

Multiple Sclerosis Followed by Neuromyelitis Optica Spectrum Disorder

From the National Multiple Sclerosis Society Case Conference Proceedings

Carolyn Goldschmidt, MD, Steven L. Galetta, Robert P. Lisak, MD, Laura J. Balcer, MD, Andrew Hellman, PhD, Michael K. Racke, MD, Amy E. Lovett-Racke, PhD, Roberto Cruz, MD, Matthew S. Parsons, PhD, Neda Sattarnezhad, MD, Lawrence Steinman, MD, Scott S. Zamvil, MD, PhD, Elliot M. Frohman, MD, PhD, and Teresa C. Frohman, MPAS, PA-C

Correspondence

Dr. Frohman
elliott.frohman@austin.utexas.edu

Neurol Neuroimmunol Neuroinflamm 2023;10:e200037. doi:10.1212/NXI.0000000000200037

Abstract

A woman presented at age 18 years with partial myelitis and diplopia and experienced multiple subsequent relapses. Her MRI demonstrated T2 abnormalities characteristic of multiple sclerosis (MS) (white matter ovoid lesions and Dawson fingers), and CSF demonstrated an elevated IgG index and oligoclonal bands restricted to the CSF. Diagnosed with clinically definite relapsing-remitting MS, she was treated with various MS disease-modifying therapies and eventually began experiencing secondary progression. At age 57 years, she developed an acute longitudinally extensive transverse myelitis and was found to have AQP4 antibodies by cell-based assay. Our analysis of the clinical course, radiographic findings, molecular diagnostic methods, and treatment response characteristics support the hypothesis that our patient most likely had 2 CNS inflammatory disorders: MS, which manifested as a teenager, and neuromyelitis optica spectrum disorder, which evolved in her sixth decade of life. This case emphasizes a key principle in neurology practice, which is to reconsider whether the original working diagnosis remains tenable, especially when confronted with evidence (clinical and/or paraclinical) that raises the possibility of a distinctively different disorder.

From the Mellen Center for Multiple Sclerosis Treatment and Research (C.G.), Cleveland Clinic, OH; Departments of Neurology (S.L.G., L.J.B.), Population Health (L.J.B.) and Ophthalmology (L.J.B., S.L.G.), New York University Grossman School of Medicine; Department of Neurology (R.P.L.), Wayne State University, Detroit MI; Quest Diagnostics (A.H., M.K.R.), Secaucus, NJ; Department of Microbial Infection and Immunity (A.E.L.-R.), Department of Neuroscience Ohio State University Wexner Medical Center, Columbus; Department of Neurology (R.C.), Doctors Hospital at Renaissance; Department of Neurology (R.C.), University of Texas Rio Grande Valley; Division of Microbiology and Immunology (M.S.P.), Yerkes National Primate Research Center, and Department of Pathology and Laboratory Medicine, Emory University, Atlanta, GA; Department of Neurology (N.S., L.S.), Stanford University School of Medicine, Palo Alto, CA; Department of Neurology and Program in Immunology (S.S.Z.), University of California San Francisco; and Distinguished Senior Fellows (Sabbatical) Neuroimmunology Laboratory of Professor Lawrence Steinman (E.M.F., T.C.F.), Stanford University School of Medicine, Palo Alto, CA.

Go to [Neurology.org/NN](https://www.neurology.org/NN) for full disclosures. Funding information is provided at the end of the article.

The Article Processing Charge was funded by the National Multiple Sclerosis Society.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0 (CC BY-NC-ND), which permits downloading and sharing the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Glossary

DMT = disease-modifying therapy; MS = multiple sclerosis; NMO/MSD = neuromyelitis optica spectrum disorder; RRMS = relapsing-remitting MS; S-1-P = sphingosine-1-phosphate; SPMS = secondary progressive MS; UTI = urinary tract infection.

Case Presentation

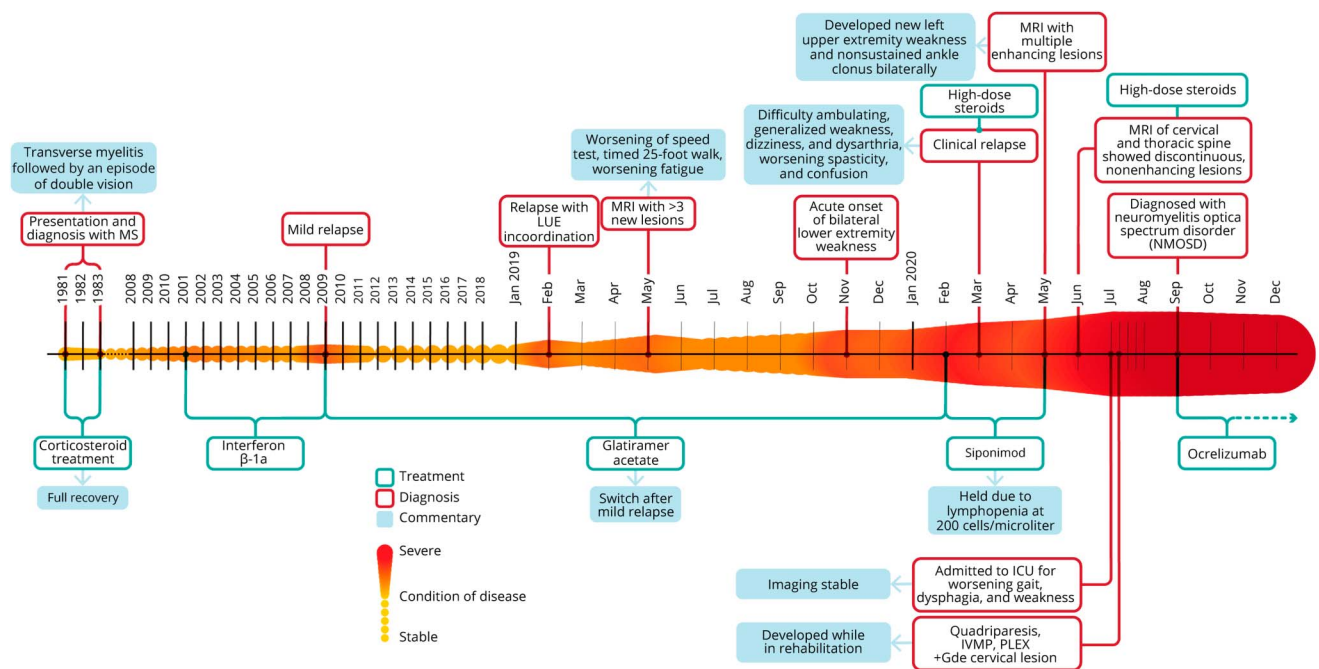
The patient is a 57-year-old woman followed at our comprehensive multiple sclerosis (MS) center at the Cleveland Clinic after decades with the diagnosis of clinically definite, relapsing-remitting MS (RRMS), followed by a transition to secondary progressive MS (SPMS), who now presents with longitudinally extensive transverse myelitis. The inception of this patient's neurologic course began in 1981 at age 18 years with partial transverse myelitis, followed by an episode of double vision (Figure 1). Following corticosteroid therapy, she recovered completely from both syndromes, and a diagnosis of clinically definite RRMS was established. She was later treated with interferon beta-1a and remained neurologically stable on this therapy for nearly 3 decades until 2009 at which time a new clinical relapse prompted the transition of her disease-modifying therapy (DMT) to glatiramer acetate (Figure 1).

Although she remained stable on glatiramer acetate with no evidence of disease activity for approximately 10 years, a follow-up visit in May 2019 revealed worsening on tests of processing speed,

timed 25-foot walk, and fatigue. A surveillance brain MRI at that time showed lesions highly characteristic for MS (ovoids, Dawson fingers, periventricular plaques, and lesions perpendicular to the long axis of the ventricles) and multiple new and/or enlarging T2 hyperintense nonenhancing lesions in the deep white matter when compared with a February 2017 scan (Figure 2). Her course at that time was most consistent with SPMS.

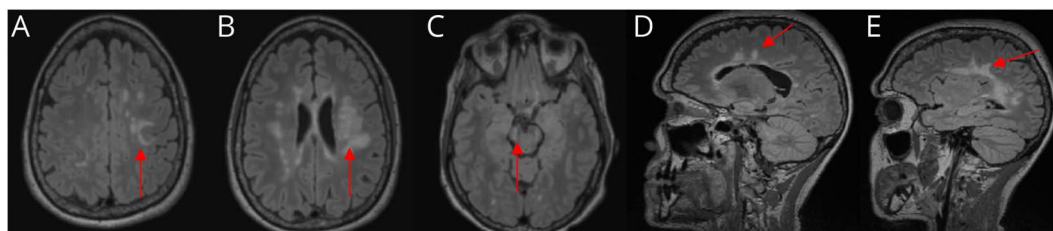
In November of the same year, the patient developed the subacute onset of bilateral lower extremity weakness, rendering her nonambulatory and requiring the use of a wheelchair (Expanded Disability Status Scale score of 7). Examination at that time revealed full strength in the upper extremities, decreased strength in the lower extremities (rated 3 on the Medical Research Council scale), diminished sensation to vibration that was worse on the left vs the right lower extremity, diffusely brisk reflexes without clonus, and finger-to-nose dysmetria. Following high-dose oral prednisone treatment, she once again exhibited significant improvement and was able to ambulate with a walker. By February 2020, the patient was transitioned to siponimod, an oral sphingosine-1-phosphate (S-1-P) receptor modulator.

Figure 1 Chronological Heat Map



In this figure, we detail the condition of the patient over time. The longitudinal axis (left to right) depicts the condition of the disease, whereas the smaller amplitude and lighter color indicates greater stability of the disease. Alternately, the expanded amplitude of the colored heat map (above and below the horizontal linear axis over time) designates increased disease activity (whether on a clinical or paraclinical basis) or complications of the treatment of disease. Other fields of information are added either above or below the heat map and include information about treatments, diagnoses, commentaries adding contextual perspectives, and results from specific test assessments from each most relevant period of clinical decision making. Each field is consistently color coded throughout as defined in the figure legend.¹⁶

Figure 2 May 2019 Brain MRI



Axial and sagittal fluid attenuated inversion recovery imaging showing (A) juxtacortical, (B) periventricular, (C) infratentorial affecting the cerebral peduncles, (D/E) classic Dawson fingers and hyperintensities in a pattern that is typical of multiple sclerosis (arrows).

One month following the transition to siponimod, she reported difficulty ambulating, generalized weakness, dizziness, dysarthria, worsening spasticity, and confusion. Brain MRI showed greater than multiple new enhancing brain lesions, most prominently in the right centrum semiovale, anterior to the right lateral ventricle, and in the right superior periventricular region (Figure 3). She was treated with high-dose steroids and antibiotics for a concomitant urinary tract infection (UTI).

Two months later, she described the new onset of weakness in the left upper extremity, which was confirmed on examination, in conjunction with nonsustained ankle clonus bilaterally. Siponimod was held due to lymphopenia at 200 cells/ μ L.

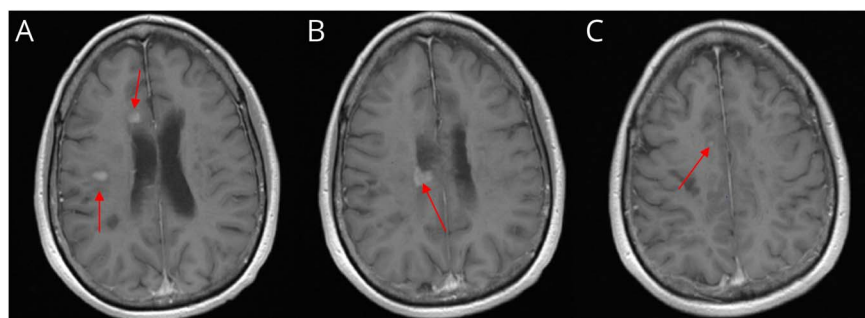
She then presented to the emergency department with difficulty ambulating and altered mental status. A brain MRI showed no abnormal enhancements and no evidence of acute ischemia. MRI of the cervical and thoracic spine showed discontinuous short-segment (i.e., skip) nonenhancing lesions. She was treated with high-dose corticosteroids and antibiotics for yet another UTI, improved, and was subsequently discharged home. However, 1 week later, the patient was admitted to the hospital for worsening gait, dysphagia, and diffuse weakness. She was transferred to the intensive care unit, where she was intubated for airway

protection and required vasopressors for blood pressure support. Imaging of the neuroaxis failed to demonstrate any interval changes. CSF analysis revealed an elevated IgG index and the presence of unmatched oligoclonal bands. Once the patient improved and stabilized, she was discharged to acute rehabilitation. While on the rehabilitation service, she developed severe weakness in the upper and lower extremities bilaterally that progressed to the point of exhibiting only trace movements in the upper extremities, paraplegia, and urinary retention.

Given the severity of deterioration, the patient was treated with IV methylprednisolone and a course of plasma exchange. Repeat imaging of the spinal cord now demonstrated a longitudinally extensive pattern of confluent hyperintensity with peripheral enhancement and marked edema that spanned from the cervicomedullary junction to the upper thoracic spinal cord (Figure 4). Serum testing by cell-based assay yielded a positive AQP4 IgG at a titer of 1:2,560, and a diagnosis of neuromyelitis optica spectrum disorder (NMOSD) was confirmed. Siponimod was discontinued while ocrelizumab, a CD20 monoclonal antibody, was initiated.

The patient currently has only trace movements in her lower extremities with limited antigravity movements in her upper extremities. She requires an indwelling Foley catheter and has significant spasticity.

Figure 3 May 2020 Brain MRI



T1 postcontrast axial images showing multiple ovoid-enhancing lesions (A) in the right frontal white matter anterior to the lateral ventricle and in the deep posterior frontal white matter (arrows), (B) in the right periventricular region (arrow), and (C) a punctate enhancing lesion in the parasagittal region.



(A) Sagittal short tau inversion recovery showing a longitudinally extensive myelitis lesion from the cervicomedullary junction to the upper thoracic spine (arrow). (B) Sagittal T1 postcontrast showing ring enhancement of the lesion (arrow). (C) Axial T1 postcontrast showing multifocal regions of both leptomeningeal and intramedullary contrast enhancement, which appears to involve both the dorsal columns and the lateral corticospinal tract systems, in keeping with the patient's clinical features of hypesthetic quadripareisis (arrow).

Differential Diagnostic Considerations

This case raises 2 intriguing possibilities: The first is that our patient was originally misdiagnosed with RRMS and followed an atypical NMOSD course until she presented with cervicothoracic myelitis. An alternative hypothesis is that she developed 2 distinctive neuroinflammatory disorders in a temporal sequence, namely the onset of MS at 18 followed by the development of NMOSD at 57.

We will first discuss perhaps the more controversial hypothesis: the prospect that our patient's presentation represented manifestations of NMOSD from the very start of her complex clinical course. This would render the original label of RRMS, the initial working diagnosis, as fundamentally incorrect. Based on the disease characteristics associated with the formulation of her working diagnosis, is there any evidence that an early misdiagnosis could have been avoided?

First, it is known that a minority of patients with NMOSD can, in fact, exhibit short-segment spinal cord lesions that are indistinguishable from the so-called classic skip lesions associated with MS.¹ Furthermore, such patients may also have brain lesions that appear consistent with MS.² Studies have shown that 60% of patients with NMOSD accumulate white matter lesions and that as many as 16% fulfill the Barkhof MRI criteria for MS.^{2,3}

A misdiagnosis of MS could explain a lack of response to escalation of MS DMTs, while the patient's previous stability on glatiramer may have been due to a protracted NMOSD remission, which can be a characteristic of the disorder.⁴ In addition, it is possible that our patient's clinical deterioration was precipitated by the transition in DMT from glatiramer acetate to siponimod, as acute inflammatory activity associated with S-1-P modulator treatment has been documented in NMOSD.^{3,5,6}

The alternate hypothesis for consideration is that the patient developed 2 distinct neuroinflammatory conditions occurring

in a temporal sequence. Although her initial presentation of partial myelitis and a brainstem syndrome can occur in both MS and NMOSD, the near-complete recovery of such syndromes with corticosteroids is highly reminiscent of, albeit not specific for, MS. Our patient was well controlled without evidence of disease activity on interferon beta-1a for nearly 30 years. Subsequently, a new exacerbation prompted a transition in DMT to glatiramer acetate, which provided another decade of disease-free remission.

Radiographically, brain imaging studies revealed enhancing and nonenhancing brain lesions, with features highly characteristic for MS including ovoids, periventricular hyperintensities, Dawson fingers, and cerebral atrophy. Spinal cord imaging performed early in the disease course exhibited multifocal and discontinuous short-segment skip lesions, in keeping with the diagnostic criteria of definite MS.⁵ Furthermore, CSF oligoclonal bands (as present in our patient) are identified in ~85% of patients with MS, but in only ~15% of patients with NMOSD.^{3,5}

The clinical course in our patient prior to 2019 included the documented transition from relapsing-remitting to SPMS. Development of progressive disability years after diagnostic confirmation and treatment of RRMS, is characteristic of SPMS, and is not an established feature of NMOSD.^{3,6} However, by mid-late 2019, our patient began to exhibit a marked escalation in both clinical and radiographic disease activity, including an episode of longitudinally extensive transverse myelitis (more than 30 years after the initial presentation), an observation that is highly atypical for MS.

Final Diagnostic Conclusions

Taken together with the highly characteristic lesions on brain imaging investigations (e.g., Dawson fingers, ovoids, periventricular lesions, and typical enhancements as demonstrated in both Figures 2 and 3), spinal cord skip lesions, and the absence of antecedent syndromes characteristic for and also part of the rigorous diagnostic criteria for NMOSD (e.g., longitudinally extensive myelitis, optic neuritis, area postrema

syndrome, or diencephalic syndrome), we believe that based on the evidence available, our patient's initial disorder of CNS inflammation was more compatible with MS than with NMOSD. Her presentation at our center decades into her disease course, with a longitudinally extensive transverse myelitis and the presence of AQP4 antibodies, supports the development of yet a second neuroinflammatory disorder, NMOSD.

A study investigated a large cohort of patients with MS for the presence of aquaporin-4 antibodies in serum samples and found that the rate of misdiagnosis of NMOSD as MS was very rare, less than 1%.⁷ Unfortunately, testing for AQP4 antibodies was not available at the time of our patient's initial presentation in 1981 and would not be widely available until some 25 years later.

Discussion

MS and NMOSD are separate diseases. MS is thought to result from an autoimmune attack targeting proteins expressed by myelin-producing oligodendrocytes. Alternately, NMOSD, a humoral autoimmune disease, was distinguished as a separate disease in 2004, with AQP4 identified as the target for the pathogenic antibody in 2005, long after the inception of our patient's disorder in 1981 (Figure 1).^{8,9} Evidence is also now well established to genetically differentiate the predilection of these 2 disorders. Specifically, MS is associated with the HLA-DR2 (DRB1*1501) and typically presents early in life (from adolescence to middle age), whereas NMOSD has been shown to be associated with HLA-DR17 (DRB1*0301) and can present at any age.¹⁰

There are highly salient and differentiating radiographic characteristics for MS and NMOSD and well-defined and evidence-based diagnostic criteria.^{3,6,11-13} However, it is important to note that patients with MS are at higher risk of developing other autoimmune disorders, making the possibility of 2 distinct neuroinflammatory disorders not untenable.^{14,15} For instance, it is clear that these 2 disorders can manifest in complex ways that raise diagnostic confusion, including the prospect that the 2 conditions might occur as separate entities in a temporally distinctive sequence. Although we cannot be certain, we believe that the analysis of the evidence available supports the contention that our patient did have RRMS, later transitioning into SPMS, and that she developed NMOSD in her sixth decade of life.

Our case report is instructive in that it emphasizes a crucial and salient principle in clinical practice. Specifically, the neurologist must remain vigilant and committed to periodically revisit a fundamental tenet in neurologic diagnosis; "does the 'working diagnosis' still work?" In our patient, answering the question with precision as to whether the working diagnosis of MS remained valid in the context of a potentially transformational clinical syndrome, longitudinally extensive transverse myelitis, required a well-codified, objective (now including the

utilization of a highly sensitive and specific molecular diagnostic tool; the cell-based assay performed on serum for the identification of the AQP4 autoantibody), and a systematic surveillance plan for disease monitoring in conjunction with the interpretation of treatment response characteristics.

At least with respect to the new syndrome, the presence of the AQP4 antibody rendered the original diagnosis of MS no longer tenable, or that a second condition in the form of NMOSD, evolved in conjunction with, and temporally after the first (i.e., MS). Modification of the working diagnosis (es) was indeed tantamount so that an alternate and more appropriate treatment strategy could be formulated, one that provided potential efficacy for one and/or both conditions.

Acknowledgment

The authors thank their medical illustrators, Mr. Jason Ooi and Dr. Matthew Parsons, for their creation of the chronological heat map (Figure 1). The authors acknowledge funding from the Frohman Foundation: Innovating Precision CARE Through Discovery in Molecular Medicine for Figure 1.

Study Funding

The authors report no targeted funding.

Disclosure

C. Goldschmidt has no disclosures. S.L. Galetta has received consultant fees from Genentech. R.P. Lisak, over the past 2 years, has been funded for research support by the NIH, National Multiple Sclerosis Society (USA), Mallinckrodt Pharmaceuticals, Genentech, Teva Pharmaceuticals, Novartis, MedImmune, and Chugai; he has served as a consultant to Gerson Lehrman Group, Syntimmune, Alexion, Alpha Sites, Insights Consulting, Informa Pharma Consulting, and Sling-shot Consulting; he has served on the speaker's bureau for Teva Pharmaceuticals (nonbranded talks only). L.J. Balcer is editor-in-chief of the *Journal of Neuro-Ophthalmology*. A. Hellman and M.K. Racke are employed by Quest Diagnostics and may own stock options. A.E. Lovett-Racke has been a consultant for Biogen and Novartis. R. Alejandro Cruz, M.S. Parsons, and N. Sattarnejhad have no disclosures. L. Steinman is on the Editorial Boards of *The Proceedings of the National Academy of Sciences* and the *Journal of Neuroimmunology*; he has served on the Editorial Board of the *The Journal of Immunology* and *International Immunology*; he has served as a member of grant review committees for the NIH and the National MS Society; he has served or serves as a consultant and received honoraria from Atara Biotherapeutics, Atreca, Biogen Idec, Celgene, Centocor, Coherus, EMD-Serono, Genzyme, Johnson and Johnson, Novartis, Roche/Genentech, Teva Pharmaceuticals, Inc., and TG Therapeutics; he has served on the Data Safety Monitoring Board for TG Therapeutics; he serves on the Board of Directors of Tolerion and Chairs the Scientific Advisory Board for Atreca. Currently, L. Steinman receives research grant support from the NIH and Atara Biotherapeutics. S.S. Zamvil is Deputy Editor of *Neurology*, *Neuroimmunology and Neuroinflammation* and is a member of the advisory board for

the International Society of Neuroimmunology; he has served as a consultant and received honoraria from Biogen Idec, EMD-Serono, Genzyme, Novartis, Roche/Genentech, and Teva Pharmaceuticals, Inc., and has served or serves on Data Safety Monitoring Boards for Lilly, BioMS, Teva, and Opexa Therapeutics. Currently, S.S. Zamvil receives research grant support from the NIH, the NMSS, The Maisin Foundation, Biogen, and Celgene. E.M. Frohman serves on the Editorial Boards of *Journal of Neurology*, *The Journal of the Neurological Sciences*, and *Neuroimmunology Reports*; he has received speaker honoraria from Genzyme, Novartis, Janssen, and Alexion. T.C. Frohman serves on the Editorial Board of *Neuroimmunology Reports*; she has received speaker fees from Alexion. Go to Neurology.org/NN for full disclosure.

Publication History

Received by *Neurology: Neuroimmunology & Neuroinflammation* June 21, 2022. Accepted in final form August 12, 2022. Submitted and externally peer reviewed. The handling editor was Josep O. Dalmau, MD, PhD, FAAN.

Appendix Authors

Name	Location	Contribution
Carolyn Goldschmidt, MD	Department of Neurology, Cleveland Clinic	Conception, manuscript drafting, clinical and imaging review, literature review, and critical revision of the manuscript
Steven L. Galetta, MD	Department of Neurology, New York University	Critical revision of the manuscript for intellectual content
Robert P. Lisak, MD	Department of Neurology, Wayne State University	Critical revision of the manuscript for intellectual content
Laura J. Balcer, MD, MSCE	Department of Neurology, New York University	Critical revision of the manuscript for intellectual content
Andrew Hellman, PhD	Quest Diagnostics	Critical revision of the manuscript for intellectual content
Michael K. Racke, MD	Quest Diagnostics	Critical revision of the manuscript for intellectual content
Amy E. Lovett-Racke, PhD	Ohio State University	Critical revision of the manuscript for intellectual content
Roberto Cruz, MD	Department of Neurology, Doctors Hospital at Renaissance Department of Neurology, University of Texas, Rio Grande Valley	Critical revision of the manuscript for intellectual content
Matthew S. Parsons, PhD	Emory University	Critical revision of the manuscript for intellectual content
Neda Sattarnejhad, MD	Department of Neurology, Stanford University School of Medicine	Critical revision of the manuscript for intellectual content

Appendix (continued)

Name	Location	Contribution
Lawrence Steinman, MD	Department of Neurology, Stanford University School of Medicine	Critical revision of the manuscript for intellectual content
Scott S. Zamvil, MD, PhD	Department of Neurology, Program in Immunology, University of California at San Francisco	Conception and critical revision of the manuscript for intellectual content
Elliot M. Frohman, MD, PhD	Distinguished Senior Fellow (Sabbatical) Laboratory of Neuroimmunology of Professor Lawrence Steinman, Stanford University School of Medicine	Conception and critical revision of the manuscript for intellectual content
Teresa C. Frohman, MPAS, PA-C	Distinguished Senior Fellow (Sabbatical) Laboratory of Neuroimmunology of Professor Lawrence Steinman, Stanford University School of Medicine	Conception and critical revision of the manuscript for intellectual content

References

- Flanagan EP, Weinschenker BG, Krecke KN, et al. Short myelitis lesions in aquaporin-4-IgG-positive neuromyelitis optica spectrum disorders. *JAMA Neurol.* 2015;72(1):81-87.
- Pittock SJ, Lennon VA, Krecke K, Wingerchuk DM, Lucchinetti CF, Weinschenker BG. Brain abnormalities in neuromyelitis optica. *Arch Neurol.* 2006;63(3):390-396.
- Wingerchuk DM, Banwell B, Bennett JL, et al. International Panel for NMO Diagnosis. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology.* 2015;85(2):177-189.
- Ayzenberg I, Schollhammer J, Hoepner R, et al. Neuromyelitis Optica Study Group. Efficacy of glatiramer acetate in neuromyelitis optica spectrum disorder: a multicenter retrospective study. *J Neurol.* 2016;263(3):575-582.
- Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol.* 2018;17(2):162-173.
- Wingerchuk DM, Lennon VA, Lucchinetti CF, Pittock SJ, Weinschenker BG. The spectrum of neuromyelitis optica. *Lancet Neurol.* 2007;6(9):805-815.
- Pittock SJ, Lennon VA, Bakshi N, et al. Seroprevalence of aquaporin-4-IgG in a Northern California population representative cohort of multiple sclerosis. *JAMA Neurol.* 2014;71(11):1433-1436.
- Lennon VA, Wingerchuk DM, Kryzer TJ, et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. *Lancet.* 2004;364(9451):2106-2112. doi: 10.1016/S0140-6736(04)17551-X.
- Lennon VA, Kryzer TJ, Pittock SJ, Verkman AS, Hinson SR. IgG marker of optic-spinal multiple sclerosis binds to the aquaporin-4 water channel. *J Exp Med.* 2005;202(4):473-477. doi: 10.1084/jem.20050304
- Brum DG, Barreira AA, dos Santos AC, et al. HLA-DRB association in neuromyelitis optica is different from that observed in multiple sclerosis. *Mult Scler.* 2010;16(1):21-29.
- Kim HJ, Paul F, Lana-Peixoto MA, et al. Guthy-Jackson Charitable Foundation NMO International Clinical Consortium & Biorepository. MRI characteristics of neuromyelitis optica spectrum disorder: an international update. *Neurology.* 2015;84(11):1165-1173. doi: 10.1212/WNL.0000000000001367
- Wattjes MP, Ciccarelli O, Reich DS, et al. 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis. MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis. *Lancet Neurol.* 2021;20(8):653-670. doi: 10.1016/S1474-4422(21)00095-8.
- Filippi M, Preziosa P, Banwell BL, et al. Assessment of lesions on magnetic resonance imaging in multiple sclerosis: practical guidelines. *Brain.* 2019;142(7):1858-1875. doi: 10.1093/brain/awz144.
- Marrie RA, Reider N, Cohen J, et al. A systematic review of the incidence and prevalence of autoimmune disease in multiple sclerosis. *Mult Scler.* 2015;21(3):282-293.
- Edwards LJ, Constantinescu CS. A prospective study of conditions associated with multiple sclerosis in a cohort of 658 consecutive outpatients attending a multiple sclerosis clinic. *Mult Scler.* 2004;10(5):575-581.
- Anadani N, Hyland M, Cruz RA, et al. Treating MS after surviving PML: discrete strategies for rescue, remission, and recovery patient 1: from the National Multiple Sclerosis Society Case Conference Proceedings. *Neurol Neuroimmunol Neuroinflamm.* 2021;8(1):e929. doi: 10.1212/NXI.0000000000000929

Neurology[®] Neuroimmunology & Neuroinflammation

Multiple Sclerosis Followed by Neuromyelitis Optica Spectrum Disorder: From the National Multiple Sclerosis Society Case Conference Proceedings

Carolyn Goldschmidt, Steven L. Galetta, Robert P. Lisak, et al.

Neurol Neuroimmunol Neuroinflamm 2023;10;

DOI 10.1212/NXI.0000000000200037

This information is current as of October 21, 2022

Updated Information & Services	including high resolution figures, can be found at: http://nn.neurology.org/content/10/1/e200037.full.html
References	This article cites 16 articles, 1 of which you can access for free at: http://nn.neurology.org/content/10/1/e200037.full.html##ref-list-1
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://nn.neurology.org/misc/about.xhtml#permissions
Reprints	Information about ordering reprints can be found online: http://nn.neurology.org/misc/addir.xhtml#reprintsus

Neurol Neuroimmunol Neuroinflamm is an official journal of the American Academy of Neurology. Published since April 2014, it is an open-access, online-only, continuous publication journal. Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Academy of Neurology. All rights reserved. Online ISSN: 2332-7812.

