sclerosis

MDPI

Case Report

From Low-Positive Fixed Cell-Based Assay to Confirmed Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease: A Paediatric Case Report

Tamara Santibáñez [1,2,3], José M. Valdés [1,2] and Lorna Galleguillos [1,2,4,*]

[1] Department of Neurology and Psychiatry, Clínica Alemana de Santiago, Santiago 7650568, Chile
[2] Facultad de Medicina, Clínica Alemana Universidad del Desarrollo, Santiago 7610315, Chile
[3] Department of Neurology, Hospital Clínico Dra. Eloísa Díaz Insunza, Santiago 8240000, Chile
[4] Neurology and Neurosurgery Department, Clínica Dávila, Santiago 8431657, Chile
* Correspondence: lgalleguillos@alemana.cl

Abstract

Background: The diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) relies on sensitive serological detection of MOG-IgG. Fixed cell-based assays (CBAs) may yield low-positive or borderline results that complicate early clinical decision-making, whereas live CBAs—recommended as the reference method—preserve native antigen conformation and offer higher analytical sensitivity. Importantly, low-positive titres should not be confused with true seronegativity, as they may nevertheless be clinically meaningful. **Case Presentation**: A 14-year-old previously healthy male presented with left optic neuritis and perineuritis following an upper respiratory infection. Initial MOG-IgG testing on a fixed CBA was low-positive (1:10). He partially responded to intravenous methylprednisolone and required intravenous immunoglobulin (IVIG) for complete resolution. Over three years, he experienced sequential, steroid-dependent bilateral optic neuritis with perineuritis, relapsing on every steroid taper. Rituximab and subsequently mycophenolate mofetil failed to induce remission. Repeat testing with a live CBA at a reference laboratory yielded a high-positive MOG-IgG titre of 1:1000, confirming MOGAD. Tocilizumab (8 mg/kg every 4 weeks) was initiated and allowed complete corticosteroid withdrawal. At age 18, the patient remained asymptomatic, with an Expanded Disability Status Scale score of 0, best-corrected visual acuity of 20/20 in both eyes, and stable peripapillary retinal nerve fibre layer thickness on spectral-domain optical coherence tomography. **Conclusions**: In paediatric patients with recurrent optic neuritis with perineural involvement and borderline fixed-CBA results, confirmatory testing with a live CBA at a reference laboratory should be considered to avoid diagnostic delay and therapeutic misdirection. In refractory, steroid-dependent cases, IL-6 receptor blockade may represent a reasonable therapeutic option, in line with emerging evidence.

Keywords: MOGAD; NMOSD; optic neuritis; perineuritis; cell-based assay; corticosteroid dependence; tocilizumab; paediatric demyelinating disease

Check for updates

Academic Editor: Maurizio A. Leone

Received: 15 March 2026
Revised: 20 April 2026
Accepted: 25 April 2026
Published: 29 April 2026

Copyright: © 2026 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license.

1. Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune disease with a predilection for the optic nerves and spinal cord. The discovery of antibodies against the aquaporin-4 (AQP4) water channel in most patients, and subsequently of serum myelin oligodendrocyte glycoprotein IgG (MOG-IgG), progressively narrowed the group

of seronegative NMOSD patients; MOG-IgG-associated disease (MOGAD) has since been recognised as a distinct clinical entity [1]. Nevertheless, a subset of patients remains truly double-seronegative (AQP4-IgG and MOG-IgG negative), without a diagnostic biomarker [2]. It is important to distinguish true seronegativity from low-positive or borderline MOG-IgG results, which describe detectable antibody at low titres (typically 1:10–1:40 on fixed CBA) and represent a different diagnostic category with its own clinical implications.

In the paediatric population, MOGAD frequently manifests as acute disseminated encephalomyelitis or optic neuritis (ON), often with prominent perineuritis [3]. Accurate diagnosis relies on the detection of MOG-IgG autoantibodies. International consensus guidelines strongly recommend using live-cell-based assays (live CBAs) due to their superior sensitivity and specificity compared to fixed-cell assays, which can yield ambiguous, low-positive, or false-negative results [4,5]. MOG-IgG is a highly specific biomarker when tested at appropriate cutoffs: at a 1:20 cutoff, the positive predictive value is only 72%, rising substantially at titres $\geq$ 1:100 [6].

While acute MOGAD exacerbations generally respond well to high-dose corticosteroids, a subset follows a highly relapsing, corticosteroid-dependent course in which conventional steroid-sparing agents such as rituximab or mycophenolate mofetil (MMF) may fail to prevent relapses [3]. Recent evidence indicates that interleukin-6 (IL-6) plays a pivotal role in NMOSD and MOGAD pathogenesis by promoting plasmablast survival and altering blood–brain barrier permeability [7,8]. Accordingly, IL-6 receptor antagonists such as tocilizumab are emerging as promising off-label options for refractory disease [9].

We report the case of a paediatric patient with sequential, bilateral, relapsing optic neuritis with perineuritis and strict corticosteroid dependence, in whom a marked analytical discrepancy between fixed (1:10) and live (1:1000) cell-based assays ultimately reclassified the diagnosis from a clinically assumed seronegative NMOSD-like presentation to definite MOGAD. The case contributes three elements to the literature: (i) the unusual magnitude of the fixed–live CBA titre discrepancy in a single patient; (ii) the downstream clinical consequences of this analytical discordance in a paediatric patient; and (iii) longitudinal paediatric data on the successful use of IL-6 receptor blockade after failure of conventional therapies.

2. Literature Review

2.1. Paediatric MOGAD: Epidemiology, Clinical Phenotypes and Prognosis

MOGAD is increasingly recognised as one of the most common antibody-mediated demyelinating disorders of the central nervous system in childhood. In a systematic synthesis of 194 cohorts encompassing 4699 paediatric and adult patients from 31 countries, optic neuritis was the most common initial phenotype (34% in children, 60% in adults), and peripapillary retinal nerve fibre layer swelling with papilloedema on fundoscopy was documented in 71% of acute attacks [10]. Although cumulative relapse rates were similar across age groups, paediatric patients relapsed earlier than adults (median time to first relapse 6 vs. 17 months), and bilateral optic nerve involvement and leptomeningeal enhancement were more frequent in children [10]. A prospective UK multicentre cohort of 276 patients confirmed that paediatric-onset disease is dominated by acute disseminated encephalomyelitis (ADEM) under 12 years (≈68%) and by optic neuritis thereafter, with an 8-year relapse risk of 36% in incident cases; first-line maintenance therapy (prednisolone, non-steroidal immunosuppression, or both) was associated with a ≈2-fold reduction in relapse risk [11]. Single-centre paediatric series reinforce that ADEM and optic neuritis are the predominant phenotypes and that, despite an overall favourable acute response to corticosteroids, visual impairment is the most frequent long-term sequela [12]. In the

absence of randomised evidence, the European Paediatric MOG Consortium endorsed intravenous methylprednisolone as first-line acute therapy, with rituximab, azathioprine, mycophenolate mofetil or monthly IVIG as first-line maintenance options for relapsing disease, and escalation strategies reserved for treatment failures [13].

2.2. Optic Neuritis with Perineural Involvement as a Phenotypic Hallmark of MOGAD

Optic perineuritis, defined as gadolinium enhancement of the optic nerve sheath on orbital MRI, is strongly related to MOG-IgG-associated optic neuritis (MOG-ON) compared with other inflammatory optic neuropathies. When combined with bilaterality, longitudinally extensive optic nerve hyperintensity and prominent disc oedema, perineural enhancement constitutes a highly suggestive radiological signature that reliably distinguishes MOG-ON from multiple sclerosis–associated optic neuritis and from AQP4-IgG-seropositive disease [14]. Individual reports of isolated optic perineuritis with confirmed serum MOG-IgG further support the view that perineural enhancement is not merely ancillary but may represent part of the core MOG-ON phenotype [15]. The radiological finding of unilateral, and subsequently bilateral, optic neuritis with perineuritis in our patient is therefore consistent with the MOGAD spectrum and reinforces the diagnostic value of dedicated orbital MRI with fat-suppressed post-gadolinium sequences in any paediatric patient presenting with acute or recurrent optic neuritis.

2.3. Analytical Performance of Fixed Versus Live MOG-IgG Cell-Based Assays

The relative performance of fixed versus live CBAs has been examined in several cross-platform studies. A Greek series comparing three of the most widely used assays showed that a live-cell IgG1-specific CBA detected MOG-IgG in 21 patients with clinico-radiological features of MOGAD, 7 of whom were seronegative on one or both IgG-total cell-based assays, suggesting that IgG1-selective live CBAs provide the highest specificity and sensitivity among available platforms [16]. In a larger real-world analysis of 322 paired clinical samples processed on commercial fixed and live CBAs, overall agreement was high (92.9%; $\kappa = 0.78$); however, discordance was concentrated in the low-positive range, and nearly all samples with high-titre live-CBA positivity corresponded to low or borderline values on the fixed assay [17]. These findings, together with previously cited work on the positive predictive value of low MOG-IgG titres [6], indicate that a 1:10 fixed-CBA titre in a patient with a compatible phenotype cannot be reliably interpreted as either confirmatory or exclusionary of MOGAD. The 100-fold fixed–live discrepancy observed in our patient, although at the extreme end of the reported spectrum, falls within this described range and underscores the clinical risk of relying solely on fixed-CBA testing for paediatric decisions involving prolonged immunosuppression.

2.4. Refractory, Corticosteroid-Dependent Paediatric MOGAD and the Emerging Role of IL-6 Receptor Blockade

Although the majority of paediatric MOGAD attacks respond to high-dose corticosteroids, a clinically relevant subset follows a highly relapsing, corticosteroid-dependent course that is not consistently prevented by rituximab, mycophenolate mofetil or IVIG. Persistent disease activity under B-cell depletion has been attributed, at least in part, to continued autoantibody production by long-lived CD20-negative plasma cells, for which IL-6 signalling is a critical survival factor [18,19]. On this mechanistic basis, tocilizumab has emerged as a rational escalation option. A European multicentre retrospective study of 57 MOGAD and NMOSD patients switched to tocilizumab after failure of prior immunotherapies (predominantly rituximab) reported, in the MOGAD subgroup ($n = 14$), a reduction in the median annualised relapse rate from 1.75 to 0 ($p = 0.001$), with 79% of MOGAD patients remaining relapse-free during treatment and stabilisation of disability [9].

Paediatric-specific evidence, although still limited, is concordant: A two-patient series documented a rapid and sustained clinical response to tocilizumab in children with life-threatening MOGAD refractory to steroids, IVIG and therapeutic plasma exchange [20], and a recent retrospective series from the Children's Hospital of Philadelphia of 11 children receiving intravenous tocilizumab for acute-severe CNS inflammation reported clinical improvement within 72 h in eight patients, including those with relapsing optic neuritis, without acute adverse events [21]. Collectively, these data support the rationale for escalating to IL-6 receptor blockade in paediatric refractory, steroid-dependent MOGAD after failure of conventional immunotherapy, while acknowledging the absence of randomised comparative data and the limitations inherent to retrospective case series.

3. Case Report

Informed consent was obtained to report the case of a 14-year-old previously healthy male who presented in September 2022 with left-eye pain triggered by upward vertical gaze, which began shortly after an upper respiratory tract infection. An initial ophthalmological evaluation was normal. Three days later, the patient experienced a sudden decrease in visual acuity in the left eye (OS) and presented to the emergency department. Fundoscopy revealed left optic disc oedema.

Magnetic resonance imaging (MRI) of the brain and orbit in September 2022 demonstrated signs of left optic neuritis with concurrent perineuritis (Figure 1), with no demyelinating lesions in the brain parenchyma or spinal cord.

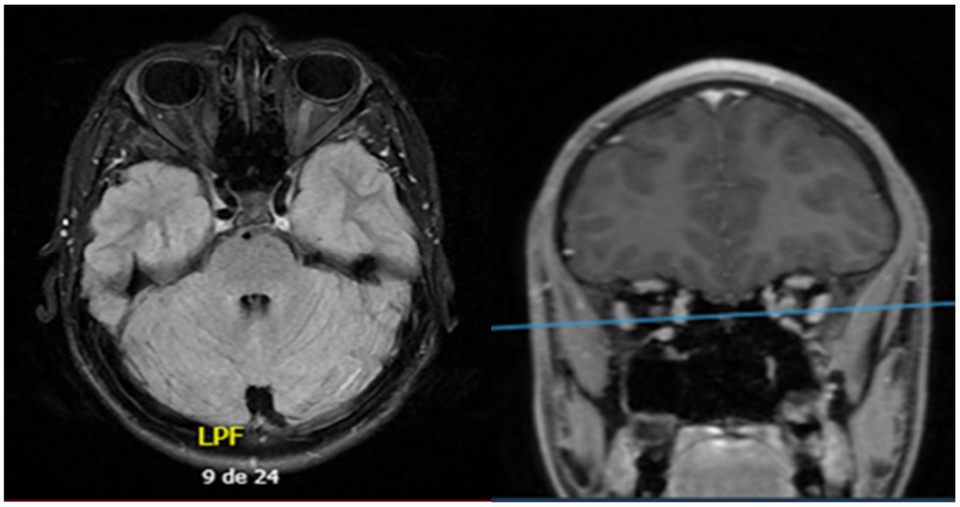


Figure 1. Brain and orbital MRI at initial presentation (September 2022). (**Left panel**) Sagittal T2-weighted fluid-attenuated inversion recovery (FLAIR) image showing hyperintensity and mild thickening of the intraorbital segment of the left optic nerve, extending along its long axis without involvement of the optic chiasm. (**Right panel**) Coronal post-gadolinium T1-weighted LAVA-FLEX sequence with fat–water separation demonstrating enhancement of the left optic nerve together with peripheral enhancement of the surrounding optic nerve sheath, consistent with concurrent optic neuritis and perineuritis. No intracranial parenchymal or spinal demyelinating lesions were identified.

Initial immunological workup showed MOG-IgG by fixed CBA at a titre of 1:10. At the time of this initial presentation, and prior to the 2023 International MOGAD Panel criteria, a 1:10 titre on fixed CBA was considered low-positive and was therefore interpreted with caution, particularly given the prospect of long-term immunosuppression in a paediatric patient. The remainder of an extensive etiological workup was unremarkable.

During the initial episode, the patient was treated with intravenous methylprednisolone (IVMP) (5 g total) followed by a prolonged oral prednisone taper (starting at

40 mg/day and progressively reduced until suspension in January 2023). Since prolonged steroids are not in the best interest of a paediatric patient, he was switched to intravenous immunoglobulin (IVIG) at a dose of 2 g/kg/month divided over 3 days for 2 consecutive months to stop prednisone, with no rebound in his visual symptoms at that time.

In August 2023, the patient developed right eye (OD) pain associated with ocular movements, without visual acuity impairment. An orbital MRI demonstrated mild thickening of the intraorbital segment of the right optic nerve adjacent to the posterior pole (Figure 2). This was associated with gadolinium enhancement of both the nerve and, mildly, the peri-optic sheath. Repeat MOG-IgG testing via fixed-cell assay remained stable at 1/10.

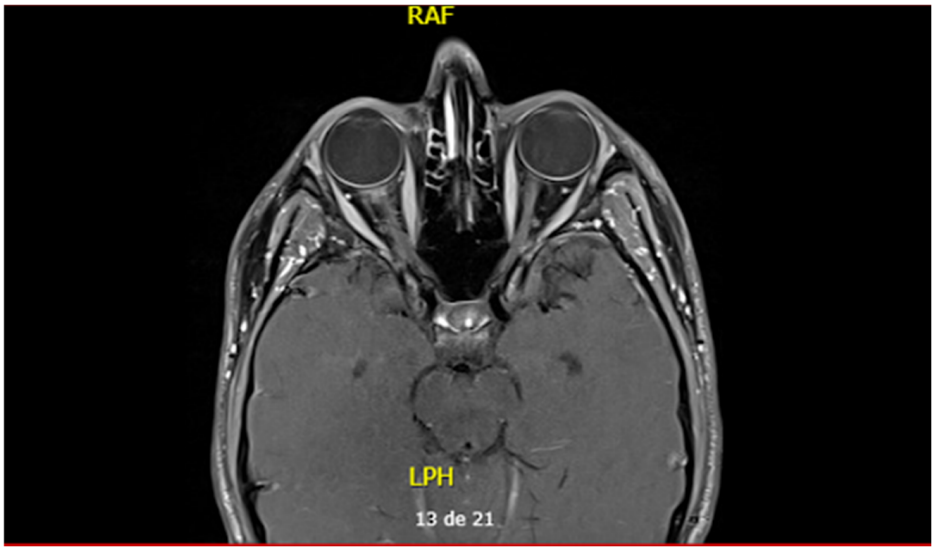


Figure 2. Orbital MRI during the second clinical episode (August 2023). Sagittal post-gadolinium T1-weighted TSE Dixon sequence with fat suppression demonstrating mild thickening and enhancement of the intraorbital segment of the right optic nerve, predominantly in its posterior portion adjacent to the globe, together with mild enhancement of the surrounding optic nerve sheath, consistent with right optic neuritis with perineural involvement (perineuritis). The intracanalicular and intracranial optic nerve segments and the optic chiasm were spared; no parenchymal demyelinating lesions were observed.

The August 2023 relapse was treated with IVIG (40 g/day for 3 days, equivalent to 2 g/kg) in combination with low-dose oral prednisone, with a good clinical response. Given a second optic neuritis event and a persistently low-positive MOG-IgG titre below the confirmatory diagnostic threshold, the patient was initially approached as having a probable low-positive/seronegative NMOSD-like presentation pending further characterisation. To prevent further relapses and accumulated disability, maintenance therapy with intravenous rituximab was initiated in September 2023 (1 g twice, two weeks apart, followed by 1 g in April 2024).

An optical coherence tomography (OCT) performed in November 2023 showed borderline thinning of the temporal retinal nerve fibre layer (RNFL) in the left eye (55–65 µm).

In March 2024, he developed a new relapse in his right eye, characterised by pain with eye movements and loss of saturation of colour vision. He started oral prednisone at a dose of 40 mg/day. Given the previous low-positive fixed-cell assay results and the highly relapsing clinical course despite rituximab therapy (already in the period of full biological effect of the monoclonal antibody), a serum sample was sent to the Mayo Clinic (Rochester, MN, USA) in March 2024 for definitive evaluation on the same day that a new fixed-cell assay for MOG-Ig was taken. While a concurrent local fixed-cell assay again returned a

titer of 1/10, the live-cell assay performed at the reference laboratory yielded a positive MOG-IgG titer of 1/1000, confirming the diagnosis of MOGAD.

Despite B-cell depletion therapy, the patient's clinical course was defined by strict corticosteroid dependence; he consistently experienced clinical deterioration and symptom recurrence whenever oral corticosteroids were tapered or suspended. To address this, his therapy was changed to oral mycophenolate mofetil (1250 mg every 12 h) in January 2025. In April, May, July, and September, he received 60 g of IVIg as combined treatment with MMF as suggested by an international paediatric neurologist.

Nevertheless, the patient presented with a new relapse characterised by right optic perineuritis in November 2025. Given the failure of rituximab, mycophenolate mofetil and IVIG, and the persistent steroid dependence, a multidisciplinary decision was made to initiate IL-6 blockade. The patient was started on intravenous tocilizumab at a dose of 8 mg/kg (500 mg total) every 4 weeks.

The transition to tocilizumab allowed for the successful withdrawal of corticosteroids. As of the current follow-up (age 18), the patient remains completely asymptomatic and clinically stable, with an Expanded Disability Status Scale (EDSS) score of 0. Best-corrected visual acuity was 20/20 in both eyes. Spectral-domain OCT performed in November 2025 (Heidelberg Spectralis®, Heidelberg Engineering, Heidelberg, Germany) showed peripapillary RNFL within normal limits in the right eye and borderline in the left eye, with persistent borderline thinning in the temporal and superotemporal sectors and remained stable compared with the baseline study of December 2024. Macular ganglion cells and total retinal thickness maps were stable bilaterally.

4. Discussion

This case illustrates two intertwined aspects of MOGAD diagnosis and management: the analytical limitations of antibody testing in the borderline range, and the challenge of highly relapsing, corticosteroid-dependent disease.

After the second relapse in 2022, he was initially approached as a possible seronegative NMOSD-like presentation: MOG-IgG was detectable by fixed CBA from the outset, albeit at a low-positive titre (1:10). The diagnostic uncertainty therefore stemmed from the borderline titre rather than from seronegativity, a distinction with important consequences for how subsequent testing and therapy should be prioritised [4,6]. Prior to the 2023 International MOGAD Panel criteria, a low-positive fixed-CBA titre frequently led to diagnostic hesitation, particularly in paediatric patients facing long-term immunosuppression. The 2023 criteria [4] formally accept a low-positive MOG-IgG result when accompanied by a core clinical demyelinating event and supportive MRI features. Nevertheless, persistent low titres on local fixed CBAs can remain a confounding factor in the face of refractoriness to standard therapies, and it was the definitive live-CBA testing at a reference laboratory that resolved the diagnostic dilemma, yielding a 1:1000 titre [5,6].

Both fixed and live CBAs have intrinsic limitations that warrant careful consideration. Fixed CBAs rely on paraformaldehyde fixation (practical, scalable, and broadly available), but fixation can distort the native conformation of the MOG protein. Because a substantial proportion of pathogenic MOG-IgG antibodies recognise conformational epitopes, particularly those in the extracellular FG loop [22], fixation may reduce antigen accessibility and generate false-negative or equivocal low-titre results. Live CBAs preserve the native conformation and typically achieve higher sensitivity and specificity at clinically relevant titres, but they are technically demanding, require flow cytometry or high-resolution microscopy, and are largely confined to reference laboratories. Additional sources of analytical discrepancy include the MOG isoform expressed (α-1 versus full-length), transfection efficiency and antigen density, secondary-antibody specificity (pan-IgG versus IgG1-selective, the

latter being more MOGAD-specific), the positivity cutoff selected, and the absence of a universal international reference standard for MOG-IgG titration. In our patient, any or several of these variables may account for the 100-fold difference.

Several differential diagnoses were critically considered. Chronic relapsing inflammatory optic neuropathy (CRION)—historically defined as an idiopathic, steroid-responsive, relapsing optic neuritis without other central nervous system involvement—overlaps strikingly with our patient's early trajectory. However, subsequent work has shown that a substantial proportion of cases previously labelled as CRION test positive for MOG-IgG once a sensitive live CBA is applied, suggesting that most of these cases fall within the MOGAD spectrum [23]. The eventual high-titre live-CBA positivity in our patient is consistent with this reclassification. Double-seronegative NMOSD was also initially entertained, but the patient never developed other core NMOSD features (area postrema, diencephalic, brainstem, cerebral, or longitudinally extensive transverse myelitis syndromes), and cerebrospinal fluid findings were non-specific. Further differentials (sarcoid-associated optic perineuritis, infectious optic neuritis, Susac syndrome, and compressive or infiltrative lesions) were systematically excluded through targeted imaging, serology, and clinical evolution.

Our patient also exhibited a hallmark feature of MOGAD: pronounced corticosteroid dependence. While acute MOGAD exacerbations respond well to high-dose steroids and IVIG, maintaining remission can be difficult. In this case, sequential rituximab, IVIG, and mycophenolate mofetil failed to achieve steroid-free remission. A significant proportion of MOGAD patients continue to exhibit disease activity despite B-cell depletion, likely reflecting continued autoantibody production by long-lived plasma cells that lack the CD20 antigen targeted by rituximab [18].

The successful induction and maintenance of remission with tocilizumab is consistent with growing evidence supporting IL-6 receptor blockade in refractory MOGAD. IL-6 is essential for B-cell differentiation into antibody-secreting plasma cells and for plasmablast survival [19], and it contributes to blood–brain barrier disruption and recruitment of pro-inflammatory T cells into the central nervous system [24]. By blocking the IL-6 receptor, tocilizumab disrupts this inflammatory cascade. In our patient, tocilizumab not only halted disease activity but also permitted safe and complete tapering of oral corticosteroids, thereby avoiding the long-term morbidity of chronic steroid exposure during adolescence.

5. Limitations

This report has several limitations that should be acknowledged. First, as a single-case observation, it cannot support causal inferences or generalisable recommendations regarding either the prevalence of fixed–live CBA discrepancies or the relative efficacy of tocilizumab. Second, MOG-IgG titration was performed at different time points and in different laboratories using different methodologies; a fully standardised, head-to-head, same-sample comparison was not feasible. Contributions from pre-analytical variability (sample handling, storage), analytical factors (MOG isoform, transfection efficiency, secondary-antibody specificity, titre cutoff), and inter-operator variability cannot be disentangled. Third, serial live-CBA titration after tocilizumab initiation was not available, limiting our ability to correlate serological dynamics with clinical response. Fourth, although best-corrected visual acuity at last follow-up was 20/20 in both eyes, serial quantitative visual-field data were not consistently available, and follow-up after tocilizumab initiation remains short in absolute terms. Finally, as is inherent to case reports, unmeasured confounders—including cumulative prior immunosuppression with rituximab, mycophenolate mofetil, and repeated IVIG cycles—may have contributed to the favourable outcome and cannot be formally dissociated from the effect of IL-6 receptor blockade.

6. Conclusions

In summary, this single case illustrates how a marked discrepancy between fixed- and live-cell-based assays may delay recognition of paediatric MOGAD and contribute to therapeutic misdirection. In patients with recurrent optic neuritis with perineural involvement and borderline fixed-CBA results, confirmatory testing with a live CBA at a reference laboratory should be considered, in line with current international recommendations. In highly relapsing, corticosteroid-dependent cases unresponsive to B-cell depletion and antimetabolite therapy, IL-6 receptor blockade with tocilizumab may constitute a reasonable therapeutic option, supported by emerging but still limited evidence from case series and small cohorts. Larger prospective studies are required before firm conclusions regarding the therapeutic hierarchy in refractory paediatric MOGAD can be drawn.

Author Contributions: T.S., J.M.V. and L.G. conceptualised the report. T.S. and J.M.V. drafted the initial manuscript. T.S., J.M.V. and L.G. critically reviewed and revised the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: The authors declare that no financial support was received for the research, authorship, and/or publication of this article.

Institutional Review Board Statement: This is a retrospective single-case report derived from routine clinical care, without any interventional or prospective research procedure. Under Chilean Law N° 20.120 (2006) on scientific research involving human beings, and in accordance with the policy of the Research Ethics Committee of Clínica Alemana de Santiago, retrospective single-patient case reports based on standard clinical care that do not meet the regulatory definition of biomedical research are exempt from formal Ethics Committee approval when written informed consent for publication has been obtained.

Informed Consent Statement: Written informed consent for the publication of clinical data and potentially identifiable images was obtained from the patient upon reaching legal majority (age 18).

Data Availability Statement: The original contributions presented in the study are included in the article; further inquiries can be directed to the corresponding author.

Acknowledgments: The authors acknowledge the use of Gemini 3 (Google) for writing assistance and language editing. The authors assume full responsibility for the final content after thoroughly reviewing the manuscript to fact-check, correct errors, verify all references, and ensure no fabricated material was included.

Conflicts of Interest: J.M.V. reports a research grant from AstraZeneca, honoraria from Merck, and support for attending meetings and/or travel from Merck. T.S. reports fees from Merck for speaker events. L.G. declare personal fees from MERCK SA., Biogen Idec, Roche Chile, Sanofi-Genzyme, TEVA, Novartis, and BMS.

References

1. Wu, Y.; Geraldes, R.; Juryńczyk, M.; Palace, J. Double-negative neuromyelitis optica spectrum disorder. *Mult. Scler. J.* **2023**, *29*, 1353–1362. [CrossRef] [PubMed]
2. Hamid, S.H.M.; Whittam, D.; Mutch, K.; Linaker, S.; Solomon, T.; Das, K.; Bhojak, M.; Jacob, A. What proportion of AQP4-IgG-negative NMO spectrum disorder patients are MOG-IgG positive? A cross sectional study of 132 patients. *J. Neurol.* **2017**, *264*, 2088–2094. [CrossRef]
3. Sechi, E.; Gastaldi, M.; Cortese, R.; Bisecco, A.; Vogrig, A.; Giannoccaro, M.P.; Zuliani, L.; Zoccarato, M.; Casagrande, S.; Sartori, S.; et al. Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD): Practical recommendations for diagnosis and management. *J. Neuroimmunol.* **2026**, *410*, 578781. [CrossRef]

4. Banwell, B.; Bennett, J.L.; Marignier, R.; Kim, H.J.; Brilot, F.; Flanagan, E.P.; Ramanathan, S.; Waters, P.; Tenembaum, S.; Graves, J.S.; et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. *Lancet Neurol.* **2023**, *22*, 268–282. [CrossRef]
5. Said, Y.; Filippatou, A.; Tran, C.; Rezavi, L.; Guo, K.; Smith, M.D.; Resto, Y.; Chen, J.J.; Calabresi, P.A.; Caturegli, P.; et al. Real-world clinical experience with serum MOG and AQP4 antibody testing by live versus fixed cell-based assay. *Ann. Clin. Transl. Neurol.* **2025**, *12*, 556–564. [CrossRef] [PubMed]
6. Sechi, E.; Buciuc, M.; Pittock, S.J.; Chen, J.J.; Fryer, J.P.; Jenkins, S.M.; Budhram, A.; Weinshenker, B.G.; Lopez-Chiriboga, A.S.; Tillema, J.-M.; et al. Positive Predictive Value of Myelin Oligodendrocyte Glycoprotein Autoantibody Testing. *JAMA Neurol.* **2021**, *78*, 741–746. [CrossRef]
7. Fujihara, K.; Bennett, J.L.; de Seze, J.; Haramura, M.; Kleiter, I.; Weinshenker, B.G.; Kang, D.; Mughal, T.; Yamamura, T. Interleukin-6 in neuromyelitis optica spectrum disorder pathophysiology. *Neurol. Neuroimmunol. Neuroinflamm.* **2020**, *7*, e841. [CrossRef]
8. Uzawa, A.; Oertel, F.C.; Mori, M.; Paul, F.; Kuwabara, S. NMOSD and MOGAD: An evolving disease spectrum. *Nat. Rev. Neurol.* **2024**, *20*, 602–619. [CrossRef] [PubMed]
9. Ringelstein, M.; Ayzenberg, I.; Lindenblatt, G.; Fischer, K.; Gahlen, A.; Novi, G.; Hayward-Könnecke, H.; Schippling, S.; Rommer, P.S.; Kornek, B.; et al. Interleukin-6 receptor blockade in treatment-refractory MOG-IgG-associated disease and neuromyelitis optica spectrum disorders. *Neurol. Neuroimmunol. Neuroinflamm.* **2022**, *9*, e1100. [CrossRef]
10. Trewin, B.P.; Brilot, F.; Reddel, S.W.; Dale, R.C.; Ramanathan, S. MOGAD: A comprehensive review of clinicoradiological features, therapy and outcomes in 4699 patients globally. *Autoimmun. Rev.* **2024**, *24*, 103693. [CrossRef]
11. Satukijchai, C.; Mariano, R.; Messina, S.; Sa, M.; Woodhall, M.R.; Robertson, N.P.; Ming, L.; Wassmer, E.; Kneen, R.; Huda, S.; et al. Factors Associated with Relapse and Treatment of Myelin Oligodendrocyte Glycoprotein Antibody–Associated Disease in the United Kingdom. *JAMA Netw. Open* **2022**, *5*, e2142780. [CrossRef]
12. Zhang, M.; Du, X.; Zhou, S.; Pan, G.; Shen, J.; Li, W.; Yu, L.; Zhou, Y.; Zhang, Y.; Wang, Y.; et al. Clinical characteristics, disease course, and outcomes of paediatric patients with myelin oligodendrocyte glycoprotein-Ab associated disease: A retrospective clinical study. *J. Clin. Neurosci.* **2021**, *94*, 1–7. [CrossRef]
13. Bruijstens, A.L.; Wendel, E.-M.; Lechner, C.; Bartels, F.; Finke, C.; Breu, M.; Flet-Berliac, L.; de Chalus, A.; Adamsbaum, C.; Capobianco, M.; et al. E.U. paediatric MOG consortium consensus: Part 5—Treatment of paediatric myelin oligodendrocyte glycoprotein antibody-associated disorders. *Eur. J. Paediatr. Neurol.* **2020**, *29*, 41–53. [CrossRef] [PubMed]
14. Jeyakumar, N.; Lerch, M.; Dale, R.C.; Ramanathan, S. MOG antibody-associated optic neuritis. *Eye* **2024**, *38*, 2289–2301. [CrossRef] [PubMed]
15. Yanagidaira, M.; Hattori, T.; Emoto, H.; Kiyosawa, M.; Yokota, T. Optic perineuritis with anti-myelin oligodendrocyte glycoprotein antibody. *Mult. Scler. Relat. Disord.* **2020**, *38*, 101444. [CrossRef]
16. Tzartos, J.S.; Karagiorgou, K.; Tzanetakos, D.; Breza, M.; Evangelopoulos, M.E.; Pelidou, S.-H.; Bakirtzis, C.; Nikolaidis, I.; Koutsis, G.; Notas, K.; et al. Deciphering anti-MOG IgG antibodies: Clinical and radiological spectrum, and comparison of antibody detection assays. *J. Neurol. Sci.* **2020**, *410*, 116673. [CrossRef]
17. Smith, T.L.; Haven, T.R.; Zuromski, L.M.; Luong, K.; Clardy, S.L.; Peterson, L.K. High level of agreement in a fixed vs. live cell-based assay for antibodies to myelin oligodendrocyte glycoprotein in a real-world clinical laboratory setting. *Front. Neurol.* **2023**, *14*, 1192644. [CrossRef]
18. Nepal, G.; Kharel, S.; Coghlan, M.A.; Rayamajhi, P.; Ojha, R. Safety and efficacy of rituximab for relapse prevention in myelin oligodendrocyte glycoprotein immunoglobulin G (MOG-IgG)-associated disorders (MOGAD): A systematic review and meta-analysis. *J. Neuroimmunol.* **2022**, *364*, 577812. [CrossRef]
19. Jego, G.; Bataille, R.; Pellat-Deceunynck, C. Interleukin-6 is a growth factor for nonmalignant human plasmablasts. *Blood* **2001**, *97*, 1817–1822. [CrossRef]
20. McLendon, L.A.; Gambrah-Lyles, C.; Viaene, A.; Fainberg, N.A.; Landzberg, E.I.; Tucker, A.M.; Madsen, P.J.; Huh, J.; Silver, M.R.; Arena, J.D.; et al. Dramatic Response to Anti-IL-6 Receptor Therapy in Children with Life-Threatening Myelin Oligodendrocyte Glycoprotein-Associated Disease. *Neurol. Neuroimmunol. Neuroinflamm.* **2023**, *10*, e200150. [CrossRef] [PubMed]
21. Marefi, A.; Grasso, E.A.; McLendon, L.A.; Narula, S.; Waldman, A.T.; Hopkins, S.; Banwell, B.L. Role of Tocilizumab in Severe CNS Inflammatory Presentations in Children. *Neurology* **2026**, *106*, e214926. [CrossRef] [PubMed]
22. Spadaro, M.; Winklmeier, S.; Beltrán, E.; Macrini, C.; Höftberger, R.; Schuh, E.; Thaler, F.S.; Gerdes, L.A.; Laurent, S.; Gerhards, R.; et al. Pathogenicity of human antibodies against myelin oligodendrocyte glycoprotein. *Ann. Neurol.* **2018**, *84*, 315–328. [CrossRef] [PubMed]

23. Lee, H.-J.; Kim, B.; Waters, P.; Woodhall, M.; Irani, S.; Ahn, S.; Kim, S.-J.; Kim, S.-M. Chronic relapsing inflammatory optic neuropathy (CRION): A manifestation of myelin oligodendrocyte glycoprotein antibodies. *J. Neuroinflamm.* **2018**, *15*, 302. [CrossRef] [PubMed]
24. Rochfort, K.D.; Collins, L.E.; Murphy, R.P.; Cummins, P.M. Downregulation of blood-brain barrier phenotype by proinflammatory cytokines involves NADPH oxidase-dependent ROS generation: Consequences for interendothelial adherens and tight junctions. *PLoS ONE* **2014**, *9*, e101815. [CrossRef]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.