ISSN: 2754-4990

Journal of Ophthalmology Research Reviews & Reports

SCIENTIFIC Research and Community

Case Report

Open Access

Optic Neuritis and Macular Edema in a Patient With NMOSD

Dimopoulos D[1]*, Markakis M[1], Zacharioudakis A[1] and Koutentakis P[1]

Ophthalmology Department, "Venizeleio" General Hospital of Heraklion

ABSTRACT

Background: Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory disease of the central nervous system caused by antibodies preferably to the optic nerve, spinal cord, and certain brain regions. Symptoms may occur at the same time or vary over a period of time. The best prognostic factor of conversion from optic neuritis to clinical definite NMO is the presence of a serum antibody to aquaporin-4 called NMO-IgG. Suspicion of NMO should be high in patients who present with simultaneous bilateral optic neuritis or recurrent attacks and in those with vision of light perception or worse or who are with acuity of 20/50 or worse after optic neuritis.

***Corresponding author**

Dimopoulos D, Ophthalmology Department, "Venizeleio" General Hospital of Heraklion, Greece. Tel: +302813408207; E-mail: dimopoulos3783@gmail.com

Received: December 31, 2021; **Accepted:** July 07, 2022; **Published:** July 21, 2022

Keywords: Neuromyelitis Optica Spectrum Disorder, NMOSD, Aquaporin Antibodies 4 immunoglobulin G, AQP4, Therapeutic Plasma Exchange, TPE, EDSS

Case Presentation

We report a case of a 57-year-old man with complaints of weakness, impaired vision, urinary incontinence, and shortness of breath. The Expanded Disability Status Scale (EDSS) was eight. Magnetic resonance imaging (MRI) of the spine showed longitudinal extensive transversal myelitis. Serum AQP4 antibody (AQP4-IgG) results were negative, cerebrospinal fluid test was normal, and the oligoclonal band was negative. Ophthalmoscopic examination revealed bilateral papillary atrophy, optical coherence tomography (OCT) showed macula edema with diffuse choroidal infiltration and FA revealed late nodular staining of the optic nerve. The patient was diagnosed with NMOSD.

Conclusion

In the case of recurrent patient with NMOSD a combination of intravitreal injections with steroids and anti-vegf, intravenous dexamethasone and TPE was used. There was ocular and neurological improvement, but during follow-up periods, the patient's visual acuity (BCVA) did not improve.

Introduction

Neuromyelitis optica spectrum disorders (NMOSD) is a group of serious inflammatory disorders of the central nervous system (CNS) that include the optic nerve and spinal cord, which can lead to paralysis and blindness [1]. The disease was first reported over 100 years ago [2]. Since then, the concept of NMOSD and the basic clinical features of diagnostic criteria have changed. It is now believed that the pathogenesis of NMOSD is regulated by the peripheral humoral immunity, with the involvement of cellular immunity. Recent studies have shown that the binding of aquaporin-4 (AQP4) antibody and antigen elicits an inflammatory response, including complement-dependent cytotoxicity (CDC), granulocyte infiltration, antibody-dependent cellular cytotoxicity (ADCC), resulting in astrocyte damage, inflamation and secondary neuronal injury [3,4].

NMOSD has been classified as AQP4-IgG positive NMOSD and AQP4-IgG negative NMOSD based on the presence of AQP4 antibodies [1]. For patients with AQP4 positive antibodies, the diagnosis of NMOSD can be made based on at least one key clinical feature (ON or myelitis or brain syndrome), while for patients with serum AQP4 negative antibodies (or unknown serum status) NMOSD, at least two or more core clinical features must be identified (one of which must be ON or MY or area postrema syndrome) [1]. Patients with negative AQP4-IgG are heterogeneous, but the current immunotherapy strategy is similar to conventional NMO.

At the Annual American Neurology 2015 Meeting, Levy and his colleagues proposed an NMO Severity Scale (NMOSS) based on the EDSS score. This method has a higher sensitivity to visual acuity and visual field impairment, focusing on the areas with the most significant impact, including 1) vision, 2) visual field, 3) motor, 4) sensory, 5) bowel and bladder, and 6) brain stem function (focusing on the area postrema and diencephalic function deficit) [5]. This scale is currently being tested in various trials. It is an urgent problem to assess the severity of the disease and the degree of disease activity in clinical trials and guidance for clinical practice. (Table 1)

Table 1: EDSS SCORE (col.A) and diagnostic criteria for NMOSD (col.B)

A. Quantification of Optic nerve and spinal cord impairment			**B. Diagnostic criteria for NMOSD with or without AQP4-IgG**
FUNCTION	**SCORE**	**DESCRIPTION**	**NMOSD with AQP4-IgG** 1. At least 1 core clinical characteristic 2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended) 3. Exclusion of alternative diagnoses
Visual acuity (VA)	0 1 2 3 4 5 6 7 8	Normal Scotoma but VA (corrected) better than 20/30 VA 20/30–20/59 VA 20/60–20/199 VA 20/200–20/800 Count fingers only Light perception only No light perception Unknown	
Motor function	0 1 2 3 4 5 6 7	Normal Abnormal signs (hyperreflexia, Babinski sign) without weakness Mild weakness (Medical Research Council grade 52 or 41) in 1 or more limbs Moderate weakness (grade 3 or 4) in 1 or more limbs Severe weakness (grade 2) in 1 or more limbs Some plegic (grade 0 or 1) muscles in 1 or more limbs Plegia (grade 0 or 1) of all muscles in 1 or more limbs Unknown	**NMOSD without AQP4-IgG or with unknown AQP4-IgG status** 1. At least 2 core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements: a. At least 1 core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome b. Dissemination in space c. Fulfilment of additional MRI requirements, as applicable 2. Negative tests for AQP4-IgG using best available detection method, or testing unavailable 3. Exclusion of alternative diagnoses
Sensory function	0 1 2 3 4 5	Normal Mild decrease in vibration Mild decrease in pinprick/ temperature/proprioception or moderate decrease in vibration Moderate decrease in touch/ pinprick/proprioception or essentially lost vibration sense Loss of all sensory modalities Unknown	Core clinical characteristics 1. Optic neuritis 2. Acute myelitis 3. Area postrema syndrome 4. Acute brainstem syndrome 5. Symptomatic narcolepsy or acute diencephalic clinical syndrome 6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions
Sphincter function	0 1 2 3 4 5	Normal Mild urinary urgency or hesitancy, constipation Moderate urinary urgency, hesitancy, or retention of bladder or bowel, infrequent urinary incontinence (less than once per week) Frequent incontinence or retention requiring intermittent bladder catheterization or aggressive (manual) bowel assistance Indwelling urinary catheter or absence of sphincter control Unknown	

Case Presentation

A 57-year-old man, who was treated with IV Methylprednisolone 1000 mg daily for 5 days for optic neuritis coming from a stroke of the medulla oblongata at our neurological clinic, developed progressive vision loss of one month with blurred vision mainly in the left eye. The Neurologists determined the score for the Expanded Disability Status Scale (EDSS) was eight and noted that steroid therapy did not improve his visual symptoms and requested an ophthalmological examination.

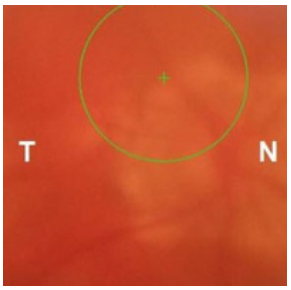
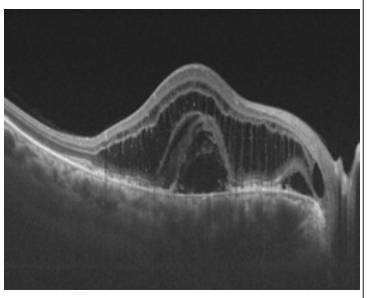
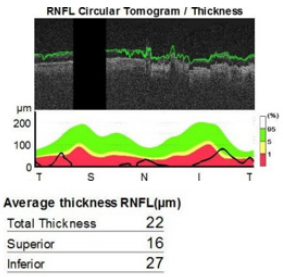
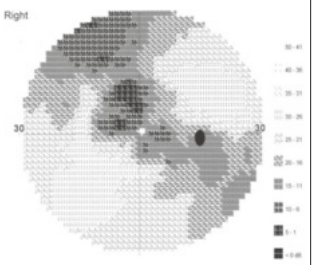
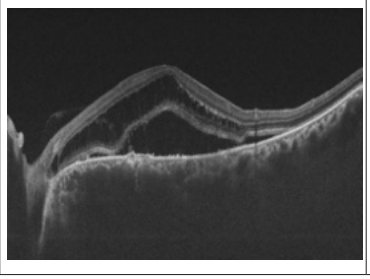
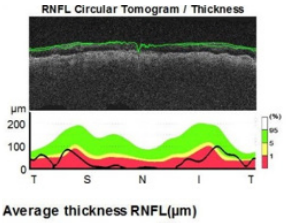
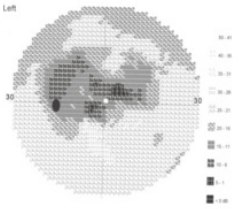
His medical history was notable for hypothyroidism and smoking history. He had no personal or family history of autoimmune disease and from his ocular history he has color blindness.

At his initial visit, the best-corrected visual acuity (BCVA) was 1/10 in the right eye (OD) and 2/10 in the left eye (OS) with intraocular pressures (IOP) of 11 and 12 mmHg, respectively. The eyes are aligned and the eye muscles seem to be working properly. The pupils respond normally, with a negative RAPD test.

Wide field Optus color fundus photos and autofluorescence, exhibited peripheral regions of RPE hyperautofluorescence, demonstrating areas of photoreceptor and RPE degeneration (Table 2).

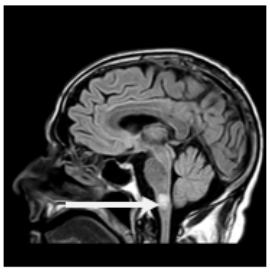
In OCT-RNFL both eyes show severe diffuse loss, with mean values of 22 μm, right eye, and 34μm, left eye. Humphrey visual fields (HVF) demonstrated a temporal field deficit OD and peripheral constriction with a central island remaining OS. OCT showed bilateral papilledema and macular edema, with diffuse choroidal infiltration. Fluorescein angiography (FA) at the mid-phase angiogram revealing early nodular staining of the optic nerve and at the late-phase angiogram showing late nodular staining of the optic nerve (Table 2).

Table 2: Fundus photos, autofluorescence, Humphrey visual fields (HVF) and RNFL (before treatment)

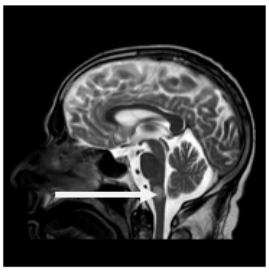
	Color fundus photos	OCT	OCT-RNFL	Humphrey visual fields (HVF)
OD				
OS				

MRI of the orbits was normal but MRI of the brain noted increased FLAIR signal and restriction of medulla oblongata diffusion (Table 3). CT scan of the thorax, abdomen and pelvis, taken in the axial, coronal and sagittal planes, were normal respectively.

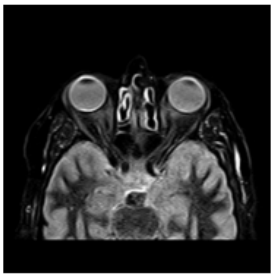
Table 3: MRI Brain, Spinal Cord and Orbits



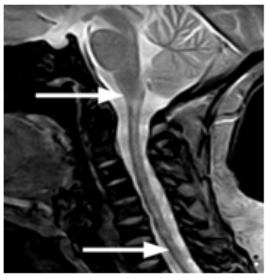
eFLAIR longTR MRI BRAIN



T2W TSE MRI BRAIN



eSTIR FLAIR SENSE MRI ORBITS



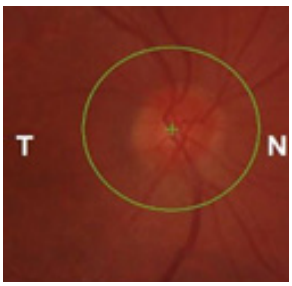
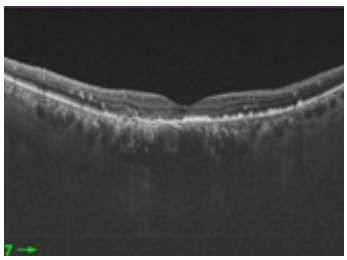
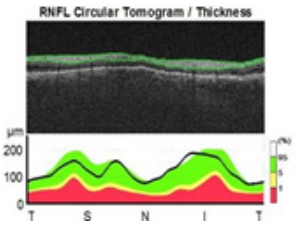
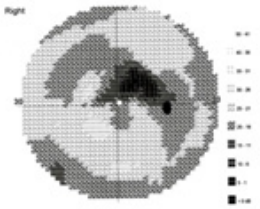
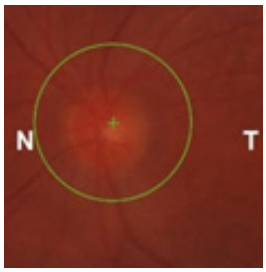
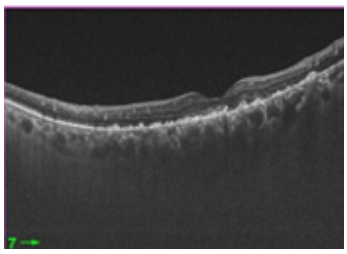
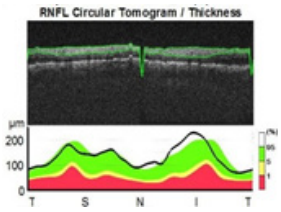
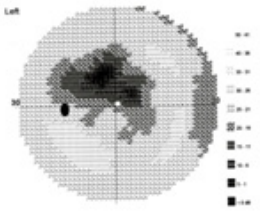
T1 SPINALCORD MRI longitudinally extensive signal change

During one month of follow-up, he reported a decrease in his ocular function. BCVA was LP in the right eye (OD) and 1/20 in the left eye (OS) with intraocular pressures (IOP) of 11 and 12 mmHg OD and OS, respectively. Blood tests results and cerebrospinal fluid analysis were within normal limits. PCR analysis on herpes simplex virus, serology for the anti-herpes simplex virus and cytomegalovirus were negative results. Serum aquaporin 4 examination (IgG-AQP4) was negative. Anti-DSA analysis and autoimmune antinuclear antibodies (ANA) were normal. We performed two VEP test for the 15 min of arc check size, the mean P100 latency was significantly delayed (OD: 107 msec, OS: 110 msec).

Based on the clinical and paraclinical data, it was suspected that the above pathology is part of NMOSD and was planned for combination therapy of intravenous dexamethasone 5 mg and 5 cycles of therapeutic plasma exchange (TPE).

After these sessions, about four months after the initial examination, he experienced significant improvement in his neurological symptoms with EDSS decreased to six, but the ophthalmological examination did not differ significantly from the previous examinations We performed intravitreal steroid injections into both eyes for the macula edema but the result was not satisfactory after 2 months follow up and we performed anti-vegf into both eyes. As shown in table 4, during one month of follow-up there was no longer any IRF or SRF in the macula area. Nevertheless, visual acuity (BCVA) was 3/10 in the right eye (OD) and 1/10 in the left eye (OS) with intraocular pressures (IOP) of 12 and 14 mmHg, respectively.

Table 4: Fundus photos, autofluorescence, Humphrey visual fields (HVF) and RNFL (after treatment)

	Color fundus photos	OCT	OCT-RNFL	Humphrey visual fields (HVF)
OD				
OS				

Conclusion

NMOSD is a rare disease, it can occur at any age and is more common in women [1]. Acute attacks of NMOSD include the first attack and subsequent acute relapses. Disability can occur after one attack and can accumulate with each relapse. Severe relapse can be associated with worse prognosis. On average, every three spinal attacks can lead to paraplegia, while every 1.5 attacks on the optic nerve may lead to blindness [6].

Thus, recovering a neurological deficit from an acute attack is essentially in the management of NMOSD. It is vital to start effective treatment as early as possible to mitigate CNS damage and reduce disability. Intravenous methylprednisolone (IVMP) and plasma exchange (PLEX) are currently the most commonly used approaches to treat NMOSD attacks [7-9]. In addition, immunoadsorption (IA) has also shown to be effective for patient's refractory to steroid or as add-on therapy [9]. However, all of these therapies have some limitations, including restricted neural function amelioration, lacking strong long-term improvement and safety issues.

In our case, we present a male patient who has severe neurological disease (NMOSD) and at the same time developed macular edema with diffuse choroidal infiltration. The patient undergoes intravitreal injections with steroids and anti-vegf, intravenous dexamethasone and TPE. He experienced improvement in his neurological symptoms but while there was a significant improvement in imaging control (OCT/FA/RNFL/HVF), his vision did not improve much.

Declaration of Patient Consent

The patient mentioned in this case has provided informed consent for the publication of identifiable details, which can include photograph (s) and/or videos and/or case history and/or details within the text to be published in the above Journal and Article.

Conflicts of Interest/Funding Statement

- The authors have no conflicts of interest to disclose.
- The authors received no specific funding for this work.

References

1. Wingerchuk, Banwell, Bennett, Cabre, Carroll, et al. (2015) International consensus diagnostic criteria for neuromyelitis optica spectrum disorders.Neurology 85: 177-189.
2. Bruce A C Cree, Douglas S Goodin, Stephen L Hauser (2002) Neuromyelitis Optica. Semin. Neurol 22: 105-122.

3. Jonathan M Crane, Chiwah Lam, Andrea Rossi, Tripta Gupta, Jeffrey L Bennett, et al. (2011) Binding Affinity and Specificity of Neuromyelitis Optica Autoantibodies to Aquaporin-4 M1/ M23 Isoforms and Orthogonal Arrays. J. Biol. Chem 286: 16516-16524.
4. Mader, Simone, Kümpfel, Tania, Meinl, et al. (2020) Novel insights into pathophysiology and therapeutic possibilities reveal further differences between AQP4-IgG- and MOG-IgGassociated diseases. Curr. Opin. Neurol 33: 362-371.
5. Levy, Mealy, Jarius S, Paul F, Aktas O, et al. (2015) New Acute Severity Scale for Neuromyelitis Optica Relapses. Presented at the AAN annual Meeting, 22 April 2015, Washington. https://n.neurology.org/content/84/14_Supplement/P5.249
6. Mickael Bonnan, Rudy Valentino, Stéphane Debeugny, Harold Merle, Jean-Louis Fergé, et al. (2018) Short delay to initiate plasma exchange is the strongest predictor of outcome in severe attacks of NMO spectrum disorders. J. Neurol. Neurosurg. Psychiatry 89: 346-351.
7. Nadja Borisow, Masahiro Mori, Satoshi Kuwabara, Michael Scheel, Friedemann Paul (2018) Diagnosis and Treatment of NMO Spectrum Disorder and MOG-Encephalomyelitis. Front. Neurol 9: 888.
8. Alice Bruscolini, Marta Sacchetti, Maurizio La Cava, Magda Gharbiya, Massimo Ralli, et al. (2018) Diagnosis and management of neuromyelitis optica spectrum disorders - An update. Autoimmun 17: 195-200.
9. Ingo Kleiter, Anna Gahlen, BMed, Nadja Borisow, Katrin Fischer, et al. (2016) Neuromyelitis optica: Evaluation of 871 attacks and 1,153 treatment courses: Therapy of NMO Attacks. Ann. Neurol 79: 206-216.