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RESEARCH

Comparison of neuroimaging and clinical findings of myelin oligodendrocyte glycoprotein antibody associated disease (MOGAD) and seronegative neuromyelitis optica spectrum disease (NMOSD)

Miyelin oligodendrosit glikoprotein antikoru ile ilişkili hastalık (MOGAD) ve seronegatif nöromiyelit optika spektrum hastalığının (NMOSD) nörogörüntüleme ve klinik bulgularının karşılaştırılması

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Abstract

Purpose: The aim of this study is to compare the clinical and neuroimaging findings of pediatric patients with myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) and seronegative neuromyelitis optica spectrum disorder (NMOSD).

Materials and Methods: This retrospective study included 8 MOGAD and 10 seronegative NMOSD patients admitted to Cukurova University between 2015 and 2025, with a minimum follow-up of one year. MOGAD was diagnosed according to the 2023 International MOGAD Panel criteria, while NMOSD was defined by the 2015 IPND criteria.

Results: The mean age at diagnosis was 12,1±2,9 years in the MOGAD group and 9,4±4.4 years in the NMOSD group. Relapse-free survival was higher in MOGAD, with 50% of patients experiencing no further attacks. In contrast, all NMOSD patients relapsed. At the end of follow-up, 87.5% of MOGAD patients achieved complete recovery, while all NMOSD patients had persistent sequelae. MRI analysis showed cortical and conus lesions as predominant in MOGAD, whereas NMOSD more frequently demonstrated long-segment spinal cord involvement, posterior orbital lesions, and brainstem or deep gray matter involvement.

Conclusion: MOGAD is associated with fewer relapses and better recovery, while NMOSD is characterized by recurrent attacks and a high rate of permanent disability. The frequency of these imaging findings may contribute to improved diagnostic accuracy and prognostic prediction.

Keywords:. Pediatric, MOGAD, seronegative NMOSD, MRI

Öz

Amaç: Çalışmanın amacı pediatrik olgularda, myelin oligodendrosit glikoprotein antikor ilişkili hastalık (MOGAD) ile seronegatif nöromiyelitis optika spektrum bozukluğu (NMOSD) hastalarının klinik ve nörogörüntüleme bulgularını karşılaştırmaktır.

Gereç ve Yöntem: Bu retrospektif çalışmaya 2015–2025 yılları arasında Çukurova Üniversitesi'nde izlenen, en az bir yıl takip edilmiş 8 MOGAD ve 10 seronegatif NMOSD hastası dahil edildi. MOGAD tanısı 2023 Uluslararası MOGAD Paneli kriterlerine, NMOSD tanısı ise 2015 IPND kriterlerine göre kondu.

Bulgular: Tanı anındaki ortalama yaş MOGAD grubunda 12,1±2,9 yıl, NMOSD grubunda 9,4±4.4 yıl idi. Relapssız sağkalım MOGAD'da daha yüksekti; hastaların %50'si tekrar atak geçirmedi. Buna karşın tüm NMOSD hastaları relaps yaşadı. Takip sonunda MOGAD hastalarının %87,5'i tamamen iyileşirken, NMOSD'de tüm olgularda kalıcı sekel saptandı. MRG analizinde MOGAD'da kortikal ve konus lezyonları ön plandayken, NMOSD'de uzun segment spinal kord tutulumu, posterior orbital lezyonlar ve beyin sapı/derin gri cevher tutulumu daha sık izlendi..

Sonuç: MOGAD daha az relaps ve daha iyi iyileşme, NMOSD tekrarlayan ataklar ve kalıcı sekel yüksek oranda saptandı. Görüntüleme bulgularının sıklıklarının tanısal doğruluk ve prognoz öngörüsünde yardımcı olabileceği düşünülmektedir.

Anahtar kelimeler: Pediatrik, MOGAD, seronegatif NMOSD, MRG

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INTRODUCTION

Myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) and neuromyelitis optica spectrum disorder (NMOSD) represent distinct yet overlapping inflammatory demyelinating disorders of the central nervous system. While aquaporin-4 antibody (AQP4-IgG) positivity defines the majority of NMOSD cases, a subset of patients remain seronegative, posing diagnostic challenges and frequently mimicking alternative demyelinating syndromes. In recent years, the identification of MOG antibodies has clarified a separate disease entity with unique clinical and radiological features, further refining the differential diagnosis among antibody-mediated demyelinating disorders[1,2].

Clinically, MOGAD is characterized by acute disseminated encephalomyelitis–like presentations, optic neuritis often bilateral and anterior and myelitis involving the conus medullaris. NMOSD, in contrast, demonstrates a predilection for severe relapsing optic neuritis and longitudinally extensive transverse myelitis, with seronegative forms frequently sharing these phenotypes but lacking confirmatory serology[3,4].

Neuroimaging has emerged as a critical tool for distinguishing these conditions: MOGAD lesions typically display cortical or "fluffy" subcortical patterns with a higher tendency for radiological resolution, whereas NMOSD lesions more often involve the optic chiasm, periependymal regions, and long spinal cord segments[5,6].

Despite these advances, considerable overlap persists, particularly between MOGAD and seronegative NMOSD, underscoring the need for systematic clinical and radiological evaluation. In this study, we aimed to contribute to the diagnostic approach by revealing the clinical and MRI differences between the two diseases and to review the literature.

MATERIALS AND METHODS

Sample

Study was conducted in accordance with the Declaration of Helsinki and approved by the Ethical Review Board for Non-interventional Studies of Cukurova University Faculty of Medicine, Adana, Turkey (Date 18 July 2025- Meeting No:154). In this study, informed consent could not be obtained because the MRI images of the patients were evaluated retrospectively. Eight patients diagnosed with myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) and ten patients diagnosed with seronegative neuromyelitis optica spectrum disease (NMOSD) who were admitted to the Pediatric Neurology and Radiology Clinics of Çukurova University between January 2015 and May 2025 and had a minimum follow-up period of one year were included in the study.

Procedure

The patients' medical records were retrospectively reviewed to collect data on age at symptom onset, age at diagnosis, number of attacks, treatments administered during attacks, follow-up duration, relapse frequency, cerebrospinal fluid (CSF) analysis, serum MOG and AQP4-IgG antibody titers determined by cell-based assay, viral panel results, rheumatological screening tests, and magnetic resonance imaging (MRI) findings.

Radiological images of the patients, obtained with and without contrast, using 3T Philips Ingenia and GE Architect MRI devices, were evaluated. Outcomes were assessed at the final visit and recorded as full recovery or presence of residual deficits (sequelae), with corresponding Expanded Disability Status Scale (EDSS) scores, which is the most frequently used assessment scale for follow-up and treatment response evaluation in daily practice of demyelinating diseases.

The diagnosis of MOGAD was made according to the International MOGAD Panel proposed criteria (2023)[7]. Inclusion criteria were: (a) Serum MOG-IgG positivity confirmed by a live cell-based assay using full-length human MOG; (b) At least one typical demyelinating syndrome (optic neuritis, acute disseminated encephalomyelitis, transverse myelitis, or other recognized phenotypes such as cerebral cortical encephalitis, brainstem or cerebellar syndromes, or tumefactive demyelinating lesions); and (c) Exclusion of alternative diagnoses including aquaporin-4 antibody–positive neuromyelitis optica spectrum disorder, multiple sclerosis, and other infectious, metabolic, or inflammatory diseases.

Antibody testing and interpretation were performed in the context of clinical and neuroimaging findings to minimize false-positive results. NMOSD was diagnosed according to the 2015 International Panel

for NMO Diagnosis (IPND) criteria[4], requiring AQP4-IgG positivity with at least one core clinical characteristic, or, in seronegative patients, two core clinical characteristics with supportive MRI findings after exclusion of alternative diagnoses.

Treatment and follow-up

All patients received standardized treatment protocols during acute attacks. Intravenous methylprednisolone (IVMP) was administered at a dose of 1 g/kg/day. Intravenous immunoglobulin (IVIG) was given at 0.5 g/kg/day for 4 consecutive days (total cumulative dose of 2 g/kg). In cases with severe neurological deficits, plasma exchange (PLEX, plasma exchange therapy) was performed as an additional treatment modality.

In terms of treatment, one MOGAD patient received IVMP, IVIG, and rituximab (RTX), while the remaining seven received IVMP and IVIG. In the NMOSD group, three patients were treated with IVMP, IVIG, PLEX, and azathioprine (AZA), whereas seven received IVMP, IVIG, PLEX, and RTX.

At the last follow-up, the median EDSS score in the MOGAD group was 0 (range 0–3), with 87.5% of patients showing complete recovery and only one patient having residual deficit (EDSS = 3). In contrast, all seronegative NMOSD patients had persistent disability, with a median EDSS score of 6 (range 3–9). Detailed demographic, clinical, and treatment characteristics are summarized in Table 1.

Table 1. Demographic and clinical findings of patients

Variable	**MOGAD (%)**	**NMOSD (%)**	**p**
Female/male ratio	50/50	20/80	0.321
No relapses	50	0	0.023
≥2 relapses	12.5	60	0.066
Full recovery	87.5	0	<0.001
Sequelae	12.5	100	<0.001

Statistical analysis

JAMOVI version 2.5.7 was used for statistical analysis. Descriptive statistical information was expressed as frequency and percentage. The Shapiro-Wilk test was used to assess normal distribution. Mean values of normally distributed parameters were reported. The chi-square method was used to evaluate categorical variables. $p<0.05$ values were considered statistically significant.

RESULTS

Among the patients included in the study, 8 were diagnosed with MOGAD and 10 with seronegative NMOSD. The mean age at initial diagnosis was 12.1 ± 2.9 years in the MOGAD group and 9.4 ± 4.4 years in the NMOSD group. The female-to-male ratio was equal (50% each) in the MOGAD cohort, whereas in the NMOSD group 2 patients (25%) were female and 8 patients (75%) were male. The mean follow-up duration was 4.7 years for MOGAD and 3.2 years for NMOSD patients.

Regarding relapse characteristics, 37% of MOGAD patients experienced one relapse after the initial attack, 12% experienced two relapses, while 50% remained relapse-free during follow-up. In contrast, all NMOSD patients experienced further relapses: 40% had one, 50% had two, and 10% had three additional attacks.

In the evaluation of MRI findings (Table 2); orbital involvement was observed in 50% of MOGAD cases (4/8) and 50% of NMOSD cases (5/10). In the MOGAD group, the most frequent patterns were anterior (25%) and pan-orbital (25%) involvement, whereas in NMOSD patients posterior (30%) and pan-orbital (20%) involvement predominated. Bilateral orbital involvement was noted in 25% (2/8) of MOGAD and 30% (3/10) of NMOSD patients. Brain parenchymal lesions were identified in 62.5% of MOGAD patients (5/8) and 70% of NMOSD patients (7/10). Regarding lesion morphology, focal (25%) and fluffy (12.5%) patterns were most frequent in MOGAD, whereas confluent (40%) and fluffy (30%) patterns were more common in NMOSD. In terms of distribution, MOGAD predominantly affected the white matter (25%) and cortex (12.5%), while NMOSD lesions were more frequently localized in the white matter (50%), brainstem (40%), and deep gray matter (30%). Spinal cord involvement was detected in 75% of MOGAD (6/8) and in all NMOSD cases (100%, 10/10). In MOGAD, long-

segment lesions were present in 50% and short-segment lesions in 25% of patients, whereas NMOSD showed a predominance of long-segment lesions (90%) with short-segment involvement being rare (10%). Lesion localization in MOGAD was most commonly cervical (37.5%) and conus (25%), while in NMOSD it was predominantly cervical (60%) and thoracic (50%). Contrast enhancement was observed in 62.5% (5/8) of MOGAD and 80% (8/10) of NMOSD patients. In MOGAD, enhancement was most frequently spinal (37.5%) and orbital (25%), whereas in NMOSD it was predominantly spinal (50%) and brain parenchymal (30%). Apart from these, only leptomeningitis was present as an additional finding in the patients and was detected in 25% (2/8) of MOGAD patients and 10% (1/10) of NMOSD patients. No significant difference was found between the findings in the statistical analysis (Table 3).

Table 2. MRI findings of patients

MRI Finding	MOGAD (n=8)	NMOSD (n=10)
Orbital involvement	4 (50.0%)	5 (50.0%)
Brain lesions	5 (62.5%)	7 (70.0%)
Spinal involvement	6 (75.0%)	10 (100.0%)
Contrast enhancement	5 (62.5%)	8 (80.0%)
Leptomeningitis	2 (25.0%)	1 (10.0%)

Table 3. Statistical comparison of groups according to MRI findings

Variable	MOGAD N:8	NMOSD N:10	p
FLAIR/T2W brain hyperintense lesions			0.636
Fluffy	1 (25.0)	1 (14.3)	
Confluent	-	3 (42.9)	
Focal	2 (50.0)	2 (28.6)	
Focal+confluent	1 (25.0)	1 (14.3)	
Spinal involvement length			0.095
Short	3 (60.0)	1 (11.1)	
Long	2 (40.0)	8 (88.9)	
Cervical spinal involvement			0.342
-	5 (62.5)	3 (30.0)	
+	3 (37.5)	7 (70.0)	
Thoracic spinal involvement			0.664
-	5 (62.5)	5 (50.0)	
+	3 (37.5)	5 (50.0)	
Conus involvement			0.444
-	7 (87.5)	10 (100.0)	
+	1 (12.5)	0	
Orbital contrast enhancement			0.314
-	7 (87.5)	6 (60.0)	
+	1 (12.5)	4 (40.0)	
Brain parenchymal contrast enhancement			0.999
-	7 (87.5)	8 (80.0)	
+	1 (12.5)	2 (20.0)	
Spinal contrast enhancement			0.999
-	3 (37.5)	4 (40.0)	
+	5 (62.5)	6 (60.0)	

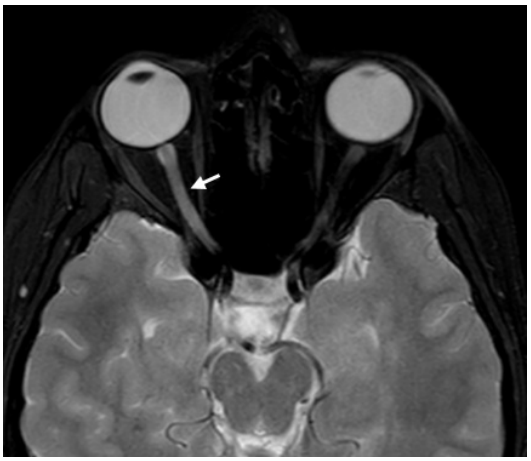

Figure 1. Axial T2A orbital MR image of a 15-year-old female patient diagnosed with MOGAD shows diffuse long-segment expansion and increased signal in the right optic nerve, consistent with optic neuritis.

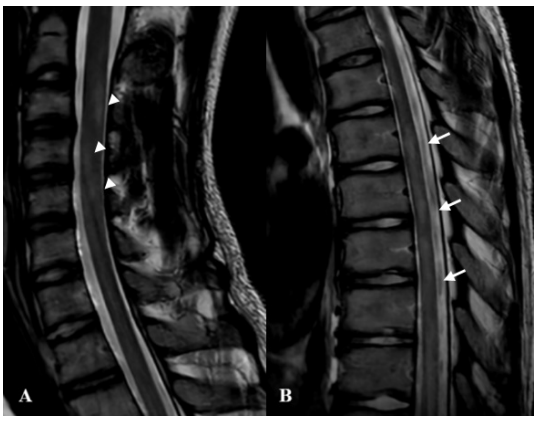

Figure 2. Sagittal cervical T2A MR image of a 10-year-old male patient diagnosed with MOGAD show faintly defined confluent increased signals (A, arrowheads), while sagittal thoracic T2A MR image show diffuse and more expansive increased signals (B, arrows) consistent with transverse myelitis.

DISCUSSION

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and neuromyelitis optica spectrum disorder (NMOSD) are rare acquired demyelinating disorders in children. Although both conditions are increasingly recognized in adults, data in pediatric populations remain limited. Most available studies are based on small case series or retrospective cohorts, and there is a lack of prospective, large-scale studies addressing clinical spectrum, treatment response, and long-term outcomes in children. This scarcity of evidence highlights the importance of further research focusing on pediatric patients to better guide diagnosis and management[3,4].

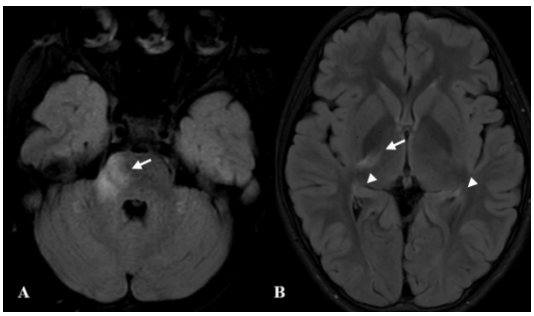

Figure 3. Axial FLAIR brain MR image (A, arrow) of a 4-year-old female patient diagnosed with NMOSD shows expansive increased signal consistent with an encephalitis focus extending from the right half of the brainstem to the peduncular area. Follow-up axial FLAIR brain MR image (B, arrow) obtained at 6 years of age shows complete regression of the brainstem-located lesion (not shown), but increased signal consistent with new foci of encephalitis, prominent in the posterior limb of the right internal capsule (arrow) and faint at both posterior peritrigonal areas (arrowheads).

In our cohort, the mean age at diagnosis was slightly higher in MOGAD patients (12.1 years) compared with the seronegative NMOSD group (9.4 years). The sex distribution also showed marked differences: while MOGAD affected males and females equally (50% each), seronegative NMOSD was predominantly observed in males (80%). These demographic findings are consistent with previous pediatric cohorts, in which MOGAD is often reported with a balanced sex ratio and a somewhat older age at presentation, whereas NMOSD tends to occur at a younger age with a clear male predominance in seronegative forms. Such demographic distinctions may provide additional clues in differentiating these two overlapping but distinct pediatric demyelinating disorders[4,7-9].

Our findings are consistent with previous pediatric cohorts. Jurynczyk et al. reported that children with MOGAD often experience relapsing courses but achieve better functional recovery compared with AQP4-positive or seronegative NMOSD patients[8]. Ramanathan et al.[5] and Cobo-Calvo et al.[9] similarly

demonstrated that pediatric MOGAD is associated with favorable outcomes despite recurrent attacks. In contrast, pediatric seronegative NMOSD has been rarely characterized in the literature, with available reports suggesting a more heterogeneous course and less favorable prognosis compared to MOGAD. The recent International MOGAD Panel criteria[7] also emphasized the importance of recognizing pediatric-specific features, particularly cortical encephalitis and conus involvement, which were reflected in our cohort. These observations highlight the necessity of differentiating MOGAD from seronegative NMOSD in the pediatric age group to optimize treatment and prognosis.

Management of acute attacks in pediatric demyelinating disorders relies primarily on high-dose intravenous methylprednisolone (1 g/kg/day), followed by intravenous immunoglobulin (0.5 g/kg/day for 4 days; total 2 g/kg) in cases with insufficient response. In our cohort, all patients received IVMP and IVIG. Plasma exchange (PLEX) was performed in patients with severe neurological deficits. Among MOGAD patients, 100% (8/8) received IVMP and IVIG, and only one patient (12.5%) required rituximab; at follow-up, 87.5% showed full recovery. In contrast, all NMOSD patients (10/10) required IVMP, IVIG, and PLEX, with 70% (7/10) treated with rituximab and 30% (3/10) with azathioprine. Despite this aggressive therapy, 100% of NMOSD patients were left with residual disability, with a median EDSS of 6 compared to 0 in the MOGAD group. These findings align with previous pediatric studies indicating favorable recovery in MOGAD after corticosteroid and IVIG therapy[2], whereas pediatric seronegative NMOSD remains difficult to treat, often requiring long-term immunosuppression with limited functional improvement[10].

The results obtained in this study highlight the differences between the clinical and radiological features of MOGAD and seronegative NMOSD. Our findings indicate that MOGAD patients have lower relapse rates and higher functional recovery rates despite longer follow-up. This is consistent with previous studies indicating that MOGAD may have a relatively better prognosis[2,9]. In contrast, recurrent attacks and permanent neurological deficits were observed in all cases in the seronegative NMOSD group. The literature indicates that seronegative NMOSD has a more heterogeneous course compared to AQP4-positive forms but generally has adverse clinical outcomes[8].

Radiologically, our study demonstrated more pronounced cortical and white matter involvement in MOGAD, while deep gray matter and brainstem involvement in NMOSD were more prominent. In a study evaluating brain T2 lesions in pediatric patients and comparing them between MOGAD, NMOSD and MS, findings were higher in MOGAD, similar to our study[10]. In addition, conus medullaris involvement is notable in MOGAD, while more widespread cervical and thoracic lesions were observed in NMOSD. These differences support studies reporting that MOGAD is more cortical and multifocal, while NMOSD is characterized by long-segment myelitis and periependymal distribution[5,8]. When orbital involvement patterns were examined, anterior/panorbital involvement was observed more frequently in MOGAD, while posterior involvement was observed more frequently in NMOSD; this finding may be helpful in differential diagnosis[11].

The strengths of our study are the relatively long follow-up period in the pediatric age group and the ability to make a detailed clinical-radiological distinction. However, there are some limitations: the relatively small number of patients, the retrospective design, and the single-center nature limit the generalizability of the findings. Furthermore, heterogeneity in treatment protocols may create variability in the assessment of clinical outcomes.

As a conclusion, MOGAD and seronegative NMOSD are two distinct entities that exhibit significant clinical and radiological differences but may partially overlap. Our study demonstrates that MOGAD may have a lower propensity for relapse and better recovery rates, while NMOSD is associated with higher recurrence and permanent sequelae. Cortical and conus involvement, in particular, provides distinguishing clues for MOGAD, while long-segment spinal and posterior orbital involvement provides clues for NMOSD. Considering these differences in diagnostic algorithms will guide clinicians in selecting appropriate treatment and predicting prognosis. Prospective multicenter studies with larger samples are necessary.

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