Inebilizumab treatment in a patient with co-occurring AQP4-IgG positive neuromyelitis optica spectrum disorder and myasthenia gravis: a case report and literature review

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Objective: This study aims to delineate the clinical features underlying the concurrent disease of neuromyelitis optica spectrum disorder (NMOSD) and myasthenia gravis (MG), and to identify efficacious therapeutic strategies.

Background: NMOSD and MG are uncommon autoimmune diseases that infrequently co-exist. Despite previous reports, a consensus on treating NMOSD concurrent with MG is lacking.

Methods: We present the case of a 55-year-old female with both anti-aquaporin-4 (AQP4) antibody-positive NMOSD and anti-acetylcholine receptor (AChR) antibody-positive MG, who achieved stable disease control following treatment with inebilizumab without significant adverse effects. We also conducted a literature review to evaluate the clinical profile of this comorbidity.

Results: Our review identified 85 patients with concurrent NMOSD and MG. In 70 well-documented cases, MG predated NMOSD in 60 (85.8%) cases, with 42 (70%) patients having undergone thymectomy. Six (8.6%) patients were first diagnosed with NMOSD, and then thymectomy was performed in 2 (33.3%) MG patients. For NMOSD treatment, although most patients received steroid hormones and immunosuppressive agents, quite a few patients had persistent severe disability. Additionally, of 44 patients with clear records of disease recurrence, 31 patients(70.5%) experienced frequent relapses of optic neuritis and myelitis, ranging from 1 to 15 attacks, averaging five. The manifestations of MG are mainly included fatigability, diplopia, and blepharoptosis, with symptoms well-controlled in most patients. Our patient treated with inebilizumab for 1 year and no relapse was recorded to date.

Conclusions: Though MG typically precedes NMOSD and thymectomy is frequently performed, it is not a prerequisite for NMOSD development but may represent a potential risk factor. MG generally follows a benign course, in contrast to the more aggressive nature of NMOSD. The utility of biological agents such as inebilizumab for patients with both NMOSD combined with MG warrants further attention.

Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is an uncommon demyelinating disorder of the central nervous system (CNS) caused by the action of the anti-AQP4 antibodies ([1]). It is marked by recurrent episodes of optic neuritis(ON) and myelitis, which often lead to significant disability if not treated promptly. Myasthenia gravis(MG) is a chronic organ-specific autoimmune disorder caused by antibody-mediated attacks on nicotinic acetylcholine receptors(AChR) at the neuromuscular junction. This interference disrupts neuromuscular transmission, ultimately leading to muscle weakness and fatigue ([2]). Moreover, the prevalence of MG varies between 0.8 and 20 per 100,000 population ([3]), and prevalence of NMOSD is reported as ranged from 0.07 to 10 per 100,000 ([4]). Although both disorders are rare, the coexistence of MG and NMOSD occurs much more common than by chance, with over 100 cases reported to date ([5]). And a study reported five of 214 reviewed patients with MG (2.3%) who had CNS demyelinating lesion or disease ([6]).

This co-occurrence can complicate the diagnosis of both conditions, as overlapping symptoms may obscure clinical presentation. Furthermore, the concurrent presence of MG complicates NMOSD treatment and may contribute to poorer outcomes ([7]). In this report, we described a patient with concurrent NMOSD and MG, highlighting their clinical course and the challenges encountered in managing these overlapping autoimmune disorders. In addition, we provide a comprehensive review of similar cases in the literature to better delineate the clinical features, potential pathogenic mechanisms, and effective therapeutic strategies for patients with these coexisting conditions. Understanding the interplay between NMOSD and MG is crucial for optimizing management, improving outcomes, and guiding future research into these complex autoimmune diseases.

Case report

A 55-year-old female was hospitalized in May 2023 due to dizziness, nausea, vomiting and gait disturbance. She had been diagnosed with MG over 10 years and had received intermittent treatment with traditional Chinese medicine. Ten years ago, she experienced episodes of ptosis and dysarthria, which was improved completely with traditional Chinese medicine. Upon this admission, she exhibited no MG symptoms, such as ptosis, dysarthria, or fatigue.

Brain magnetic resonance images (MRI) revealed abnormal lesions around the third ventricle (Figure 1). Wernicke's encephalopathy was first considered due to the brain MRI lesions, but was then ruled out because of her persistent symptoms without improvement. Cerebrospinal fluid (CSF) examination demonstrated a normal protein level (404mg/L, normal range 120-600mg/L) and white blood cell count of 8/mm^3(normal range 0-8/mm^3). Thyroid testing indicated anti-thyroglobulin antibody level was 669 IU/mL (normal range <115 IU/ml), and anti-thyroid peroxidase antibody level was 170 IU/mL (normal range <34 IU/ml). Thyroid ultrasound findings were consistent with Hashimoto's thyroiditis. Serum analysis showed a positive AQP4 antibody titer of 1:1000(cell-based assay). Given the high specificity of AQP4 antibodies, she was diagnosed with NMOSD. Then she received intravenous methylprednisolone (500 mg/day) for 5 days, which partially improved her neurological symptoms. She was discharged on oral prednisone (50 mg/day) and mycophenolate mofetil (MMF) (500 mg twice daily). Five months later, she presented with visual blurring in right eye with visual acuity reduced to 0.12 over about 2 weeks. At this admission, her visual evoked potential response was absent on the right eye. Neurological examination showed grade V muscle strength in all limbs. Her quantitative myasthenia gravis score (QMGS) was 0 and Expanded Disability Status Scale (EDSS) score was 3. Her anti-AChR antibodies were positive (6.36 nmol/L, serum ELISA, normal range <0.45nmol/L),while other autoantibodies including MuSK, LRP4, RyR, Titin, antinuclear antibodies (ANA) profile, anti-neutrophil cytoplasmic antibodies (ANCA), and T-SPOT testing were negative. Chest CT showed no thymus abnormalities, and spinal and orbital MRI revealed no notable findings.

She was then treated with methylprednisolone (1 g/day for 5 days) and initiated with inebilizumab (300 mg at day 0,15, and then every 6 months). After two doses, her CD19 B-cell count decreased to 0.1%, and she tolerated well without adverse effects. Over the following year, the patient remained relapse-free after 3 doses, with a stable QMGS of 0 and EDSS score of 2.
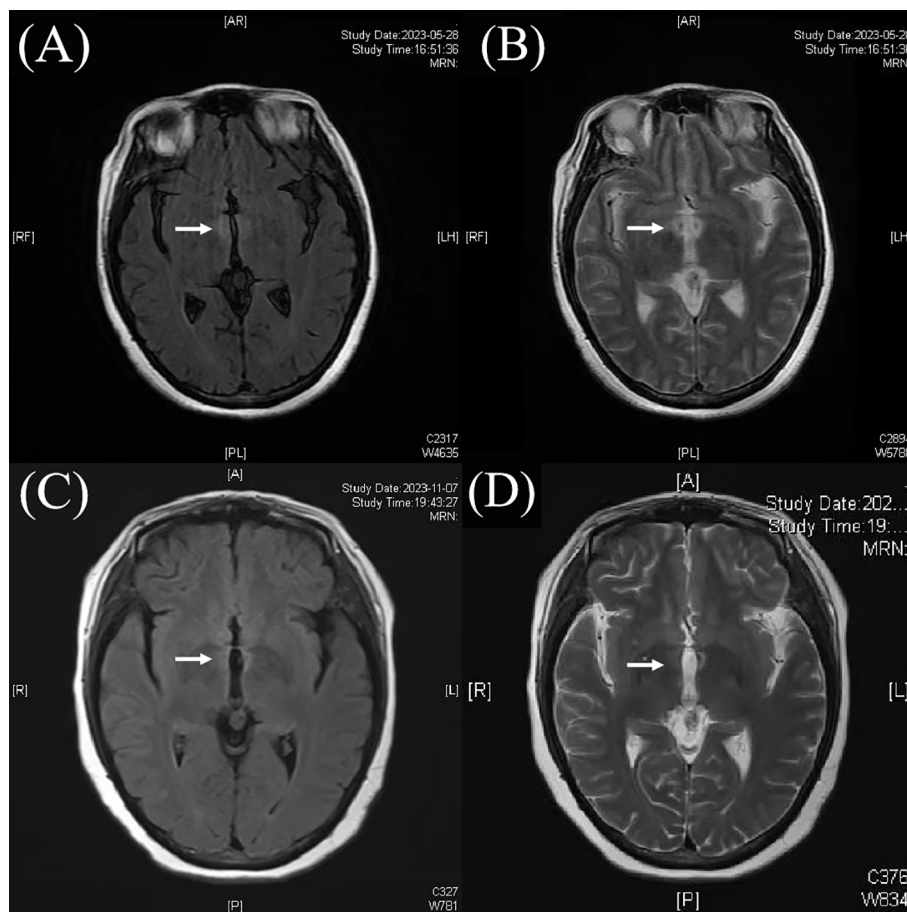
FIGURE 1
Magnetic resonance images (MRI) showed abnormal lesions around the third ventricle **(A, B)**. After treatment, the abnormal lesions of the third ventricle was weaker than before **(C, D)**.

Results: literature review and our case

A total of 27 articles were searched, including a cohort study, a multicentre study (8, 9). Those cases were identified with a PubMed search using the terms "neuromyelitis optica spectrum disorder," "neuromyelitis optica," "myelitis," "optic neuritis," "multiple sclerosis" and "myasthenia gravis."

A total of 85 patients were identified with comorbid NMOSD and MG, including our patient (Table 1). Among 70 patients with well-documented reports, MG predated NMOSD in 60 (85.8%) cases, with 54 (94.7%) being female. MG onset occurred between the ages of 8 and 63 years (median 27.5 years). Of these, 46 patients (76.7%) were aged ≤50 years. Forty-two (70%) had undergone thymectomy, with thymoma confirmed in 3 cases. NMOSD occurred first in 6 cases, with 5 patients (83.3%) being female, and one patient (16.7%) being male. NMOSD onset occurred between the ages of 16 and 79 years (median 41.5 years). Two of these patients had undergone thymectomy, one confirmed case of thymoma. Among patients with both MG and NMOSD, 74 patients (91.3%) were positive for anti-AChR antibodies, and anti-AQP4 antibodies were detected in 62 cases (83.8%). Thirteen patients (26%) also had concurrent other autoimmune diseases, such as thyroid disease, systemic lupus erythematosus (SLE), and Sjögren's syndrome (SS). Additionally, 9 patients (18%) tested positive for other immune-related antibodies, including ANA and double-stranded DNA (dsDNA). These results are summarized in Table 1.

In 50 patients with treatment details, 21 patients started with ON, 16 with myelitis, and 13 were diagnosed with NMOSD in the beginning. Additionally, of 44 patients with clear records of disease recurrence, 31 patients (70.5%) experienced frequent relapses of ON and myelitis, ranging from 1 to 15 attacks, averaging five. Twenty-three patients (63.9%) were treated with intravenous methylprednisolone (IVMP), 6 (16.7%) with plasma exchange (PE), and one (2.7%) with intravenous immunoglobulin (IVIG) during NMOSD acute phases. Regarding the treatment during remission phases, 10 patients (37.0%)were maintained with steroid or prednisolone alone, 14 patients(51.9%) had additional immunosuppressive agents, and 3 patients (11.1%) were supplemented with biological agents, including our patient. One patient passed away in ICU despite IVMP treatment, and 8 patients (28.6%) experienced persistent severe disabilities. Ten patients (35.7%) received completely symptom improvement, and 7 patients (25%) received partially symptoms improvement. Furthermore, most cases responded well to MG therapy, and the

TABLE 1   Clinical and laboratory findings in 50 patients with MG and NMOSD.

No	Sex	Age at onset MG	Age at thymectomy	Histology of thymus	Age at onset of NMOSD	MG treatment	MG prognosis	First Attack of NMOSD	Symptoms at NMOSD onset	No. of ON attacks	No. of Myelitis attacks	NMOSD Treatment (acute phases)	NMOSD Treatment (remission phases)	NMOSD prognosis	Anti-AchR-Ab	Anti-AQP-4-IgG	Other immunological diseases or related antibodies
Uzawa (2)	F	20	28	hyperplasia	41	thymectomy, prednisolone, PE, IVMP, tacrolimus	ptosis and nasal voice were occasionally observed	ON	acute visual loss	4	4	IVMP,PE	prednisolone	severe disabilities persisted	P	P	NA
Uzawa (2)	F	18	20	NA	29	steroid, thymectomy	clinical remission	ON	NA	8	3	IVMP	prednisolone	severe tetraplegia and visual loss persisted	N	P	NA
Isbister (10)	F	28	NA	hyperplasia	36	NA	NA	ON	NA	NA	NA	NA	NA	NA	P	NA	NA
Kay (11)	F	44	not done	not done	49	pyridostigmine	remission	NMOSD	weakness, abnormal sensibility in all limbs, urinary and fecal incontinence	3	3	prednisone AZA	prednisone, AZA	marked and prompt improvement of symptoms.	P	P	NA
Furukawa (12)	F	23	NA	hyperplasia	48	thymectomy	clinical remission	NMOSD	band-like thoracic pain, ophthalmic pain	1	1	IVMP	prednisolone	symptoms improved modestly	P (1304)	N	chronic thyroiditis, ANA 1: 720
Kister (13)	F	38	38	hyperplasia	39	pyridostigmine bromide, thymectomy	symptoms resolved	ON	acute visual loss	7	3	AZA	NA	She had only shade perception and ambulated with assistance	P	P	stiff-person syndrome.
Kister (13)	F	36	37	hyperplasia	42	pyridostigmine, thymectomy	symptoms resolved	ON	acute visual loss	1	2	IVMP, IVIG	methylprednisolone AZA	NA	P	P	ANA1:80 Anti-GAD
Kister (13)	F	17	17	hyperplasia	19	pyrostigmine, thymectomy	well-controlled	ON	acute visual loss	6	9	NA	NA	required a cane for walking	P	N	ANA1:1024, anti-cardiolipin antibodies
Kister (13)	F	27	28	NA	38	pyridostigmine, prednisone, thymectomy, AZA	clinical remission	NMOSD	vision acutely declined, weakness, abnormal sensation and urinary retention	2	2	NA	NA	vision deteriorated acutely in both eyes	P	NA	NA
Nakamura (14)	F	28	30	NA	38	thymectomy	NA	ON	NA	7	2	IVMP	methylprednisolone	sensory disturbance	P	P	NA
Bichuetti (15)	F	26	27	hyperplasia	32	pyridostigmine, thymectomy	NA	NMOSD	truncal and gait ataxia associated to horizontal nystagmus	NA	NA	IVMP	methylprednisolone	symptoms resolved	NA	P	NA
Bichuetti (15)	M	27	not done	not done	45	pyridostigmine, AZA, cyclosporine	remain stable	ON	pain, low visual acuity	NA	NA	NA	cyclosporine	symptoms resolved	NA	P	NA
Bichuetti (15)	F	27	28	NA	31	prednisone, thymectomy, pyridostigmine, AZA	NA	AM	left side paresthesia	3	2	IVMP	prednisone AZA	symptoms resolved	NA	NA	ANA 1:320
Kohsaka (16)	F	NA	NA	hyperplasia	60	cortin, thymectomy, cyclosporine	NA	AM	NA	NA	NA	IVMP , tacrolimus	NA	NA	P	NA	NA

(Continued)

TABLE 1 Continued

No	Sex	Age at onset MG	Age at thymectomy	Histology of thymus	Age at onset of NMOSD	MG treatment	MG prognosis	First Attack of NMOSD	Symptoms at NMOSD onset	No. of ON attacks	No. of Myelitis attacks	NMOSD Treatment (acute phases)	NMOSD Treatment (remission phases)	NMOSD prognosis	Anti-AchR-Ab	Anti-AQP-4-IgG	Other immunological diseases or related antibodies
Ogaki (17)	F	30	40	NA	43	pyridostigmine bromide, thymectomy	well-controlled	ON	visual field defect in left eye	2	2	prednisone	metacortandracin	NA	P	P	ANA1:1280, hyperthyroidism
Hironishi (18)	F	23	NA	NA	30	thymectomy	complete remission	MNOSD	NA	NA	NA	IVMP	steroid AZA	NA	P	NA	NA
Jarius (19)	F	31	36	hyperplasia	59	thymectomy	NA	AM	NA	0	2	NA	NA	NA	P (6.8)	P	ANA 1:640, TPO-Ab
Jarius (19)	F	26	not done	not done	26	NA	NA	ON	NA	several	2	NA	NA	NA	P (26.3)	P	ANA
Jarius (19)	F	23	23	hyperplasia	43	NA	NA	AM	NA	0	3	NA	NA	NA	P (29)	P	ANA, anti-dsDNA-Ab
Jarius (19)	F	25	not done	not done	66	NA	NA	AM	NA	0	2	NA	NA	NA	NA	P	ANA
Jarius (19)	F	21	35	hyperplasia	67	NA	NA	AM	NA	0	2	NA	NA	NA	P (12.5)	P	anti- GAD Ab,
Jarius (19)	F	33	35	normal	47	NA	NA	AM	NA	3	2	NA	NA	NA	P	P	SS
Jarius (19)	F	13	14	normal	28	NA	NA	ON	NA	1	1	NA	NA	NA	P	P	NA
Jarius (19)	F	11	13	thymitis	32	NA	NA	ON	NA	1	1	NA	NA	NA	P (63.4)	P	SLE
Jarius (19)	F	29	not done	not done	55	NA	NA	ON	NA	1	2	NA	NA	NA	P (7.6)	P	NA
Spillane (20)	F	23	24	normal	31	pyridostigmine, prednisolone, thymectomy	remain stable	MNOSD	nausea, vomiting and hiccups, altered sensation in right arm	0	1	prednisolone, AZA	NA	limb power returned to normal	P	P	NA
Ikeguchi (21)	F	25	29	normal	49	prednisolone, thymectomy	symptoms improved	AM	gait disturbance	0	1	IVMP	prednisolone	able to walk unassisted	P	P	NA
Ikeguchi (21)	F	47	not done	not done	79	prednisolone	NA	ON	acute vision loss in left eye	2	0	IVMP	prednisolone	right eye blindness and disability	P	P	NA
Ikeguchi (21)	M	41 (preceded NMOSD)	41	thymoma	41	steroid	NA	NMOSD	NA	NA	0	steroid	NA	NA	P	NA	NA
Balarabe (22)	F	8	not done	not done	16	pyridostigmine	remain stable	AM	visual impairment, numbness and paraesthesia of lower limbs, urinary and fecal incontinence	NA	2	methylprednisolone, physiotherapy	NA	NA	P	P	NA
O'Riordan (23)	F	NA (preceded NMOSD)	NA	NA	41	NA	well-controlled	ON	acute vision loss in the left eye	1	2	steroids CTX	NA	moderate paraparesis	NA	NA	SLE,ANA, anti-dsDNA Ab
Kimura (24)	F	47	48	hyperplasia	48	steroid, thymectomy	NA	AM	NA	1	3	steroid tacrolimus	steroid tacrolimus	evolved to recurrent myelitis	P	P	NA

(Continued)

TABLE 1 Continued

No	Sex	Age at onset MG	Age at thymectomy	Histology of thymus	Age at onset of NMOSD	MG treatment	MG prognosis	First Attack of NMOSD	Symptoms at NMOSD onset	No. of ON attacks	No. of Myelitis attacks	NMOSD Treatment (acute phases)	NMOSD Treatment (remission phases)	NMOSD prognosis	Anti-AchR-Ab	Anti-AQP-4-IgG	Other immunological diseases or related antibodies
Kimura (24)	M	48	50	normal	61	steroid, tacrolimus	worsening of MG was seen three times	ON	NA	1	1	NA	steroid tacrolimus	evolved to recurrent ON and myelitis	P	P	NA
Bibic (7)	F	36	not done	not done	40	PE,IVMP,RTX, IVIG	passed away in ICU	ON	NA	1	0	IVMP	AZA,HCQ, metacortandracin	passed away in ICU	N	P	hypothyroidism SLE anti-MuSK Ab
Bibic (7)	F	32	not done	not done	36	pyridostigmine	well-controlled	NMOSD	leg weakness, numbness, and pain in the lower extremities bilaterally	1	1	IVMP,PE,RTX,CTX	preventative immunotherapy was not initiated as NMOSD had been quiescent	quiescent	P	N	NA
Bates (25)	F	39	49	NA	54	pyridostigmine, thymectomy	well-controlled	NMOSD	right sided weakness	NA	NA	IVMP	eculizumab	improvement of strength nearly to baseline	P	P	anti-MOG Ab 1:40
Gotkine (26)	F	23	NA	NA	41	pyridostigmine, steroids,AZA, thymectomy	clinical remission	AM	paresthesia	0	2	NA	steroid	NA	P	NA	NA
Gotkine (26)	F	10	12	NA	26	pyridostigmine, steroids,AZA, thymectomy	full remission	AM	neck pain, upper and lower limb weakness, and urinary urgency	0	3	IVMP,PE	NA	remained wheelchair bound	P	P	ANA
Gotkine (26)	F	14	NA	NA	23	steroid, thymectomy	clinical remission	AM	acute bilateral leg weakness and urinary retention	0	1	NA	steroid	bilateral leg weakness and urinary retention improved	P	NA	NA
Tola (27)	F	27	37	hyperplasia	58	anticholinesterase thymectomy	well-controlled	ON	NA	2	4	IVMP,PE,	NA	symptoms partially improved	P	NA	dsDNA1:180, ANA1:360, SLE
PIñAR (28)	F	NA	not done	not done	49	prednison, pyridostigmine bromide	well-controlled	AM	weakness, hypoesthesia in the right leg back pain	NA	1	IVMP	prednison MMF	symptoms partially improved, but dysuria persisted	P	P(6.99)	NA
PIñAR (28)	F	NA	NA	NA	76	pyridostigmine	well-controlled	NMOSD	paresthesia weakness and urinary retention	NA	2	IVMP	prednison MMF RTX	symptoms partially improved, and mild paresis persisted	P	P	ANA,ENA, SS, hypothyroidism
Jarius (19)	F	22	not done	not done	20	NA	NA	ON	NA	6	5	NA	NA	NA	P	P	Hashimoto's thyroditis; TPOAb, TG-Ab
Kimura (24)	F	32	NA	NA	31	thymectomy	NA	AM	NA	0	7	IFN β	steroid, tacrolimus;	NA	NA	P	NA
Etemadifar (29)	F	42	not done	not done	33	pyridostigmine, AZA;	NA	ON	NA	3	1	PE mitoxantrone	prednisolone AZA	NA	P	P	NA
Yau (30)	F	56	not done	not done	51	pyridostigmine	well-controlled	ON	visual impairment in right eye	4	0	IVMP	AZA	no relapse of ON	P (8.83)	P	ANA
Bonner (31)	F	44 (3months since	not done	not done	44	pyridostigmine	complete remission	AM	headache followed by imbalance, right sided extremity numbness and weakness	0	1	IVMP RTX	MMF	no relapse of NMOSD	P (0.53)	P	N-methyl-D Aspartate receptor encephalitis,

(Continued)

TABLE 1 Continued

No	Sex	Age at onset MG	Age at thymectomy	Histology of thymus	Age at onset of NMOSD	MG treatment	MG prognosis	First Attack of NMOSD	Symptoms at NMOSD onset	No. of ON attacks	No. of Myelitis attacks	NMOSD Treatment (acute phases)	NMOSD Treatment (remission phases)	NMOSD prognosis	Anti-AchR-Ab	Anti-AQP-4-IgG	Other immunological diseases or related antibodies
		NMOSD diagnosis)															
Antoine (32)	M	49	49	thymoma	49	thymectomy, IVIG,PE	complete remission	NMOSD	dmyalgia, weakness, and blind ultimately	1	1	IVMP,PE, CTX	NA	able to walk using a cane blind	P	NA	NA
Furukawa (12)	F	63	not done	not done	63	prednisolone	remission	NMOSD	impairment of right visual, gait disturbance	1	1	IVMP	NA	neurological symptoms improved	P (141)	N	ANA,SLE, Grave's disease, autoimmune thyroid disease
Our patient	F	45	not done	not done	55	traditional Chinese medicine	well-controlled	NMOSD	dizziness, nausea, vomiting, gait disturbance	2	0	IVMP	prednison MMF inebilizumab	no obvious improvement in vision	P	P	Hashimoto's thyroditis

MG, myasthenia gravis; NMOSD, neuromyelits optica spectrum disorders; AChR, acetylcholine receptor; ON, optic neuritis; AM, acute myelitis; P, Positive; N, Negative; NA, not available; F, female; M, male; AZA, azathioprine; HCQ, hydroxychloroquine; PE, plasma exchange; CTX, cytoxan; ANA, antinuclear antibody; SLE, systemic lupus erythematosus; SS, Sjögren's syndrome; IVMP, intravenous methylprednisolone pulse; MMF, mycophenolate mofetil.

prognosis is often favorable. In our review, 13 out of 29 patients (44.8%) exhibited well-controlled symptoms or remained stable, while clinical remission or complete remission was reported in 11 patients (37.9%). However, 3 patients experienced MG crises. Therefore, for individuals with concurrent NMOSD and MG, it is essential to pay attention to the management of MG alongside NMOSD treatment.

Discussion

Our patient was diagnosed with both AQP4 antibody-positive NMOSD and AChR antibody-positive MG. She initially presented with dizziness, nausea, vomiting, gait disturbance, and then vision loss. However, despite receiving standard treatment, her vision improved only slightly. In contrast, her MG symptoms, such as ptosis and dysarthria, were well-controlled prior to the NMOSD onset, with a QMGS score of 0. She had been treated with inebilizumab for one year follow-up, with no relapses reported to date.

Although the mechanisms underlying co-occurrence of NMOSD and MG remain unclear, it is hypothesized that the two diseases share common immune pathological mechanisms. In NMOSD, B cells contribute to pathogenesis through the production of pathogenic AQP4-IgG antibodies by plasmablasts (PBs) and plasma cells (PCs) (33), secretion of pro-inflammatory cytokines, and antigen presentation that activates autoreactive T cells (34). MG is due to the action of pathogenic antibodies secreted by PCs at the neuromuscular junction, leading to neuromuscular dysfunction. Both diseases have highly specific autoantibodies, which secreted by PBs and PCs differentiated from B cells. Moreover, genetic predispositions also contribute to the co-occurrence of NMOSD and MG. Human Leukocyte Antigen (HLA) -DPB1*05:01 in both southern Han Chinese and Japanese populations are linked to an increased risk of developing NMOSD (35). HLA-C07:01:01 is a well-characterized risk factor for MG. Additionally, HLA-DRB1*03:01 and HLA-DRB1*15:01 have been emerged as an independent risk allele for both disease (36). Certain HLA types have been pinpointed that correlate with the susceptibility to developing NMOSD and MG (37). When appropriate, HLA genotyping should be considered.

In patients with both conditions, MG typically precedes NMOSD and is often associated with thymectomy. A previous study reported that more than 50% of MG patients have their thymus removed (38). Our literature review showed that approximately 70% patients with both NMOSD and MG had undergone thymectomy. It is a higher proportion than in MG patients without NMOSD. However, it has been reported that NMOSD can develop in MG patients without thymectomy (8), as observed in our case. This indicates that thymectomy is not a necessary factor for the occurrence of NMOSD. One possible explanation is that AQP4, expressed at the peripheral neuromuscular junction, may act as a shared target for both diseases (39). The degeneration of the postsynaptic membrane induced by AChR antibodies may trigger AQP4 sensitization within the inflammatory environment of MG, consequently leading to

autoimmunity against AQP4 (7). This explains why the MG patients without thymectomy would develop NMOSD. Therefore, thymectomy is not prerequisite for NMOSD onset in MG patients. In contrast, for patients who develop NMOSD after thymectomy, the expression of AQP4 in the thymus gland may play a role. The abnormal thymus associated with MG could generate anti-AQP4 antibodies (6). In some cases, an immune response against AQP4 on thymoma cells may trigger NMOSD. And there is another viewpoint that regulatory T cells in the adult thymus play a role in preventing the emergence of autoimmune diseases by keeping autoreactive cells in check. A reduction in regulatory T cells after thymectomy may contribute to the development of NMOSD (40).

In the literature review, many patients were found to have concurrent autoimmune conditions or other immune-related antibodies, such as ANA and dsDNA. Evidence suggests that over 25% of patients with autoimmune disorders are likely to develop another autoimmune condition, which can be either organ-specific or systemic-specific (40). Common co-occurring conditions include thyroid disease, SLE, SS, rheumatoid arthritis, antiphospholipid syndrome, ulcerative colitis and sarcoidosis, et al. Therefore, after the diagnosis of an autoimmune disease, screening for antibodies related to other autoimmune disorders is recommended. A similar situation is observed in patients with both NMOSD and MG. In most cases, MG precedes NMOSD by more than 10 years. Additionally, AQP4-Abs have been detected in some MG patients years even in the absence of clinical manifestations of NMOSD (8). Based on this, we recommend routine evaluation of AQP4-Abs in MG patients, as well as thyroid antibodies, ANA, and dsDNA et al. Moreover, clinical symptoms and signs are essential for determining whether MG coexists with NMOSD or only antibodies are present without active disease. It is also recognized that NMOSD can occur in MG patients even in the absence of AQP4-Abs. This highlights the importance of screening for NMOSD in MG patients, especially when clinical features overlap, regardless of antibody status. A thorough clinical evaluation and the use of advanced diagnostic techniques are crucial for accurately identifying coexisting autoimmune conditions.

The treatment strategies for NMOSD and MG have advanced rapidly in recent years, with novel therapeutic biologics targeting diverse mechanisms emerging. For NMOSD, three biologics have been approved by the U.S. Food and Drug Administration (FDA) for patients with NMOSD: eculizumab, satralizumab, and inebilizumab (41–43). Furthermore, rituximab (RTX) has class I evidence supporting its use in AQP4-IgG positive NMOSD (44). For MG, eculizumab is FDA-approved for refractory cases with efficacy supported by phase III trial data. Efgartigimod has also been approved for the treatment of generalized MG (45). Interleukin-6 inhibitors like satralizumab are under active evaluation (46). RTX has demonstrated promising results in MG, with studies reporting reductions in autoantibody levels and improvements in clinical symptoms (47).

MG tends to be a milder condition in patients with comorbid NMOSD and MG, and its relapse was rare once NMOSD developed. NMOSD appears to be more aggressive and tends to have recurrent attacks. In the case of our patient, MG remained stable, so a special focus on the treatment of NMOSD. NMOSD and

MG are both B cell-mediated autoimmune diseases, making B cell-depleting therapies a logical therapeutic approach. Inebilizumab is FDA-approved for NMOSD. And evidence supports inebilizumab is effective for MG and may even outperform other anti-CD20 therapies such as ocrelizumab, ofatumumab, and obinutuzumab in this context (48). Additionally, inebilizumab has demonstrated potential in other humoral immune-mediated autoimmune diseases. Studies have indicated that it reduces the risk of flares in IgG4-related disease and increases the likelihood of achieving flare-free complete remission within one year (49). Phase I clinical trials of inebilizumab for the treatment of multiple sclerosis (NCT01585766) and systemic sclerosis (NCT00946699) have been completed, showing signals of clinical effectiveness (50). Phase III clinical trials for the treatment of systemic sclerosis (NCT05198557) and N-methyl-D-aspartate receptor encephalitis (NCT04372615) are currently underway (51).

It is important to acknowledge the limitations of our study to provide a balanced perspective on the findings. Firstly, the duration of the follow-up period was relatively short, limited to one year, which restricts conclusions about the long-term sustainability of the observed effects. Secondly, other than monitoring the quantity and functionality of immune cells such as T cells and B cells, glial fibrillary acidic protein(GFAP), neurofilament light chain(NfL) and AQP4 antibody level is crucial for comprehensively evaluating treatment efficacy and predicting prognosis. In light of these limitations, we encourage future research to address these gaps through studies with extended follow-up periods and more robust assessments in patients with NMOSD and MG.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

XS: Writing – original draft. JC: Writing – review & editing. CJ: Writing – original draft. YP: Writing – original draft. YS: Writing – original draft. XZ: Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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