RESEARCH LETTER

Coexistence of Myelin Oligodendrocyte Glycoprotein and Aquaporin-4 Antibodies in Adult and Pediatric Patients

Myelin oligodendrocyte glycoprotein (MOG)–IgG is a biomarker associated with central nervous system–demyelinating disorders termed MOG-IgG–associated disorders. These disorders have overlapping clinical features, including optic neuritis and myelitis, with aquaporin-4 (AQP4)–IgG-positive neuromyelitis optica spectrum disorders. These disorders are hypothesized to be biologically distinct; AQP4-IgG–positive neuromyelitis optica spectrum disorders are autoimmune astrocytopathies, whereas MOG-IgG-associated disorders are postulated to be autoimmune oligodendrocytopathies.1 Despite their immunopathogenic differences, there are rare reports of patients with dual positivity of MOG-IgG and AQP4-IgG.2,3 We aimed to determine the frequency, sex ratio, and coexistence of glial antibodies (AQP4-IgG and MOG-IgG) in adult and children undergoing evaluation for suspected central nervous system–demyelinating diseases.

Methods | This is a retrospective cohort study approved by the Mayo Clinic institutional review board and ethics committee with a waiver of informed consent because of the restricted, deidentified nature of the data used. All patients who had serum samples tested for AQP4-IgG and MOG-IgG from October 2017 to May 2019 were evaluated using a clinically validated flow cytometric assay (BD FACSCanto II [BD Biosciences]).4 All samples were repeated to confirm positivity. We have used basic demographic data (age and sex) provided through the clinical testing request forms. We used χ² tests to compare the proportions of female and male individuals within the antibody-positive groups. All tests were 2-sided, and P values less than .05 were considered significant. The statistical software R version 3.5.1 (R Foundation for Statistical Computing) was used.

Results | Over a 20-month period, 15 598 patients (1862 children [<18 years] and 13 736 adults) were tested for both AQP4-IgG and MOG-IgG (Figure 1). In 1291 patients (8.3%), MOG-IgG was detected; AQP4-IgG was detected in 387 patients (2.3%). Of the adults, 899 (6.5%) were MOG-IgG positive, and 351 (2.6%) were AQP4-IgG positive (Figure 2A). Of the adults with MOG-IgG, 546 were female (60.7%); 303 of the adults with AQP4-IgG (86.3%) were female (P < .001) (Figure 2C). Of the children, 392 were MOG-IgG positive (21.1%), and 36 were AQP4-IgG positive (1.9%) (Figure 2B). Of all children with MOG-IgG, 214 were female (54.6%) vs 21 (58.3%) of all children with AQP4-IgG (P = .79) (Figure 2D).

In the subgroup of patients with serum testing completed on the same sample (n = 8 276), similar proportions of antibody positivity were observed as in those with separate samples tested (Figure I). The median serum titers for the cohort were 1:10 000 (range, 1:5 to 1:100 000) for AQP4-IgG and 1:100 (range, 1:20 to 1:100 000) for MOG-IgG (Figure 2E and F). The adult and children subgroups had the same median titers.

Of 15 598 patients, 10 patients (0.06%) had dual positivity. All 10 patients with dual positivity had high-titer AQP4-IgG (median, 1:10 000; range, 1:100 to 1:100 000) and low-titer MOG-IgG (median, 1:100; range, 1:10 to 1:100 000) (Figure 2G and H). All of the patients with dual positivity were adults.
(median age, 47 years [range, 30-61 years]), and 9 of the 10 patients were female (90%).

Conclusions | In this large cohort of patients undergoing evaluation for suspected central demyelinating diseases, MOG-IgG were detected almost 3 times as often as AQP4-IgG in adults; in children, MOG-IgG was detected more than 11 times as often as AQP4-IgG. In this study, MOG-IgG and AQP4-IgG rarely coexisted in a single patient (0.06%).

We have confirmed the previously described female predominance in adults who are positive for AQP4-IgG.5 Furthermore, we have demonstrated that there is a distinct differ-
ence in the female predominance in adults with AQP4-IgG compared with MOG-IgG. Together, these sex differences and the greater detection of MOG-IgG, especially in children, suggest that central demyelinating diseases associated with these biomarkers may have different drivers of autoimmunity.

The rare coexistence of these 2 antibody biomarkers also points to distinct immunopathogeneses of these diseases. It has been postulated that MOG-IgG is an epiphenomenon, occurring with exposure of antigen in the AQP4-IgG disease. However, the rarity of dual positivity is this large cohort is evidence against an epiphenomenon. All individuals with dual positivity had high titers of AQP4-IgG and low titers of MOG-IgG, suggesting the disease phenotype may be more compatible with AQP4-IgG-positive neuromyelitis optica spectrum disorders.

These findings suggest that MOG-IgG may occur more frequently than AQP4-IgG in patients tested for central demyelinating diseases, particularly in children. However, because the study population was derived from patients who had undergone a central demyelinating disease serological evaluation, these data should not be interpreted as representing sero-prevalence in the general population. Further population-based studies are required to determine the prevalence and incidence of MOG-IgG–associated disorders. That MOG-IgG and AQP4-IgG rarely coexist highlights the immunopathogenic distinction of these biomarkers.

Amy Kunchok, MBBS, MMed
John J. Chen, MD, PhD
Andrew McKeon, MD
John R. Mills, PhD
Eoin P. Flanagan, MB, BCh
Sean J. Pittcock, MD

Author Affiliations: Department of Neurology, Mayo Clinic, Rochester, Minnesota (Kunchok, Chen, McKeon, Flanagan, Pittcock); Department Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota (Kunchok, McKeon, Mills, Flanagan, Pittcock); Center for Multiple Sclerosis and Autoimmune Neurology, Mayo Clinic, Rochester, Minnesota (Kunchok, Chen, McKeon, Mills, Flanagan, Pittcock); Department of Ophthalmology, Mayo Clinic, Rochester, Minnesota (Chen).

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Corresponding Author: Sean J. Pittcock, MD, Department of Neurology, Mayo Clinic, 200 First St SW, Rochester, MN 55905-0001 (pittcock.sean@mayo.edu).

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Perception of Dementia Risk and Preventive Actions Among US Adults Aged 50 to 64 Years

Disease-preventing or disease-modifying treatments do not exist for Alzheimer disease or other dementias. Adults may be unaware of strategies to reduce their risk1 and resort to marketed but ineffective options, such as ginkgo biloba or vitamin E. While these so-called treatments are relatively inexpensive, new preventive therapies may not be. Thus, individuals overestimating their risk of developing dementia could lead to inappropriate use and excessive costs.2 This analysis explores how adults aged 50 to 64 years estimate their lifetime risk of dementia and the risk-reducing strategies they pursue.

Methods | The University of Michigan National Poll on Healthy Aging (NPHA) is a nationally representative survey of adults ages 50 to 80 years, sponsored by AARP and Michigan Medicine. The NPHA uses KnowledgePanel (Ipsos Public Affairs LLC), a probability-based panel of the civilian, noninstitutionalized US population. This survey was fielded in October 2018; questions for this analysis were asked of respondents aged 50 to 64 years. The University of Michigan institutional review board reviewed this study and deemed it exempt from human subjects review because it was a study of deidentified respondents. The requirement for informed consent was therefore waived.

Along with demographic information and self-reported health status, respondents were asked, “How likely are you to develop dementia during your lifetime?” (with the possible answers being “very likely,” “somewhat likely,” and “not likely”); “Have you ever discussed ways to prevent dementia with your...