STEPHY Publishers

SOJ Medical and Clinical Case Reports

Case Report

ISSN: 2834-5517

# Successful Treatment of a Severe Attack of Neuromyelitis Optica Spectrum Disorder Associated with Myasthenia Gravis using Plasmapheresis and Rituximab

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**Abstract**

A 36-year-old woman with a history of myasthenia gravis (MG), who underwent thymectomy surgery 4 years ago, was hospitalized with bilateral leg paralysis and dysesthesia. The patient was diagnosed with concurrent neuromyelitis optica spectrum disorder (NMOSD) and MG, which are both rare autoimmune diseases. The patient was treated with high-dose intravenous methylprednisolone, plasmapheresis and rituximab. She was discharged with significantly improved symptoms. This is a rare clinical case that helps physicians enhance their understanding of the possibility of NMOSD co-occurring with other autoimmune diseases and provides appropriate treatment options.

**Keywords:** Myasthenia, Neuromyelitis optica spectrum disorder, Plasmapheresis, Rituximab

## Introduction

We present a case of a patient with a coexisting diagnosis of myasthenia gravis (MG) and neuromyelitis optica spectrum disorder (NMOSD), highlighting the challenges in managing such cases due to potential overlap in clinical symptoms and the need for tailored treatment approaches. This report describes the successful utilization of plasmapheresis (PLEX) and rituximab, which resulted in clinical improvement for both conditions.

## Case Presentation

A 36-year-old Vietnamese woman, diagnosed with MG (MGFA: IIa) 4 years ago and tested positive for acetylcholine receptor antibodies (AChR Ab), underwent surgery to remove the thymus gland. Her MG was well-controlled on Pyridostigmine (60mg x 8 tablets/day) and Medrol (2mg/day).

Five days prior to admission, she developed weakness in both legs and numbness in the lower extremities bilaterally. Examination

Quick Response Code:

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**Received:** 13 November, 2023 **Published:** 29 November, 2023

**Citation:** Hong KV, Thi ML, Thi AN. Successful Treatment of a Severe Attack of Neuromyelitis Optica Spectrum Disorder Associated with Myasthenia Gravis using Plasmapheresis and Rituximab. *SOJ Med Clin Case Rep*. 2023;3(2):1–4. DOI: 10.53902/SOJMCCR.2023.03.000524

revealed remarkable weakness in the lower extremities bilaterally, with predominance on the right side. Muscle strength in the right leg was rated 0/5, while the left leg 4/5. Additionally, there was a decreased sensation to pinprick below T-4. MRI brain was normal. Thoracic spinal MRI with contrast demonstrated a non-enhancing longitudinally extensive cord T2/STIR hyper intensity from T2-T3 and T4-T6 Figure 1. The CSF analysis showed a slight increase in protein (0.51g/L) along with an elevated leukocyte count (91 cells/mm3), predominantly comprising lymphocytes (70%). Therefore, investigations are undertaken Table 1.

Initial treatment and response: the patient was initially treated with high-dose methylprednisolone (1g/day) for five consecutive days but no significant clinical improvement. Subsequently, she underwent PLEX for a total of seven sessions, which resulted in partial improvement of muscle strength (right leg: 2/5, left leg: 5/5). Due to the patient's partial response and the need for suitable treatment to prevent relapses, the decision was made to administer rituximab. The patient received an initial dose of rituximab (1g) followed by a repeat dose after two weeks. Following rituximab therapy, the patient demonstrated further improvement in muscle strength, reduced numbness in both legs, and regained the ability to walk 100 meters without aids. At discharge, the muscle strength in the right leg improved to 4/5, while the left remained at 5/5. The outpatient treatment will continue with pyridostigmine 60mg x 8 tablets per day, discontinuing Medrol and receiving rituximab infusions every 6 months according to the schedule.

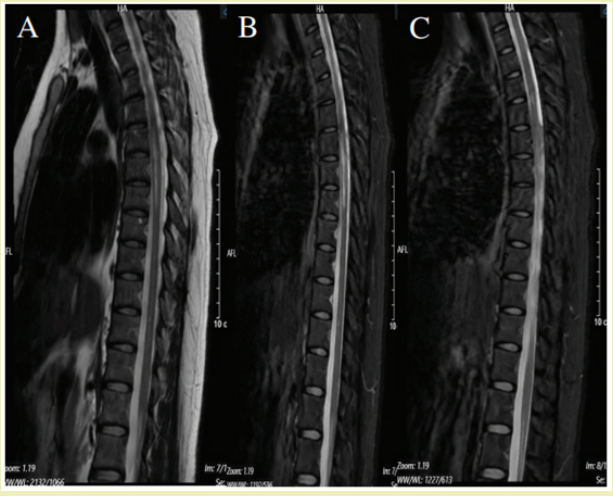


**Figure 1A,B,C:** Sagittal T2 and Short tau inversion recovery (STIR) MRI imaging showing T2-3 central cord hyper intensity and T4-T6 longitudinally extensive central cord hyper intensity in keeping with longitudinally extensive transverse myelitis (LETM) as can be seen in NMOSD.

**Table 1:** Serum Paraclinical studies.

| Test | Result | Test | Result |
|---|---|---|---|
| HIV ELISA Test | Negative | Anti- dsDNA Antibodies | Positive |
| HBs Ag | Negative | Anti- ANA Antibodies | Negative |
| HCV Antibodies | Negative | Anti - Phospholipid IgG Antibodies | Negative |
| Glucose | Normal | Anti - Phospholipid IgM Antibodies | Negative |
| Potassium | Normal | Anti - Cardiolipin IgG Antibodies | Negative |
| Sodium | Normal | Anti- Cardiolipin IgM Antibodies | Negative |
| Serum Protein | Normal | Anti Beta2 - Glycoprotein IgG Antibodies | Negative |
| FT4 | Normal | Anti Beta2 - Glycoprotein IgM Antibodies | Negative |
| TSH | Normal | LAC/ LA screen | Negative |
| Complete Blood count | Normal | LAC/ LA confirm | Negative |
| Creatinin | Normal | APQ - 4 Antibodies | Positive |
| ALT | Normal | | |
| AST | Normal | | |

HIV: Human immunodeficiency viruses; ELISA: Enzyme - linked immune sorbent assay; HBsAg: Hepatitis B Surface Antigen; HCV Ab: Hepatitis C virus antibodies; FT4: Free Thyroxine; TSH: Thyroid stimulating hormone; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; dsDNA: Double stranded deoxyribonucleic acid; ANA: Antinuclear antibodies; LAC/ LA screen: Lupus Anticoagulant screen; LAC/ LA confirm: Lupus Anticoagulant confirm; AQP 4: Aquaporin 4

## Discussion

Both NMO and MG present low prevalence in the general population.[1,2] Our clinical case is a rare example of the combination of both diseases in one individual. The presence of MG and NMO was first reported in 1995. NMO is an inflammatory disorder of the central nervous system characterized by severe demyelination, mediated by the immune system, and primarily targeting the optic nerve and spinal cord fibers. The AQP4 - antibodies are present in 60%- 80% of patients.[3] MG is a neuromuscular disorder associated with the presence of anti–acetylcholine receptor antibodies (AChR-Ab) and characterized by fluctuating muscle weakness.[4] Patients with autoimmune diseases such as systemic lupus erythematosus,

Sjögren syndrome, and MG may have an increased risk of developing NMOSD.[3] In fact, some studies have shown that up to 20% - 30% of patients with NMOSD also have other autoimmune diseases Figure 2.[5] The coexistence of AChR antibodies was found in 11% of NMOSD but only 2% of the NMOSD patients had a clinical diagnosis of MG.[6] Explanation for this mechanism: AQP4 is not only expressed in the central nervous system but also in the bones and epithelial cells of the thymus gland. Abnormalities in the thymus gland that occur in patients with MG may constitute a risk factor for AQP4-Ab production due to AChR-Ab – induced degeneration of the postsynaptic membrane.[7] A history of thymectomy could be a possible risk factor for the later development of NMOSD. A temporal pattern that echoes a previous study investigating NMOSD and comorbid MG, in which 20 of 25 patients developed NMOSD following thymectomy.[3]

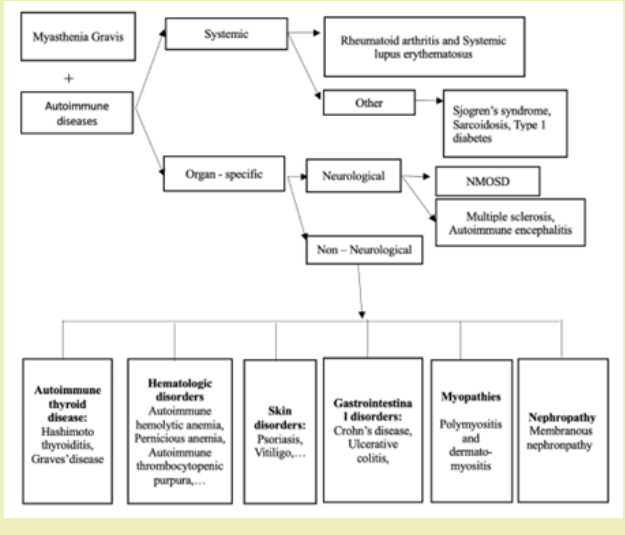


**Figure 2:** Coexistence of autoimmune diseases and MG.[12]

Rituximab has been predominantly used in NMO patients as immunosuppressive therapy to prevent relapses, especially in those who do not respond well to other drugs such as AZA and mycophenolate. It is also being increasingly used as a first-line drug in patients with severe form of NMO. Rituximab is a monoclonal antibody that depletes CD20+ B cells, which are precursors of short-lived antibody-producing plasma cells. This depletion helps suppress antibody-mediated immunity and reduce AQP4 antibody levels as well.

Our patient was initially treated with high-dose intravenous Methylprednisolone (1 gram per day for five consecutive days), however, her clinical condition only improved partially. Therefore, a plasma exchange was performed, following the recommendations of the expert panel.[8-11] Rituximab was started with two 1g infusions separated by a two-week interval, followed by a 1g infusion every six months. However, due to facility constraints, we were unable to quantify CD19+ and CD27+ for monitoring. The patient was discharged with an EDSS score decreased from 9 to 5.5.

## Conclusion

In conclusion, healthcare professionals should recognize the potential overlap between Myasthenia Gravis (MG) and Neuromyelitis Optica Spectrum Disorder (NMOSD) to enhance diagnostic accuracy and optimize treatment strategies. Further research and clinical studies are necessary to deepen our understanding of the relationships between these conditions and explore additional therapeutic avenues that can benefit affected patients.

Moreover, a comprehensive approach that incorporates the use of plasmapheresis (PLEX) and rituximab can greatly benefit the management of NMOSD exacerbations and the long-term treatment of both MG and NMOSD. These therapeutic interventions share a mechanism of action, targeting the underlying pathogenesis of both conditions.

## Acknowledgements

None.

## Funding

None.

## Conflicts of Interest

The authors declare that there are no conflicts of interest.

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