

MOG antibody-associated diseases

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Markus Reindl, PhD
Kevin Rostasy, MD

Correspondence to
Dr. Reindl:
markus.reindl@i-med.ac.at

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In the past few years several studies have consistently reported the presence of high-titer serum IgG antibodies to conformational epitopes of the myelin oligodendrocyte glycoprotein (MOG) in predominantly pediatric patients with acquired demyelinating diseases.¹ Moreover, MOG antibodies seem not only to distinguish patients with clinically isolated syndromes or multiple sclerosis (MS) from monophasic or relapsing demyelinating events other than MS but also to be associated with a better prognosis. The inflammatory demyelinating disease subtypes in which MOG antibodies have been reported are monophasic acute disseminated encephalomyelitis (ADEM), ADEM followed by episodes of optic neuritis (ON), multiphasic demyelinating encephalomyelitis, and recurrent ON. Most recently, MOG antibodies have also been observed in aquaporin-4 (AQP4) antibody-negative neuromyelitis optica (NMO).¹⁻⁵

This finding has motivated authors Zamvil and Slavin to write the article “Does MOG Ig-positive AQP4-seronegative opticospinal inflammatory disease justify a diagnosis of NMO spectrum disorder?” published in this issue of *Neurology® Neuroimmunology & Neuroinflammation*.⁶ This article addresses an important issue with important implications for patients, treating physicians, and scientists involved in basic or clinical research. Despite the development of highly sensitive and specific assays for AQP4 antibodies, up to 40% of patients will not have AQP4 antibodies at initial presentation and during the course of NMO and related disorders such as monophasic or recurrent longitudinally extensive transverse myelitis (LETM) or ON.⁷ Studies suggest that AQP4 antibodies are even less frequent in children with NMO. Zamvil and Slavin first summarize the studies reporting the presence of a subpopulation of AQP4 antibody-negative NMO patients who presented with serum MOG antibodies. When comparing clinical and outcome data, these studies showed that patients with serum MOG antibodies do have a distinct clinical phenotype from AQP4 antibody-seropositive NMO that is characterized by fewer relapses, a better clinical outcome,

and a wider spectrum of MRI features, such as ADEM-like presentation. Further, Zamvil and Slavin describe histopathologic and neuroimmunologic differences between patients with MOG and AQP4 antibodies and emphasize the point that 2 different disease entities likely exist and that they should be clearly separated in view of the potential therapeutic and clinical implications. Whereas AQP4 antibody-associated NMO spectrum disorder (NMOSD) is an astrocytopathy, MOG antibody-associated inflammatory demyelinating diseases represent an oligodendropathy. The authors therefore suggest classifying MOG antibody-positive disease with a NMO-like presentation as a variant of opticospinal MS.

Although this possibility is intriguing, we would like to remind readers about the substantial literature on MOG antibodies and the fact that they are mainly found in pediatric cases with ADEM but are almost absent in adult patients with MS and other demyelinating diseases. In comparison to the larger number of pediatric cases with acquired demyelinating diseases associated with MOG antibodies, adult cases with NMO or opticospinal MS are rare, and some recent studies provided clear evidence that MOG antibody-positive ADEM cases have clinical presentations resembling NMO (e.g., LETM and recurrent ON).^{8,9} Therefore, MOG antibody-positive cases with NMO could also be cases with monophasic or multiphasic ADEM since ON and/or myelitis are typical clinical presentations of this disorder. It is also important to note that the initial clinical presentation of ADEM often suggests an autoimmune encephalitis (but without neuronal antibodies), and ADEM and NMO sometimes overlap with anti-NMDA receptor encephalitis.¹⁰

It therefore seems to be more appropriate to include these clinical presentations under the term “MOG antibody-associated diseases,” with a much broader clinical spectrum than AQP4 antibody-positive NMOSD. Further, these presentations are often monosymptomatic, with MOG antibodies seen only transiently during relapse. This might have consequences for

From the Clinical Department of Neurology (M.R.), Medical University of Innsbruck, Austria; and Division of Pediatric Neurology (K.R.), Children's Hospital Datteln, University Witten/Herdecke, Datteln, Germany.

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patient care, as mentioned by Zamvil and Slavin, since many of these patients may not need any immunomodulatory or immunosuppressive treatment after clinical recovery. However, before MOG antibodies are used for the laboratory diagnosis of neurologic diseases, the validation and improvement of currently used immunoassays is urgently needed (and already ongoing).

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