Myelin oligodendrocyte glycoprotein antibodies associated disease: how important are B cells?

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Myelin oligodendrocyte glycoprotein antibodies (MOG-Ab) are detected in 30% to 50% of children at first presentation of acquired demyelinating syndrome.¹ Children are less likely than adults to relapse, with about a third having a second clinical event.¹ But identification of MOG-Ab in those with presumed low relapse risk, such as children with acute disseminated encephalomyelitis or isolated optic neuritis, raises the question of whether we should change our paediatric protocols and treat them as neuromyelitis optica spectrum disorder (NMOSD).

Patients with MOG-Ab appears extremely steroid responsive, with many relapsing on steroid wean. In such cases, it is reasonable to add a corticosteroid-sparing agent with the usual precautions and monitoring.
The decision whether to treat children who clinically relapse is easier. In these children it is reasonable to add a corticosteroid-sparing agent, for example, maintenance therapy with monthly intravenous immunoglobulins\textsuperscript{2}. Other options include azathioprine and mycophenolate mofetil, but it may take months before these agents are fully effective. Rituximab, an anti-CD20 chimeric monoclonal antibody that results in B cell depletion, was initially used to treat B-cell neoplasms, but is now commonly used in autoimmune disorders, including inflammatory central nervous system disorders. In aquaporin-4 autoantibody NMOSD, rituximab was shown to reduce the number of relapses and disability.

Albassam et al\textsuperscript{3}. report 12 children with MOG-Ab associated diseases treated with rituximab.\textsuperscript{2} These children were part of a larger cohort of 39 children with MOG-Ab presenting over the study period of which only 16 (41\%) relapsed and remained persistently MOG-Ab positive at 12 weeks from onset. Median time from presentation to first relapse was 2.4 months and the clinical course was in keeping with previous reports. Three patients relapsed during the year after rituximab and by 2 years after rituximab induction, six patients had relapsed: two despite the absence of B cells, and four during B cell reconstitution. Among the eight patients whose MOG-Ab titres were retested, three became negative. Although none of the patients developed severe life-threatening events, side effects were common with leukopenia reported in 7(58.3\%) and serum immunoglobulin decrease in 5 (41.6\%).

The utility of MOG-Ab in making treatment decisions remains an area of active debate. A study of 197 adults with MOG-Ab observed that titres were higher at relapse than in remission.\textsuperscript{4} In a large paediatric study, high MOG-Ab titres (≥1:1280) predicted a recurrent non-multiple sclerosis course with 46\% sensitivity and 86\% specificity.\textsuperscript{5} Overall, patients may remain seropositive for years, despite having a monophasic disease. Although the risk of
relapse is lower if patients become seronegative, seronegative patients may still relapse (and become seropositive at the time of relapse).\textsuperscript{1}

Albassam et al.’s\textsuperscript{3} report adds to a subgroup of patients with MOG-Ab associated diseases who relapsed on rituximab despite B cell depletion, suggesting that the pathobiology of the disease may be different in these patients.\textsuperscript{2} Alternatively, treatment failure might be explained by antibody-producing cells in the central nervous system, despite peripheral B cell depletion. Thus, further studies, particularly of treatment-resistant patients, may provide insight into this complex disease.

REFERENCES