

MOG Antibody Disease (MOGAD) Presenting as Acute Disseminated Encephalomyelitis (ADEM): Insights from Cerebrospinal Fluid Cytokine Profiling

Doença Associada a Anticorpos contra MOG (MOGAD) Apresentando-se como Encefalomielite disseminada aguda (ADEM): Contribuições do Perfil de Citocinas no Líquido Cefalorraquidiano

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ABSTRACT

This study reports a pediatric case of MOG-antibody-associated disease (MOGAD) presenting as acute disseminated encephalomyelitis (ADEM) following a febrile episode. The patient, a 6-year-old female, exhibited progressive neurological deficits that resolved after treatment with intravenous corticosteroids. We characterized the cerebrospinal fluid (CSF) inflammatory profile, which revealed significant elevations of pro-inflammatory cytokines, including TNF, IL-6, IL-8, and IL-1 β . In contrast, the anti-inflammatory cytokine IL-10 was also markedly increased, suggesting an endogenous mechanism to limit the inflammatory cascade. The robust neuroinflammatory response, combined with the favorable clinical outcome after immunosuppression, highlights the complex response of pro- and anti-inflammatory pathways in MOGAD. Our findings reinforce the potential of CSF cytokine profiling to advance the understanding of the immunopathogenesis of MOGAD and to guide personalized therapeutic interventions, particularly with agents targeting key mediators.

Keywords: Myelin oligodendrocyte glycoprotein; acute disseminated encephalomyelitis; Cytokines.

RESUMO

Este estudo relata um caso pediátrico de doença associada ao anticorpo MOG (MOGAD) apresentando-se como encefalomielite disseminada aguda (ADEM) após um episódio febril. A paciente, uma menina de 6 anos, exibiu déficits neurológicos progressivos que foram resolvidos após tratamento com corticosteroides intravenosos. Nós caracterizamos o perfil inflamatório do líquido cefalorraquidiano (LCR), que revelou elevações significativas de citocinas pró-inflamatórias, incluindo TNF, IL-6, IL-8 e IL-1 β . Em contraste, a citocina anti-inflamatória IL-10 também estava marcadamente aumentada, sugerindo um mecanismo endógeno para limitar a cascata inflamatória. A robusta resposta neuroinflamatória, combinada com o desfecho clínico favorável após a imunossupressão, destaca a complexa resposta das vias pró e anti-inflamatórias na MOGAD. Nossos achados reforçam o potencial do perfil de citocinas do LCR para avançar a compreensão da imunopatogênese da MOGAD e para guiar intervenções terapêuticas personalizadas, particularmente com agentes que visam mediadores-chave.

Palavras-chaves: Glicoproteína Mielina-Oligodendrócito; Encefalomielite Aguda Disseminada; Citocinas.

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INTRODUCTION

Paediatric acquired demyelinating syndromes (ADS) encompass a broad spectrum of immune-mediated disorders of the central nervous system (CNS), including acute disseminated encephalomyelitis (ADEM), optic neuritis, transverse myelitis, neuromyelitis optica spectrum disorders (NMOSD), and multiple sclerosis¹. Over the past decade, the identification of myelin oligodendrocyte glycoprotein antibodies as a biomarker of CNS demyelination has defined a distinct clinical entity known as MOG-antibody-associated disease (MOGAD)^{2,3,4}. Clinical presentation varies by age, with ADEM being the most common phenotype in children. Notably, antecedent infections have been reported in 20–57% of individuals with MOGAD, supporting the hypothesis of a post-infectious trigger, particularly for the ADEM phenotype¹.

Identifying new biomarkers is crucial to improve understanding of encephalitis, since treatment differs between viral and autoimmune forms. Such biomarkers could help distinguish persistent symptoms caused by ongoing CNS inflammation from those due to residual injury. Chemokines (CKs) and other cytokines, as key inflammatory mediators measurable in the cerebrospinal fluid (CSF), represent promising candidates for more accurately characterizing the underlying inflammatory processes⁵.

The present study aims to report the case of a pediatric patient with ADEM and positive anti-MOG antibodies, characterizing the inflammatory profile in the cerebrospinal fluid through cytokine and chemokine analysis, and correlating the immunological findings with the clinical presentation and neurological course.

CASE REPORT

A 6-year-and-11-month-old girl was admitted for evaluation of progressive lower limb weakness and urinary dysfunction. Her illness had begun approximately 18 days earlier with fever (maximum 39 °C) and mild headache. After transient improvement, symptoms recurred five days later with fever (38 °C) and vomiting. Three days after completing an antibiotic course for a presumed urinary tract infection, she developed worsening headache and weakness in the lower limbs. Amoxicillin was then prescribed for a suspected sinus infection; however, the following day, she experienced marked motor deterioration, became unable to walk without assistance, and developed urinary retention, leading to hospital admission at the referral center.

On admission, the patient presented with a distended bladder and subsequently developed sphincter dysfunction. Neurological examination showed muscle strength grade 2/2 in the lower limbs, with reduced movement on the left side. Deep tendon reflexes were brisk (3/3), with fatigable clonus on the left and bilateral Babinski signs. A cranial CT scan was unremarkable. The initial diagnostic hypothesis was transverse myelitis of infectious or inflammatory origin.

Lumbar puncture showed lymphomonocytic pleocytosis and elevated protein. CSF was stored at –20 °C for cytokine/chemokine analysis. IL-1 β , IL-6, IL-8, IL-10, TNF, and IL-12p70 were quantified by flow cytometry (CBA Human Inflammatory Cytokine Kit; BD Biosciences, San Jose, CA, USA). The study was approved by the institutional ethics committees (CAAE 21781914.2.0000.5119).

The patient was isolated with suspected meningitis and empirically treated with intravenous ceftriaxone (100 mg/kg/day, 10 days) and acyclovir (10 mg/kg every 8 h, 9 days). Acyclovir was discontinued after negative herpesvirus PCR. Due to suspected ADEM, intravenous methylprednisolone (30 mg/kg/day, 5 days) was administered. Cranial and thoracic spinal MRI subsequently demonstrated hyperintense T2/FLAIR lesions in the right cerebral peduncle and cerebellum (figure 2).

Following corticosteroid pulse therapy, the patient showed progressive clinical improvement. At discharge, she was alert, oriented, and able to follow commands, with preserved extraocular movements and only a subtle deviation of the left oral commissure. Muscle strength was grade 4– in the lower limbs and 4+ in the upper limbs, deep tendon reflexes were brisk in the lower limbs with bilateral fatigable clonus, and plantar responses were in extension. No dysmetria or ataxia was observed. She was discharged on oral prednisolone (1 mg/kg/day) with a tapering plan over 4–6 weeks.

At follow-up, five months after symptom onset, neurological examination was essentially normal, with only mild flattening of the right nasolabial fold and a slightly atypical gait as residual findings. Anti-MOG antibody testing was performed late (18 weeks after symptom onset), due to limited availability, and returned positive.

The cytokine analysis revealed a markedly proinflammatory profile: TNF (7,733.59 pg/mL), IL-6 (5,127.16 pg/mL), IL-8 (4,853.25 pg/mL), and IL-1 β (4,437.54 pg/mL) were strongly elevated. IL-10 was also substantially increased (6,219.14 pg/mL), likely reflecting a counter-regulatory mechanism, as described in neuroinflammatory and post-infectious conditions. IL-12p70, although lower in magnitude (1,655.89 pg/mL), indicated activation of adaptive immune pathways.

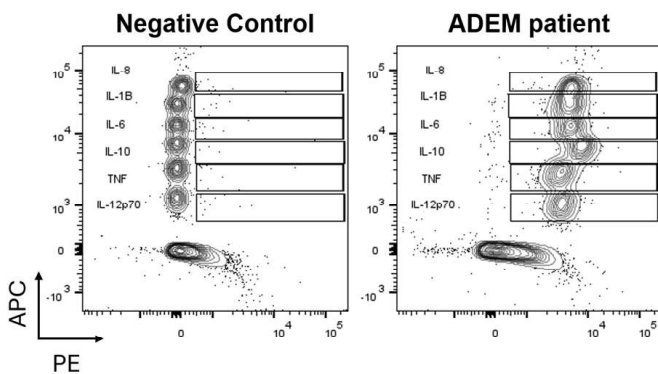


Figure 1: Cytokine Profile in Cerebrospinal Fluid of a Pediatric Patient with ADEM and positive anti-MOG antibodies Compared to a Negative Control.

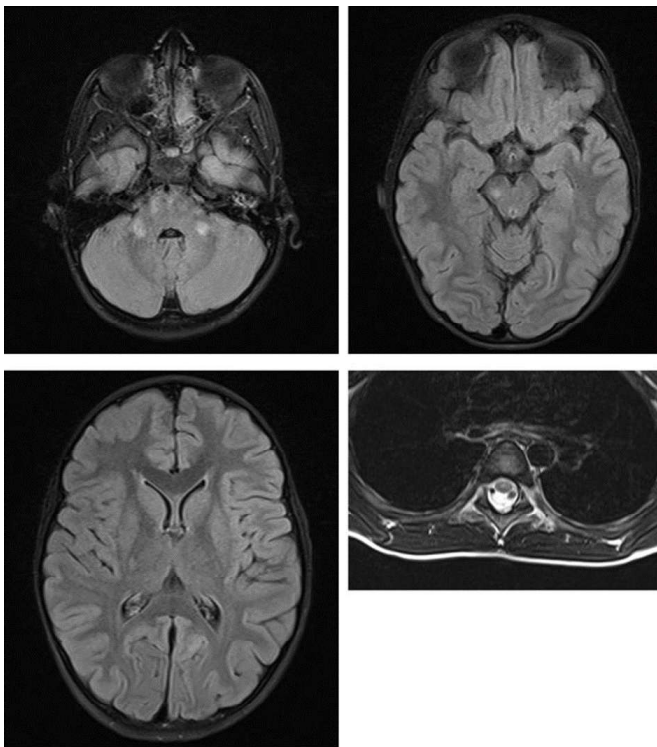


Figure 2: Cranial and thoracic spinal MRI subsequently demonstrated hyperintense T2/FLAIR lesions in the right cerebral peduncle and cerebellum, with thoracic spine demonstrating discrete intramedullary foci of hyperintensity spanning T9 to T12 (in the central cord, anterior funiculi, and posterior funiculi), notable for the absence of gadolinium enhancement.

DISCUSSION

We report a pediatric MOGAD case presenting as ADEM post-febrile episode. CSF cytokine profiling showed a concomitant increase in pro-inflammatory cytokines (TNF, IL-1 β , IL-6, IL-8) and the anti-inflammatory cytokine IL-10, reflecting a robust acute CNS inflammatory response^{6,7}. Similar patterns have been observed in other MOGAD patients, with CSF elevations of humoral and Th17-related cytokines as well as IL-10 compared to MOG-negative demyelinating conditions^{7,8}. IL-6 and IL-17A correlate with MOG-IgG titers, highlighting Th17 activation's role in

pathogenesis via neutrophil recruitment and inflammation^{8,9}. IL-1 β and IL-8 amplify inflammatory cascades and promote leukocyte recruitment, likely causing our patient's rapid motor deterioration⁶.

As a key driver of blood–brain barrier disruption, IL-6's persistent elevation in pediatric MOGAD is associated with higher protein levels and sustained inflammation, suggesting it may guide therapeutic strategies like IL-6 inhibition¹⁰. The concomitant IL-10 increase likely reflects its role as a key immunoregulator limiting tissue damage during excessive inflammation^{6,11}. This interplay of pro- and anti-inflammatory cytokines influences clinical course, including relapse risk and neurological deficit severity^{7,11}.

The favorable response to methylprednisolone highlights the benefit of early immunosuppression. Substantial recovery five months post-onset aligns with the favorable prognosis of pediatric MOGAD, where over 70% achieve near-complete recovery¹². This complex profile underscores the dual nature of immune responses. Mapping this balance could refine prognosis, guide therapy, and improve outcomes.

Despite the scarcity of studies characterizing this inflammatory response in ADEM, recent evidence highlights the central role of IL-6 in MOGAD pathogenesis. IL-6 promotes Th17 differentiation, directly contributing to demyelination and establishing a positive feedback loop that sustains neuroinflammation⁹. Unlike NMOSD, MOGAD is less complement-dependent with limited therapeutic responses to complement-targeting strategies¹³. Tocilizumab (TCZ), an IL-6 receptor antibody, is a promising alternative for rituximab-refractory cases. Case reports confirm TCZ's efficacy and safety, reinforcing the rationale for IL-6-targeted therapies in severe or refractory MOGAD, and suggesting cytokine profiling may guide future personalized strategies¹³.

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