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Case report

# A rare concurrence: Antibodies against Myelin Oligodendrocyte Glycoprotein and *N*-methyl-D-aspartate receptor in a child

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ABSTRACT

*Background:* Myelin Oligodendrocyte Glycoprotein antibodies (MOG) may be used as a biomarker for diagnosis of many demyelinating diseases. Especially, patients of acute disseminated encephalomyelitis (ADEM), multiple sclerosis (MS), aquaporin-4 (AQP4) seronegative neuromyelitis optica spectrum disorder (NMOSD), monophasic or recurrent optic neuritis (ON), transverse myelitis and *N*-methyl-D-aspartate (NMDA) receptor encephalitis (NMDARe) can overlap with Myelin Oligodendrocyte Glycoprotein antibodies. We present a child with autoimmune encephalitis in whom antibodies against Myelin Oligodendrocyte Glycoprotein (MOG) and *N*-methyl-D-aspartate receptor (NMDAR) were simultaneously detected. The clinical manifestation was characteristic of NMDAR encephalitis, and cranial and spinal magnetic resonance imaging showed no signs of encephalomyelitis. On the other hand, complete recovery within first days of steroid treatment was more compatible with the course of MOG antibody-related disease.

*Conclusions:* We emphasize the rarity of this antibody combination in children and suggest these patients, although clinically improved, may require longer follow-up due to the risk of recurrence of two autoimmune disorders.

## 1. Background

Serum autoantibodies against Myelin Oligodendrocyte Glycoprotein (MOG) are associated with clinical pictures of acute disseminated encephalomyelitis (ADEM), neuromyelitis optica spectrum disorder (NMOSD), monophasic or recurrent optic neuritis (ON), transverse myelitis and rarely, multiple sclerosis (MS) in children (Peschl et al., 2017). Anti-*N*-methyl D-aspartate receptor antibody (anti NMDAR ab) is associated with autoimmune encephalitis (NMDARe). MOG-Ab disease and NMDARe can occur in the same patient simultaneously or sequentially: several adult and a few pediatric cases have been reported (Fan et al., 2018; Dalmau et al., 2011). We present a child with encephalopathy in whom anti-NMDAR and anti-MOG antibodies have been detected simultaneously, and whose normal imaging findings added to the diagnostic challenge.

## 2. Case presentation

A six-year old boy was admitted with alteration of gait, speech, behavior (agitation, aggression, irritability) and insomnia for the last week. He had an upper respiratory tract infection two weeks ago. Prenatal, perinatal and family histories were unremarkable. Physical examination was normal. Neurological examination revealed reduced response to stimuli, ataxic gait, and hyporeflexia. Routine blood count, biochemistry, and metabolic tests (ammonia, lactate, blood gas, tandem mass spectroscopy, urine organic acid analysis) were normal. Serological investigations for infectious agents (Epstein-Barr virus, adenovirus, cytomegalovirus, herpes simplex virus types 1 and 2, varicella zoster virus, chlamydia, mycoplasma) and systemic autoimmunity (antinuclear antibodies, anti-double-stranded DNA, perinuclear and cytoplasmic anti-neutrophil cytoplasmic antibodies, thyroglobulin, thyroperoxidase and phospholipid antibodies) were negative. Cerebrospinal fluid (CSF) contained no cells, normal protein and glucose levels, but an elevated IgG index (0.84, normal: 0.2–0.6) and

*Abbreviations:* ADEM, Acute disseminated encephalomyelitis; anti NMDAR ab, Anti-*N*-methyl D-aspartate receptor antibody; NMDARe, Anti-*N*-methyl D-aspartate receptor encephalitis; CSF, Cerebrospinal fluid; MS, Multiple sclerosis; MOG, Myelin Oligodendrocyte Glycoprotein; NMDAR, *N*-methyl-D-aspartate receptor; NMOSD, Neuromyelitis optica spectrum disorder; ON, Optic neuritis; VEP, Visual evoked potential

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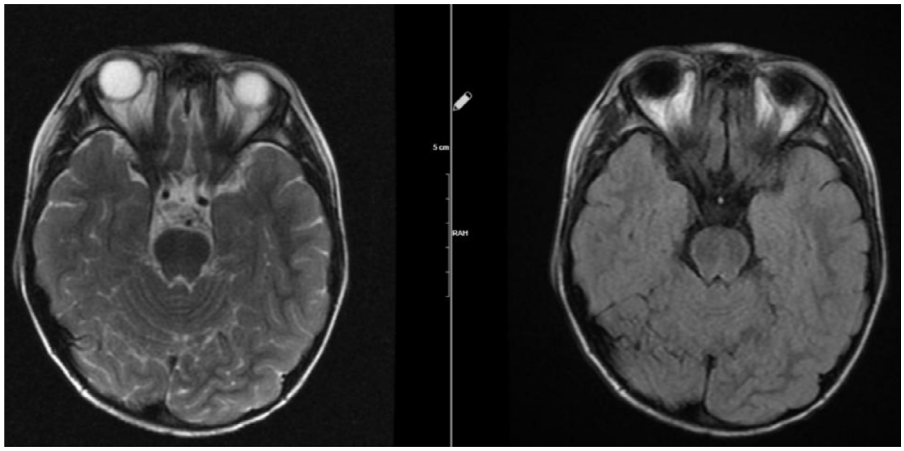

**Fig. 1.** Normal T2 ve flair axial sequence on MRI.

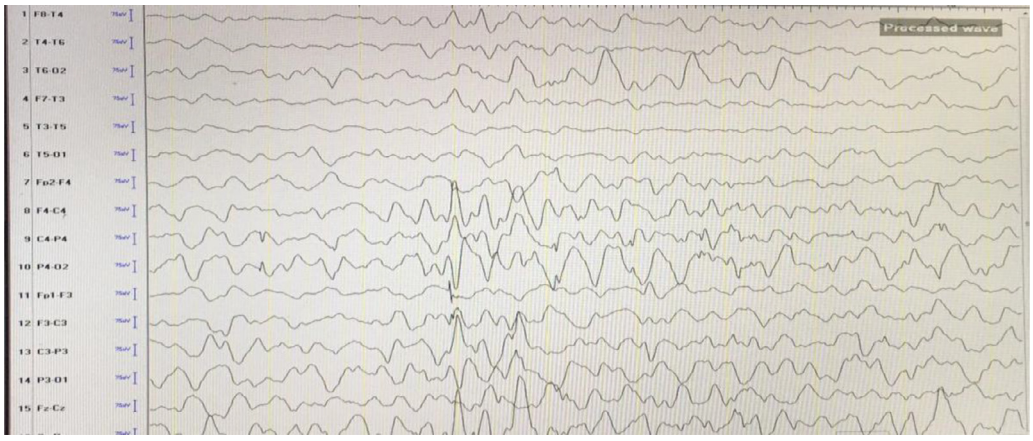


**Fig. 2.** Posterior slow waves and spike waves in the right parietooccipital zone.

oligoclonal bands (where these bands were unique to CSF and there were four bands, two of them were weak). Brain and spinal MRI were normal (Fig. 1). Visual evoked potential (VEP) study presented normal P100 wave latency bilaterally. EEG showed bilateral posterior slow waves of 1–2 Hz more prominent on the right hemisphere, and intermittent spike waves in the right parietooccipital zone (Fig. 2).

In the presence of marked behavioral and sleep disturbances, the diagnosis of autoimmune encephalitis was considered. Anti-NMDAR IgG in CSF and anti-MOG IgG (1/320 – where antibodies were tested with Immunofluorescence method at Euroimmun Labs in Germany) in serum were found positive.

Methylprednisolone 30 mg/kg was given for three days, followed by 20 mg/kg for two days. Consciousness started to improve on the third day of the treatment. The patient was discharged with full recovery. Neurological examination was normal on the 3-month follow-up visit.

## 3. Discussion

The concurrence of MOG and NMDAR antibodies is infrequent. In a series collected in Fan et al. (2018) accompanied by a review of literature, five patients, three of them of childhood onset (3–9 years old), had MOG and NMDAR antibodies simultaneously or sequentially. All had recurrent episodes of demyelinating syndrome and/or NMDAR encephalitis manifesting behavior, sleep, memory problems; they showed fast and satisfactory response to treatment. MRI was abnormal in 9/10 episodes (But all patients had normal MRI during the first attack) (Fan et al., 2018). Our case presented with the clinical and picture of NMDARe rather than NMOSD: the normal MRI findings, elevated IgG index (observed in 15% of MOG Ab disease and 60% of NMDARe cases), occipital intermittent rhythmic delta activity on EEG are more supportive of NMDARe compared to MOG Ab-disease (Fan et al., 2018; Titulaer et al., 2014; Yıldırım et al., 2018). On the other hand, our case's prompt response to treatment and full recovery within days is expected in MOG Ab-positive disease, as NMDARe usually requires a combination of steroid and intravenous immunoglobulin or plasma exchange (Suppiej et al., 2016). In our case, clinical improvement on the third day of treatment obviated consideration of other therapeutic agents.

In pediatric series, relapses occur more frequently in anti-MOG-associated demyelinating disease compared to NMDARe: 65% and 15% respectively (Konuskan et al., 2018a,b; Armangue et al., 2013). As MOG seropositivity can serve as a biomarker for relapse, the test is to be repeated during follow-up of our patient.

## 4. Conclusions

Our “double seropositive” patient carried both antibodies’ clinical features: behavioral and sleep disturbances, EEG findings and normal MRI described in NMDARe, but rapid response to steroid treatment supportive of MOG Ab-disease. Multiple seropositivity may be more frequent than presumed in children. The presence of multiple antibodies does not necessarily complicate the clinical course, and treatment response can be favorable although follow-up for recurrences is recommended.

### *4.1. Ethics approval and consent to participate*

The presentation of the case was approved by the Clinical Research Ethics Committee of the Mersin University. Informed consent was

obtained.

## Conflict of interest

The authors declare that they have no conflict of interest to disclose. There is no funding support available for this study.

## References


Armangue, T., Titulaer, M.J., Malaga, I., et al., 2013. Pediatric Anti-NMDAR encephalitis-clinical analysis and novel findings in a series of 20 patients. J. Pediatr. 162 (4), 850–856. https://doi.org/10.1016/j.jpeds.2012.10.011.

Dalmau, J., Lancaster, E., Martinez, H.E., et al., 2011. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. Lancet Neurol. 10, 63–74. https://doi.org/10.1016/S1474-4422(10)70253-2.

Fan, S., Xu, Y., Ren, H., et al., 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. Scler. Relat. Disord. 20, 144–152. https://doi.org/10.1016/j.msard.2018.01.007.

Konuskan, B., Yildirim, M., Topaloglu, H., et al., 2018a. Clinical presentation of anti-*N*-methyl-D-aspartate receptor and anti-voltage-gated potassium channel complex antibodies in children: a series of 24 cases. Eur. J. Paediatr. Neurol. 22 (1), 135–142. https://doi.org/10.1016/j.ejpn.2017.10.009.

Konuskan, B., Yildirim, M., Gocmen, R., et al., 2018b. Retrospective analysis of children with myelin oligodendrocyte glycoprotein antibody-related disorders. Mult. Scler. Relat. Disord. 26, 1–7. https://doi.org/10.1016/j.msard.2018.07.02.

Peschl, P., Bradl, M., Hoftberger, R., et al., 2017. Myelin oligodendrocyte glycoprotein: deciphering a target in inflammatory demyelinating diseases. Front. immunol. 8 (8), 529. https://doi.org/10.3389/fimmu.2017.00529.

Suppiej, A., Nosadini, M., Zuliani, L., et al., 2016. Plasma exchange in pediatric anti-NMDAR encephalitis: a systematic review. Brain and Dev. 38, 613–622. https://doi.org/10.1016/j.braindev.2016.01.009.

Titulaer, M.J., Hoftberger, R., Lizuka, T., et al., 2014. Overlapping demyelinating syndromes and anti-*N*-methyl-D-aspartate receptor encephalitis. Ann. Neurol. 75, 411–428. https://doi.org/10.1002/ana.24117.

Yildirim, M., Konuskan, B., Yalnizoglu, D., et al., 2018. Electroencephalographic findings in anti-*N*-methyl-D-aspartate receptor encephalitis in children: a series of 12 patients. Epilepsy Behav. 78, 118–123. https://doi.org/10.1016/j.yebeh.2017.09.022.