

# Neuromyelitis Optica Spectrum Disorder: A Case Report of Effective Combination Immunosuppressant, Corticosteroids, and Therapeutic Plasma Exchange

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## Abstract

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**BACKGROUND:** Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune disease that causes severe demyelination, especially in the optic nerve and spinal cord with typical clinical manifestations of acute optic neuritis and transverse myelitis. The symptoms can occur simultaneously or separated by a variable period. NMOSD is associated with serum aquaporin antibodies 4 immunoglobulin G (AQP4-IgG).

**CASE PRESENTATION:** We report a case of a 22-year-old male with complaints of weakness of all four limbs, impaired vision, urinary incontinence, and dyspnea. The Expanded Disability Status Scale (EDSS) was nine. Spinal magnetic resonance imaging (MRI) showed longitudinal extensive transversal myelitis. The brain MRI showed a normal impression, whereas the brain magnetic resonance spectroscopy (MRS) examination showed a description of the mild demyelination process. The serum antibody AQP4 (AQP4-IgG) results were seronegative, the cerebrospinal fluid examination was normal, and the oligoclonal band was negative. The ophthalmoscopic examination found bilateral papillary atrophy but optical coherence tomography (OCT) was still normal. Somatosensory evoked potential and visual evoked potential examinations were abnormal. The patient was diagnosed with NMOSD and was given combination immunosuppressant therapy, corticosteroids, and therapeutic plasma exchange. The patient experienced significant improvement with EDSS decreased to six.

**CONCLUSION:** In the case of relapsing NMOSD patient, combination therapy of immunosuppressant's, corticosteroids, and TPE was used. There were significant improvements from EDSS nine to six.

## Introduction

Neuromyelitis optica spectrum disorder (NMOSD), formerly known as neuromyelitis optica (NMO) or Devic's syndrome or Devic's disease, was initially considered as part of multiple sclerosis (MS) because the symptoms were considered overlapping. But now, it is known that the pathophysiology of these two diseases is different [1].

NMOSD is a central nervous system inflammatory syndrome that is different from MS, which is associated with serum aquaporin-4

immunoglobulin G (AQP4-IgG) antibodies [1], [2], [3].

NMOSD is an autoimmune disease that causes severe demyelination, especially in the optic nerve with typical clinical manifestations in the form of acute optic neuritis and transverse myelitis which can occur simultaneously or separated by a variable period [1], [2], [3], [4], [5], [6].

It is more common in the form of polyphasic (90%) such as optic neuritis or myelitis, or both occurring together. The monophasic form has only occurred in 10% of cases [1], [2].

## Case report

We report a case of a 22-year-old male with complaints of weakness in all four limbs, impaired vision, urinary incontinence, and dyspnea. Previously the patient had experienced six similar attacks and the longer, the worse the symptoms got. A history of low back pain, muscle spasms, and numbness were found. Neurological examination found a weakness in all four limbs accompanied by increased physiological reflexes and the presence of pathological reflexes. Visual acuity examination on the right and left eyes showed a visual of 1/300 and 1/∞, respectively. Funduscopy examination revealed a picture of bilateral atrophic papillae (Figure 1). The optical coherence tomography (OCT) examination was normal. The presence of exteroceptive and proprioceptive disorders was accompanied by urinary incontinence. The score for the Expanded Disability Status Scale (EDSS) was nine.

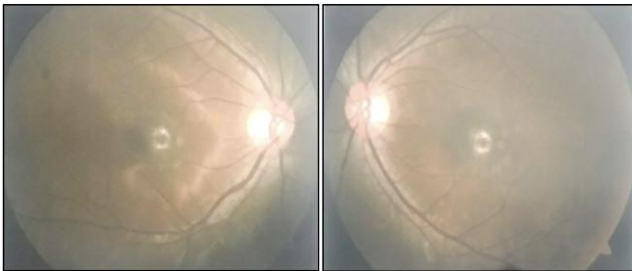


Figure 1: The ophthalmoscopic examination results of a 22-year-old male NMOSD patient with bilateral papillary atrophy

Blood tests results and analysis of brain fluid were within normal limits. Serology for the anti-herpes simplex virus, PCR analysis on herpes simplex virus and cytomegalovirus were negative results. Serum aquaporin 4 examination was negative. Autoimmune antinuclear antibodies (ANA) and anti-DSA analysis were normal. Electrophysiological examination of somatosensory evoked potential (SEP) found lesions between C2-7 and Th2-7 and visual evoked potential (VEP) found partial blocks of bilateral visual pathways. The spinal MRI examination showed a picture of myelitis involving C3-6 and Th2-6 (Figure 2). Brain magnetic resonance spectroscopy (MRS) showed a description of mild demyelination process. Brain magnetic resonance imaging (MRI) showed a normal impression.

Differential diagnosis at that time was NMOSD, MS, acute disseminated encephalomyelitis (ADEM), acute idiopathic myelitis transversalis (iATM) and systemic lupus erythematosus (SLE). Based on the results of clinical symptoms and other investigations, the patient was diagnosed with NMOSD.

Treatment to prevent relapse in this patient was azathioprine at a dose of 50 mg given twice a day. Nevertheless, the patient remained to experience

recurrences. During an acute exacerbation, he was treated with intravenous methylprednisolone but no improvement was noted and his neurological symptoms worsened.

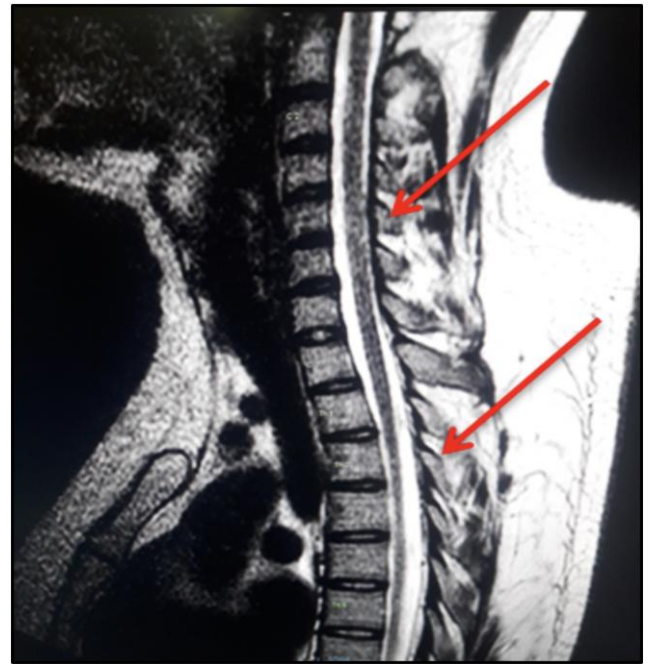


Figure 2: Spinal MRI result of NMOSD patient of a 22-year-old male with longitudinal extensive transversal myelitis involving C3-6 and Th2-6

The patient was then treated with combination therapy of intravenous dexamethasone 5 mg and 7 cycles of therapeutic plasma exchange (TPE) along with physiotherapy. He experienced significant improvement in his neurological symptoms with EDSS decreased to six.

## Discussion

NMOSD is an autoimmune disease that causes severe demyelination, especially in the optic nerve and spinal cord with typical clinical manifestations of acute optic neuritis and transverse myelitis. It has been associated with serum AQP4-IgG [1], [2], [3], [4], [5], [6].

Eugene Devic (1858-1930) who first introduced the French term acute neuromyelitis optic "neuro-myélite optique aiguë" to show a new syndrome characterised by myelitis and acute optic neuritis. Lennon and Wingerchuck (2004) detected the presence of IgG-NMO or IgG-AQP4, the specific antibodies that distinguish NMOSD from MS [1], [7].

NMOSD is a rare syndrome with less than 1% demyelinating disease and the incidence varies in various countries. In general, the incidence of NMOSD ranges from 0.05-4.4 per 100,000 [1], [6]. It generally occurs in Asian, African and Hispanic

descendants [6]. It is more dominant to attack female than the man with a ratio of 3-9: 1, and in adults age between 30.5 and 55.2 years, but can also occur children and elderly [1], [6], [8]. NMOSD cases have been reported in a 3-year-old and a 90-years-old [7].

To date, the pathogenesis of NMOSD is still not fully understood [7], [9]. Antibodies to AQP4 play a key role in the pathogenesis of NMOSD. AQP4 is a water channel that is mostly expressed on podocytes of astrocytic cell membrane forming part of the blood-brain barrier [1], [7], [9].

The clinical features of NMOSD are severe recurrent attacks of myelitis and bilateral and unilateral optical neuritis that can occur simultaneously. It is more common to be found in the form of polyphasic (90%) than monophasic (10%) [1], [2]. In this patient, we found a weakness in all four limbs, accompanied by visual impairment, urinary incontinence, and dyspnea. Previously, he had experienced 6 attacks which at each time was increasingly worsened. Other clinical symptoms include brain stem symptom, posterior reversible encephalopathy syndrome (PRES), coma, hypothalamic dysfunction, depression, cognitive disorders, psychiatric symptoms, and abnormal endocrinopathy [1], [2], [10], [11], [12]. In this patient, no other clinical symptom was found.

Immunological and autoimmune examinations in NMOSD are generally normal [8]. In this patient, the immunological examination against the anti-herpes simplex virus, PCR analysis on herpes simplex virus and cytomegalovirus were negative. An examination of autoimmune antinuclear antibodies (ANA) and anti-DSA was normal.

Serum AQP4-Ig is detected in 60-90% of patients who met NMOSD clinical and radiological criteria [5]. In seronegative AQP4-IgG patients who met the clinical and radiological criteria of NMOSD, serum myelin oligodendrocyte glycoprotein (MOG) antibodies can be detected [2]. In this patient, AQP4-IgG examination was negative, but serum MOG antibody examination was not tested.

Cerebrospinal fluid examination in positive NMOSD patients with AQP4-Ab can be found moderate with normal pleocytosis in about 40% of cases during acute recurrence. Oligoclonal bands (OCB) are usually not found, the intrathecal polyspecific antiviral immune response against-Measles, Rubella and Varicella-Zoster viruses (MRZ reaction) are negative, and increased glial fibrillary acidic protein and neurofilament heavy chain (nfH) are commonly found [8]. In this patient, the cerebrospinal fluid examination gave a normal impression and OCB was negative.

The results of the ophthalmoscopic examination in NMOSD patients varied from optic neuritis, atrophic papillae, to normal features [10]. In this patient, the ophthalmic examination showed

bilateral atrophy. A thinning nerve layer may also be seen in the OCT examination, but the changes take a long time after the development of optic neuritis [3]. In this patient, the OCT examination showed normal findings.

The electrophysiological examination on SEP and VEP often show changes in patients with NMOSD, with prolonged latency at around 40% of cases and decreased amplitude or potential loss in about 25% of patients [8]. In this patient, the SEP examination showed lesions between C2-7 and suspicious lesions between Th2-7. While VEP showed a partial block of bilateral visual pathways.

The MRI examination on the spinal cord in NMOSD have typical features of longitudinal extensive transversal myelitis (LETM), a lesion that extends over 3 or more segments of the adjacent spinal cord [1], [5], [13], [14]. MRI of the optic nerve can be seen as hyperintensity in optic neuritis and tends to have more posterior involvement of the optic nerve. Brain MRI features can vary, such as normal or periependymal lesions surrounding the ventricular system, dorsal brain stem lesions bordering the fourth ventricle, periependymal lesions that surround the lateral ventricles, white matter hemispheres, lesions involving the corticospinal tract, non-specific lesions and enhancing lesions [14], [15]. In this patient, an MRI examination of the spinal cord showed with the features of myelitis involving C3-6 and Th2-6 while a brain MRI examination was normal.

In general, the MRS examination for normal N-acetyl-aspartate (NAA), choline and Myo-inositol parameters are appropriate for normal axonal loss, inflammation, and gliosis [14], [15], [16], [17], [18]. In this patient, MRS examination found an increase in choline levels and the ratio of mild choline/creatine with the impression of a mild demyelination process.

The differential diagnosis of NMOSD is multiple sclerosis, acute disseminated encephalomyelitis, idiopathic acute transversal myelitis, and systemic lupus erythematosus [1], [5], [15], [16], [17], [19].

Therapy in NMOSD consists of acute exacerbation phase therapy to reduce the risk of relapse and long-term care [10], [20]. Treatment options for prevention of relapse include oral corticosteroids, immunosuppressant therapy, TPE, immunomodulatory therapy, and other new therapies. Azathioprine is the main treatment option for preventing relapse at a dose of 75-100 mg/day and is more effective when combined with oral prednisolone (1 mg/kg/day). Evaluation on hematology and long-term side effects including gastrointestinal complaints, leukopenia, infections, allergies, hematological general disorders, and congenital disorders are required [10].

Corticosteroids are the main choice in the acute phase. Intravenous methylprednisolone is

administered with a dose of 1-1.5 grams in 3-5 days [1], [2], [6], [7], [8]. Intravenous dexamethasone at a dose of 5 mg can be also a choice of corticosteroids [21]. Therapeutic plasma exchange (TPE) can be considered if the patient's condition does not improve or neurological symptoms worsen. Therapeutic plasma exchange dosage is carried out by giving 5-7 cycles in a period of 2 weeks with a dose of 1-1.5 plasma per time TPE [1], [6], [8], [9], [10], [20].

This patient has been treated with a dose of 50 mg azathioprine twice a day to prevent relapse, but the patient still had a recurrence. In acute exacerbations, initially, he was given intravenous methylprednisolone but there was no improvement in neurological disorders. Next, he was treated with the combination therapy of intravenous dexamethasone and 7 cycles of TPE. Azathioprine was also continued to be given with physiotherapy. He experienced significant neurological symptoms improvement from EDSS nine to six.

Long-term care is also needed such as medical rehabilitation, management of anxiety and depression, treatment of gastrointestinal problems and bladder, and pain management [20].

The probability of recurrence of disease activity is greater than 90% [21]. Attacks on NMOSD can be very severe, NMOSD can be life-threatening if the lesion extends to the cervical spinal cord and brain stem because it has the potential to cause respiratory failure [1], [7].

In conclusion, in the case of relapsing NMOSD patient, combination therapy of immunosuppressants, corticosteroids, and TPE was used. There were significant improvements from EDSS nine to six.

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