# ABDUCENS NERVE MONONEURITIS AS A MANIFESTATION OF PEDIATRIC MYELIN OLIGODENDROCYTE GLYCOPROTEIN ANTIBODY ASSOCIATED DISEASE (MOGAD): A CASE REPORT

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**Abstract**
**Introduction:**
Antibodies targeting myelin oligodendrocyte glycoprotein (MOG-ab) have been reported as one of the causes of demyelinating syndromes of the central nervous system. It's also well established that MOG-antibodies are found more often in pediatric patients presenting with demyelinating events. Recent studies have shown the expanding clinical spectrum of MOG-antibodies-associated disorders giving birth to the term MOG antibodies-associated disease (MOGAD).
**Case report:**
Herein, we report the case of a 2.5-year-old boy, who presented with acute isolated left sixth cranial nerve palsy. The only abnormal laboratory test finding in our patient was the presence of IgG1 MOG-ab in the serum. The patient recovered fully after treatment with methylprednisolone.
**Conclusion**:
This case proposes the abducens nerve mononeuritis as a possible phenotype of MOGAD and highlights the need for MOG-ab testing in children with isolated cranial mononeuritis. To our knowledge this is the first report of this kind of disorder.

**Keywords:** MOG-ab, MOGAD, abducens nerve, cranial mononeuritis, case report

# ΠΑΡΕΣΗ ΑΠΑΓΩΓΟΥ ΝΕΥΡΟΥ ΣΕ ΠΑΙΔΙΑΤΡΙΚΟ ΑΣΘΕΝΗ ΩΣ ΕΚΔΗΛΩΣΗ ΝΟΣΟΥ ΣΧΕΤΙΖΟΜΕΝΗΣ ΜΕ ANTI-MOG ΑΝΤΙΣΩΜΑΤΑ (MOGAD) - ΠΑΡΟΥΣΙΑΣΗ ΠΕΡΙΣΤΑΤΙΚΟΥ

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**Περίληψη**
**Εισαγωγή:**
Τα αντισώματα έναντι της μυελινικής γλυκοπρωτεΐνης των ολιγοδενδροκυττάρων (anti-MOG) είναι πλέον μια από τις αναγνωρισμένες αιτίες των απομυελινωτικών συνδρόμων του Κεντρικού Νευρικού Συστήματος. Είναι επίσης γνωστό ότι η εύρεση anti-MOG αντισωμάτων εμφανίζεται με υπεροχή στα απομυελινωτικά σύνδρομα των παιδιατρικών ασθενών. Πρόσφατες έρευνες αναφέρουν ένα ολοένα και μεγαλύτερο φάσμα κλινικών συνδρόμων που σχετίζονται με τα αντισώματα αυτά, στοιχειοθετώντας έτσι τη Νόσο Σχετιζόμενη με anti-MOG Αντισώματα (MOGAD).
**Περιγραφή περιστατικού:**
Το περιστατικό που περιγράφεται αφορά σε παιδιατρικό ασθενή 2,5 ετών, που εμφάνισε αιφνίδια πάρεση της έκτης εγκεφαλικής συζυγίας αριστερά. Από τον παρακλινικό έλεγχο ανιχνεύθηκαν IgG1 anti-MOG αντισώματα στον ορό χωρίς κάποιο άλλο παθολογικό εύρημα. Ο ασθενής βελτιώθηκε κλινικά έπειτα από τη χορήγηση αγωγής με μεθυλπρεδνιζολόνη.

**Συμπέρασμα:**
Το περιστατικό αυτό εισάγει τη μονονευρίτιδα του απαγωγού νεύρου στο ευρύ φάσμα κλινικών εκδηλώσεων της MOGAD και υπογραμμίζει την ανάγκη για έλεγχο των anti-MOG αντισωμάτων σε περιπτώσεις παιδιών με κρανιακή μονονευρίτιδα. Από ότι γνωρίζουμε πρόκειται για την πρώτη περιγραφή παρόμοιας βλάβης.

**Λέξεις ευρετηρίου:** αντι-MOG, MOGAD, απαγωγό νεύρο, κρανιακή μονονευρίτιδα

## Introduction

Myelin oligodendrocytes glycoprotein (MOG) is a transmembrane protein, expressed in the surface of neuronal cells in the nervous system. It is well-known that myelin oligodendrocyte glycoprotein antibodies (MOG-abs) cause demyelination and the detection of these antibodies is related to a plethora of demyelinating syndromes and clinical phenotypes that constitute MOG-associated disease (MOGAD). Additionally, MOG-abs present with a higher frequency in the pediatric population and with a greater heterogeneity in their clinical phenotypes.[1(p1)]increasing interest in the role of autoantibodies against myelin oligodendrocyte glycoprotein (MOG-abs).

The most common clinical syndromes associated with pediatric MOGAD include Acute Disseminated Encephalomyelomyelitis (ADEM), Optic Neuritis (ON), Transverse Myelitis (TM) and Neuromyelitis Optica Spectrum Disorder (NMOSD).[2] Atypical clinical presentations consist of 10% of MOGAD cases and include, among others, encephalitis, leukodystrophy-like phenotype, a combination of central and peripheral demyelination with cranial nerve involvement.[1]increasing interest in the role of autoantibodies against myelin oligodendrocyte glycoprotein (MOG-abs).

Here we report a pediatric case of MOG-abs Associated Disease presenting with acute unilateral abducens nerve palsy. To our own knowledge, this is the first-ever reported case of sixth nerve palsy as a clinical manifestation of MOGAD.

Our report is in accordance with the CARE guidelines. Written informed consent for the publication of the case report and the image included was given by the patient's caregivers. Detailed information is available on request.

## Case report

A previously healthy 2.5-year-old boy with a normal antenatal and developmental profile presented with a 10-day history of acute strabismus (figure 1). On initial examination, the toddler manifested with difficulty in the abduction of the left eye, esotropia of the affected eye and compensatory right head tilt, suggestive of diplopia. Based on these findings the diagnosis of 6$^{th}$ cranial nerve palsy was established. The rest cranial nerves were intact. A thorough neurological examination followed without noted deficits.

A series of laboratory and imaging tests followed. Brain Computed Tomography (CT) on the first day of admission, demonstrated no abnormalities. Diagnostic evaluation continued with cerebrospinal fluid (CSF) analysis and extensive serum laboratory studies. CSF analysis showed two white blood cells, normal protein and glucose. CSF culture and PCR test for meningitis and encephalitis pathogen panel were negative as were the PCR tests for herpes viruses in the serum. The serum immunology analysis showed positive IgG1 MOG-abs (titter 1:40), using cell-based assay technique. Serum and CSF oligoclonal bands were identical, indicating systemic immune reaction. Brain Magnetic Resonance Imaging (MRI) with contrast agent, showed no abnormalities. (Table 1)

Figure 1. Clinical presentation of the patient on diagnosis. Inability to abduct the left eye on left horizontal lateral gaze, indicating weakness of the ipsilateral lateral rectus muscle.

The patient was initially treated with intravenous methylprednisolone (30mg/kg/d) for five days. He made a satisfactory clinical improvement and was able to partially abduct the affected eye upon discharge. The toddler's treatment continued with oral prednisolone (2mg/kg/d), in a weaning course with over 2 months duration.

On the patient's reassessment, 2 months after the initial diagnosis, the neurological examination was normal and there were no clinical signs suggestive of diplopia. In accordance with the proposed guidelines [3]optic neuritis (ON , IgG1 MOG-abs were tested again during the 3 months follow-up and were found positive (titter 1:40), even though the

patient remained clinically recovered. In the subsequent review, 6 months after the initial presentation, IgG1 MOG-abs remained positive (titter 1:40).

**Table 1. Laboratory tests**

| Laboratory analysis | Result |
|---|---|
| CSF profile | Normal |
| CSF culture | Negative |
| Oligoclonal bands | Type IV |
| IgG index | 0.654 |
| Serum autoantibodies<br>ANA, anti-dsDNA, anti-ENA, anti-RNP, anti-SM, anti-SSA, anti-SSB, anti-scl70, anti-MPO, anti-PR3, anti-LE, c-anca, p-anca, antimitochondrial, anti-cardiolipin, anti-DNA ,IgG1 anti-MOG, anti-AQP4, anti-AQP1 | IgG1 anti-MOG 1:40 |
| Blood Serology<br>SARS-CoV-2, HSV, CMV, EBV, VZV, Adenovirus, Echovirus, Coxsackie, Mumps, RSV, PIV, Influenza (A,B), Mycoplasma, Brucella | EBV IgG (+) |
| CSF serology<br>Antobodies for: West Nile Virus, Leptospira Interrogans, Borrelia Burgdorferi, Adenovirus, Picorna, Polio, RSV, HSV, CMV, EBV, VZV, HHV6, HHV7, PIV | Negative |
| Serum PCR<br>HSV1, CMV, HHV6, HHV7, HHV8, EBV, Enterovirus | Negative |
| CSF PCR<br>HSV1, CMV, HHV6, HHV7, HHV8 | Negative |
| Serological/Virological Hepatitis Markers | Anti-HBs (+) (immunization) |

## Discussion

MOG-Associated Disease presents as a variety of clinical phenotypes, most of which are demyelinating syndromes of the central nervous system (CNS)[4]. The atypical clinical presentations of MOGAD consist of a wider range of manifestations that haven't been completely elucidated yet. In any case, the higher frequency of anti-MOG presence in pediatric patients compared to adults, is well established, as is the more benign course of the disease in children[4].

In a cohort of 252 pediatric and adult patients who tested positive for serum IgG1 anti-MOG-abs, 78% showed sufficient recovery, the majority of which were children [1(p1),5]increasing interest in the role of autoantibodies against myelin oligodendrocyte glycoprotein (MOG-abs. In another study using exclusively pediatric patients, complete recovery was observed in 75%-96% of them [6]this part of the Paediatric European Collaborative Consensus provides an oversight of existing knowledge of clinical outcome assessment in paediatric MOG-ab-associated disorders (MOGAD. Although the outcome of the disease is usually favorable, it appears that multiple prognostic factors, like the severity of the initial clinical presentation, the relapses and the persistence of possitive IgG1 anti-MOG-abs, can affect the course of the disease. It should be noted that the antibody titter value does not correlate with the outcome of the disease[6] this part of the Paediatric European Collaborative Consensus provides an oversight of existing knowledge of clinical outcome assessment in paediatric MOG-ab-associated disorders (MOGAD,[7].

Regarding the pathophysiology of cranial nerve involvement, even though anti-MOG-abs traditionally target central nervous system cells[8]with the number of CCLs being significantly lower in MOGAD (median (interquartile range (IQR, studies in primates, have shown the expression of MOG antigen in cells of the peripheral nervous system [9]. The involvement of anti-MOG-abs in a syndrome combining central and peripheral demyelination has also been reported [10].

This case we report contributes to the broadening spectrum of clinical manifestations of MOGAD as it proposes cranial mononeuritis, and specifically abducens nerve mononeuritis, as an atypical presentation of the disease. Recent studies report anti-MOG-abs-positive cases manifesting with cranial nerve palsies (vestibulocochlear, trigeminal, oculomotor) along with CNS involvement [11]. There

has also been reported a single case of oculomotor nerve palsy in a 2-year-old patient with anti-MOG-abs, without evidence of CNS lesions on the MRI [11, 12].

The case of our patient is unique, as it appears to be the first reported abducens nerve palsy in a seropositive anti-MOG pediatric patient, without evidence of central nervous system involvement. The underlying pathophysiology of cranial mononeuritis in MOG-abs-IgG-positive patients remains elusive.

## Conclusion

This case-report proposes abducens nerve mononeuritis as an atypical manifestation of MOG associated disorder. The involvement of peripheral nervous system demyelination in MOGAD is underlined, expanding the spectrum of possible clinical phenotypes, especially in the pediatric population. In conclusion, given the great heterogeneity of clinical manifestations of the pediatric MOGAD, this case highlights the need for MOG-abs testing in children with acute cranial mononeuritis of unspecified etiology.

## References

[1] Bruijstens AL, Lechner C, Flet-Berliac L, et al. E.U. paediatric MOG consortium consensus: Part 1 - Classification of clinical phenotypes of paediatric myelin oligodendrocyte glycoprotein antibody-associated disorders. Eur J Paediatr Neurol EJPN Off J Eur Paediatr Neurol Soc. 2020;29:2-13. doi:10.1016/j.ejpn.2020.10.006

[2] Armangue T, Olivé-Cirera G, Martínez-Hernandez E, et al. Associations of paediatric demyelinating and encephalitic syndromes with myelin oligodendrocyte glycoprotein antibodies: a multicentre observational study. Lancet Neurol. 2020;19(3):234-246. doi:10.1016/S1474-4422(19)30488-0

[3] Cobo-Calvo Á, Ruiz A, D'Indy H, et al. MOG antibody-related disorders: common features and uncommon presentations. J Neurol. 2017;264(9):1945-1955. doi:10.1007/s00415-017-8583-z

[4] de Mol CL, Wong Y, van Pelt ED, et al. The clinical spectrum and incidence of anti-MOG-associated acquired demyelinating syndromes in children and adults. Mult Scler Houndmills Basingstoke Engl. 2020;26(7):806-814. doi:10.1177/1352458519845112

[5] Jurynczyk M, Messina S, Woodhall MR, et al. Clinical presentation and prognosis in MOG-antibody disease: a UK study. Brain J Neurol. 2017;140(12):3128-3138. doi:10.1093/brain/awx276

[6] Bruijstens AL, Breu M, Wendel EM, et al. E.U. paediatric MOG consortium consensus: Part 4 - Outcome of paediatric myelin oligodendrocyte glycoprotein antibody-associated disorders. Eur J Paediatr Neurol EJPN Off J Eur Paediatr Neurol Soc. 2020;29:32-40. doi:10.1016/j.ejpn.2020.10.007

[7] Tzartos JS, Karagiorgou K, Tzanetakos D, et al. Deciphering anti-MOG IgG antibodies: Clinical and radiological spectrum, and comparison of antibody detection assays. J Neurol Sci. 2020;410:116673. doi:10.1016/j.jns.2020.116673

[8] Tzanetakos D, Tzartos JS, Vakrakou AG, et al. Cortical involvement and leptomeningeal inflammation in myelin oligodendrocyte glycoprotein antibody disease: A three-dimensional fluid-attenuated inversion recovery MRI study. Mult Scler J. 2022;28(5):718-729. doi:10.1177/13524585211034362

[9] Pagany M, Jagodic M, Schubart A, et al. Myelin oligodendrocyte glycoprotein is expressed in the peripheral nervous system of rodents and primates. Neurosci Lett. 2003;350(3):165-168. doi:10.1016/s0304-3940(03)00899-1

[10] Vazquez Do Campo R, Stephens A, Marin Collazo IV, Rubin DI. MOG antibodies in combined central and peripheral demyelination syndromes. Neurol Neuroimmunol Neuroinflammation. 2018;5(6):e503. doi:10.1212/NXI.0000000000000503

[11] Cobo-Calvo A, Ayrignac X, Kerschen P, et al. Cranial nerve involvement in patients with MOG antibody–associated disease. Neurol Neuroimmunol Neuroinflammation. 2019;6(2):e543. doi:10.1212/NXI.0000000000000543

[12] Kawakami S, Akamine S, Chong PF, et al. Isolated cranial neuritis of the oculomotor nerve: Expanding the MOG phenotype? Mult Scler Relat Disord. 2020;41:102040. doi:10.1016/j.msard.2020.102040.