Clearing the fog: MOG-antibody associated disease – an emerging clinical picture

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Myelin oligodendrocyte glycoprotein (MOG) is a membrane protein expressed on oligodendrocytes and on the outermost surface of the myelin sheath. Anti-MOG antibodies (MOG-Ab) recently emerged as potential biomarkers in a phenotypically-distinct group of patients with inflammatory demyelinating diseases (IDD). More described and defined forms of IDD include multiple sclerosis (MS) and aquaporin-4 (AQP4)-Ab associated neuromyelitis optica spectrum disorders (NMOSD), but a separate MOG-Ab-specific disease profile is now emerging.

Accurate diagnosis of IDD aetiology is essential as disease course and treatment options vary. Immunomodulatory therapies that work for MS have been shown not to benefit or have a detrimental impact in NMOSD, which is more effectively treated with immunosuppressant therapy.

Within the past month, four large case-series have been published detailing MOG-Ab disease. A clinical picture is now emerging that includes a female predominance and an average onset in the early to mid-thirties. Ramanathan et al published a retrospective case series of 59 (33 paediatric and 26 adult) patients with relapsing demyelination (≥2 episodes) and MOG-Ab seropositivity. Bilateral optic neuritis was the most common initial presentation and unilateral optic neuritis was the most frequent phenotype throughout disease. ADEM was prominent in children, while transverse myelitis was more common in adults. Demyelinating episodes in almost half the patients were preceded by an infectious prodrome, a finding shared by Mariotto et al, who published a cases series of 22 seropositive MOG-Ab patients, suggesting the potential role for an uknown pathogen acting as a self-mimic agent leading to direct damage and further activation of the immune system.

Both papers emphasise the vast diversity in phenotypes associated with MOG-Ab demyelination, and the overlap that may be present between patients with clinically definite MS and NMOSD. Possibly refining the picture slightly, Hamid et al published a retrospective case series of 34 MOG-Ab patients, comparing them with 100 patients with AQP4-Ab NMOSD in a tertiary neurological centre. Interestingly, five of the 34 patients with MOG-Ab (14.7%) had seizures compared with just 1 patient with AQP4-Ab (2-sided P<.008, Fisher test). All MOG-Ab with seizures had inflammatory cortical brain lesions on MRI, and 3 out of 5 presented with seizure as part of their index event.

Not only distinct at onset, Jurynczyk et al, who have published the largest case-series of MOG-Ab seropositive patients yet (252 patients acors at least 16 months), suggest MOG-Ab disease also runs a different disease course. Their paper suggests MOG-Ab prognosis is generally favourable; recovery from onset attack was full or good in 78%, and relapse rate at 16-months was 36%. After median disease duration of 28 months, the paper found that permanent disability occurred in about half of patients and more often involved bladder/bowel sphincter (28% and 20% respectively) and erectile function (21%) than vision (16%) or mobility (7%). When compared to previous work, NMOSD appears far more disabling – after 25 months from onset, disability (as defined by an Expanded Disability Status Scale score >6) occurred in 4% on MOG-Ab compared to 25% of those with AQP4-Ab disease.

All four papers comment on MRI appearance. The MRI Brain of MOG-Ab positive cases show nil abnormality, unspecific findings, optic nerve involvement, or other abnormalities resembling those observed in NMOSD and MS (though only a small percentage fulfill revised McDonald Criteria). Supporting previous data, Mariotto et al and Ramanathan et al note the prevalence of fewer brain lesions (< 2) in patients with MOG-Ab compared to seronegative ones. Both further agree that optic neuritis (unilateral/bilateral/both) and/or radiological involvement of the optic nerve appears to be the predominant finding in MOG-Ab cases. Spinal lesions, if present, were usually short. Further refining the diagnostic process, Mariotto et al analysed seropositive cases for MOG-IgG subtype. IgG1 was the most predominant subtype and results suggested that both anti-total IgG and IgG1 based assays could give comparable results. Due to the high sensitivity of IgG subclass test, IgG1 assay could even identify also patients below the cut-off for total IgG. MOG-Ab titres decrease in non-relapsing cases, regardless of level of recovery, and could fall below the cut-off, highlighting the importance of testing patients during the acute phase.

Regarding treatment, Jurynczyk et al showed that immunosuppression with steroids longer than 3 months following the onset attack was associated with a lower risk of a second relapse. Ramanathan et al suggest that patients with relapsing MOG-Ab disease are also steroid responsive, but frequently relapse with low doses or with rapid taper. Interestingly, some patients on maintenance low-dose prednisone alone had a relapse-free course, suggesting this may be effective in sustaining remission. A subgroup of MOG-Ab patients remained relapse free on no immunotherapy for a long time after initial steroid treatment with steroids, and had a relapse many years later.

Ramanthan et al. Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination.
J Neurol Neurosurg Psychiatry. 2018 Feb;89(2):127-37.

Marrioto et al. Clinical spectrum and IgG subclass analysis of anti-myelin oligodendrocyte glycoprotein antibody-associated syndromes: a multicenter study. Journal of Neurology. 2017 Dec;264(12):2420-30.

Hamid et al. Seizures and Encephalitis in Myelin Oligodendrocyte Glycoprotein IgG Disease vs Aquaporin 4 IgG Disease. JAMA Neurol. 2018 Jan;75(1):65-71.

Jurynczyk et al. Clinical presentation and prognosis in MOG-antibody disease: a UK study. Brain. 2017;140(12):3128-38.

A packed programme to ensure attendees, including social care staff, NHS workers, students, charities and anyone involved in rehabilitation get the most out of the day will include a client's story of their rehab experience with arts therapies.

Dr Jeanette Tamplin of the University of Melbourne will provide an introduction to the evolving field of the creative arts therapies within brain injury rehabilitation, covering current research and practice. Sarah O'Doherty and Rebecca O'Conner of the National Rehabilitation Hospital will present their Music Therapy Neuropsychology Assessment Model.

The day will also provide practical hands-on workshops, which allows delegates to experience, engage with and understand an art therapy process from a client's/patient's point of view. A special workshop brings together physiotherapy and music therapy approaches to introduce the neuro-scientific framework for motor symptoms in neurology and movement stimulation by music and rhythm.

Dr Wendy Magee from the US will showcase the MATADOC assessment for patients with prolonged disorders of consciousness (PDOC) that she and her colleagues pioneered.

The completion session will be a commissioner 'insight' piece about using the neurologic music therapy within a leading paediatric neuro rehab hospital.

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