Optic neuritis and MOGAD

ZM Htet[1*] and E Tallantyre[2]

1. Department of Neurology, University Hospital of Wales, Heath Park, Cardiff, United Kingdom, CF14 4XN

2. Department of Neurology, Division of Psychological Medicine and Clinical Neuroscience, Cardiff University, University Hospital of Wales, Heath Park, Cardiff, UK, CF14 4XN.

*Corresponding author

Optic neuritis (ON) is one of the most common causes of monocular visual loss but has several mimics that result in relatively frequent misdiagnosis. In recent years there has been a growing recognition of the distinct entities of antibody-associated ON (associated with antibodies to myelin oligodendrocyte glycoprotein (MOG) or Aquaporin 4 (AQP4), which have implications for treatment. Some cases of ON represent the first symptom of multiple sclerosis, while other cases of ON are (para)infectious or associated with alternate causes of more widespread systemic inflammatory disease. The prevalence of these aetiologies varies according to age, geographical location, and ethnicity. Imaging of the optic nerve using MRI and OCT have continued to improve over recent years as well as becoming more available and has facilitated diagnosis. However, consensus definitions for classification and diagnostic criteria have been lacking. In this month's journal club, we present a consensus paper that proposes new criteria for the diagnosis of ON, and two papers reporting the clinical features of MOG-antibody associated disease.

Diagnosis and classification of optic neuritis

This paper describes consensus definitions for ON diagnosis, established by over 100 international experts using a Delphi process. The consensus recommended that diagnosis can be assigned as definite (typical clinical features of ON plus confirmation on one paraclinical test) or possible (positive paraclinical tests in context of a retrospective history compatible with ON). The paraclinical assessments used in the diagnostic criteria include MRI, OCT and antibodies/OCB, but exclude VEPs since these are influenced by central macular response and more useful in follow up or in considering differential diagnoses.

The same group proposes that cases of ON are considered according to 3 levels of evidence. Level 1 dichotomises autoimmune (typically relapsing) versus infectious or systemic (usually monophasic). They acknowledge that there is a small degree of overlap, but this dichotomy may help to guide on the appropriateness of long term immunosuppressants. Level 2 divides Autoimmune ON according to antibody serostatus e.g., MOG, AQP4, and evidence of wider neuroinflammatory disease e.g., multiple sclerosis. Isolated ON is divided into likely systemic versus (para-/post-) infectious or post-vaccine using anatomical clues, biomarkers, clinical features, and paraclinical tests. Level 3 collated free text suggestions of all contributors on subtypes of optic neuritis that may be considered in future iterations.

Comment: The authors have provided a system for classification that includes anatomical, clinical and paraclinical features to provide some insights into aetiology and treatment. However, they also highlight the need for additional biomarkers to predict risk of relapse. The panel did not reach consensus on certain aspects of treatment such as when to initiate

immunosuppression after corticosteroids for optic neuritis. Future treatment trials in a wider geographic range and age range are proposed.

Petzold A, et al. Lancet Neurol. 2022 Dec;21(12):1120-1134. doi: 10.1016/S1474-4422(22)00200-9. Epub 2022 Sep 27. PMID: 36179757.

Factors Associated With Relapse and Treatment of Myelin Oligodendrocyte Glycoprotein Antibody–Associated Disease in the United Kingdom

This retrospective cohort study was conducted amongst 276 patients with Myelin Oligodendrocyte Glycoprotein Antibody–Associated Disease (MOGAD) at 5 healthcare centres in the UK, collating data from January 1973 to March 2020. Risk of relapse and annualized relapse rate were evaluated according to differences in baseline features, including onset age, onset phenotype, and between.

Incident cases (diagnosed with antibodies against myelin oligodendrocyte glycoprotein before a second attack) were considered as a subgroup of the overall cohort. Time to next relapse among people with relapsing MOGAD was compared between the maintenance therapy subgroup and each first-line treatment group.

183 patients were considered to be incident cases and were representative of the overall cohort in terms of age at onset and sex. Female patients were predominant in the overall cohort (60%). The most common presentation of MOGAD in adults was optic neuritis (ON) (52%), whereas in childhood, 52% of onset attacks involved the brain/ brainstem and included acute disseminated encephalomyelitis (ADEM). In the incident group, the overall 8-year risk of relapse was 36.3%. TM at onset (either alone or in combination with ON or ADEM, brain, or brain stem) was associated with decreased risk of relapse compared with no TM, even when adjusted for whether or not patients received a follow-on dose of prednisolone after their incident event. Young adult age at onset (18-40 years) was associated with increased risk of relapse compared with both children, and also older adult age at onset (>40 years). First-line maintenance therapy was associated with decreased risk of relapse compared with the no-treatment group. Specifically, standard first-line immunosuppression or prednisolone were associated with a decrease in relapse-risk of almost one-half versus no treatment.

Comment: This is a relatively large study of a rare disease, has a long duration of follow-up and wide age range, enabling the authors to investigate relapse risk by age. However, small numbers of patients in some subgroups, and the complexity of multiple treatments in some patients, reduced the ability to separate out individual treatment effects and adjust for indication bias. This was countered by including covariates that may affect relapse risk and studying only first-line treatments. This study looked at time to next relapse only; recurrent relapses should be studied in future studies to assess association of treatment with long-term relapse rates.

Satukijchai C, et al. JAMA Netw Open. 2022 Jan 4;5(1):e2142780. doi: 10.1001/jamanetworkopen.2021.42780. Erratum in: JAMA Netw Open. 2022 Mar 1;5(3):e225056. PMID: 35006246; PMCID: PMC8749481.

MOG-IgG Among Participants in the Pediatric Optic Neuritis Prospective Outcomes Study

This paper reports outcomes of all 44 participants of the Paediatric Optic Neuritis Prospective Outcomes Study, which included children (aged 3-15 years) presenting with a first episode of ON within 2 weeks of symptom onset, who had either measurable visual acuity deficit, colour vision, optic disc swelling or field defect in the affected eye. Thirteen out of 44 had been tested for MOG IgG. Demographic and clinical characteristics at enrolment and visual outcomes after 6 months were compared between children with MOG-IgG–positive versus MOG-IgG–negative ON.

In the 7 out of 13 participants who were MOG positive, the majority were male, had bilateral disease and a younger age of onset compared to the 6 participants who were MOG antibody negative. Gender balance was equal in the 6 patients who were MOG negative and bilateral involvement was uncommon. Visual acuity at onset was also worse in the MOG positive group (Snellen equivalent worse than 20/800) versus the MOG-negative group (Snellen equivalent 20/50). However, after 6 months, the recovery of visual acuity was similar (Snellen equivalent of 20/25 in MOG-positive and 20/20 in MOG-negative).

Comment; The findings of this cohort are consistent with prior studies suggesting that ~30% of children with demyelinating disease are positive for MOG-IgG, with higher rates in association with paediatric ON and acute disseminated encephalomyelitis. This contrasts lower rates of MOG-IgG positive testing in adults with demyelinating disease (~5%). The study reports a small cohort, and those with bilateral ON were more likely to have had MOG antibody testing, introducing some potential for bias. Similar to previous studies, despite severe visual loss at presentation in people with MOG antibody ON, substantial visual recovery was observed after 6 months, indicating a good prognosis.

Chen JJ, et al. JAMA Ophthalmol. 2021 May 1;139(5):583-585. doi: 10.1001/jamaophthalmol.2021.0349. PMID: 33764379; PMCID: PMC7995133.

Summary: Optic neuritis is a common cause of visual loss in paediatric and adult populations. The aetiology and prognosis of optic neuritis can be informed by a range of paraclinical tests including MRI, OCT and antibodies for MOG and AQP4. Consensus recommendations are now available to guide the evaluation of patients with optic neuritis. MOG-associated optic neuritis appears to have an overall good prognosis in both adult and paediatric populations, although certain clinical features may be helpful in better predicting outcomes and guiding treatment.