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

Myelin oligodendrocyte glycoprotein (MOG) is a membrane protein expressed on oligoden-
drocytes 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 aqua-
porin-4 (AQP4)-Ab associated neuromyeli-
itis optica spectrum disorders (NMOSD), but a separate MOG-Ab-specific disease profile
is now emerging.

Accurate diagnosis of IDD aetiology is essen-
tial 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 immunosup-
pressant 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 (39 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 infec-
tious prodrome, a finding shared with Jurynczyk et al, who published a cases series of 22
seropositive MOG-Ab patients, suggesting the
potential role for an unknown 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 demyel-
ination, 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 initial
event. Not only distinct at onset, Jurynczyk et al,
who have published the largest case-series of
MOG-Ab seropositive patients yet (252 patients
across 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 appear-
ance. The MRI Brain of MOG-Ab positive cases
show nil abnormality, unspecific findings,
optic nerve involvement, or other abnor-
malities 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 ster-
oids 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. Interest-
ingly, 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.

Ramanathan et al. Clinical course, therapeutic
responses and outcomes in relapsing MOG anti-
body-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.

Hamid et al. Seizures and Encephalitis in Myelin
Oligodendrocyte Glycoprotein IgG Disease vs
Aquaporin 4 IgG Disease. JAMA Neurol. 2018

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nosis in MOG-antibody disease: a UK study. Brain.
2017;140(12):3128-38.