



## Short Communication

# A case of recurrent MOG antibody positive bilateral optic neuritis and anti-NMDAR encephalitis: Different biological evolution of the two associated antibodies

Bojan Rojc<sup>a,\*</sup>, Barbara Podnar<sup>a</sup>, Francesc Graus<sup>b</sup><sup>a</sup> General Hospital Izola, Izola, Slovenia<sup>b</sup> Neuroimmunology Program, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

## ARTICLE INFO

## Keywords:

Myelin-oligodendrocyte-glycoprotein antibody  
 Optic neuritis  
 Anti-N-methyl-D-aspartate receptor encephalitis  
 N-methyl-D-aspartate receptor antibody

## ABSTRACT

We report the clinical association of myelin-oligodendrocyte-glycoprotein (MOG) IgG-associated encephalomyelitis (MOG-EM) and anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis. A 47-year old male presented to our hospital with right eye optic neuritis in February 2018. He had a history of recurrent bilateral optic neuritis since 2001 and in 2013 was treated of a anti-NMDAR encephalitis. He never had any CNS demyelination event besides optic neuritis. At the time of anti-NMDAR encephalitis both NMDAR and MOG antibodies were positive in serum and CSF. At the last visit, serum aquaporin-4 (AQP-4) and NMDAR antibodies were negative but MOG antibodies remained positive.

MOG-EM and NMDAR encephalitis can present over an extended period of time without other signs of CNS demyelination and with a different temporal evolution of the associated antibodies.

## 1. Introduction

In the past years, a considerable amount of knowledge has been obtained regarding neurological syndromes associated with myelin-oligodendrocyte-glycoprotein (MOG) antibodies. MOG antibodies are present in a wide clinical spectrum of central nervous system (CNS) demyelinating diseases, including optic neuritis, myelitis, neuromyelitis optica spectrum disorder (NMSOD), acute disseminated encephalomyelitis (ADEM), brainstem syndromes and encephalitis (Chalmoukou et al. 2015; dos Passos et al. 2018; Sepúlveda et al. 2016; Wang et al. 2018). Recently, recommendations on MOG antibodies testing and proposed criteria for MOG IgG-associated encephalomyelitis (MOG-EM) were published (Jarius et al. 2018). In adults, MOG-EM represents an important differential diagnostic option, especially in aquaporin 4 (AQP-4) antibody negative neuromyelitis optica (NMO) or NMSOD patients. About 20% of seronegative NMSOD patients are positive for MOG antibodies (de Sèze et al. 2016). Evidence from clinical cohorts shows that MOG-positive NMSOD patients have better outcomes and a distinctive clinical picture compared to AQP-4 positive or seronegative NMSOD patients (Cobo-Calvo et al. 2016; Fan et al. 2018; Hoftberger et al. 2015).

Anti-N-Methyl-D-aspartate receptor (NMDAR) encephalitis can occur simultaneously or separated in time with a demyelinating

syndrome (Kruer et al. 2010; Titulaer et al. 2014). In a cohort of 691 anti-NMDAR encephalitis patients, 23 suffered an overlapping demyelinating syndrome, and in the majority of cases, antibodies to AQP-4 or MOG were identified (Titulaer et al. 2014).

Thus, the aim of this case report is to add knowledge on the possible clinical spectrum of anti-NMDAR encephalitis and MOG-EM overlapping syndrome.

## 2. Case report

A 47-year-old Caucasian male presented to the ophthalmology department in February 2018 with complaints of decrease in visual acuity, unpleasant sensations, and photophobia of his right eye (OD) that started the day prior to examination. The patient denied regular alcohol consumption, smoking or illicit drug use.

The patient had a history of recurrent bilateral optic neuritis, which had first appeared in July 2001 in his left eye (OS) and had by the time of presentation recurred twice in his left eye (2004, 2012) and twice in his right eye (2002, 2014). Visual evoked potentials were performed and were in line with demyelinating optic neuropathy. MR imaging of brain and spinal cord never showed demyelinating lesions apart from thinned left optic nerve in 2004. CSF examination performed the same year (2004) disclosed no cells and normal protein level with negative

\* Corresponding author: Neurology Service, General Hospital Izola, Polje 40, Izola, Slovenia  
 E-mail address: [bojan.rojc@sb-izola.si](mailto:bojan.rojc@sb-izola.si) (B. Rojc).

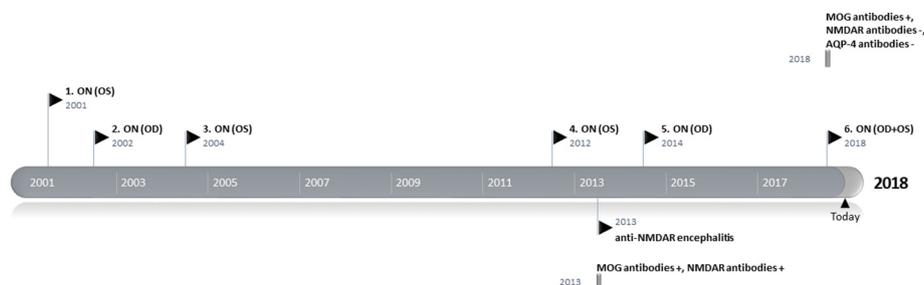


Fig. 1. Timeline of symptoms and antibodies detection.

IgG oligoclonal bands. The optic neuritis episodes always improved after 3-day IV methylprednisolone treatment (1 g/day). In February 2013 the patient was successfully treated in another hospital for anti-NMDAR encephalitis. At that time, brain MR showed T2 and FLAIR nonspecific hyper-intense lesions in right frontoparietal white matter. There was also mild pleocytosis in CSF. EEG was normal. NMDAR antibodies were positive in CSF and serum.

At presentation, best-corrected visual acuity was 6/20 in OD and 6/12 in OS, Ishihara's test showed impaired colour perception bilaterally (OD 2/14, OS 5/14), and there was pain on ocular movement of OD. An Octopus visual field examination revealed an almost complete visual field loss in both eyes with minimal area of preserved sensitivity centrally and inferotemporally in OD and a slightly larger area of preserved sensitivity centrally in OS. Pupillary examination revealed relative afferent pupillary defect (RAPD) in OD. Fundus examination showed pale and sharply demarcated optic discs and optic disc OCT showed considerably thinned retinal nerve fibre layer (RNFL) bilaterally. Blood tests showed minimally elevated leukocyte count ( $(16 \times 10^9/L)$ ), but were otherwise unremarkable. MRI of the brain, cervical and thoracic spine did not show any demyelinating lesions or signs of optic nerve oedema. Serum AQP-4 antibodies were negative and the MOG antibodies positive. Neurological examination did not reveal any further abnormalities.

A diagnosis of recurrent bilateral optic neuritis was established and the patient was admitted for high-dose IV steroid therapy. The 3-day-regimen was extended to 5 days since the visual acuity in OD kept falling during the first three days of hospitalisation. The visual acuity in OS had improved after the first dose of methylprednisolone. At discharge best corrected visual acuity was 6/15 in OD and 6/6 in OS and Ishihara's test was 0/14 in OD and 12/14 in OS. Best corrected visual acuity after 2 months was 6/7 in OD and 6/9 in OS and Ishihara's test was 10/14 in OD and 12/14 in OS. The visual field examination after 2 months showed substantially smaller visual field loss. The patient refused a long-term immunosuppressive treatment.

Retrospectively, we analysed blood and CSF samples from the 2013 period, when he was diagnosed anti-NMDAR encephalitis, which were also positive for MOG antibodies. We also analysed the blood samples for NMDAR antibodies during the last ON episode and were negative.

### 3. Discussion

In this case report we present a patient with two autoimmune diseases of CNS; MOG-EM presented as relapsing bilateral optic neuritis and anti-NMDAR encephalitis. As this combination has been reported in only a few previous case reports or cohort studies, it is evident that both diseases can occur simultaneously in the same patient (Fan et al. 2018; Ran et al. 2017; Titulaer et al. 2014; Zhou et al. 2018). The two diseases can be at different time points or even concomitant (Titulaer et al. 2014). Our case has some distinctive properties that expand the knowledge of the MOG-EM anti-NMDAR encephalitis overlapping syndrome. The anti-NMDAR encephalitis was diagnosed nearly 12 years (139 months) after first optic neuritis attack. This time period is in line with previously reported data or even longer (Titulaer et al. 2014). In

this period, the patient had 4 additional attacks of optic neuritis in both eyes, always recovering substantially after methylprednisolone treatment. It is also evident that our patient fulfilled the proposed criteria for MOG-EM (Jarvis et al. 2018). The clinical history, with recurrent bilateral optic neuritis and a good clinical outcome, is in line with previous reports of patients with MOG antibodies positive demyelinating CNS disorders (Cobo-Calvo et al. 2016; Hoftberger et al. 2015; Sepúlveda et al. 2016). But no other patients reported till now with MOG-EM and anti-NMDAR encephalitis had only bilateral optic neuritis and no other signs of CNS demyelination (Fan et al. 2018; Titulaer et al. 2014; Zhou et al. 2018). The MR imaging of the brain was performed at different time points and there were no signs of demyelinating changes in brain, cervical or thoracic spinal cord apart from thinned left optic nerve. There were only nonspecific T2 hyperintense lesions during the anti-NMDAR encephalitis, in line with the expected changes for this entity (Titulaer et al. 2014). In our case NMDAR and MOG antibodies show two distinct time patterns for each antibody type. NMDAR antibodies were detected in CSF and serum only during the episode of anti-NMDAR encephalitis, on the other hand serum MOG antibodies were detected during last optic neuritis episode and even during anti-NMDAR encephalitis episode. This finding indicates that two different overlapping autoimmune diseases with different immune mechanisms and distinctive clinical pictures coexist, as it was previously postulated by Titulaer et al. (2014) (Fig. 1).

### 4. Conclusion

Our case report expands the knowledge of the clinical spectrum of patients with MOG-EM and anti-NMDAR encephalitis adding new data on the possible time frame, clinical presentation and antibody profile.

### Declarations of interest

None.

### References

- Chalmoukou, K., Alexopoulos, H., Akrivou, S., Stathopoulos, P., Reindl, M., Dalakas, M.C., 2015. Anti-MOG antibodies are frequently associated with steroid-sensitive recurrent optic neuritis. *Neurol. Neuroimmunol. Neuroinflamm.* 2, e131. <https://doi.org/10.1212/NXI.0000000000000131>.
- Cobo-Calvo, Á., Sepúlveda, M., Bernard-Valnet, R., Ruiz, A., Brassat, D., Martínez-Yélamos, S., Saiz, A., Marignier, R., 2016. Antibodies to myelin oligodendrocyte glycoprotein in aquaporin 4 antibody seronegative longitudinally extensive transverse myelitis: Clinical and prognostic implications. *Mult. Scler.* 22, 312–319. <https://doi.org/10.1177/1352458515591071>.
- dos Passos, G.R., Oliveira, L.M., da Costa, B.K., Apostolos-Pereira, S.L., Callegaro, D., Fujihara, K., Sato, D.K., 2018. MOG-IgG-associated optic neuritis, encephalitis, and myelitis: lessons learned from neuromyelitis optica spectrum disorder. *Front. Neurol.* 9. <https://doi.org/10.3389/fneur.2018.00217>.
- Fan, S., Xu, Y., Ren, H., Guan, H., Feng, F., Gao, X., Ding, D., Fang, F., Shan, G., Guan, T., Zhang, Y., Dai, Y., Yao, M., Peng, B., Zhu, Y., Cui, L., 2018. Comparison of myelin oligodendrocyte glycoprotein (MOG)-antibody disease and AQP4-IgG-positive neuromyelitis optica spectrum disorder (NMOSD) when they co-exist with anti-NMDA (N-methyl-D-aspartate) receptor encephalitis. *Mult. Sclerosis Relat. Disorders* 20, 144–152. <https://doi.org/10.1016/j.msard.2018.01.007>.
- Hoftberger, R., Sepúlveda, M., Armangue, T., Blanco, Y., Rostasy, K., Cobo Calvo, A.,

- Olascoaga, J., Ramio-Torrenta, L., Reindl, M., Benito-Leon, J., Casanova, B., Arrambide, G., Sabater, L., Graus, F., Dalmau, J., Saiz, A., 2015. Antibodies to MOG and AQP4 in adults with neuromyelitis optica and suspected limited forms of the disease. *Mult. Scler. J.* 21, 866–874. <https://doi.org/10.1177/1352458514555785>.
- Jarius, S., Paul, F., Aktas, O., Asgari, N., Dale, R.C., de Seze, J., Franciotta, D., Fujihara, K., Jacob, A., Kim, H.J., Kleiter, I., Kümpfel, T., Levy, M., Palace, J., Ruprecht, K., Saiz, A., Trebst, C., Weinschenker, B.G., Wildemann, B., 2018. MOG encephalomyelitis: international recommendations on diagnosis and antibody testing. *J. Neuroinflammation* 15. <https://doi.org/10.1186/s12974-018-1144-2>.
- Kruer, M.C., Koch, T.K., Bourdette, D.N., Chabas, D., Waubant, E., Mueller, S., Moscarello, M.A., Dalmau, J., Woltjer, R.L., Adams, G., 2010. NMDA receptor encephalitis mimicking seronegative neuromyelitis optica. *Neurology* 74, 1473–1475. <https://doi.org/10.1212/WNL.0b013e3181dc1a7f>.
- Ran, Y., Wang, L., Zhang, F., Ao, R., Dong, Z., Yu, S., 2017. Anti-NMDAR encephalitis followed by seropositive neuromyelitis optica spectrum disorder: a case report and literature review. *Clin. Neurol. Neurosurg.* 155, 75–82. <https://doi.org/10.1016/j.clineuro.2017.02.016>.
- Sepúlveda, M., Armangue, T., Martínez-Hernández, E., Arrambide, G., Sola-Valls, N., Sabater, L., Téllez, N., Midaglia, L., Ariño, H., Peschl, P., Reindl, M., Rovira, A., Montalban, X., Blanco, Y., Dalmau, J., Graus, F., Saiz, A., 2016. Clinical spectrum associated with MOG autoimmunity in adults: significance of sharing rodent MOG epitopes. *J. Neurol.* 263, 1349–1360. <https://doi.org/10.1007/s00415-016-8147-7>.
- de Sèze, J., Kremer, L., Collongues, N., 2016. Neuromyelitis optica spectrum disorder (NMOSD): a new concept. *Rev. Neurol. (Paris)* 172, 256–262. <https://doi.org/10.1016/j.neurol.2016.03.003>.
- Titulaer, M.J., Höftberger, R., Iizuka, T., Leypoldt, F., McCracken, L., Cellucci, T., Benson, L.A., Shu, H., Irioka, T., Hirano, M., Singh, G., Cobo Calvo, A., Kaida, K., Morales, P.S., Wirtz, P.W., Yamamoto, T., Reindl, M., Rosenfeld, M.R., Graus, F., Saiz, A., Dalmau, J., 2014. Overlapping demyelinating syndromes and anti-N-methyl-D-aspartate receptor encephalitis. *Ann. Neurol.* 75, 411–428. <https://doi.org/10.1002/ana.24117>.
- Wang, L., Zhangbao, J., Zhou, L., Zhang, Y., Li, H., Li, Y., Huang, Y., Wang, M., Lu, C., Lu, J., Zhao, C., Quan, C., 2018. Encephalitis is an important clinical component of MOG-antibody-associated demyelination: a single-center cohort study in Shanghai, China. *Eur. J. Neurol.* <https://doi.org/10.1111/ene.13790>.
- Zhou, J., Tan, W., Tan, S.E., Hu, J., Chen, Z., Wang, K., 2018. An unusual case of anti-MOG CNS demyelination with concomitant mild anti-NMDAR encephalitis. *J. Neuroimmunol.* 320, 107–110. <https://doi.org/10.1016/j.jneuroim.2018.03.019>.