Epidemiology of Neuromyelitis Optica in the United States

A Multicenter Analysis

Maureen A. Mealy, RN; Dean M. Wingerchuk, MD; Benjamin M. Greenberg, MD; Michael Levy, MD, PhD

Background: Rare diseases require integrated multicenter clinical networks to facilitate clinical research. Neuromyelitis optica (NMO) and NMO spectrum disorders (NMOSDs) are uncommon neuroinflammatory syndromes that are distinct from multiple sclerosis and associated with NMO-IgG, a serologic antibody against aquaporin 4.

Objective: To develop a national multicenter NMO clinical consortium and report initial demographic, clinical, and radiographic features of a cohort of patients with NMO/NMOSD in the United States.

Design: Review of medical records from patients undergoing evaluation during a 5-year period. We used uniform diagnostic criteria and clinical, laboratory, and neuroimaging definitions to describe the cohort.

Setting: Three academic medical centers.

Patients: One hundred eighty-seven patients with NMO/NMOSD.

Results: Of the 187 patients included in the analysis, 86 had NMO-IgG–seropositive NMO; 40, NMO-IgG–seronegative NMO; and 61, NMO-IgG–seropositive NMOSD. Altogether, 29.4% of our patients were initially misdiagnosed with multiple sclerosis. The average age at onset of NMO/NMOSD was 41.1 years with a strong female predilection, similar to other autoimmune disorders. Nonwhite patients constituted 52.4% of the cohort. The hallmark of NMO and NMOSD is recurrent longitudinally extensive transverse myelitis, but patients with NMO tend to initially present with optic neuritis.

Conclusions: A national multicenter consortium to study NMO/NMOSD is feasible and facilitates accurate clinical diagnosis. This network establishes a foundation for determining disease prevalence, translational research, and clinical trials.


EUROMYELITIS OPTICA (NMO) is an inflammatory demyelinating disease that preferentially targets the spinal cord and optic nerves. The disease is distinct from multiple sclerosis (MS), and the natural history of the disorder has a poorer prognosis, underscoring the importance of early diagnosis and appropriate treatment. The serum autoantibody NMO-IgG, which targets aquaporin 4, is highly specific for NMO and has led to appreciation of a wider spectrum of clinical and radiologic characteristics associated with the disorder, including patterns of brain involvement and topographically limited forms of the disease.

The incidence and prevalence of NMO and NMOSD have been inconsistently described. Studies from Japan, Cuba, and the French West Indies suggest incidence rates of 0.053 to 0.4 per 100 000 patient-years and prevalence rates of 0.52 to 4.4 per 100 000 people. In the United States, NMO prevalence is estimated to be approximately 1% to 2% of MS, suggesting that there may be 4000 to 8000 patients.

We developed a multicenter NMO clinical consortium of 3 tertiary centers experienced in the diagnosis and treatment of NMO/NMOSD to systematically characterize NMO in terms of epidemiology, clinical course, serology, and treatment.

METHODS

We retrospectively characterized cases of NMO and NMOSD evaluated at the Johns Hopkins University, The University of Texas Southwestern Medical Center, and Mayo Clinic, Scottsdale/Phoenix. We obtained institutional review...
RESULTS

We found 187 patients who had NMO and NMOSD, including 88 at Johns Hopkins University, 63 at Mayo Clinic, and 36 at The University of Texas Southwestern Medical Center. Of these patients, 126 (67.4%) met 2006 NMO diagnostic criteria, and 86 of the 126 (68.3%) were NMO-IgG seropositive (Table 1). Patients were followed up for an average of 6.8 (median, 4.9) years.

The average age at onset was 41.1 (range, 3-81) years (Table 1). The age distribution of patients with NMO and NMOSD was unimodal. The sex distribution was strongly skewed toward female, with a female to male ratio of 6.5:1. Men with NMO had a slightly tendency to be seronegative for NMO-IgG. White patients constituted the largest race group (47.6%), but patients of African descent were overrepresented at 36.9%.

All NMO patients had a history of optic neuritis and transverse myelitis, but NMOSD patients were much more likely to present with transverse myelitis (Table 2). In contrast, the initial event in NMO was slightly more likely to be optic neuritis. The classic presentation of simultaneous optic neuritis and transverse myelitis occurring within 3 months was found in 10.2% of our population. The disease course was recurrent in 94.1% of patients; of the 11 patients with a monophasic presentation, 3 had NMO (2 of whom were NMO-IgG seronegative) and 8 had NMOSD followed up for a median of 3.0 (range, 0.1-32.0) years. During the course of the disease, each NMO and NMOSD patient developed an average of 3.6 events, with a relapse rate of 1.3 events per year. Patients with NMO and NMOSD had an average of 2.6 to 2.7 transverse myelitis events, but given that NMOSD patients had a shorter duration of disease, their relapse rate was higher at 1.4 events per year compared with 0.8 events per year for NMO patients. Optic neuritis was much more common in NMO patients, who averaged 1.8 events and 0.8 events per year; however, in the few NMOSD patients with recurrent optic neuritis (who have no history of transverse myelitis), the relapse rate was an aggressive 1.5 events per year.

The MRI data of acute events were available in 84.0% of patients with transverse myelitis and optic neuritis (Table 3 and Table 4). A total of 202 myelitis lesions characterized by MRI found that cervical and thoracic spinal cords were equally susceptible in NMO and NMOSD and that most of the lesions were longitudinally extensive (≥3 vertebral segments). Approximately one-third of patients had longitudinally extensive lesions in the cervical and thoracic spinal cord. During a transverse myelitis event, MRI showed gadolinium enhancement in 87.1% of cases. A total of 281 events of optic neuritis were imaged by MRI (Table 4), and 23.8% were simultaneous bilateral optic neuritis, which was much more likely to occur in NMO than in NMOSD. Recurrence of unilateral optic neuritis was 3 times more likely to strike the affected optic nerve than the healthy one, and gadolinium enhancement was noted in 77.0% of cases. Brain MRI findings were characterized as normal findings, non-specific white matter lesions, or MS-like in 80.7% of patients (Table 5). Magnetic resonance imaging revealed normal brain findings or non-specific white matter lesions in 87.4% of NMO and NMOSD patients. Thirty patients developed brainstem lesions, 24 (80%) of whom were of African descent.

<table>
<thead>
<tr>
<th>Table 1. Demographics of the NMO Consortium Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristic</strong></td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
</tr>
<tr>
<td>NMO</td>
</tr>
<tr>
<td>Seropositive NMO</td>
</tr>
<tr>
<td>Seronegative NMO</td>
</tr>
<tr>
<td>NMOSD</td>
</tr>
<tr>
<td><strong>Age at onset, y</strong></td>
</tr>
<tr>
<td>Mean (range)</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td><strong>Duration of disease, y</strong></td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>Median (range)</td>
</tr>
<tr>
<td><strong>Age at onset, y</strong></td>
</tr>
<tr>
<td>Mean (range)</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female to male ratio</td>
</tr>
<tr>
<td><strong>Race</strong></td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>African descent</td>
</tr>
<tr>
<td>Latin American</td>
</tr>
<tr>
<td>Asian</td>
</tr>
<tr>
<td>Native American</td>
</tr>
</tbody>
</table>

Abbreviations: NMO, neuromyelitis optica; NMOSD, NMO spectrum disorder.

²Unless otherwise indicated, data are expressed as number (percentage) of patients. Percentages have been rounded and might not total 100.
Cerebrospinal fluid was collected in 16.4% of acute events, typically during the initial presentation and workup. These studies revealed a pleocytosis (mean, 95/µL; median, 13/µL; range, 0/µL-2150/µL); the mean protein level was also high at 128 (median, 57) mg/dL (Table 6). Only 12.1% of patients had 2 or more oligoclonal bands.

More than half of patients had antinuclear antibodies and approximately one-quarter also had positive findings for another autoantibody, such as SS-A, antiacetylcholine receptor, or double-stranded DNA antibodies. The erythrocyte sedimentation rate was slightly elevated but consistent with age, and the C-reactive protein marker of peripheral inflammation was largely normal (median, 0.3 mg/L; to convert to nanomoles per liter, multiply by 9.524).

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>Data</th>
<th>MRI Characteristic of NMO Acute Transverse Myelitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. of patients</td>
<td>187</td>
<td>MRI availability</td>
</tr>
<tr>
<td>No. (%) with transverse myelitis</td>
<td>179 (95.7)</td>
<td>All</td>
</tr>
<tr>
<td>No. (%) with optic neuritis</td>
<td>137 (73.3)</td>
<td>NMO</td>
</tr>
<tr>
<td>No. of NMO patients</td>
<td>61</td>
<td>NMOSD</td>
</tr>
<tr>
<td>No. (%) with transverse myelitis</td>
<td>52 (85.2)</td>
<td>No. of lesions detected</td>
</tr>
<tr>
<td>No. (%) with optic neuritis</td>
<td>11 (18.0)</td>
<td>All</td>
</tr>
<tr>
<td>Mean No. of events/patient</td>
<td>3.6</td>
<td>NMO</td>
</tr>
<tr>
<td>All</td>
<td>1.0</td>
<td>NMOSD</td>
</tr>
<tr>
<td>Monophasic NMO/NMOSD</td>
<td>4.2</td>
<td>Cervical lesions</td>
</tr>
<tr>
<td>Recurrent NMO</td>
<td>3.2</td>
<td>All</td>
</tr>
<tr>
<td>Recurrent NMOSD</td>
<td>2.7</td>
<td>Longitudinally extensive</td>
</tr>
<tr>
<td>Transverse myelitis, mean No. of events/patient</td>
<td>2.5</td>
<td>NMO</td>
</tr>
<tr>
<td>All</td>
<td>1.0</td>
<td>NMOSD</td>
</tr>
<tr>
<td>Monophasic NMO/NMOSD</td>
<td>2.7</td>
<td>Focal</td>
</tr>
<tr>
<td>Recurrent NMO</td>
<td>2.6</td>
<td>NMO</td>
</tr>
<tr>
<td>Recurrent NMOSD</td>
<td>3.2</td>
<td>NMOSD</td>
</tr>
<tr>
<td>Optic neuritis, mean No. of events/patient</td>
<td>1.3</td>
<td>Cervical lesions</td>
</tr>
<tr>
<td>All</td>
<td>1.2</td>
<td>All</td>
</tr>
<tr>
<td>Monophasic NMO/NMOSD</td>
<td>1.3</td>
<td>Longitudinally extensive</td>
</tr>
<tr>
<td>Recurrent NMO</td>
<td>0.8</td>
<td>NMO</td>
</tr>
<tr>
<td>Recurrent NMOSD</td>
<td>0.6</td>
<td>NMOSD</td>
</tr>
<tr>
<td>Total relapse rate, mean No. of events/y</td>
<td>1.3</td>
<td>Focal</td>
</tr>
<tr>
<td>All relapses</td>
<td>1.2</td>
<td>NMO</td>
</tr>
<tr>
<td>Recurrent NMO</td>
<td>0.8</td>
<td>NMOSD</td>
</tr>
<tr>
<td>Transverse myelitis</td>
<td>1.4</td>
<td>Thoracic lesions</td>
</tr>
<tr>
<td>Optic neuritis</td>
<td>1.4</td>
<td>All</td>
</tr>
<tr>
<td>Recurrent NMOSD</td>
<td>1.5</td>
<td>Longitudinally extensive</td>
</tr>
<tr>
<td>Transverse myelitis</td>
<td>1.5</td>
<td>NMO</td>
</tr>
<tr>
<td>Optic neuritis</td>
<td>1.4</td>
<td>NMOSD</td>
</tr>
<tr>
<td>Initial event, No./total No. (%) of patients</td>
<td>94/187 (50.2)</td>
<td>Focal</td>
</tr>
<tr>
<td>Transverse myelitis only</td>
<td>46/94 (48.9)</td>
<td>NMO</td>
</tr>
<tr>
<td>NMO</td>
<td>48/94 (51.1)</td>
<td>NMOSD</td>
</tr>
<tr>
<td>Optic neuritis only</td>
<td>66/187 (35.3)</td>
<td>Gadolinium enhancement, No. (%) of lesions</td>
</tr>
<tr>
<td>NMO</td>
<td>59/66 (89.4)</td>
<td>All</td>
</tr>
<tr>
<td>NMOSD</td>
<td>7/66 (10.6)</td>
<td>NMO</td>
</tr>
<tr>
<td>Simultaneous optic neuritis plus transverse myelitis</td>
<td>19/187 (10.2)</td>
<td>NMOSD</td>
</tr>
<tr>
<td>Other CNS lesion</td>
<td>8/187 (4.3)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: NMO, neuromyelitis optica; NMOSD, NMO spectrum disorder.

We included all NMO patients meeting 2006 diagnostic criteria and all NMO-IgG-seropositive patients who developed demyelinating diseases of the central nervous system, such as transverse myelitis, who did not meet the Wingerchuk 2006 criteria for clinically definite NMO. The rationale for including only NMO-IgG-seropositive patients who did not meet the Wingerchuk 2006 criteria, rather than all patients with recurrent transverse myelitis and recurrent optic neuritis, was to avoid the possibility of inadvertently including patients who actually had a central nervous system manifestation of another diagnosis other than NMO, including rheumatologic disorders, sarcoidosis, or vascular disease. Although many of these disorders may be treated similarly with immunosuppressive therapy, the biological mechanism of these other disorders is quite different and could therefore confound our data set. It is difficult to precisely characterize the incidence and prevalence of a rare disease in the United States.
In this study, we analyzed NMO/NMOSD in 187 patients across 3 major NMO centers in the United States. Compared with patients with MS, NMO and NMOSD patients are older on average at presentation, but they are somewhat younger than patients presenting with other autoimmune diseases, including lupus and Sjögren syndrome. We found no differences in the disease course based on the age at onset, although NMO-IgG findings tended to be seronegative in children with transverse myelitis. The race distribution in NMO and NMOSD is mixed; the proportion of white patients, however, is less than typically seen in most MS clinics. Patients of African descent constitute only 12% of the US population but in this study constituted 36.9% of the NMO/NMOSD population, unlike MS, in which patients of African descent account for a small percentage of the total MS population in the United States. The female to male ratio of 6.5:1 for NMO and NMOSD is greater than that for MS (2:1 to 3:1) but similar to the ratios for lupus (9:1), Sjögren syndrome (19:1), and other autoimmune disorders.

Cases of NMOSD may represent early, incompletely developed NMO, but some may also represent a group of patients who are less likely to acquire certain typical manifestations, such as optic neuritis. Consider that NMO and NMOSD patients equally developed an average of 2.6 to 2.7 events of transverse myelitis, but NMOSD patients only rarely developed solely optic neuritis (18.0%). In contrast, NMO patients were more likely to have optic neuritis at the initial presentation than transverse myelitis and were more likely to have recurrent events of optic neuritis compared with NMOSD patients. This difference be-

### Table 4. Clinical Characterization of NMO Acute Optic Neuritis

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>Data</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral simultaneous</td>
<td>All</td>
<td>50 (100.0)</td>
</tr>
<tr>
<td></td>
<td>NMO</td>
<td>48 (96.0)</td>
</tr>
<tr>
<td></td>
<td>NMOSD</td>
<td>2 (4.0)</td>
</tr>
<tr>
<td>Bilateral nonsimultaneous</td>
<td>All</td>
<td>36 (100.0)</td>
</tr>
<tr>
<td></td>
<td>NMO</td>
<td>29 (80.6)</td>
</tr>
<tr>
<td></td>
<td>NMOSD</td>
<td>7 (19.4)</td>
</tr>
<tr>
<td>Unilateral</td>
<td>All</td>
<td>107 (100)</td>
</tr>
<tr>
<td></td>
<td>NMO</td>
<td>97 (90.7)</td>
</tr>
<tr>
<td></td>
<td>NMOSD</td>
<td>10 (9.3)</td>
</tr>
<tr>
<td>Optic neuritis, No. (%) of lesions</td>
<td>All</td>
<td>281 (100.0)</td>
</tr>
<tr>
<td></td>
<td>Unilateral</td>
<td>214 (76.2)</td>
</tr>
<tr>
<td></td>
<td>Bilateral simultaneous</td>
<td>67 (23.8)</td>
</tr>
<tr>
<td>Gadolinium enhancement, No. (%) of lesions</td>
<td>MRI availability</td>
<td>74 (100.0)</td>
</tr>
<tr>
<td></td>
<td>All enhancements</td>
<td>57 (77.0)</td>
</tr>
</tbody>
</table>

**Abbreviations:** MRI, magnetic resonance imaging; NMO, neuromyelitis optica; NMOSD, NMO spectrum disorder.

*a* Unless otherwise indicated, data are expressed as number (percentage) of patients.

*b* Seventeen events consisting of bilateral simultaneous optic neuritis and 107 consisting of unilateral optic neuritis were recurrent.

### Table 5. Characteristics Found on MRI of the Brain in NMO Patients

<table>
<thead>
<tr>
<th>MRI Characteristic</th>
<th>Data, No. (%) of Patients</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI availability</td>
<td>All</td>
<td>151/187 (80.7)</td>
</tr>
<tr>
<td></td>
<td>NMO</td>
<td>108/126 (85.7)</td>
</tr>
<tr>
<td></td>
<td>NMOSD</td>
<td>43/61 (70.5)</td>
</tr>
<tr>
<td>Normal MRI findings</td>
<td>All</td>
<td>61/151 (40.4)</td>
</tr>
<tr>
<td></td>
<td>NMO</td>
<td>45/61 (73.8)</td>
</tr>
<tr>
<td></td>
<td>NMOSD</td>
<td>16/61 (26.2)</td>
</tr>
<tr>
<td>Nonspecific white matter lesions</td>
<td>All</td>
<td>71/151 (47.0)</td>
</tr>
<tr>
<td></td>
<td>NMO</td>
<td>49/71 (69.0)</td>
</tr>
<tr>
<td></td>
<td>NMOSD</td>
<td>21/71 (31.0)</td>
</tr>
<tr>
<td>MS-like lesions</td>
<td>All</td>
<td>19/151 (12.6)</td>
</tr>
<tr>
<td></td>
<td>NMO</td>
<td>14/19 (73.7)</td>
</tr>
<tr>
<td></td>
<td>NMOSD</td>
<td>5/19 (26.3)</td>
</tr>
<tr>
<td>All brainstem lesions</td>
<td>30/151 (19.9)</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** MRI, magnetic resonance imaging; MS, multiple sclerosis; NMO, neuromyelitis optica; NMOSD, NMO spectrum disorder.

*a* Twenty-four patients with brainstem lesions (80%) were of African descent.

### Table 6. Laboratory Values

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Data</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell count, No./µL</td>
<td>Mean</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>Median (range)</td>
<td>13 (0-2150)</td>
</tr>
<tr>
<td></td>
<td>Reference range</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Protein level, mg/dL</td>
<td>Mean</td>
<td>128</td>
</tr>
<tr>
<td></td>
<td>Median (range)</td>
<td>57 (17-2149)</td>
</tr>
<tr>
<td></td>
<td>Reference range</td>
<td>&lt;50</td>
</tr>
<tr>
<td>Glucose level, mg/dL</td>
<td>Mean</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td>Median (range)</td>
<td>62 (29-264)</td>
</tr>
<tr>
<td></td>
<td>Reference range</td>
<td>50-80</td>
</tr>
<tr>
<td>Oligoclonal bands, No. (%) of patients</td>
<td>0 (Normal finding)</td>
<td>68/99 (69.7)</td>
</tr>
<tr>
<td></td>
<td>1 (Monoclonal)</td>
<td>18/99 (18.2)</td>
</tr>
<tr>
<td></td>
<td>≥2 (Oligoclonal)</td>
<td>12/99 (12.1)</td>
</tr>
<tr>
<td>Serum measurements, No. (%) of patients</td>
<td>Antinuclear antigen</td>
<td>Negative finding</td>
</tr>
<tr>
<td></td>
<td>1:40-1:160 titer</td>
<td>39/121 (32.2)</td>
</tr>
<tr>
<td></td>
<td>≥1:320 titer</td>
<td>34/121 (28.1)</td>
</tr>
<tr>
<td>Sjögren syndrome antigens SS-A</td>
<td>Positive finding</td>
<td>25/95 (26.3)</td>
</tr>
<tr>
<td></td>
<td>Negative finding</td>
<td>70/95 (73.7)</td>
</tr>
<tr>
<td>SS-B</td>
<td>Positive finding</td>
<td>10/92 (10.9)</td>
</tr>
<tr>
<td></td>
<td>Negative finding</td>
<td>82/92 (89.1)</td>
</tr>
<tr>
<td>Antiacetylcholine receptor</td>
<td>Positive finding</td>
<td>7/31 (22.6)</td>
</tr>
<tr>
<td></td>
<td>Negative finding</td>
<td>24/31 (77.4)</td>
</tr>
<tr>
<td>Double-stranded DNA antibodies</td>
<td>Positive finding</td>
<td>9/28 (32.1)</td>
</tr>
<tr>
<td></td>
<td>Negative finding</td>
<td>19/28 (67.9)</td>
</tr>
</tbody>
</table>

**Abbreviations:** MRI, magnetic resonance imaging; MS, multiple sclerosis; NMO, neuromyelitis optica; NMOSD, NMO spectrum disorder.

*a* Measurements include 110 patients with cerebrospinal fluid samples available.

*b* Indicates number of bands in cerebrospinal fluid minus serum.

SI conversion factors: To convert glucose to millimoles per liter, multiply by 0.0555; white blood cell count to $10^9$ per liter, multiply by 0.001.

The race distribution in NMO and NMOSD is mixed; the proportion of white patients, however, is less than typically seen in most MS clinics. Patients of African descent constitute only 12% of the US population but in this study constituted 36.9% of the NMO/NMOSD population, unlike MS, in which patients of African descent account for a small percentage of the total MS population in the United States. The female to male ratio of 6.5:1 for NMO and NMOSD is greater than that for MS (2.1 to 3.1) but similar to the ratios for lupus (9:1), Sjögren syndrome (19:1), and other autoimmune disorders.

Cases of NMOSD may represent early, incompletely developed NMO, but some may also represent a group of patients who are less likely to acquire certain typical manifestations, such as optic neuritis. Consider that NMO and NMOSD patients equally developed an average of 2.6 to 2.7 events of transverse myelitis, but NMOSD patients only rarely developed solely optic neuritis (18.0%). In contrast, NMO patients were more likely to have optic neuritis at the initial presentation than transverse myelitis and were more likely to have recurrent events of optic neuritis compared with NMOSD patients. This difference be-
tween the initial presentations of NMO and NMOSD patients may result from a combination of testing biases because many patients with isolated optic neuritis do not undergo testing for NMO-IgG and, for those who do, the sensitivity for detection of NMO-IgG is poor.\textsuperscript{11} Susceptibility of different central nervous system areas to inflammation in NMO and NMOSD is similarly reflected in the marked predilection of brainstem lesions to be found in patients of African descent. Almost half our patients of African descent had an MRI-confirmed brainstem lesion, accounting for 80.0% of all brainstem lesions.

As expected, most NMO/NMOSD patients had longitudinally extensive transverse myelitis given that this is one of the criteria for NMO, albeit nonmandatory. In contrast, the MRIs of the brain in these patients accumulated nonspecific cortical and subcortical hyperintensities that were largely asymptomatic. The contribution of these lesions to the overall neurologic disability was undetectable compared with the spinal cord lesions. As seen in some recently reported cases, a few rare patients with NMO developed large cerebral lesions atypical for MS.\textsuperscript{18,19}

A key observation of this multicenter study is that 29.4% of our cohort was diagnosed as having MS before the final diagnosis of NMO/NMOSD. The MRI findings in the brain may have been among the factors that influenced the initial misdiagnosis given that 66.7% of those misdiagnosed have abnormal findings on their brain MRI. In addition, 38.2% of the misdiagnoses predated the availability of the NMO-IgG blood test. This finding is of critical importance given the different therapeutic regimens for NMO/NMOSD and MS and the observation that use of interferon beta may aggravate NMO.\textsuperscript{20}

In summary, a national, multicenter NMO/NMOSD consortium is feasible. Expansion of this type of national or international NMO center network could facilitate more accurate assessments of disease incidence and prevalence and comparison of these rates between people of different racial and geographic backgrounds. This consortium also provides the infrastructure for future prognostic biomarker studies and therapeutic clinical trials.

Accepted for Publication: February 14, 2012.
Published Online: June 25, 2012. doi:10.1001/archneur.2012.314

Correspondence: Michael Levy, MD, PhD, Department of Neurology, Johns Hopkins University, 600 N Wolfe St, Pathology 509, Baltimore, MD 21287 (mlevy@jhmi.edu).

Author Contributions: Study concept and design: Mealy, Wingerchuk, Greenberg, and Levy. Acquisition of data: Mealy, Wingerchuk, and Greenberg. Analysis and interpretation of data: Mealy and Greenberg. Drafting of the manuscript: Mealy and Levy. Critical revision of the manuscript for important intellectual content: Mealy, Wingerchuk, and Greenberg. Statistical analysis: Mealy and Greenberg. Obtained funding: Wingerchuk, Greenberg, and Levy. Administrative, technical, and material support: Mealy. Study supervision: Levy.

Financial Disclosure: Ms Mealy has received honoraria from EMD Serono, Novartis, and the Multiple Sclerosis Association of America and receives research funding from the Guthy Jackson Charitable Foundation. Dr Wingerchuk has received research support from Genzyme, Genentech, Alexion, Guthy Jackson Charitable Foundation, the National Institutes of Health, and the National Multiple Sclerosis Society. Dr Greenberg has received honoraria from EMD Serono, Advanced Studies in Medicine, CME Logix, the Multiple Sclerosis Association of America, the American Academy of Neurology, and the National Multiple Sclerosis Society; consulting fees from the Greater Good Foundation and DioGenix; research funding from the Guthy Jackson Charitable Foundation, Amplimmune, and the Accelerated Cure Project; and legal fees for expert witness services and has equity in DioGenix. Dr Levy has received commercial research support and honoraria from ApoPharma Inc, travel funding from Amplimmune, academic research support from the Guthy Jackson Charitable Foundation; book royalties from Lippincott, and legal fees for expert witness services.

Funding/Support: This study was supported by the Guthy Jackson Charitable Foundation.

REFERENCES


©2012 American Medical Association. All rights reserved.