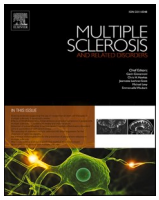
Multiple Sclerosis and Related Disorders 72 (2023) 104613

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard



Editorial

Multiple types of relapses in MOG antibody disease

Myelin oligodendrocyte glycoprotein antibody disease (MOGAD) is a relatively newly recognized entity among the autoimmune diseases of the central nervous system (CNS), defined as an inflammatory demyelinating attack in the context of circulating MOG antibodies (Banwell et al., 2023). Relapsing MOGAD occurs in ~50% of cases (Armangue et al., 2020; Cobo-Calvo et al., 2018; Jurynczyk et al., 2017; Waters et al., 2020) but varying definitions of what constitutes a relapse can affect the estimate. In related conditions such as multiple sclerosis and neuromyelitis optica spectrum disorder (NMOSD), a relapse is typically defined as new or worsening neurological symptoms that last for at least 24 hours and are not due to other factors such as infection or medication side effects (Cree et al., 2019; Inusah et al., 2010; Pittock et al., 2019; Yamamura et al., 2019). Attacks also need to be separated from the prior relapse by at least 30 days. The presence of new or active lesions on MRI may provide supportive evidence for diagnosing a relapse, but is not necessary. In MOGAD, there are three additional issues that need to be considered to develop a useful definition of relapse: clustered inflammatory events within the 30-day period, steroid withdrawal-triggered events, and variable timing of the MRI.

In the recently published "International MOGAD Panel proposed criteria," a relapse is defined as "a new clinical attack occurring more than 30 days following onset of a previous attack" (Banwell et al., 2023). However, this definition does not address the scenario of a patient having a new clinical attack within 30 days that is disseminated in space; for example, optic neuritis in the left eye followed 20 days later by optic neuritis in the right eye or optic neuritis occurring 20 days after transverse myelitis. Moreover, this also does not address the scenario of a patient having sequential attacks in the same location; for example, left optic neuritis that recovers and is followed 20 days later by a second episode of left optic neuritis. We propose the term *polyphasic relapse* to refer to a cluster of attacks occurring within 30 days, either sequentially in the same location or in another location in the CNS.

Corticosteroids such as prednisone are commonly used for the treatment of a MOGAD relapse. In some cases, patients are prescribed long-term corticosteroid treatment to manage their symptoms and prevent relapses, while in other cases, corticosteroids may be used only during acute relapses and gradually tapered off once symptoms have improved. MOGAD is different from NMOSD and MS in that there is high risk of relapse during or shortly after tapering off corticosteroids (Huda et al., 2021; Marignier et al., 2021; Ramanathan et al., 2018). We propose that a relapse that occurs within 4 weeks of corticosteroid cessation or taper should be considered a *triggered relapse*. A triggered relapse should be treated acutely to mitigate neurological damage and optimize long-term outcomes; however, a triggered relapse should not necessarily be interpreted as relapsing MOGAD.

Finally, MOGAD lesions tend to heal and pseudo-normalize on MRI (Fadda et al., 2021; Sechi et al., 2022, 2021a, 2021b). Thus, MRI scans performed too late may miss a recent lesion. Similarly, imaging too early may result in missing lesions that have not yet become inflamed enough to be visible on MRI. A negative MRI is not as specific in ruling out a MOGAD relapse as it is in NMOSD. We propose the term *MRI-negative relapse* to refer to a clinical presentation that is strongly supportive of a relapse but associated with a negative MRI. MRI-negative relapses should prompt acute treatment to try to improve symptoms, but whether they should be considered *bona fide* relapses and affect long-term treatment decisions should be determined on an individual patient basis.

The table below summarizes the types of relapses that can occur in MOGAD and proposed treatment options. Future research may elucidate the prognostic and therapeutic implications of the disparate types of relapses.

Type of Relapse	Definition	Treatment
Typical relapse	New or worsening neurological symptom(s) lasting more than 24 h occurring more than 30 days after the previous relapse, associated with an exam change and/or a new or enhancing MRI lesion	Acute treatment with corticosteroids or IVIG (2 g/kg ideal body weight), plus strong consideration for preventive therapy for at least one year.
Triggered relapse	New or worsening neurological symptom(s) lasting more than 24 h occurring within 4 weeks of corticosteroid taper or discontinuation, associated with an exam change and/or a new or enhancing MRI lesion.	Acute treatment with higher doses of corticosteroids, plus consideration of a prolonged corticosteroid taper or preferably a 3–6 month course of monthly IVIG (2 g/kg ideal body weight).
Polyphasic relapse	New or worsening neurological symptom(s) lasting more than 24 h occurring within 30 days of the previous relapse, associated with an exam change and/or a new or enhancing MRI lesion.	Acute treatment with higher doses of corticosteroids, plus consideration of a prolonged corticosteroid taper or preferably a 3–6 month course of monthly IVIG (2 g/kg ideal body weight).
MRI-negative relapse	New or worsening neurological symptom(s) lasting more than 24 h, associated with an exam change and a negative MRI.	Consideration of acute treatment with corticosteroids or a single dose of IVIG (2 g/kg ideal body weight), and individualized discussions about preventative treatment changes or initiation.

https://doi.org/10.1016/j.msard.2023.104613

Available online 12 March 2023

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