Neuromyelitis Optica Spectrum Disorders With Aquaporin-4 and Myelin-Oligodendrocyte Glycoprotein Antibodies: A Comparative Study

Joanna Kitley, BMBS; Patrick Waters, PhD; Mark Woodhall, PhD; M. Isabel Leite, DPhil; Andrew Murchison, BM BCh; Jithin George, BMBS; Wilhelm Küker, FRCR; Saleel Chandratre, FRCPCH; Angela Vincent, FRS; Jacqueline Palace, DM

**IMPORTANCE** Most patients with neuromyelitis optica (NMO) and many with NMO spectrum disorder have autoantibodies against aquaporin-4 (AQP4-Abs), but recently, myelin-oligodendrocyte glycoprotein antibodies (MOG-Abs) have been found in some patients. Here, we showed that patients with NMO/NMOSD with MOG-Abs demonstrate differences when compared with patients with AQP4-Abs.

**OBJECTIVE** To characterize the features of patients with NMO/NMOSD with MOG-Abs and compare them with patients with AQP4-Ab–positive NMO/NMOSD.

**DESIGN, SETTING, AND PARTICIPANTS** This observational study was conducted at a single UK specialist center for NMO. Patients with a first demyelinating event between January 1, 2010, and April 1, 2013, seen within the Oxford NMO service and who tested positive for MOG-Abs or AQP4-Abs were included in the study.

**EXPOSURE** Cell-based assays using C-terminal–truncated human MOG and full-length M23-AQP4 were used to test patient serum samples for AQP4-Abs and MOG-Abs.

**MAIN OUTCOMES AND MEASURES** Demographic, clinical, and disability data, and magnetic resonance imaging findings.

**RESULTS** Twenty AQP4-Ab–positive patients and 9 MOG-Ab–positive patients were identified. Most patients in both groups were white. Ninety percent of AQP4-Ab–positive patients but only 44% MOG-Ab–positive patients were females (P = .02) with a trend toward older age at disease onset in AQP4-Ab–positive patients (44.9 vs 32.3 years; P = .05). MOG-Ab–positive patients more frequently presented with simultaneous/sequential optic neuritis and myelitis (44% vs 0%; P = .005). Onset episode severity did not differ between the 2 groups, but patients with MOG-Abs had better outcomes from the onset episode, with better recovery Expanded Disability Status Scale scores and a lower risk for visual and motor disability. Myelin-oligodendrocyte glycoprotein antibody–positive patients were more likely to have conus involvement on spinal magnetic resonance imaging (75% vs 17%; P = .02) and involvement of deep gray nuclei on brain magnetic resonance imaging (P = .03). Cerebrospinal fluid characteristics were similar in the 2 groups. A higher proportion of AQP4-Ab–positive patients relapsed (40% vs 0%; P = .03) despite similar follow-up durations.

**CONCLUSIONS AND RELEVANCE** Despite the fact that patients with MOG-Abs can fulfill the diagnostic criteria for NMO, there are differences when compared with those with AQP4-Abs. These include a higher proportion of males, younger age, and greater likelihood of involvement of the conus and deep gray matter structures on imaging. Additionally, patients with MOG-Abs had more favorable outcomes. Patients with AQP4-Ab-negative NMO/NMOSD should be tested for MOG-Abs.

Published online January 13, 2014.
Neuromyelitis optica (NMO) is a severe inflammatory disorder of the central nervous system (CNS), which predominantly affects the optic nerves and spinal cord. Limited forms of the disease are known as NMO spectrum disorder (NMOSD). Most patients with NMO and many with NMOSD have autoantibodies against the water channel aquaporin-4 (AQP4-Ab), which are thought to be pathogenic. However, some patients are seronegative for AQP4-Abs; the lack of a biomarker makes diagnosis and management of these patients difficult. Many clinicians perceive these patients to be similar to those with AQP4-Ab and manage them in the same way. However, when sensitive AQP4-Ab assays are used to define seropositivity, there do appear to be differences between patients with and without AQP4-Abs, and it is possible that patients with seronegative NMO have different etiopathogenic mechanisms.

Recently, we and others have shown that some AQP4-Ab-seronegative patients have antibodies against myelin-oligodendrocyte glycoprotein (MOG-Abs). Here, we describe the clinical and paraclinical characteristics of patients with NMO/NMOSD with MOG-Abs who have been under our care and follow-up with prospective clinical examination and investigations. We demonstrate differences when compared with patients with NMO/NMOSD with AQP4-Abs.

Methods

Ethical approval was obtained from the Oxfordshire Regional Ethics Committee and patients provided written consent. Since January 2010, data on all patients seen within the Oxford clinical NMO service have been entered prospectively into a clinical database and patient serum samples routinely tested for AQP4-Abs and MOG-Abs. The database was searched for all patients with a first demyelinating event between January 1, 2010, and April 1, 2013, who were positive for AQP4-Abs or MOG-Abs. Positivity for AQP4-Abs and MOG-Abs was determined by visualization of binding to human embryonic kidney cells transiently transfected with full-length M23-AQP4 or the extracellular and transmembrane domains of human MOG, as described previously. Myelin-oligodendrocyte glycoprotein cDNA was courtesy of Kevin O’Connor, PhD, (Yale University). Samples were analyzed blind to clinical details and other autoantibody results. All patients were followed up prospectively, and clinical examination, magnetic resonance imaging (MRI) findings, evoked potentials (EPs), cerebrospinal fluid (CSF) results, and ophthalmological assessments recorded on the database. The Expanded Disability Status Scale (EDSS) scoring system was used to estimate disability during and after the onset episode. The nadir EDSS score was taken as the maximum EDSS score during the acute episode, and recovery EDSS scores were taken at last follow-up prior to any further episodes. Disability outcomes from the onset episode were defined as the inability to walk 100 m unaided for motor disability and Snellen visual acuity of worse than 6/36 for visual disability. Relapses were defined as new neurological symptoms lasting at least 24 hours and accompanied by new neurological examination findings and/or new lesions on MRI. Spinal cord MRI scans were evaluated for lesions with no MS features. Lesions were classified as NMO-like when surrounding the fourth ventricle, hypothalamus, or aqueduct with or without small deep white matter lesions, as previously described, and scans with lesions in deep gray nuclei or fluffy white matter lesions of similar age were classed as ADEM-like. Spinal cord MRI scans were evaluated for lesion length, axial and sagittal location, and the presence of cord edema, hypointensity on T1-weighted imaging, and postcontrast enhancement.

The features of AQP4-Ab-positive patients were compared with those of MOG-Ab-positive patients. Statistical analysis was performed using GraphPad Prism version 4. The Mann-Whitney U test was used to compare continuous variables and the Fisher exact test was used to compare frequencies. Statistical significance was set at $P < .05$.

Results

Forty-six patients were identified with a first CNS demyelinating episode between January 1, 2010, and April 1, 2013. Of these, 20 were AQP4-Ab positive and 9 were MOG-Ab positive, and they were included in the study. No patients have been identified as positive for both MOG-Abs and AQP4-Abs within this cohort or as part of the UK screening service. Three of the MOG-Ab-positive patients have been described previously.

Demographic Features in AQP4-Ab–Positive and MOG-Ab–Positive Patients With NMO/NMOSD

Table 1 summarizes the demographic and clinical features of the patients. The median follow-up duration was similar in the 2 groups. Both groups comprised predominantly white patients but there was a significantly higher proportion of males in the MOG-Ab–positive group and a trend toward AQP4-Ab–positive patients being older at disease onset than MOG-Ab–positive patients. Nine AQP4-Ab–positive patients had evidence of other autoimmunity (6 had coexisting autoimmune disorders with or without autoantibodies and an additional 3 were positive for antinuclear antibodies). One MOG-Ab–positive patient had hypothyroidism but no other MOG-Ab-positive patients had autoimmune disorders or other autoantibodies.

Features of the Onset Episode

Patients who were MOG-Ab positive were more likely to present with simultaneous (within 1 week) or rapidly sequential...
(within 1 month) optic neuritis (ON) and transverse myelitis (TM) \((P = .005)\). No AQP4-Ab–positive patients presented with both ON and TM, and most presented with either ON or TM. Thus, 4 MOG-Ab–positive patients (44%) but no AQP4-Ab–positive patients fulfilled the clinical diagnostic criteria for NMO11 at disease onset. Onset episodes in both groups tended to be severe, and the median EDSS score at nadir did not differ between the 2 groups.

Four of 9 MOG-Ab–positive patients and 6 of 20 AQP4-Ab–positive patients had optic nerve involvement as part of the onset episode; the proportion of these patients with bilateral ON was higher in the MOG-Ab–positive group (75% vs 33%), although because of the small numbers, this difference was not significant \((P = .52)\). All affected eyes in both groups had evidence of optic disc swelling on fundoscopy (no documentation was available for 1 patient in each group). Optic neuritis in both groups tended to be severe, with visual acuities of less than 6/60 at nadir in at least 1 affected eye in all MOG-Ab–positive patients and 5 of 6 AQP4-Ab–positive patients with optic nerve involvement. Overall, 5 of 7 affected eyes in the MOG-Ab–positive group and 5 of 8 affected eyes in the AQP4-Ab–positive group had acuities of less than 6/60.

Twelve of 20 AQP4-Ab–positive patients and all 9 MOG-Ab–positive patients had spinal cord involvement at disease onset. The median EDSS score at nadir in these patients did not differ between AQP4-Ab–positive and MOG-Ab–positive patients \((7.0 \text{ vs } 6.0)\). One notable difference between myelitis episodes in the 2 groups was that there was a trend toward bladder involvement as the first neurological symptom being more common in MOG-Ab–positive patients \((33\% \text{ vs } 0\%\); \(P = .06)\), whereas sphincter disturbance occurred after development of sensory and motor deficits in AQP4-Ab–positive patients with myelitis.

### Treatment Details and Disability Outcomes

A high proportion of patients in each group received corticosteroids in the acute setting \((100\% \text{ MOG-Ab positive vs } 75\% \text{ AQP4-Ab positive; } P = .15)\) and similar proportions additionally underwent plasma exchange \((PLEX)\) \((33\% \text{ vs } 25\%; P = .68)\). A standard regime of intravenous methylprednisolone, 1g, daily for 3 days, extending to 5 days if no clinical improvement occurred, was used (with the exception of 1 patient in each group treated with oral methylprednisolone, 500 mg, daily for 5 days). Plasma exchange was then instituted if patients showed no or limited clinical improvement within 7 days, with 5 exchanges performed over a period of 5 to 7 days. Intravenous corticosteroids were followed by a tapering course of oral prednisolone, starting at 60 mg daily. AQP4-Ab–positive patients were maintained indefinitely on oral prednisolone at 10 to 20 mg daily with azathioprine or methotrexate, while in MOG-Ab–positive patients, corticosteroids were withdrawn after several months.

The median EDSS score at recovery was significantly better in the MOG-Ab–positive group \((P = .01)\) and the median change in EDSS score was significantly greater in the MOG-Ab–positive patients \((P < .001; \text{ Figure 1})\). The 5 AQP4-Ab–positive patients who were not treated acutely with steroids tended to have relatively mild episodes and all made a full \((\text{EDSS score, } 0; n = 4)\) or good \((\text{EDSS score, } 2; n = 1)\) recovery and thus these untreated patients did not skew the recovery EDSS scores.

Six AQP4-Ab–positive patients but no MOG-Ab–positive patients were left motor disabled after the onset episode, and 1 additional AQP4-Ab–positive patient became wheelchair dependent. Of those with spinal cord involvement at the onset episode, patients in the AQP4-Ab–positive group were significantly more likely to be left motor disabled than the MOG-Ab–positive group \((58\% \text{ vs } 0\%\); \(P = .007)\). Two of 6 AQP4-Ab–positive patients developed additional MS during follow-up, whereas none of the MOG-Ab–positive patients developed additional MS.

### Table I. Comparison of Clinical Features in Patients With MOG-Ab–Positive and AQP4-Ab–Positive NMO/NMOSD

<table>
<thead>
<tr>
<th>Feature</th>
<th>MOG-Ab Positive ((n = 9))</th>
<th>AQP4-Ab Positive ((n = 20))</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up, median (range), mo</td>
<td>18.00 (2.2-38.5)</td>
<td>20.47 (5.0-36.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Female, %</td>
<td>44</td>
<td>90</td>
<td>.02</td>
</tr>
<tr>
<td>White, %</td>
<td>78</td>
<td>60</td>
<td>NS</td>
</tr>
<tr>
<td>Age at onset, mean (SD), y</td>
<td>32.29 (17.1)</td>
<td>44.86 (14.8)</td>
<td>.05</td>
</tr>
<tr>
<td>Coexisting autoimmunity, No. (%)</td>
<td>1 (11)</td>
<td>9 (45)</td>
<td>NS</td>
</tr>
<tr>
<td>Onset episode, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ON only</td>
<td>0 (0)</td>
<td>6 (30)</td>
<td>NS</td>
</tr>
<tr>
<td>TM only</td>
<td>3 (33)</td>
<td>12 (60)</td>
<td>NS</td>
</tr>
<tr>
<td>ON+TM</td>
<td>4 (44)</td>
<td>0 (0)</td>
<td>.005</td>
</tr>
<tr>
<td>Brain/brainstem+TM</td>
<td>2 (22)</td>
<td>0 (0)</td>
<td>NS</td>
</tr>
<tr>
<td>Brain only</td>
<td>0 (0)</td>
<td>2 (10)</td>
<td>NS</td>
</tr>
<tr>
<td>Nadir EDSS score, median (range)</td>
<td>6.0 (4-8.5)</td>
<td>5.5 (1-8.5)</td>
<td>NS</td>
</tr>
<tr>
<td>EDSS score at best recovery, median (range)</td>
<td>0 (0-2.5)</td>
<td>4.0 (0-8)</td>
<td>.01</td>
</tr>
<tr>
<td>Patients with TM at onset left motor disabled, No. (%)</td>
<td>0 (0)</td>
<td>7 (58)</td>
<td>.007</td>
</tr>
<tr>
<td>Patients with ON at onset left visually disabled, No. (%)</td>
<td>0 (0)</td>
<td>2 (33)</td>
<td>NS</td>
</tr>
<tr>
<td>Subsequent relapse, No. (%)</td>
<td>0 (0)</td>
<td>8 (40)</td>
<td>.03</td>
</tr>
</tbody>
</table>

Abbreviations: Ab, antibody; AQP4, aquaporin-4; EDSS, Expanded Disability Status Scale; MOG, myelin-oligodendrocyte glycoprotein; NMO, neuromyelitis optica; NS, not significant; ON, optic neuritis; SD, spectrum disorder; TM, transverse myelitis.
positive patients (33%) with ON but none of 4 MOG-Ab–positive patients were left visually disabled in 1 eye after the onset episode.

Eighty-nine percent of MOG-Ab–positive patients and 70% of AQP4-Ab–positive patients were started treatment with immunosuppression at or shortly after disease onset. All AQP4-Ab–positive patients ultimately started long-term immunosuppression (range, 0-17 months) and all were taking treatment at last follow-up, whereas immunosuppression was withdrawn gradually over 9 to 24 months in 6 of the MOG-Ab patients and 3 remain on low-dose tapering steroids. Despite this, a greater proportion of AQP4-Ab–positive patients relapsed during the follow-up (40% vs 0%; \( P = .03 \)).

**Brain and Spinal Cord MRI Findings**

Twenty-one patients (12 AQP4-Ab positive and 9 MOG-Ab positive) had clinical evidence of spinal cord involvement at presentation. One AQP4-Ab–positive patient with sensory cord symptoms but normal neurological examination had a normal MRI findings. The spinal cord MRI features of the remaining patients are shown in Table 2. The conus was significantly more likely to be involved in patients with MOG-Ab (\( P = .02 \); Figure 2) but there were no differences in terms of central gray matter involvement, presence of cord edema, postcontrast enhancement, or T1 hypointensity in the 2 groups. And the median length of the longest lesion did not differ between AQP4-Ab–positive and MOG-Ab–positive patients. There was complete resolution of T2 high signal in 6 of 7 MOG-Ab–positive patients who had follow-up imaging (performed after median follow-up of 9.5 months; range, 5-17 months) with no evidence of cord atrophy. One patient with follow-up imaging at 3 months had mild residual signal abnormality. By contrast, 3 of 4 AQP4-Ab–positive patients with follow-up cord imaging (prior to a second episode) showed residual T2 hyperintensity (performed after median follow-up of 14.5 months; range, 7-16 months); none had atrophy.

Twenty-seven patients (18 AQP4-Ab positive and 9 MOG-Ab positive) had an MRI brain scan performed during the acute episode (Table 2). Patients with MOG-Ab were significantly more likely to have a scan classified as ADEM-like (44%) than patients with AQP4-Ab (0%); consequently, deep gray matter lesions were significantly more common in MOG-Ab–positive patients (\( P = .02 \)). Surprisingly, lesions adjacent to the fourth ventricle were also more common in MOG-Ab–positive patients. All 6 MOG-Ab–positive patients with abnormal brain scans at onset had follow-up imaging performed following clinical recovery and 5 showed complete resolution of all abnormalities (after median follow-up 7 months; range, 5-15 months). The patient with residual signal change had follow-up imaging performed only 3 months following the acute episode. By contrast, when follow-up imaging was performed (prior to a second episode) in AQP4-Ab disease, brain abnormalities persisted (n = 4; performed after median follow-up of 14.5 months; range, 7-16 months).

**CSF Findings and Evoked Potentials**

Cerebrospinal fluid examination was performed during the acute episode in 12 AQP4-Ab–positive (60%) and 9 MOG-Ab–positive (100%) patients, and findings were similar in the 2 groups (Table 2).

Visual evoked potentials (VEPs) were performed acutely in 6 MOG-Ab–positive patients (66%) and 10 of those with AQP4-Ab (50%). Only affected eyes had delayed VEPs in those with MOG-Ab, whereas 2 AQP4-Ab–positive patients had delayed VEPs in 3 clinically unaffected eyes. Three of 4 MOG-Ab–positive patients who had VEPs performed following clinical recovery returned to normal and the fourth markedly improved (performed after median follow-up of 13.5 months; range, 6-17 months). Follow-up VEPs in the AQP4-Ab–positive patients were not performed. While sensory EPs were not generally performed in the acute setting, 5 MOG-Ab–positive patients had sensory EPs performed following clinical recovery and all findings were normal.

**MOG-Ab and AQP4-Ab Serology**

All patients had repeat AQP4-Ab and MOG-Ab testing following recovery from the acute episode. Five MOG-Ab-
positive (56%) and 3 AQP4-Ab–positive (15%) patients have seroconverted, with no detectable antibodies during disease remission.

### MOG-Ab– and AQP4-Ab–Negative Patients

Seventeen patients were negative for both AQP4-Abs and MOG-Abs. These patients were predominantly white (82%), with an almost equal sex ratio (53% were males and 47% females), and the median age at presentation was 35.9 years (range, 17.6-75.6 years). Most (n = 9; 53%) presented with longitudinally extensive transverse myelitis, 5 (29%) presented with severe ON, and 3 (18%) presented with simultaneous or rapidly sequential LETM and ON. Two patients with LETM became wheelchair dependent and 2 presenting with simultaneous ON and TM were left with bilateral visual disability after the onset episode; all were monophasic. Thirteen patients (76%) experienced a single episode, and 4 (24%) experienced a relapsing-remitting course (episodes of both ON and TM) over a median follow-up period of 13.1 months (range, 1.9-38.4 months). Of note, no seronegative patients with a relapsing NMO phenotype had reached the visual or motor disability end points after median follow-up of 23.2 months (range, 9.7-28.8 months).

### Discussion

The discovery of AQP4-Ab has revolutionized NMO/NMOSD but there are patients fulfilling diagnostic criteria without the antibodies. We have characterized a MOG-Ab phenotype to account for some cases of AQP4-Ab–seronegative NMO/NMOSD and in patients with new-onset NMO/NMOSD seen within the Oxford clinical NMO service over a 3-year period, patients with MOG-Abs accounted for nearly one-third of antibody-positive cases (9 patients with MOG-Abs and 20 patients with AQP4-Abs identified). Although nearly half of the MOG-Ab–positive patients fulfilled the 2006 diagnostic criteria for NMO, there were differences between patients with MOG-Abs and AQP4-Abs.
Differences between patients with monophasic NMO and those with recurrent episodes were noted even before the discovery of NMO IgG, with observations that monophasic patients were younger, had equal sex ratios, more commonly presented with simultaneous ON and TM, and had better outcomes.12 Many of the characteristics of patients with monophasic NMO described historically are reflected in our current observations of MOG-Ab–positive patients, and MOG-Abs appear to be an important biomarker in monophasic NMO.

Myelin-oligodendrocyte glycoprotein is a CNS-specific myelin protein that provides an accessible target for autoantibodies in the extracellular space. With the exception of early studies using assays detecting antibodies to denatured MOG, MOG-Abs have largely been reported in childhood demyelinating disorders particularly ADEM.13-17 However, recently, we and others reported MOG-Abs in adult patients with NMO/NMOSD.6,7 In the current study, 4 of 9 MOG-Ab–positive patients had Devic disease as it was originally described,18 with simultaneous or sequential ON and TM, and some had ADEM-like brain lesions and/or mild encephalopathy. These findings suggest that MOG-Ab NMO/NMOSD may account for some cases of Devic disease as it was originally described and that MOG-Ab–positive NMO/NMOSD may be an adult version of the childhood MOG-Ab–associated ADEM reported by others.

Despite the fact that nearly half of MOG-Ab–positive patients fulfilled NMO diagnostic criteria at onset, the MOG-Ab–positive patients showed differences compared with patients with AQP4-Ab–positive NMO/NMOSD. Aquaporin-4–Ab disease has a striking female preponderance. By contrast, most MOG-Ab–positive patients were male, and there was a trend toward younger age at disease onset. Delayed VEPs in clinically asymptomatic eyes occurred in 2 AQP4-Ab–positive patients, whereas in MOG-Ab–positive patients, delayed VEPs were only seen in symptomatic eyes. Thus, subclinical demyelination may occur in the optic nerves of AQP4-Ab–positive patients and this observation warrants investigation in future studies. Although MOG-Ab–positive patients had severe onset episodes, with comparable nadir EDSS scores with AQP4-Ab–positive patients, they showed remarkable recovery, and EDSS scores at follow-up were significantly lower than those with AQP4-Ab, with no MOG-Ab–positive patients being left with significant visual or motor disability. Moreover, MRI abnormalities resolved completely on follow-up imaging in most patients and EPs normalized in most. Our findings suggest that MOG-Ab–positive patients have more favorable outcomes than patients with AQP4-Ab. We cannot exclude the possibility that minor variations in treatments may have contributed to the differences in outcomes observed because a greater proportion of MOG-Ab–positive patients received PLEX in the acute setting. However, the treatment protocol we used was identical for patients no matter what their diagnosis and depended solely on severity and response to initial treatment. Thus, the greater PLEX use in MOG-Ab–positive patients was simply a reflection of the greater severity of the acute episode. Good clinical and radiological recovery in pediatric patients with NMO/NMOSD and ADEM with MOG-Abs have also been noted.8,19

Despite the relatively short follow-up period and use of immunosuppression, a substantial proportion of AQP4-Ab–positive patients relapsed following the onset episode. By contrast, no MOG-Ab–positive patients relapsed despite immunosuppression being completely withdrawn in 6 patients. However, we cannot exclude the possibility that some may relapse over a longer follow-up period, and we are aware of 2 MOG-Ab–positive adult patients seen at other UK centers with relapsing NMO.

Another group6 has also found MOG-Abs in patients with NMO/NMOSD, some with relapsing disease; low titers of MOG-Abs were also found in a small number of adult
patients with MS or other neurological conditions, whereas we have not found MOG-Abs when screening adult MS and neurological control individuals. This likely reflects differences in the assays since we used cells transfected with a C-terminal–truncated MOG, whereas Mader and colleagues used full-length MOG. In our hands, MOG-Abs in adults seem to be a useful biomarker, defining a severe NMO-like illness, overlapping with ADEM, with more favorable outcomes than AQP4-Ab disease. However, we do encounter patients with similar characteristics without MOG-Abs, and it is possible that some of these patients may have low levels of MOG-Abs below the detection limit of the current assay. We are aware of some children testing positive for MOG-Abs with other phenotypes, such as pediatric MS or ADEM, followed by recurrent ON. Further optimization of the assays and direct comparisons between groups and between assays (in particular comparisons between assays using C-terminal–truncated MOG and full-length MOG) is now needed to better define the role of MOG-Abs in CNS-demyelinating disease in both adults and children.

Our study has several limitations. First, all patients were seen within a specialist NMO service, and we cannot exclude the possibility that MOG-Abs may also be seen in non-NMO adult phenotypes. Second, owing to the rarity of NMO/NMOSD, the numbers of patients were relatively small and we could not make statistical corrections for multiple comparisons. Nevertheless, there did appear to be differences between patients with AQP4-Ab and MOG-Abs. The significant differences noted here and the differences that showed a trend require a priori analysis in further cohorts. Finally, some clinical data were recorded with knowledge of antibody status and thus we cannot exclude the possibility that this may have biased outcomes. However, we feel that this is unlikely since EDSS scores and decision of relapses were done independently of the data analysis.

Conclusions

We have found MOG-Abs in some patients with AQP4-Ab-negative NMO/NMOSD. Our results support our original observations that these patients show some overlap with ADEM and have more favorable outcomes than patients with AQP4-Ab disease. Patients with MOG-Abs may not require long-term immunosuppression after a single episode but extended follow-up studies of these patients will be important. Patients with AQP4-Ab-negative NMO/NMOSD should be tested for MOG-Abs.
Biogen Idec, Novartis, and Teva; speaker honoraria from Novartis and Terumo BCT; and is supported by the National Health Service (NHS) National Specialised Commissioning Group for Neuromyelitis Optica. Dr Waters is a named inventor on patents for antibody assays and has received royalties, and he has received a speaker honorarium from Biogen-Idec Japan. Dr Woodhall is involved in aquaporin-4 and myelin-oligodendrocyte glycoprotein antibody testing and is supported by the NHS National Specialised Commissioning Group for Neuromyelitis Optica. Dr Leite is involved in aquaporin-4 and myelin-oligodendrocyte glycoprotein antibody testing, is supported by the NHS National Specialised Commissioning Group for Neuromyelitis Optica and by the National Institute for Health Research Oxford Biomedical Research Centre, and has received speaking honoraria from Biogen Idec and travel grants from Novartis. Dr George has received support for scientific meetings from Biogen Idec. Dr Chandratre has received unrestricted educational grants from Novartis and Eisai. Prof Vincent and the Nuffield Department of Clinical Neurosciences, Oxford University Hospitals NHS Trust, hold patents and receive royalties and payments for antibody tests. Dr Palace has received support for scientific meetings and honoraria for advisory roles from Merck Serono, Biogen Idec, Novartis, Teva, Chugai Pharma, and Bayer Schering, and unrestricted grants from Merck Serono and Bayer Schering. She has held MS Society and Guthy-Jackson Charitable Foundation grants, is a clinical lead for the UK Department of Health risk-sharing scheme, and is supported by the NHS National Specialised Commissioning Group for Neuromyelitis Optica. No other disclosures were reported.

Additional Contributions: We thank the National Health Service National Specialised Commissioning Group for Neuromyelitis Optica and the National Institute for Health Research Oxford Biomedical Research Centre for funding antibody testing. No specific funding was received for this study.

REFERENCES


