

Late Recurrence of Neuromyelitis Optica Spectrum Disorder Following Multiple COVID-19 Vaccinations After Nearly Four Decades of Clinical Stability: A Case Report

Katharine Gen

katiegen@me.com

Gershon Pain Specialists

Dr. Steven Gershon

Gershon Pain Specialists

Case Report

Keywords: Neuromyelitis Optica Spectrum Disorder, COVID-19, vaccination, disease relapse, case report.

Posted Date: September 30th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10530425/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background: Neuromyelitis Optica Spectrum Disorder (NMO) is a rare autoimmune inflammatory disease of the central nervous system characterized by recurrent episodes of optic neuritis, transverse myelitis, and other neurologic manifestations.

Case presentation: We report the case of a 75-year-old white woman with NMO who remained clinically stable for nearly four decades following her initial diagnosis in 1982. In 2021, after receiving multiple doses of the Moderna COVID-19 vaccine, she developed progressive neurologic symptoms including worsening lower extremity spasticity, visual decline, and intractable nausea. Evaluation confirmed recurrent disease activity, and she underwent treatment with IV corticosteroids, plasma exchange, and multiple pharmacologic therapies. Due to refractory lower extremity spasticity, she was subsequently treated with serial botulinum toxin injections, which provided transient symptomatic improvement.

Conclusion: This case highlights an unusual presentation of late NMO recurrence following a prolonged period of clinical quiescence and contributes to the growing literature describing disease activity temporally associated with COVID-19 vaccination. Further investigation is needed to better understand potential immunologic triggers of NMO relapse and the role of botulinum toxin in managing refractory spasticity in this patient population.

Introduction

Neuromyelitis Optica spectrum disorder (NMO) is a rare autoimmune inflammatory disorder of the central nervous system characterized by recurrent attacks involving the optic nerves, spinal cord, and brainstem [1]. Most attacks occur without an identifiable trigger, although infection and, less commonly, vaccination have been reported before disease onset or relapse. We describe a 75-year-old woman with longstanding quiescent NMO who developed progressive neurologic deterioration temporally associated with multiple Moderna COVID-19 vaccine doses and later received botulinum toxin for refractory lower-extremity spasticity.

Previously considered a variant of multiple sclerosis (MS), NMO was established as a distinct condition after the discovery of immunoglobulin G autoantibodies against aquaporin-4 (AQP4-IgG) [2]. AQP4-IgG binding activates complement and antibody-dependent cellular injury, producing astrocyte damage, demyelination, and neuronal loss. The antibody is detectable in more than 80% of patients, although diagnosis may also be supported by characteristic clinical and MRI findings [1, 2].

NMO accounts for approximately 1–2% of inflammatory demyelinating disease in the United States and Europe, with an estimated worldwide prevalence of 1.82 cases per 100,000 [4]. It predominantly affects women and is more prevalent among Black individuals in the United States neuropathic pain, bowel and bladder dysfunction, and spasticity. Spasticity may present as increased resistance to movement, involuntary spasms, or paroxysmal tonic spasms and can cause substantial functional impairment [5].

SARS-CoV-2 infection and vaccination have been temporally associated with the immune-mediated neurologic disease, including MS and NMO, although causality has not been established [6, 8, 9]. In a review of 41 patients with NMO temporally associated with COVID-19 infection or vaccination, 15 developed disease after infection, 21 after vaccination, 3 with established NMO relapsed after vaccination, and 2 initially diagnosed with MS were subsequently identified as having NMO. Transverse myelitis was the most frequent manifestation [7]. Other reports include AQP4-IgG-positive NMO after Oxford-AstraZeneca and Sputnik vaccination and worsening paraparesis with new NMO-consistent spinal lesions 23 days after vaccination in a 68-year-old woman previously diagnosed with MS [7, 10].

Acute NMO attacks are generally treated with intravenous glucocorticoids and, for moderate or severe relapses, plasma exchange. Long-term relapse prevention may include prednisone, azathioprine, mycophenolate, rituximab, eculizumab, inebilizumab, or satralizumab [2]. Botulinum toxin does not treat the underlying disease but may be used for symptoms such as focal spasticity, bladder dysfunction, or dysphagia; one NMO case report described its use alongside swallowing rehabilitation for cricopharyngeal dysfunction [3]. Evidence specific to NMO is limited.

Despite these reported benefits, data on Botox treatment with NMO is limited. We report another example of a patient who was found to have an exacerbation of her NMO after several COVID-19 vaccinations and subsequently underwent treatment with botulinum toxin injections as part of the management of refractory lower extremity spasticity.

Case presentation

A 75-year-old white woman developed progressive spasticity and other neurologic symptoms beginning in 2021. She had been diagnosed with NMO in 1982 at age 31 after a headache followed three days later by peripheral vision loss and paralysis below the torso. The diagnosis was made clinically, with MRI confirmation obtained in 1983. Despite an initially poor prognosis, physical therapy, corticosteroids, and baclofen produced approximately 75% functional recovery. From 1983 through 2020, she remained clinically stable without recognized relapse or neurologic deterioration. Relevant family, genetic, and psychosocial history was not available for review.

She received an initial Moderna mRNA COVID-19 vaccine in January 2021, followed by additional doses in February and August 2021, and May and October 2022. During this period, she developed progressive peripheral vision loss, lower-extremity spasticity, neuropathic symptoms, intractable nausea, and gait impairment. She did not initially recognize the visual deterioration, which was documented by her ophthalmologist. She also experienced a stroke in July 2022.

Baclofen, which had previously been effective, no longer provided relief and appeared to worsen stiffness. Clonazepam produced only mild improvement, and gabapentin was ineffective. Pregabalin provided partial symptomatic relief without restoring functional mobility. With progression, particularly in the quadriceps, she developed severely restricted knee flexion, ankle clonus, and marked gait

impairment. Following confirmation of recurrence, she received intravenous corticosteroids and plasma exchange.

Beginning in January 2025, she received onabotulinumtoxinA injections at approximately three-month intervals. Initial injections targeted the vastus lateralis and rectus femoris. Doses were escalated over five cycles from a total of 100 units to 500 units. Several cycles produced transient relief lasting only weeks, without weakness, but sustained functional improvement was not achieved. In April 2026, treatment was changed to incobotulinumtoxinA, with a total of 300 units distributed among the vastus medialis, vastus lateralis, vastus intermedius, rectus femoris, and medial and lateral gastrocnemius. Weakness developed following this treatment. Overall, botulinum toxin provided limited and short-term symptomatic benefit.

Timeline

Date	Event
1982	Initial NMOSD Diagnosis
1983-2020	Stable
January 2021	Moderna Initial Vaccine
February 2021	Moderna Booster: Progressive visual loss
August 2021	Moderna Booster
May 2022	Moderna Booster
October 2022	Moderna Booster
2022-2023	Mild progressive exacerbation of NMOSD symptoms: loss of peripheral vision, spasticity, intractable nausea.
July 2022	Stroke
December 2023	IV corticosteroid therapy and plasma exchange (apheresis).
2024	Symptom Progression
January 2025	OnabotulinumtoxinA injections 75/25 units into Vastus Lateralis and Rectus Femoris. Transient relief for only a few weeks, no weakness
April 2025	OnabotulinumtoxinA injections 100/100 units into Vastus Lateralis and Rectus Femoris. Transient relief for several weeks, no weakness
July 2025	OnabotulinumtoxinA injections 75/25 units into Vastus Lateralis and Rectus Femoris. Transient relief for several weeks, no weakness
October 2025	OnabotulinumtoxinA injections 150/150 units into Vastus Lateralis and Rectus Femoris. Better transient relief, but only lasting weeks, no weakness
February 2026	OnabotulinumtoxinA injections 150/350 units into Vastus Lateralis and Rectus Femoris. Minimal relief, no weakness
April 2026	IncobotulinumtoxinA injections: 50/50/25/125/25/25 units into the Vastus medialis, vastus lateralis, vastus intermedius, rectus femoris, medial & lateral gastrocnemius. The patient developed weakness.

Discussion

This case is distinguished by approximately four decades of clinical stability before progressive neurologic deterioration temporally associated with repeated COVID-19 vaccination. A causal relationship cannot be inferred from a single case. Nevertheless, the temporal sequence and published reports of NMO onset or relapse after COVID-19 vaccination raise the possibility that immune activation contributed to recurrence in a susceptible patient [7–10]. The unusually long period between the initial episode and deterioration further differentiates this case from the more typical relapsing course.

Important limitations complicate interpretation. The original diagnosis predated contemporary NMO criteria and serologic testing, and AQP4-IgG testing during recurrence was negative. However, a subset of patients with clinically diagnosed NMO are seronegative, and the historical combination of optic neuropathy and transverse myelitis was consistent with NMO. Contemporary diagnosis reassessment, including testing for myelin oligodendrocyte glycoprotein antibodies if not previously performed, may help clarify the diagnosis. The intervening stroke is also a potential contributor to spasticity and neurologic decline. Moreover, the gradual symptom progression across repeated vaccine doses, rather than a clearly documented acute relapse within a defined post-vaccination interval, limits causal attribution. Spontaneous recurrence or progression remains possible.

The limited response to botulinum toxin should also be interpreted cautiously. Several onabotulinumtoxinA cycles reduced spasticity transiently, but neither onabotulinumtoxinA nor incobotulinumtoxinA produced sustained functional improvement. Response to chemodenervation depends on the severity and chronicity of spasticity, fixed contracture, muscle selection, dose distribution, rehabilitation, underlying neurologic injury, and baseline function. Botulinum toxin is established for focal spasticity caused by upper motor neuron disorders such as stroke, MS, traumatic brain injury, and spinal cord injury, but NMO-specific evidence remains sparse. In this patient, the history of stroke and possible mixed etiologies further limits conclusions about treatment response.

This case therefore contributes a clinically informative, limited response rather than evidence against botulinum toxin for NMO-related spasticity. It illustrates the difficulty of treating severe chronic spasticity when systemic agents are ineffective or poorly tolerated and highlights the need to individualize target-muscle selection, dosing, and concurrent rehabilitation. Further study is needed to define which patients with NMO-related spasticity may benefit from chemodenervation and how outcomes should be measured.

Conclusion

We describe progressive neurologic deterioration after approximately four decades of quiescent NMO, temporally associated with repeated Moderna COVID-19 vaccination. Although causality cannot be established, the case adds to the reports of immune-mediated neurologic events following vaccination and emphasizes the need for cautious assessment of temporal association and alternative explanations. It also demonstrates the challenge of managing refractory lower-extremity spasticity:

escalating onabotulinumtoxinA and subsequent incobotulinumtoxinA produced only transient benefit and, after the latter, weakness. Additional research is needed to clarify potential relapse triggers and optimize symptomatic treatment for NMO-related spasticity.

Patient Perspective

The patient described the progressive lower-extremity spasticity and loss of mobility as the most significant effects of her neurological deterioration. Medications that had previously been helpful, particularly baclofen, no longer provided meaningful relief, while pregabalin produced only partial improvement. She reported that several botulinum toxin treatment cycles temporarily reduced her spasticity. Overall, she viewed the botulinumtoxin injections as providing limited symptomatic relief.

Declarations

Ethics approval and consent to participate:

The manuscript describes a single-patient case report and did not involve prospective research or an experimental intervention.

Consent for publication:

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor in Chief of this journal.

Funding:

Not applicable.

Author Contribution

K.G. performed the literature review, analyzed the case, and drafted the initial and final manuscript. S.G. supervised the project, provided clinical guidance, critically reviewed and revised the manuscript. Both authors read and approved the final manuscript.

Acknowledgements:

Not applicable.

Availability of data and materials:

Not applicable. No datasets were generated or analyzed for this case report.

Competing interests: The authors declare that they have no competing interests.

References

1. Mora Cuervo DL, Hansel G, Sato DK. Immunobiology of neuromyelitis optica spectrum disorders. *Curr Opin Neurobiol.* 2022;76:102618. doi:10.1016/j.conb.2022.102618
2. Wingerchuk DM. Neuromyelitis optica spectrum disorder. *N Engl J Med.* 2022;387(7):631- 639. doi:10.1056/NEJMra1904655
3. He Z, Zhao F, Shan Y, Dou Z, Wen H. *Botulinum toxin injection combined with traditional swallowing rehabilitation improved cricopharyngeal dysfunction in neuromyelitis optica spectrum disorder: A case report.* *Front Neurol.* 2022;13:939443
4. Kim HJ, Paul F, Lana-Peixoto MA, et al. MRI characteristics of neuromyelitis optica spectrum disorder: an international update. *Neurology.* 2015;84(11):1165-1173. doi:10.1212/WNL.0000000000001367
5. Traboulsee A, Greenberg BM, Bennett JL, et al. Safety and efficacy of satralizumab monotherapy in neuromyelitis optica spectrum disorder: a randomized, double-blind, multicenter, placebo-controlled phase 3 trial. *Lancet Neurol.* 2020;19(5):402-412. doi:10.1016/S1474-4422(20)30078-8
6. Kim S, Seok HY. Evaluation of the safety profile of COVID-19 vaccines in patients with MS, NMOSD, and MOGAD. *Neurol Sci.* 2023;44(6):1841-1848. doi:10.1007/s10072-023-06676-1
7. Harel T, et al. New onset or relapsing neuromyelitis optica temporally associated with SARS-CoV-2 infection and COVID-19 vaccination: a systematic review. *Front Neurol.* 2023;14:1099758. doi:10.3389/fneur.2023.1099758.
8. Stastna D, Menkyova I, Drahota J, et al. To be or not to be vaccinated: The risk of MS or NMOSD relapse after COVID-19 vaccination and infection. *Mult Scler Relat Disord.* 2022;65:104014. doi:10.1016/j.msard.2022.104014.
9. Kim SH, Mealy MA, Levy M, et al. Relapse after COVID-19 vaccination in patients with neuromyelitis optica spectrum disorder and multiple sclerosis. *Mult Scler Relat Disord.* 2023;75:104743. doi:10.1016/j.msard.2023.104743.
10. Lohmann L, Glaser F, Möddel G, Lünemann JD, Wiendl H, Klotz L. Severe disease exacerbation after mRNA COVID-19 vaccination unmasks suspected multiple sclerosis as neuromyelitis optica spectrum disorder: a case report. *BMC Neurol.* 2022;22(1):185. doi:10.1186/s12883-022-02698-y.