though it is now recognised that NMOSD usually has a relapsing course, which is seen in up to 90% of patients. Relapses more commonly occur in the first year after initial attack, however, remote relapses beyond 10 years have also been reported [19].

Prior studies have reported ON as the initial presentation in 42% of NMOSD patients. It has also been found that close to two-third of patients with NMOSD will eventually develop ON during the disease course [20]. Distinguishing NMOSD ON (NMOSD-ON) from other forms of ON can be challenging at the time of initial presentation, but there are some clinical clues that should raise the suspicion of NMOSD. NMOSD-ON often causes severe vision loss with over 75% having a visual acuity of 20/200 or worse at nadir. Severe visual acuity loss of 20/200 or worse at nadir was also reported in 35.9% of ONTT patients and therefore severe vision loss alone at presentation does not perfectly stratify NMOSD-ON from other forms of ON [21–25]. However, NMOSD-ON outcomes tend to be worse with less recovery. Over one-third of patients with NMOSD-ON have a final visual outcome of 20/200 or worse, which is a significant morbidity compared to improvement to 20/40 or better in over 90% of patients in the ONTT [1, 26] (Table 2).

Other helpful distinguishing factors is simultaneous or rapidly sequential bilateral ON that are seen more commonly associated with NMOSD-ON and MOGAD optic neuritis (MOGAD-ON), while rare in MS and typical ON [27–30]. Bilateral simultaneous ON in NMOSD is 20% in NMOSD compared to almost 50% in MOGAD. However, both are far higher than MS where it is likely 1% at most (Table 2). NMOSD-ON has higher optic chiasm involvement ranging from 20–64%, which is rare in MS (Fig. 1) [31]. Optic disc oedema in only noted in 5–33% of NMOSD-ON cases given its propensity to involve the more posterior aspects of the optic nerve [32].

Diagnosis and testing

Visual fields and OCT. NMOSD-ON can lead to any pattern of visual field loss on automated perimetry, with central scotoma being the most common pattern followed by altitudinal hemianopia and less commonly bitemporal hemianopsia from chiasmal involvement [33, 34]. However, often the vision is so severe at nadir that automated visual fields cannot be performed.

Neuroaxonal damage is often significant in NMOSD-ON, which can be evaluated by optical coherence tomography (OCT) after ON. This damage leads to an average peripapillary retinal nerve fibre layer (pRNFL) loss that is almost two-fold higher than seen in MS-ON (38.4 µm thinning in NMOSD-ON compared to 20 µm thinning in MS-ON). Macular ganglion cell and inner plexiform layer (GCIPL) thinning in NMOSD-ON has been reported as 1.5-fold higher than MS-ON [35, 36]. Severe pRNFL and GCIPL loss correlates with the worse visual outcomes in NMOSD-ON compared to MS-ON or MOGAD-ON [37].

Neuroimaging. Simultaneous bilateral optic nerve enhancement, longitudinally extensive enhancement (≥50% of the optic nerve) and chiasmal involvement [38], should raise the suspicion for

Table 2. Comparison of clinical and paraclinical findings in NMOSD vs. MOGAD.

	NMOSD	MOGAD
Characteristics		
Median age (years)	30–40s	30s (adults) and children (<18)
Gender (F:M)	9:1	1:1
Ethnicity preference	Asian, African American	No clear predilection
Clinical and imaging features		
Optic neuritis:		
• Optic disc oedema	+	+++
• Bilateral optic nerve involvement	++	++
• Pain	++	+++
• Severe vision loss at nadir	+++	+++
• Recurrent visual loss	+++	+++
• Steroid dependence	+	++
• Visual recovery	Poor	Favourable
• Optic chiasm involvement	+++	+
• MRI enhancement location	Posterior optic nerve	Anterior optic nerve
• MRI perineural enhancement	Rare	++
Myelitis:		
• LETM	+++	++
• Conus medullaris involvement	+	+++
• MRI gadolinium enhancement	++	+
• H sign	+	++
Area postrema syndrome	++	Rare
Seizure	Rare	+
Encephalopathy	Rare	++
Diencephalic symptoms	++	Rare
Brainstem syndromes	+	++
ADEM	Rare	++
CSF		
White blood cell count (cells/μl)	Normal to mild elevation	Normal to mild elevation
• >50 cells/μl	35%	13–35%
Protein mg/dl	Normal to mild/ moderate elevation	Normal to mild elevation
Oligoclonal bands	<20%	<20%

Rare or less than 5%, + infrequent, ++ frequent, +++ very frequent.
ADEM acute disseminated encephalomyelitis, *CSF* cerebrospinal fluid, *LETM* longitudinally extensive transverse myelitis, *MOGAD* myelin oligodendrocyte glycoprotein antibody-associated disease, *MRI* magnetic resonance imaging, *NMOSD* neuromyelitis optica spectrum disorder.

atypical ON associated with NMOSD (Fig. 1). The most commonly described intracranial brain lesions have non-specific characteristics presenting as small hyperintensities on T2-weighted or FLAIR sequences in the deep white matter; however, certain localisation of lesions make them more unique for NMOSD [39]. NMOSD brain lesions have increased preference to the areas with high AQP4 expression such as diencephalon surrounding the third ventricle and cerebral aqueduct, posterior brainstem adjacent to the fourth ventricle, and periependymal adjacent to lateral ventricles [40, 41]. Involvement of the area postrema is frequent in NMOSD, which is the third most common presentation of NMOSD behind ON and transverse myelitis. Periventricular white matter lesions that are typically seen in MS are rare in NMOSD.

Serum and cerebrospinal fluid. Detection of serum AQP4-IgG by live cell-based assays has been shown to have a sensitivity of ~75% and specificity of >99%, which is superior to other assays such as ELISA, and therefore are the gold standard for the detection of AQP4-IgG [42]. Serological testing for AQP4-IgG is crucial for treatment as well as prognostication. Prior studies have shown a statistically significant correlation between AQP4 seropositivity and higher risk of ON and myelitis recurrence, thus leading to poorer visual outcome and overall disability [43]. Cerebrospinal fluid (CSF) evaluation for AQP4-IgG was determined to be less sensitive and not cost effective, and is therefore not recommended in the setting of ON or suspected NMOSD [44].

There are no unique CSF characteristics in NMOSD, however, up to 35% of AQP4-IgG + NMOSD cases have shown pleocytosis with >50 cells/μl of either neutrophilic or monocular predominance [45]. Protein elevations can be seen in up to 44% of cases. Oligoclonal bands is only seen in 15–30% of cases, compared to 90% in MS. High levels of glial fibrillary acidic protein (GFAP) in the CSF of NMOSD patients during acute attack further suggest astrocytic damage [46]. Interestingly, studies have also shown that higher serum GFAP level is associated with 3-fold increased risk of relapses [47, 48].

Treatment

While the ONTT showed that steroids do not alter the visual outcome of typical ON, NMOSD-ON has a worse prognosis and therefore treatment with both IVMP and plasma exchange are recommended. Early treatment of NMOSD-ON is likely important in reducing the risk of visual morbidity as prior retrospective studies have shown better preservation of vision and pRNFL in NMOSD-ON when treated with early IVMP [49–51]. IVMP is usually used at 1000 mg/day for 3 to 5 consecutive days with or without an oral prednisone taper. High-dose oral corticosteroids (1250 mg prednisone, which is the bioequivalent of 1000 mg IVMP) has been shown to be equivalent to high-dose IVMP for the treatment of ON [52], and is therefore also an acute treatment option for NMOSD-ON. In addition, multiple case series and retrospective studies have demonstrated benefits of using plasma exchange as first line or in corticosteroid-refractory NMOSD-ON [53]. Plasma exchange is typically administered every other day for a total of 5 to 7 sessions with most benefits in visual outcomes when initiated within 7 days from symptom onset [54]. Retrospective studies have shown that the use of IVMP and plasma exchange in combination leads to a better final visual acuity than IVMP alone [55]. Therefore, most experts recommend both high-dose corticosteroids and plasma exchange as the first line treatment for acute NMOSD-ON.

All NMOSD patients require long-term immunosuppressive therapy (IST) given the high rate of relapses (67–90%) and high risk of morbidity and even potential for mortality [38]. Traditional off label ISTs, such as mycophenolate mofetil and azathioprine, have been shown to be associated with a reduction in relapses based on multiple retrospective studies [56]. Rituximab, a chimeric monoclonal antibody targeting CD20, has been shown to very effective in relapse prevention based on retrospective and randomised clinical trials [57, 58], and therefore has traditionally been the most commonly employed treatment for NMOSD. More recently, results of four randomised clinical trials have led to Food and Drug Administration (FDA) approval of three ISTs

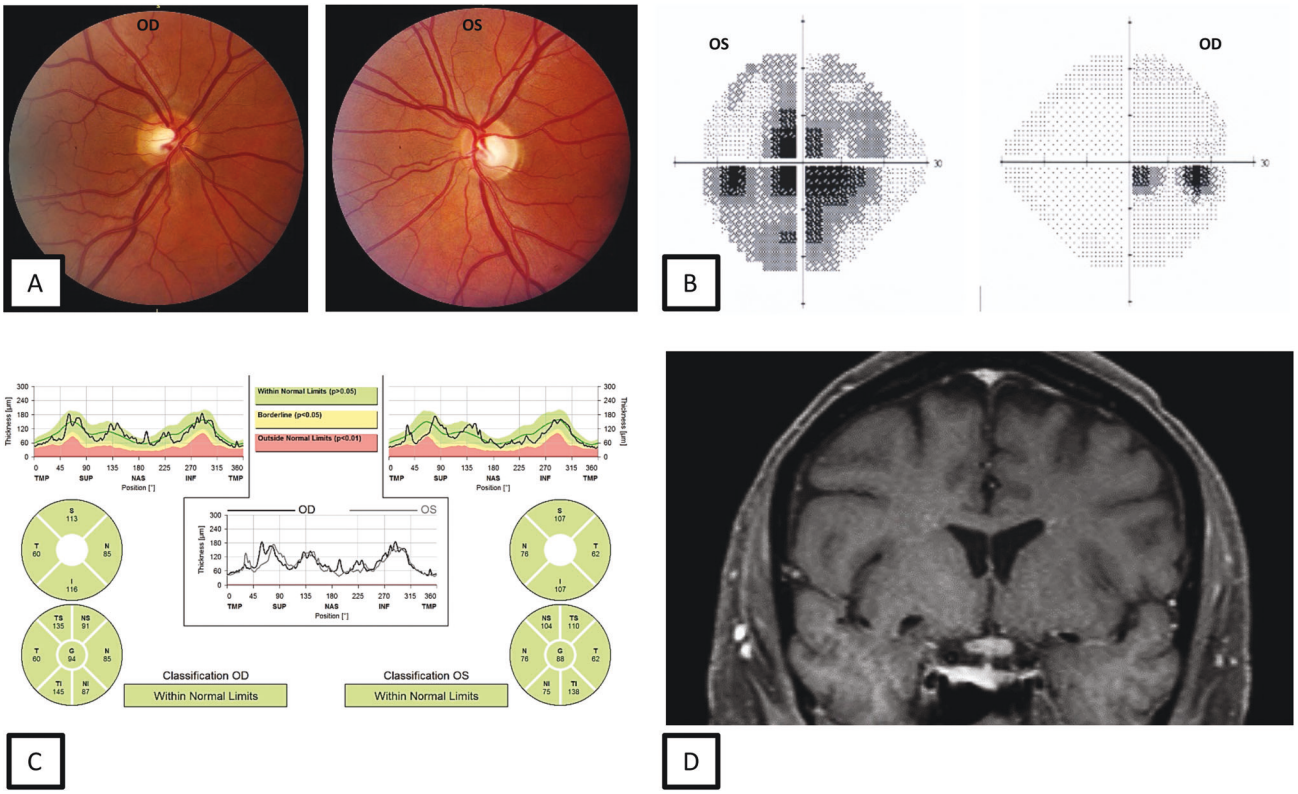

Fig. 1 57-year-old male with AQP4-IgG positive neuromyelitis optica spectrum disorder (NMOSD) optic neuritis. During the acute optic neuritis attack, fundus photographs demonstrate no optic disc oedema (**A**). Automated visual field testing shows a junctional scotoma (**B**). OCT shows a normal pRNFL thickness (**C**). Coronal, fat saturated T1-weighted post contrast MRI of the orbits shows enhancement of the optic chiasm and left optic nerve at the junction of the chiasm correlating with the visual field defects (**D**).

demonstrating lower relapse rates in NMOSD patients compared to placebo. These three ISTs include eculizumab—an anti-C5 complement inhibitor [59], inebilizumab—a CD19 monoclonal antibody [60], and satralizumab—a interleukin 6 receptor (IL-6) monoclonal antibody [61], which all greatly improve our treatment armamentarium for NMOSD.

MYELIN OLIGODENDROCYTE GLYCOPROTEIN ANTIBODY-ASSOCIATED DISEASE (MOGAD)

Historical overview and epidemiology

MOGAD is a recently described inflammatory demyelinating condition, which can present with ON and other CNS demyelinating phenotypes, including transverse myelitis, acute disseminated encephalomyelitis (ADEM), brainstem syndromes, seizure and cerebral cortical encephalitis [62, 63]. While MOG-IgG was previously erroneously thought to be a marker of MS based on non-specific older generation assays using MOG in its denatured form [64], the use of transfected cell-based assays with MOG in its native conformation has led to MOG-IgG becoming a reliable biomarker for a new entity, MOGAD, which is distinct from both MS and NMOSD [62, 63, 65, 66].

The median age of onset for MOGAD is mid-30s, but can affect any age, including a predilection for children [62, 67]. Unlike MS and NMOSD, there is no clear gender or racial predilection [62, 68]. However, studies in predominantly White populations suggest that it is likely 2 to 3-fold more common than AQP4-IgG + NMOSD [69, 70].

Clinical presentation

Optic neuritis is the most common phenotype of MOGAD in adults, while ADEM is more frequent in the paediatric population [62]. In adults, MOGAD accounts for ~5% of ON [68, 70, 71] while in children, MOGAD accounts for a much higher percentage of ON, ranging from 20–50% [68, 72–74]. While there are overlapping features of ON with other demyelinating conditions, there are some salient clinical characteristics that should alert the clinician to the possibility of MOGAD (Table 2). Unlike other forms of ON where visible optic disc oedema is present in only a third of cases, optic disc oedema is present in ~80% of MOGAD-ON, which can sometimes be severe and associated with peripapillary haemorrhages [66, 67, 75–77] (Fig. 2). Up to 50% can be bilateral at presentation [66, 67, 76, 78]. Pain is a prominent feature of most MOGAD-ON attacks, and can be severe enough to manifest as headache [79]. MOGAD-ON typically has severe vision loss at nadir (similar to AQP4-IgG + NMOSD ON), but often has significant recovery leading to better visual outcomes, with only 5–14% of patients with a final visual acuity of 20/200 or worse [29, 62, 67, 76, 80].

Approximately 50% of patients with MOGAD will have relapsing disease, which is most commonly in the form of ON [62, 81]. The ON attacks are often steroid responsive, but some are steroid dependent and can follow a chronic relapsing inflammatory optic neuropathy (CRION)-like phenotype. Recent studies have shown that MOGAD accounts for many cases of CRION that were previously thought to be idiopathic [82–84]. Less common ophthalmic manifestations reported in MOGAD include uveitis, macular neuro-retinopathy, neuroretinitis, retinopathy secondary to venous stasis and increased intracranial pressure, orbital inflammatory syndrome, and cranial neuropathies [85].

Diagnosis and testing

Visual fields and OCT. Automated perimetry during an acute MOGAD-ON attack can reveal any pattern of field loss, including central scotoma or severe generalised depression, which can affect one or both eyes.

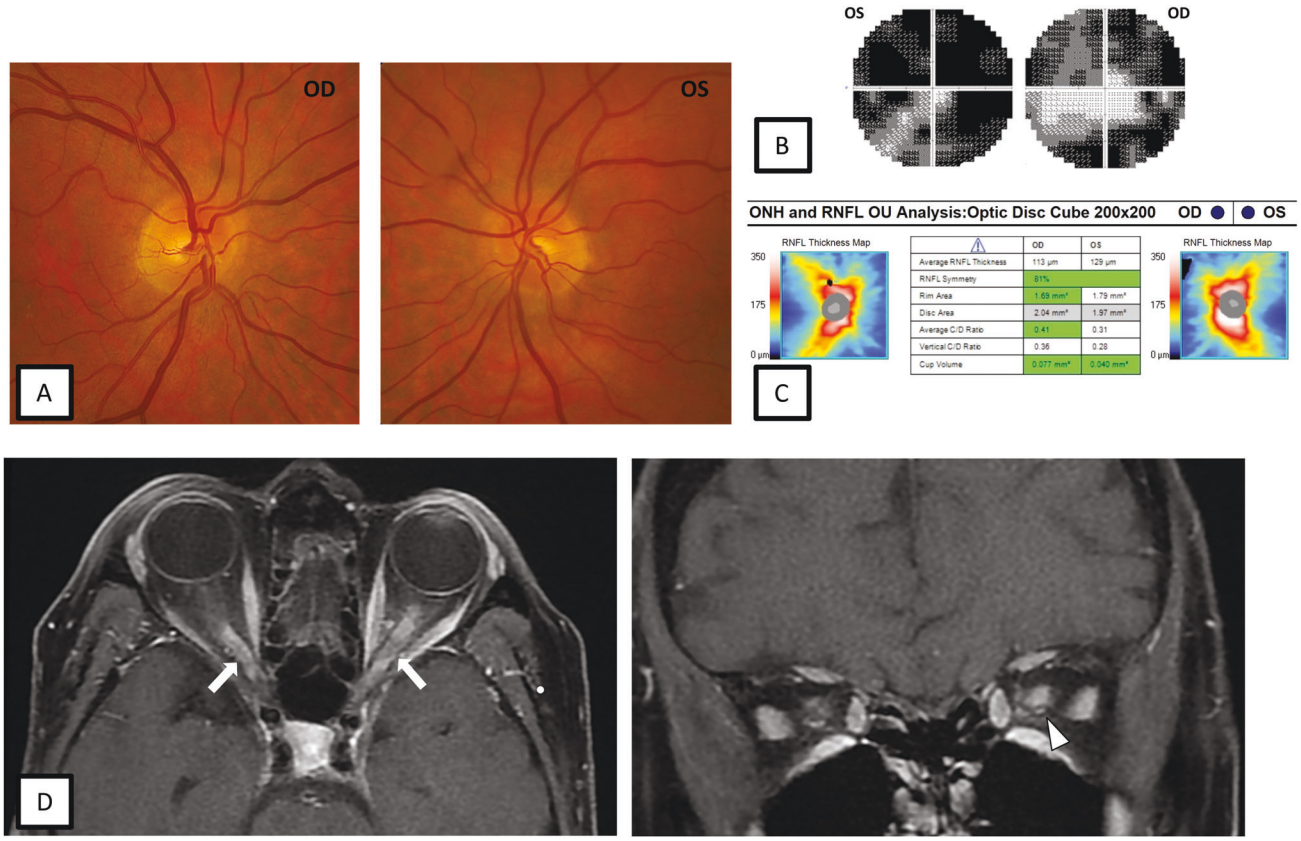

Fig. 2 67-year-old female with myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) optic neuritis. During the acute optic neuritis attack, fundus photographs show trace bilateral optic disc oedema (**A**). Automated visual field testing demonstrates bilateral generalised constriction (**B**). OCT shows mild bilateral pRNFL thickening (**C**). Axial and coronal, fat saturated T1-weighted post contrast MRI of the orbits shows bilateral longitudinally optic nerve enhancement (white arrows) with mild perineural enhancement on the left (white arrowhead) (**D**).

OCT during the acute phase of ON typically shows pRNFL thickening consistent with the optic disc oedema [86, 87]. A study comparing MOGAD-ON to MS-ON found that a pRNFL thickness of ≥175 µm had a 96% specificity of distinguishing MOGAD-ON from MS-ON [88]. Progressive optic atrophy with pRNFL and GCIPL thinning is seen in the chronic phase despite usually having significant recovery of vision [37]. Although the visual acuity loss at nadir is often as severe as NMOSD-ON, recurrent attacks are often required in MOGAD-ON to reach similar severe levels of pRNFL and GCIPL thinning seen in NMOSD [80, 89].

Neuroimaging. Optic nerve gadolinium enhancement is typically longitudinally extensive (≥50% of the optic nerve) (90% of cases) with evidence of perineural enhancement involving the optic nerve sheath and peribulbar fat (50% of cases) [67, 77] (Fig. 2). Chiasmal involvement occurs in ~15% of cases [76], which is often from a longitudinally extensive lesion involving the entire optic nerve, unlike NMOSD, which more commonly causes isolated chiasmal involvement [31]. Intracranial lesions can be present in both white and deep grey matter and are typically characterised as large T2-weighted hyperintensities with indistinct margins [90].

Serum and cerebrospinal fluid. The detection of MOG-IgG should be done in the serum and tested with a cell-based assay, which provides a specificity of about 98%. The sensitivity and specificity of cell-based assays in identifying MOG-IgG are significantly higher than other assays, such as ELISA [91, 92]. Despite an excellent specificity of 98%, a study looking at MOG-IgG testing over 2 years at a tertiary centre found that the positive predictive value was only 72%, which was even poorer for lower titres of 1:20 and 1:40. Higher titres of ≥1:100 had higher a positive predictive value [93]. Therefore, patients with a low MOG-IgG titre should be reviewed in detail to make sure the disease is compatible with a MOGAD phenotype.

While CSF testing for AQP4-IgG has been shown to be not clinically useful [44], the utility of MOG-IgG testing is still being evaluated. There may be some cases of MOGAD that are negative in the serum, but positive in the CSF [48, 94]. However, the specificity of CSF MOG-IgG testing is still being elucidated. Overall, testing the serum for MOG-IgG remains the gold standard, but CSF MOG-IgG testing can be considered in patients with a MOGAD phenotype who are seronegative for MOG-IgG.

During an acute attack, CSF can show mild pleocytosis (>5 cells/µl) in more than 50% of patients (less commonly with isolated ON clinical phenotype when compared to myelitis or multifocal CNS involvement) [95]. Marked pleocytosis of >50 cells/µl has been reported in about 30% of patients during acute attacks, which is an uncommon finding in comparison to MS [96]. Oligoclonal bands are seen in <20%, which can help differentiate MOGAD from MS.

Treatment

Acute MOGAD-ON is often very responsive to high-dose corticosteroids. In addition, retrospective studies have suggested that early treatment with corticosteroids may lead to better outcomes [51, 97]. Because some patients are both steroid responsive and steroid dependent, an oral prednisone taper over 1–2 months is often recommended [38]. However, it is important to note that spontaneous improvement without steroid treatment can occur as well [7, 97, 98]. In a small percentage of the patient

with significant visual loss and no improvement after the high-dose corticosteroid administration, additional treatment with plasma exchange should be considered [97].

Because only 50% of MOGAD patients will have relapsing disease and recovery from attacks is typically good, chronic immunotherapy is usually reserved for patients with relapsing disease or severe disease with significant residual disability after the first attack. Similar to NMOSD, MS medications have been shown to be ineffective for MOGAD [66, 99–101]. Many of the chronic therapies that have been employed in MOGAD have been extrapolated from the treatment of NMOSD, which includes rituximab, mycophenolate mofetil, and azathioprine [99–104]. Retrospective studies have suggested these are all partially beneficial in reducing relapses in MOGAD, but rituximab may be less effective in MOGAD than in NMOSD [105, 106]. Chronic prednisone has been shown to be very effective in preventing relapses in MOGAD, but its use can be limited because of the side effects of chronic steroid treatment [66]. Recent case series have suggested that targeting IL-6 with tocilizumab may be effective in patients with refractory MOGAD [107, 108]. Lastly, several retrospective studies have suggested that maintenance IVIG may be one of the most effective treatments for patients with relapsing MOGAD [73, 99, 109]. Future randomised clinical trials will be required to determine the optimal therapy for MOGAD. Upcoming randomised clinical trials for satralizumab (IL-6 inhibitor) and rozanolixizumab (neonatal Fc receptor inhibitor) are underway, which will hopefully lead to FDA approved medications for MOGAD and a better understanding of the disease.

CONCLUSIONS

The discovery of AQP4 and MOG antibodies have facilitated the recognition of NMOSD and MOGAD as separate neuroimmunological disease entities. Early diagnosis of each disorder is crucial as it impacts the course of treatment, clinical outcomes and morbidity. Because NMOSD-ON is associated with poor outcomes, early treatment with high-dose corticosteroids and plasma exchange are recommended for acute attacks. Patients with NMOSD also require long-term ISTs, such as rituximab or one of the recently FDA approved monoclonal antibody treatments. In contrast, MOGAD-ON is usually responsive to high-dose corticosteroids and has a generally favourable visual outcome. However, some cases are corticosteroid dependent or have relapsing disease and require maintenance therapy with either chronic prednisone or long-term immunotherapy, such as maintenance IVIG. The optimal long-term treatment for relapsing MOGAD will be elucidated in future randomised clinical trials.

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AUTHOR CONTRIBUTIONS

JJC and NM were involved in the study conception and design, review of the literature, drafting of the manuscript, and approval of the final version of the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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