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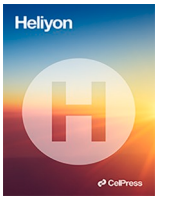

Case report

Visual improvement in a case of neuromyelitis optica spectrum disorder-related optic neuritis after 18 months of treatment with satralizumab: A case report

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A B S T R A C T

Neuromyelitis optica spectrum disorder-related optic neuritis (NMOSD-ON) is an autoimmune disease that affects the astrocytes. NMOSD-ON is one of the core clinical phenotypes of neuromyelitis optica spectrum disorder and its most-common initial symptom. NMOSD-ON is characterized by severe vision loss, poor prognosis and high recurrence, mainly affecting young and middle-aged individuals. It is a challenge to know how to improve patients' visual outcomes. In this report, we present a refractory case of NMOSD-ON treated with satralizumab after multiple conventional therapies proved ineffective. Satralizumab was found to effectively control relapses in this patient and visual improvement was found after 18 months of treatment. Given to that, satralizumab may have a potential longitudinal effect on visual improvement in NMOSD-ON.

1. Introduction

Neuromyelitis optica spectrum disorder-related optic neuritis (NMOSD-ON) is a rare autoimmune disease, with an incidence of 0.039–0.73 cases per 100,000 people [1]. It targets astrocytes in the central nervous system, particularly in the optic nerve and spinal cord. Neuromyelitis optica spectrum disorder (NMOSD) has a high relapse rate, and repeated episodes of NMOSD-ON result in irreversible damage to the visual system. Studies have shown that only 25 % of the long-term disabilities in patients with NMOSD result from the initial attack, highlighting the critical role of recurrence prevention in reducing disability status [2].

With the discovery of the main pathogenic antibody (aquaporin-4 (AQP4) antibody) and the progress of the pathogenesis research, there has been progress in the treatment and prevention of NMOSD, including the use of eculizumab, inebilizumab and satralizumab. In particular, interleukin-6 receptor (IL-6r) inhibitors, such as satralizumab, are known for their ability to not only inhibit lymphocyte activation, but also to alleviate blood-brain barrier damage. Satralizumab acts by inhibiting immune inflammation and reducing the production of autoimmune antibodies [3–5]. However, its impact on visual function recovery is still unknown. Herein, we present a refractory case of NMOSD-ON, in which the patient was switched to satralizumab after multiple treatments with conventional immunosuppressants had proven ineffective. Not only was satralizumab found to effectively control relapses, but the patient's visual function showed improvement 18 months later.

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1.1. Case presentation

A 44-year-old female was admitted to our hospital in December 2021, with a sudden decrease in visual acuity (VA) in her right eye (RE), accompanied by eye movement pain. No associated symptoms, such as dizziness, headache, nausea, vomiting or limb weakness, were reported.

The patient had a history of NMOSD, first diagnosed in 2011. Between 2011 and 2021, the patient experienced a single episode of optic neuritis (ON) in the left eye (LE) and three episodes in the RE, with severe residual visual field (VF) defects in both eyes, more extensive in the LE. The patient also experienced three episodes of myelitis involving motor and sensory impairments, but had no lasting related symptoms. Azathioprine (AZA) treatment for relapse prevention was started after the second ON attack in 2011. However, because there were three more relapses, despite the AZA treatment, the patient was switched to oral mycophenolate mofetil (MMF) therapy at 500 mg twice daily (BID) in 2019. Nonetheless, the patient had two more relapses, in 2019 and 2020 (Fig. 1). The patient had no relevant family medical history.

Upon the patient's admission in December 2021, her best-corrected VA values were 0.5 (RE) and 0.025 (LE). Fundus examination revealed pale optic discs, with clear margins in both eyes. VF mean deviation (MD) values were −7.27 dB (RE) and −27.85 dB (LE). Optical coherence tomography showed extremely thin retinal nerve fiber layers in both eyes, measuring 43 μm (RE) and 48 μm (LE). Her serum AQP4 antibody titer was 1:100. Magnetic resonance imaging using T1-weighted and T2-weighted scans revealed slightly elevated T2-weighted signals in the bilateral intraorbital segments and nerve sheath segments of the optic nerves, with mild and uneven enhancement after contrast administration (Fig. 2). In addition, magnetic resonance imaging of her spine showed intramedullary lesions at the level of the C1, T4 and T7 vertebrae, suggesting demyelinating disease (Fig. 3). The final diagnosis was NMOSD-ON.

Visual deterioration stabilized after one course of high-dose methylprednisolone pulse therapy; however, numbness occurred in her left lower limb, so another course of methylprednisolone pulse therapy, combined with immunoglobulin therapy at 20 g per day for 5 days, was given. Following methylprednisolone pulse therapy, the patient was switched to 56 mg oral methylprednisolone, with weekly tapering over 7 months. The MMF dosage was also increased to 750 mg BID. The patient started treatment with satralizumab in September 2022, at a dosage of 120 mg every 4 weeks, with MMF continued at 750 mg BID.

After 18 months of satralizumab treatment (27 months after the onset of NMOSD-ON), the patient reported slightly improved vision in both eyes, with best-corrected VA values of 0.63 (RE) and 0.05 (LE). VF tests (STATPAC, Allergan Humphrey, San Leandro, CA) also showed improvement in both eyes, especially in the LE, with MD values increasing from −28 dB to −25 dB and macular microperimetry (CenterVue S.p.A., Padova, Italy) average thresholds increasing from 0 dB to 2.5 dB. The VF of the RE remained stable (MD: −6 dB) (Fig. 4). No significant changes in retinal nerve fiber layer thicknesses were found.

2. Discussion

This patient with NMOSD experienced eight relapses despite treatment with conventional immunosuppressants (AZA and MMF) [6]. After switching to satralizumab, not only were her relapses effectively controlled but, unexpectedly, VF improvement was found after 18 months of treatment. Responses to immunosuppressive treatment are less commonly reported in recurrent ON than in other clinical phenotypes of NMOSD [7,8].

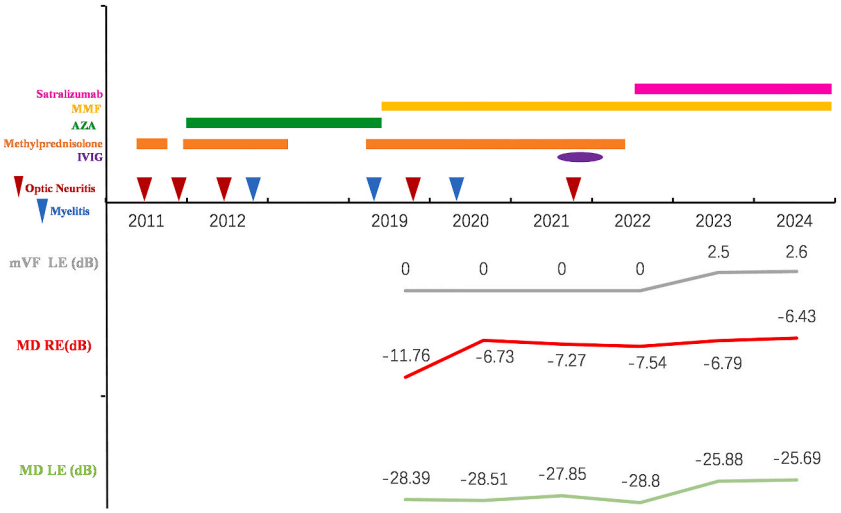

Fig. 1. Timeline of recurrence and treatment during a 13-year course of neuromyelitis optica spectrum disorder-related optic neuritis. Higher mean deviation (MD) and microperimetry (mVF) values indicate better visual function. MMF: mycophenolate mofetil, AZA: azathioprine, IVIG: intravenous immunoglobulins, LE: left eye, RE: right eye.

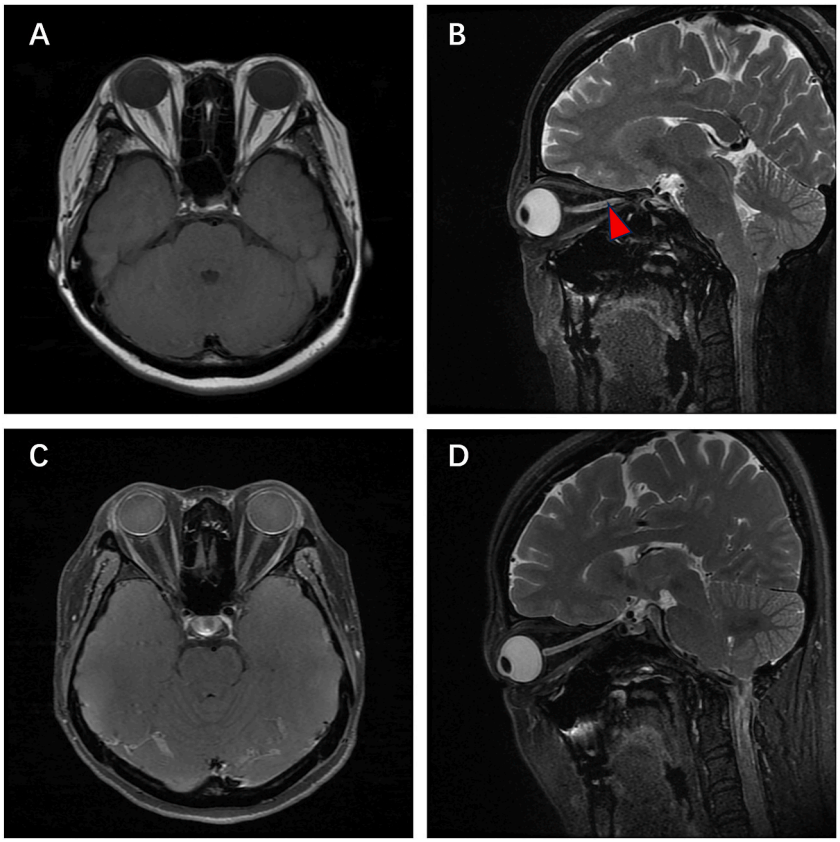

Fig. 2. Orbit magnetic resonance images of a patient diagnosed with neuromyelitis optica spectrum disorder-related optic neuritis. A and C: T1-weighted images showing no apparent abnormality, with mild and uneven enhancement after contrast administration. B (right eye) and D (left eye): slightly elevated T2-weighted image signals in bilateral optic nerves, with the obviously elevated signal on the right side indicated by the red arrow.

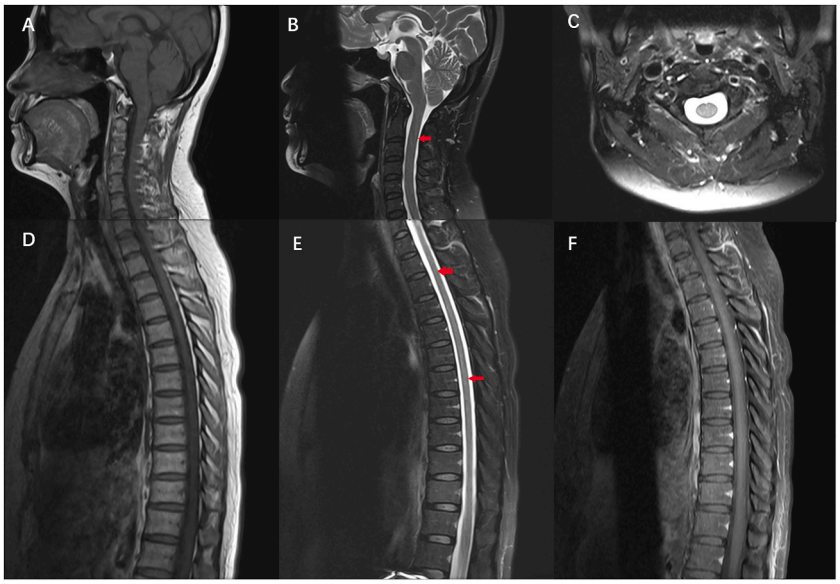

Fig. 3. Magnetic resonance images of a 44-year-old woman with neuromyelitis optica spectrum disorder (NMOSD). Sagittal T1-weighted (A, D), T2-weighted (B, E) and T1 Gd (C: transverse, F: sagittal) images show cervical and thoracic cord involvement (arrows) with slightly elevated signal shown as T2WI hyperintensity without significant enhancement.

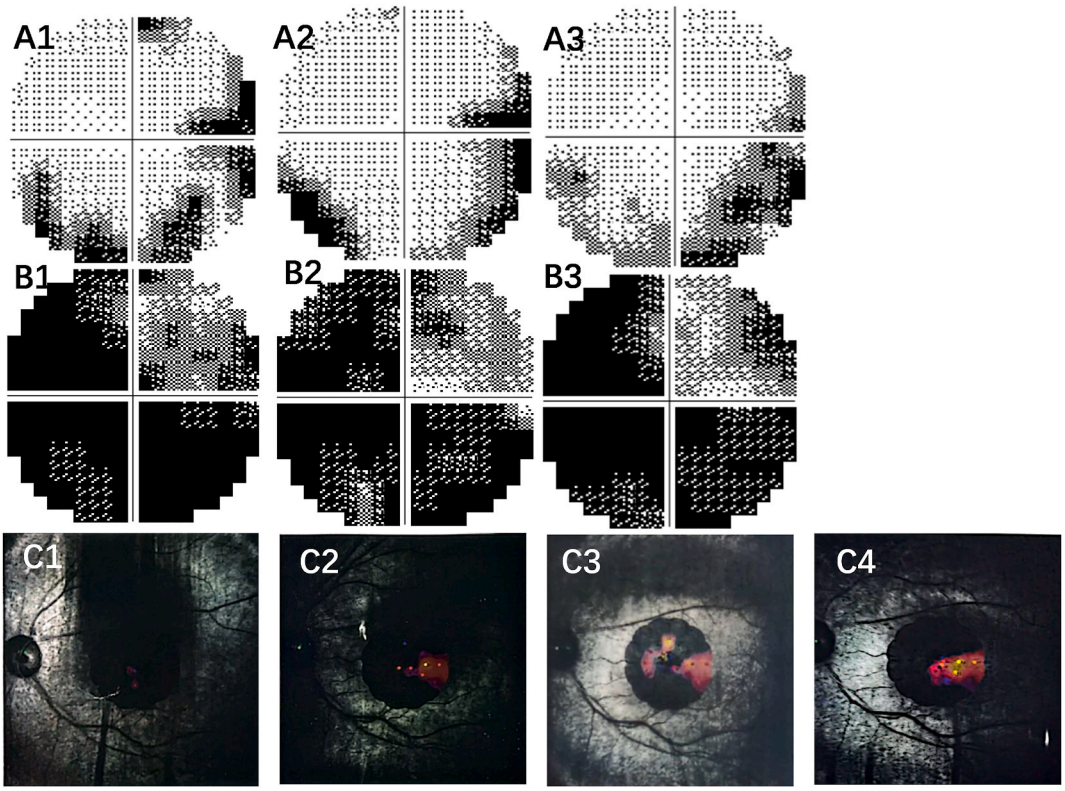

Fig. 4. Visual field (VF) and microperimetry (mVF) test results for the right (RE) and left (LE) eyes before and after 12, 15 and 18 months of treatment with satralizumab. A: VF of the RE (A1: before, −7.54 dB; A2: after 15 months, −6.79 dB; A3: after 18 months, −6.43 dB). B: VF of the LE (B1: before, −28.8 dB; B2: after 15 months, −25.88 dB; B3: after 18 months, −25.69 dB), indicating an improvement in both the superior and inferior arcuate VF defects after treatment. C: mVF of the LE (C1: before, 0 dB; C2: after 12 months, 0.6 dB; C3: after 15 months, 2.5 dB; C4: after 18 months, 2.6 dB).

Satralizumab is a humanized monoclonal immunoglobulin G2 (IgG2) antibody, targeting the IL-6r, which has been found to significantly reduce NMOSD relapses, achieving a 92 % relapse-free rate after 96 weeks of combined baseline immunosuppressive therapy [9]. In the present case, the patient was relapse-free after 27 months of MMF treatment and 18 months of satralizumab treatment. Furthermore, in the Sakura-Moon study, with follow-up as long as 8–9 years, 91 % of patients with NMOSD treated with satralizumab experienced no severe relapses, and 83 % showed no worsening of disability [10]. Satralizumab has been shown to be safe and efficacious in preventing relapses, whether used as monotherapy or in combination with baseline immunosuppressants [9,11]. Consistent with previous studies, satralizumab therapy was safely employed in this patient, with no side effects observed during treatment.

Reports have also indicated that IL-6r inhibitors, including satralizumab and tocilizumab, improve neurologic function, reducing expanded disability status scale (EDSS) scores [12,13]; however, a meta-analysis of tocilizumab therapy data did not support this finding [14]. Nevertheless, EDSS scores alone may not provide a comprehensive neurologic evaluation, especially for ON patients, for whom detailed ophthalmic assessments are essential.

The prognosis for patients with NMOSD-ON is poor and the recovery window is very narrow, with no visual improvement typically found beyond 3–6 months after onset [15]. However, this patient showed visual improvement at 27 months after onset, after 18 months of satralizumab treatment. Because no visual recovery was found after the acute phases of her four previous ON episodes, her visual improvement in this case is considered to be associated with the satralizumab treatment, suggesting that IL-6r inhibitors have an impact on visual function.

There is only one previously documented case of VA improvement associated with satralizumab [16]. However, VA only represents the visual function of the very central retina. Therefore, that patient's visual improvement was not confirmed, because of the absence of VF testing or other visual function examinations. In light of the multifaceted effects of IL-6, some nerve fibers may be dormant and not completely dead during the remission period of inflammation [17,18]. Whether the improvements in VA and VF in the present case are due to the strong inflammatory regulation function of IL-6r inhibitors, which restores the function of dormant nerve fibers, is worthy of further investigation.

It is to be remembered that this case represents a clinical experience, so does not allow for definitive conclusions. Therefore, further research with a larger sample size is needed to confirm the effects of satralizumab on visual function in NMOSD-ON patients. Research on the use of IL-6r inhibitors during acute-phase treatment for improving visual recovery may also be warranted.

3. Conclusions

Herein, we report the case a patient with NMOSD-ON with visual improvement after 18 months of treatment with satralizumab, indicating the potential of IL-6r inhibitors in the recovery of dormant optic nerve function because of multiple mechanisms of IL-6 involved in the inflammation process. Furthermore, prospective, observational studies of visual function in patients treated with IL-6r inhibitors are warranted.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case and any potentially identifiable images or data included in this article.

Statements and declarations

The authors have no conflicts of interest to declare.

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Data availability statement

The original details in this study are included in the article; further inquiries can be directed to the corresponding author.

CRediT authorship contribution statement

Yao Qiu: Writing – original draft, Visualization, Data curation, Conceptualization. **Ting Shen:** Validation, Resources, Data curation. **Wei Qiu:** Validation, Supervision, Resources. **Hui Yang:** Writing – review & editing, Validation, Supervision.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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