American Journal of Ophthalmology Case Reports 22 (2021) 101060

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Anti-myelin oligodendrocyte glycoprotein antibodies in a girl with good recovery after five episodes of prior idiopathic optic neuritis

Mathias Falck Schmidt [a,*], Gorm Pihl-Jensen [b], Margrethe Bastholm Bille [c], Jette Lautrup Frederiksen [a]

[a] Clinic of Optic Neuritis, The Danish Multiple Sclerosis Center (DMSC), Department of Neurology, Rigshospitalet – Glostrup, University of Copenhagen, Valdemar Hansens Vej 13, 2600, Glostrup, Denmark
[b] Clinic of Optic Neuritis, The Danish Multiple Sclerosis Center (DMSC), Department of Neurology, Rigshospitalet – Glostrup, Valdemar Hansens Vej 13, 2600, Glostrup, Denmark
[c] Department of Neurophysiology, Rigshospitalet, Valdemar Hansens Vej 13, 2600, Glostrup, Denmark

ARTICLE INFO

Keywords:
Myelin oligodendrocyte glycoprotein (MOG)
Neuromyelitis optica spectrum disorder (NMOSD)
Optic neuritis (ON)
Multiple sclerosis (MS)
Visual evoked potentials (VEP)

ABSTRACT

Purpose: To describe the clinical, radiological, immunological and electrophysiological features of a myelin oligodendrocyte glycoprotein (MOG)-IgG positive girl with five prior episodes of idiopathic bilateral optic neuritis (ON).

Observations: We report a Danish girl who has been followed by pediatricians and pediatric neurologists since the age of 10 with recurrent episodes of idiopathic bilateral ON. Since the age of 15 there has been no recurrence of ON, and the patient has been thoroughly investigated for Multiple Sclerosis (MS) several times, but with negative findings. At the age of 19 the patient was referred to the Clinic of Optic Neuritis where she was tested seropositive for antibodies against MOG (MOG- IgG) on a conventionally cell-based assay. Despite 5 previous episodes of ON, the latency and amplitude signals of pattern-reversal visual evoked potentials (pVEP) including multifocal VEP were detected within the normal range.

Conclusion: The clinical implications of MOG- IgG are not yet clear, but in cases where the diagnosis of MS is less likely and where ON is the main symptom, testing for both IgG antibodies against AQP4 and MOG while having atypical optic neuropathies in mind is important. MOG-IgG positive patients may have a good prognosis with regards to visual function.

1. Introduction

The myelin oligodendrocyte glycoprotein (MOG) is a glycoprotein expressed on the outer membrane of myelin in the central nervous system (CNS). Neuroinflammatory autoimmune diseases involving IgG antibodies against MOG (MOG-IgG) are termed MOG-IgG associated disease [MOG-AD] or MOG-IgG associated encephalomyelitis and is considered as a distinct disease entity from both multiple sclerosis (MS) and aquaporin-4 antibody (AQP4-IgG)- neuromyelitis optica spectrum disorders (NMOSD).[1–4] Detection of antibodies to the astrocytic AQP4 water channel is currently considered as a highly sensitive and specific diagnostic biomarker in NMOSD, but up to 42% of the NMOSD patients who are tested seronegative for the AQP4-IgG are tested positive for MOG-IgG.[5]

Here we present a case report of a Caucasian girl with a long pediatric history of recurrent episodes of idiopathic bilateral ON who is finally tested positive for MOG-IgG.

2. Case report

In April 2016 a 19-year-old girl is referred to the Clinic of Optic Neuritis and Multiple Sclerosis for an investigation of demyelinating disease. The patient has been followed by pediatricians and pediatric neurologists since the age of 10 with recurrent episodes of idiopathic bilateral optic neuritis (rON). Previous ophthalmologic examinations showed a best-corrected visual acuity (VA) of 0.08 in the left eye and 1.2 in the right eye with a positive relative afferent pupillary defect (RAPD) in the left eye. Superior and inferior temporal visual field defects were

* Corresponding author.
E-mail addresses: mathias.falck.schmidt@regionh.dk (M.F. Schmidt), gorm.pihl-jensen@regionh.dk (G. Pihl-Jensen), margrethe.bastholm.bille.01@regionh.dk (M.B. Bille), jette.lautrup.battistini@regionh.dk (J.L. Frederiksen).

https://doi.org/10.1016/j.ajoc.2021.101060
Received 26 May 2020; Received in revised form 19 January 2021; Accepted 20 February 2021
Available online 24 March 2021

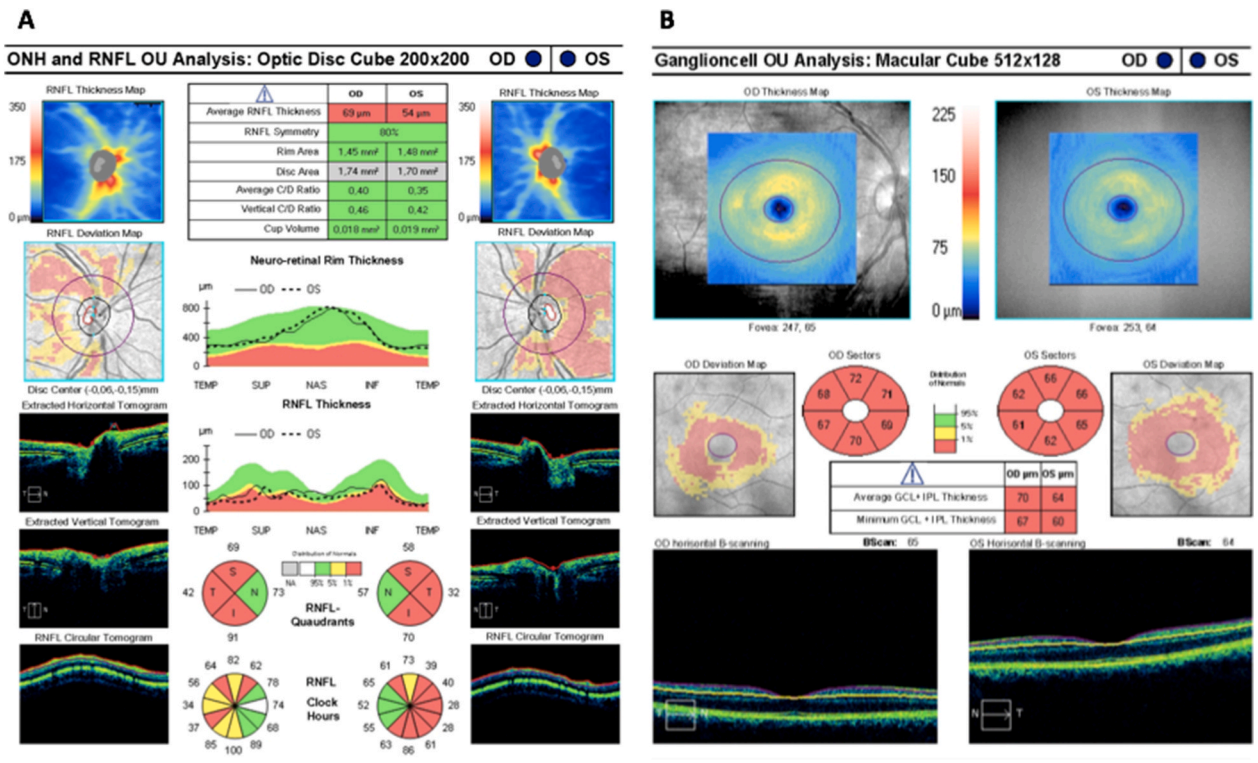
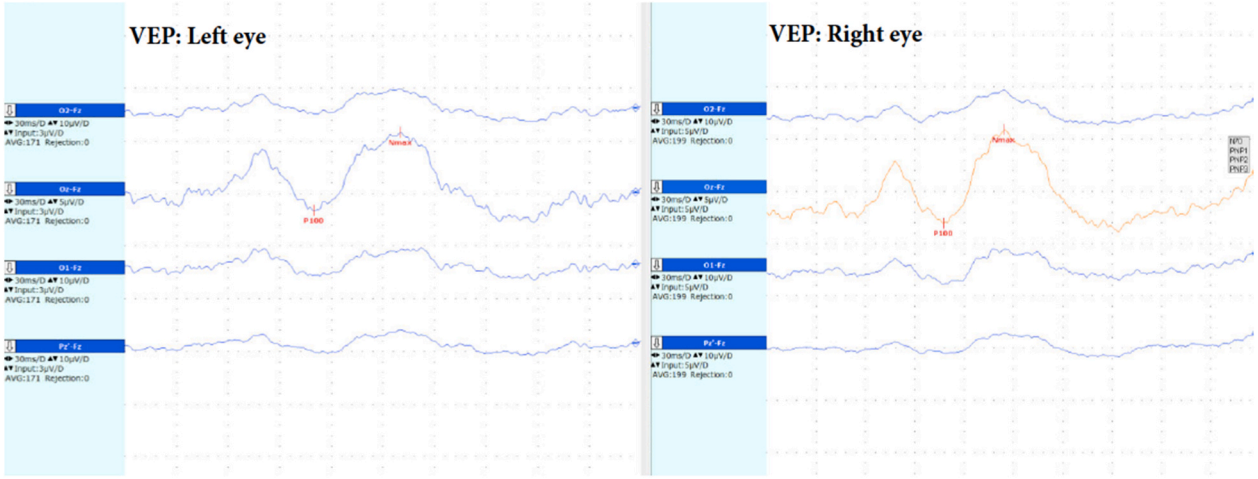


Fig. 1. OCT report obtained with the Cirrus HD-OCT (model 4000, software V.7.0.1.290, Carl-Zeiss Meditec, Dublin, CA). A) Optic nerve head and peripapillary retinal nerve fiber layer (RNFL) analyses and B) macular ganglion cell layer (GCL) analyses. There is RNFL and GCL loss in both eyes, as indicated by the averaged thicknesses of RNFL and GCL.



Check size of VEP stimuli: 4.5 mm

			Latency						Amplitude					
			Left		Right		Inter-ocular latency difference		Left		Right		Inter-ocular amplitude difference	
			ms	SD	ms	SD	ms		µV	SD	µV	SD	µV	
Average	Oz'-Fz	P100	110	1.03	107	0.32	3.0							
	Oz'-Fz - Oz'-Fz	P100 - Nmax							7.4	-1.31	8.9	-0.85	1.50	

Fig. 2. Pattern-reversal visual evoked potentials (pVEP) recorded from a female with 5 prior episodes of idiopathic optic neuritis. Nmax and P100 waves are labeled. VEP traces of the right and left eye stimulation are displayed. The left and right eye peak times are within normal range. The interocular differences are shown in the lowest box and are within the normal range. The pVEP was performed by the use of the DantecTM, Keypoint.NET (Natus Medical Incorporated, San Carlos, CA).

confirmed in the left eye using perimetry tests, whereas the visual field was normal in the right eye. Initially a 3- days course of methylprednisolone was given intravenously (1000 mg/day) followed by 2 months of daily oral prednisolone until tapering off during another 4 months (5 mg–2.5 mg). In the beginning, the patient experienced relapses of ON when steroids were tapered down but at the end the patient had good recovery (i.e. normal VA and visual fields). Since the age of 15 no recurrence of ON and the patient had several times been thoroughly investigated for MS, but with negative findings. The suspicion of MS arises again because the patient experienced progressive paraesthesia in the left extremities for 2–3 weeks.

During hospitalization magnetic resonance imaging (MRI) scanning (1.5T Siemens) of the central nervous system (CNS) was performed, and it revealed only a cervical demyelinating lesion, extending above C3 and down to C6/C7. The radiological diagnosis was acute transverse myelitis. The chest X-ray was normal and lumbar puncture (the patient had not been given any treatment in two months) showed normal conditions with regard to leukocytes, protein, glucose, oligoclonal bands, immunoglobulin G index, borrelia and herpes viruses. The patient was screened extensively with blood samples including the complete blood count with differential, common electrolytes and liver functions tests, glucose and coagulation factors, thyroid stimulating hormone (TSH), folate, 25-hydroxy vitamin D test, cobalamin, immunoglobulins, antinuclear antibody (ANA), anti-neutrophil cytoplasmic antibody (ANCA), IgM-Rheumatoid Factor, Sjögren's Syndrome-B Extractable Nuclear Antibodies, angiotensin converting enzyme test (to exclude sarcoidosis). The above blood tests were all normal including negative test for IgG autoantibodies against aquaporin-4 (AQP4-IgG), but with a weak positive test for IgG autoantibodies against the myelin oligodendrocyte glycoprotein (MOG-IgG). MOG-IgG analysis were performed with a cell based assay (CBA) which is an internationally recognized assay method for detecting MOG-IgG. The technique indirectly detects immunofluorescence on live transfected CBA and results are recorded on a semi-quantitative scale (negative, grey-zone, weak positive, medium positive, or strong positive). A standard 1:10 dilution was used.

Due to the symptoms of paraesthesia the patient was treated with a 5-days course of methylprednisolone (given intravenously 1000 mg/day). Two months later, the pattern-reversal visual evoked potentials (pVEP) and multifocal VEP showed normal latency and amplitude in both eyes (Fig. 2). VA was 1.2 in both eyes and the visual fields of both eyes were normal and the pupils did not show a RAPD. Optical coherence tomography (OCT) was also performed using the Cirrus HD-OCT, model 4000, software V.7.0.1.290 and it showed bilateral loss of the peripapillary retinal nerve fiber layer (RNFL) (i.e. the average RNFL thickness was 69 μm in the right eye and 54 μm in the left eye). Furthermore OCT showed bilateral loss of the ganglion cell layer (GCL) with an average GCL thickness of 70 μm in the right eye and 64 μm in the left eye (see Fig. 1). MOG-IgG was again measured by the same method and this time the test was strong positive. The paraesthesia in the extremities was no longer present and a signal intensity decrease was observed on T2-weighted images of the cervical spine on MRI (extending from C3 to C6/C7).

Finally, the patient was diagnosed with MOG-AD based also on her medical history with a normal cerebrospinal fluid (CSF) and MRI of the brain, rON, transverse myelitis as well as a negative AQP4-IgG status.

3. Discussion

MOG-IgG seropositivity most often predicts a better prognosis than MS or AQP4-IgG NMOSD, and it is much more common in the pediatric population.[6]However, data on VEP latency in MOG-AD have been less extensively studied to date.[7]This is a rare case report of a MOG-IgG seropositive patient with normal pVEP and mfVEP latency/amplitude and VA despite 5 prior episodes of ON and evidence supporting retinal GCL and RNFL loss. The diagnosis of MS was less likely since MRI of the cerebrum repeatedly was confirmed normal with no presence of oligoclonal bands or elevated IgG index in the CSF.

Most likely MOG-AD results directly from an autoimmune response directed against MOG on myelin sheaths, and therefore, we would expect VEP to reflect demyelination secondary to damage of the myelin sheath. Recently, one study[8] reported worse visual outcomes after ON in patients with AQP4-IgG seropositivity compared to MOG-ON and MS-ON, even with similar severity of macular GCIPL thinning. Interestingly, the authors argue that the relatively preserved visual acuity in MOG-ON compared to AQP4-ON may reflect differences in the relative contributions of the retinal ganglion cells to GCIPL and RNFL thickness between these two conditions.

Further studies will be needed to elucidate whether a particular VEP pattern in amplitude and P100 wave latency exists in a subset of patients with MOG-AD compared with AQP4-IgG positive NMOSD or MS.

It is currently difficult to treat MOG-AD patients due to the heterogeneous clinical spectrum and the lack of data indicating a need for evidence-based treatment guidelines. Although no clinical trial has been performed to determine the effectiveness of the maintenance therapy in such patients, most physicians will nowadays consider treatment with chronic immunosuppression agent in relapsing MOG-AD.[9]

In 2016 MOG analysis was a rather new analysis and at that time there were no guidelines for treatment of MOG-AD patients. Remission after ON was seen in this patient with gradual steroid tapering, but even though the patient later had persistently raised MOG-Ab titers, chronic immunotherapy was not considered since 1) there were no signs of MS and because 2) the patient had experienced good recovery after 5 prior episodes of ON (normal VA and visual fields and normal pVEP) and 3) improvement regarding MRI of the spinal cord.

4. Conclusions

MOG-AD is rare, but it is a severe demyelinating inflammatory disorder in the CNS that may be clinically difficult to differentiate from MS. In cases where the MS diagnosis is less likely but where ON is the main symptom, it is crucial to test for both AQP4-IgG and MOG-IgG while having atypical optic neuropathies in mind. MOG-IgG positive patients may have a good prognosis with regards to visual function.

Patient consent

The patient gave written consent to publication of the case. This case report does not contain any personal information that could lead to the identification of the patient.

Funding

No funding or grant support.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The following authors have no financial disclosures: Mathias Falck Schmidt. The following authors have no financial disclosures: Gorm Pihl-Jensen. The following authors have no financial disclosures: Jette Lautrup Frederiksen. The following authors have no financial disclosures: Margrethe Bastholm Bille.

Acknowledgements

None.

References

1. Jarius S, Paul F, Aktas O, Asgari N, Dale RC, et al. MOG encephalomyelitis: international recommendations on diagnosis and antibody testing. *J Neuroinflammation*. 2018;15(1):134.
2. Weber MS, Derfuss T, Bruck W, et al. Anti-myelin oligodendrocyte glycoprotein antibody-associated central nervous system demyelination-a novel disease entity? *JAMA Neurol*. 2018;75(8):909–910.
3. Dos Passos GR, Oliveira LM, da Costa BK, et al. MOG-IgG-associated optic neuritis, encephalitis, and myelitis: lessons learned from neuromyelitis optica spectrum disorder. *Front Neurol*. 2018 Apr 4;9:217.
4. van Pelt ED, Wong YY, Ketelslegers IA, et al. Neuromyelitis optica spectrum disorders: comparison of clinical and magnetic resonance imaging characteristics of AQP4-IgG versus MOG-IgG seropositive cases in The Netherlands. *Eur J Neurol*. 2016;23(3):580–587.
5. Narayan R, Simpson A, Fritsche K, et al. MOG antibody disease: a review of MOG antibody seropositive neuromyelitis optica spectrum disorder. *Mult Scler Relat Disord*. 2018 Oct;25:66–72.
6. Lock JH, Newman NJ, Biousse V, Peragallo JH. *Curr Opin Ophthalmol*. 2019 Nov;30(6):418–425.
7. Vabanesi M, Pisa M, Guerrieri S, et al. In vivo structural and functional assessment of optic nerve damage in neuromyelitis optica spectrum disorders and multiple sclerosis. *Sci Rep*. 2019 Jul 17;9(1):1–5.
8. Sotirchos ES, Filippatou A, Fitzgerald KC, et al. Aquaporin-4 IgG seropositivity is associated with worse visual outcomes after optic neuritis than MOG-IgG seropositivity and multiple sclerosis, independent of macular ganglion cell layer thinning. *Multiple Sclerosis Journal*. 2019 Jul 31:9–10. https://doi.org/10.1177/1352458519864928.
9. Whittam DH, Karthikeayan V, Gibbons E, et al. Treatment of MOG antibody associated disorders: results of an international survey. *J Neurol*. 2020 Jul 4. https://doi.org/10.1007/s00415-020-10026-y.