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Original article

Visual outcome measures in pediatric myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD)

Flavia C. Gericke [a], James V.M. Hanson [b], Annette Hackenberg [c], Christina Gerth-Kahlert [b,*]

[a] University of Zurich, Zurich, Switzerland
[b] Department of Ophthalmology, University Hospital Zurich and University of Zurich, Zurich, Switzerland
[c] Department of Neuropediatrics, University Children's Hospital Zurich, Switzerland

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ABSTRACT

Background: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) comprises various age-dependent clinical phenotypes and may be monophasic, multiphasic, or chronic. Optic neuritis (ON) is a common manifestation and frequently appears in combination with other MOGAD phenotypes, particularly in young children. Despite permanent structural damage to the retinal nerve fiber layer (RNFL), children often experience complete visual recovery.
Aims: To analyze the progression and impact of MOGAD on the visual system of pediatric patients independently of the history of ON.
Methods: This retrospective study included children who met specific criteria: myelin oligodendrocyte glycoprotein (MOG) immunoglobulin G (IgG) seropositivity, acute presentation of MOGAD, and written general consent. Main outcome measures were global peripapillary retinal nerve fiber layer (pRNFL) thickness, and near and distance visual acuity, analyzed using descriptive statistics.
Results: We identified 10 patients with median age of 7.7 years at first event: 7 patients manifested with acute disseminated encephalomyelitis (ADEM) (with ON 5/7, ADEM only 1/7, with transverse myelitis (TM) 1/7), 2 with isolated ON, and 1 patient with neuromyelitis optica spectrum disorder (NMOSD)-like phenotype with ON. Among ON patients, 5/8 were affected bilaterally, with 3 initially diagnosed with unilateral ON but experiencing subsequent involvement of the fellow eye. None of the patients without previous ON showed a deterioration of visual acuity and, if evaluated, a reduction of the pRNFL.
Conclusion: Most pediatric MOGAD-ON patients in our cohort presented with acute vison loss and optic disc edema. All patients achieved complete visual recovery, independent of number of relapses or initial visual loss. The pRNFL thickness decreased for several months and stabilized at reduced levels after 12 months in the absence of further relapses. MOGAD may not have subclinical/'silent' effects on the visual system, as visual acuity and pRNFL were not affected in patients without ON.

1. Introduction

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an acute autoimmune disorder characterized by the presence of high-titer serum immunoglobulin G (IgG) antibodies that target conformational epitopes of myelin oligodendrocyte glycoproteins (MOG) leading to an acquired demyelinating disease [1]. The clinical phenotypes of MOGAD appear to be age-dependent, with children <10 years more likely to develop an acute disseminated encephalomyelitis (ADEM), and children ≥10 more likely to show an opticospinal phenotype consisting of optic neuritis (ON) or transverse myelitis (TM) [2–4]. Within a clinical phenotype, however, the MOG antibody status does not appear to differ with age [4]. A common clinical manifestation in both pediatric and adult patients is ON, which can present isolated or recurrent, uni- or bilateral [2,5] and may be due to high MOG antibody titers and enhanced blood-brain barrier permeability in the optic nerve that allows B cells, plasma cells, and autoantibodies to cross and mediate their pathogenic effects [2,6–8]. Other phenotypes include MOG encephalitis or in rare cases a leukodystrophy-like phenotype, which may all occur in any combination with either a monophasic or relapsing disease course [2,9]. The heterogeneity of clinical phenotypes is a determinant for the diverse functional outcomes of MOGAD patients: ADEM presents with encephalopathy, ON may cause severe visual

* Corresponding author.
E-mail address: christina.gerth-kahlert@usz.ch (C. Gerth-Kahlert).

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Abbreviations

ADEM	Acute disseminated encephalomyelitis
CNS	Central nervous system
IgG	Immunoglobulin G
MOGAD	Myelin oligodendrocyte glycoprotein antibody-associated disease
MS	Multiple sclerosis
NMOSD	Neuromyelitis optica spectrum disorder
OCT	Optical coherence tomography
ON	Optic neuritis
pRNFL	Peripapillary retinal nerve fiber layer
TM	Transverse myelitis
VA	Visual acuity

impairment and functional blindness [2], TM leads to motor and bladder problems, and encephalitis may trigger epilepsy [4].

Studies have shown that acute and chronic neurological impairment depends on the clinical phenotype and the central nervous system (CNS) structures involved, and age [4]. For instance, the occurrence of a single episode of ON is associated with a low risk of permanent disability and good functional visual outcome even when severe axonal degeneration with loss of retinal ganglion cells is present [4]. In particular, pediatric ON patients show a better visual recovery than adult patients, although the degree of neuroaxonal retinal atrophy is comparable [2]. These pediatric patients may experience a severe loss of vision during an acute episode of isolated MOGAD-ON, with 44–80 % having a Snellen visual acuity (VA) of 0.1 or less. They demonstrate a good response to steroid treatment, with a final visual acuity of ≥0.5 in 98 % [10], ≥0.8 in 89 % [11] and ≥1.0 in 56–73 % [4,12,13]. The recovery rate in pediatric patients with bilateral ON showed similar results [13]. A possible explanation for the discrepancy between functional visual outcome and structural changes in pediatric patients may be age-related cortical neuroplasticity [2,14].

Given the heterogenous nature of the disease, it remains unclear what factors, apart from the clinical phenotype [4] and age, contribute to the disease course and outcome, especially in the pediatric subgroup. Pediatric patients may display progressive retinal damage upon repeated examination with optical coherence tomography (OCT) [4], despite functional visual recovery and the absence of clinical relapses. OCT is a rapid, non-invasive imaging technique that enables detailed *in vivo* imaging of the retina and optic nerve head, allowing for the visualization and measurement of relevant structural changes such as peripapillary retinal nerve fiber layer (pRNFL) thinning or optic disc edema [15–17]. Additionally, the relationship between the number of relapses and visual outcome requires further exploration in pediatric patients as, to date, studies have described findings primarily in adult MOGAD-ON patients. These studies showed that an increasing number of relapses leads to an accumulation of structural damage and functional visual impairment in adults [4,18].

Therefore, in this study, we retrospectively analyzed data available in medical records to assess longitudinal changes in pRNFL thickness along with the near and distance visual acuity of pediatric MOGAD patients.

2. Study population and methods

2.1. Study population

This was a retrospective study conducted at the Department of Ophthalmology at the University Hospital in Zurich in collaboration with the Department of Neuropediatrics at the University Children's Hospital Zurich.

During the data collection period from November 2022 to August 2023, we identified all pediatric MOGAD patients who had been treated at the respective hospitals from August 2017 to August 2023. The inclusion criteria were as follows: MOG-IgG-seropositivity, acute presentation of a clinical phenotype associated with MOGAD, and general written consent given by the parents. Clinical manifestations other than ON were not an exclusion criterion.

Seropositivity for anti-MOG-antibodies was confirmed by two independent clinical institutions (Medical University of Innsbruck and the University Hospital of Zurich), using live-cell based assays.

2.2. Data analyzed

The following clinical data were collected from each pediatric patient through a review of the electronic medical records at our center: date of birth, age at first event, sex, date of appointments, medical history with diagnosis, presence and laterality of ON (if applicable), time of follow-up, and number of relapses.

The following functional and morphological data were extracted for each eye: near- and distance visual acuity (Snellen), visual acuity test type, refractive error (spherical equivalent), description of the fundus and optic nerve head appearance, and the global (averaged through 360° around the optic nerve head) thickness of the pRNFL as measured by OCT (SPECTRALIS, Heidelberg Engineering, Heidelberg, Germany). Near visual acuity was included because of potentially increased sensitivity in detecting the development of amblyopia at baseline and follow up [14].

A relapsing disease course, in contrast to progression to the fellow eye, is characterized by the occurrence of MOGAD symptoms after at least 30 days or more following a previous attack [9,19]. In this study, we classified another attack at 30 days following initial presentation as a flare-up if the attack occurred during steroid tapering or shortly after cessation.

Segmentation of the pRNFL was performed automatically by the proprietary software of the OCT manufacturer (Eye Explorer 1.9.10, Heidelberg Engineering) and was then manually verified and, when necessary, manually corrected by a single author (FCG). Scan quality and centration were also verified to ensure adequate quality, particularly in areas of optic disc edema and/or atrophy [20,21]. All OCT data included in the study fulfilled the OSCAR-IB quality criteria [22].

2.3. Statistical analysis

Due to the limited size of the patient population, we performed qualitative and quantitative analyses. We described categorical variables by frequencies and continuous variables by medians [23]. Graphs were created using the commercially available software Prism 9 (GraphPad Software Inc, La Jolla, CA, USA)).

2.4. Ethical approval and consent

The study protocol was approved by the cantonal ethics committee of Zurich (Switzerland) (BASEC- 2022-01562) on November 15th, 2022. Written general consent was provided by the parents of all patients.

3. Results

3.1. Cohort description and clinical features

We identified 10 MOG-IgG-positive pediatric patients with a median age of 7.7 years at the time of the first attack (range 5.1–13.3 years), including 7 females and 3 males. Among them, 5/10 patients were diagnosed with ADEM and ON, 2/10 patients with ON only, 1/10 patient with isolated ADEM, 1/10 patient with ADEM and TM, and 1/10 patient with neuromyelitis optica spectrum disorder (NMOSD) and ON.

Of the 8 patients with ON, 3/8 had unilateral involvement and 5/8

had a bilateral disease course. Of the latter, 3 patients were initially diagnosed with unilateral ON and subsequently experienced disease progression to the fellow eye over a median period of 1 month (range: 1–28 months). One of these three cases had relapsing ON with persistently high MOG-IgG titers, with 4 relapses over a follow-up period of 62 months despite immunosuppressive therapy.

The remaining 7/8 pediatric patients with a monophasic course of ON were followed up for a median of 12 months (range: 0–38 months).

The patient with ADEM only had a monophasic disease course and a follow-up of 12 months. There were no relapses other than ON.

All patients were initially treated with high dose methylprednisolone, which was repeated once in 3 patients with ADEM. Steroids were not uniformly tapered. Two patients had additional immunosuppressive therapy over 25 or 23 months due to a relapsing disease course or severe damage to the pRNFL and late occurring disease flare, respectively. The former patient received azathioprine, rituximab, and intravenous immunoglobulins as part of their treatment, while the latter underwent immunoadsorption and received intravenous immunoglobulins. Both patients received additional pulse steroid therapy.

The main clinical characteristics for each patient are reported in Table 1.

3.2. Visual acuity

At initial presentation, patients with showed a median distance VA of 0.35 (range: 0.014–1.0) and a median near VA of 0.5 (range: 0.014–1.0), in affected eyes (see Tables 2 and 3). Severe distance visual acuity reduction ≤0.1 was observed in 5/8 patients, with 4 patients having hand movements or counting fingers vision only. Near visual acuity reduction ≤0.1 was seen in 3/6 patients with ON, in whom this specific vision assessment was performed.

Visual acuity recovery ≥0.8 was observed in 4 patients after 2 months at both near and distance, except for 1 patient whose near VA decreased by 0.1. For the remaining patient, visual acuity was not recorded. At 6 months, all patients in whom follow-up data were available (5/8) attained a VA ≥0.8.

At the 12-month-analysis, all patients with ON had near VA and distance VA ≥0.8 with a median of 1.0 (range near VA: 0.8–1.0, range distance VA: 0.9–1.6). The VA of patients without a history of ON was not affected and remained normal.

3.3. Peripapillary retinal nerve fiber layer

At initial presentation, optic disc edema was present in 5 out of 7 patients with ON who received OCT testing, which consequently affected scan quality [20]. In the remaining 2 patients with ON, OCT scans were not performed during the acute phase but 1 or 5 months later, respectively, when the inflammation had already begun to subside (see Table 4). Fundoscopic descriptions from the medical records documented corresponding swelling of the optic disc at the time of the acute inflammation in patients with OCT testing.

The edema subsided in 3/5 patients after 2 months. At the 6-month-analysis, all 4/7 ON patients with available scans showed a reduction of the pRNFL with a median global thickness of 63 µm (range: 55–84 µm). The pRNFL thinned further in all MOGAD-ON patients with available OCT scans (6/7) over the following months, with a median global pRNFL thickness of 61 µm (range: 43–84 µm) at the 12-month-follow-up.

After the 12-month analysis, subsequent follow ups (18–60 months) revealed stabilization of the reduced global pRNFL thickness in patients with the history of ON who underwent regular OCT scans (3/7). The only patient without previous ON in whom OCT was performed had normal RNFL thickness.

A comparison of the progression of the visual acuity and global pRNFL thickness is shown in Fig. 1. In the initial 2 months, both pRNFL thickness and visual acuity show high variability, with an increased pRNFL thickness corresponding to optic disc swelling on fundoscopy and decreased visual acuity. By the 12-month-analysis, VA had recovered while the global pRNFL thickness stabilized at reduced levels. Overall, the near and distance VA showed similar development and results with minor discrepancies, as both measures were not always available at each timepoint due to the retrospective nature of the analysis.

Table 1
Main Clinical Characteristics
ADEM, Acute disseminated encephalomyelitis; Age, Age at first presentation in years and months [y.m]; BE, Both eyes; distance VA, distance visual acuity at initial presentation and at the 12-month-analysis; FU, Follow-up time in months; LE, Left eye; ME, Meningoencephalitis; NMOSD, Neuromyelitis optica spectrum disorder; NOE, Number of events; near VA, near visual acuity at initial and at the 12-month-analysis; ON, Optic neuritis; PN-S, patient number and sex; pRNFL, global thickness of the peripapillary retinal nerve fiber layer at initial presentation and at the 12-month-analysis in micrometers; RE, Right eye; SE, Spherical equivalent in diopter; Side ON, describes which eye is affected by optic neuritis; TM, Transverse myelitis.
In this table, the value in the upper row for each patient corresponds to the right eye, while the value in the lower row represents the left eye.

PN-S	Diagnosis	Age	Side ON	NOE	FU	near VA		distance VA		pRNFL		SE	OpD initial	OpD 12 m
						initial	12 months	initial	12 months	initial	12 months			
1-F	ADEM-ON	7.7	LE	2	38	0.6	1.0	1.25	1.0	n/a	75	n/a	normal	temporal pale
						0.014	0.8	0.014	1.0		52		swollen	temporal pale
2-F	ADEM-ON	7.1	BE	1	5	0.5	n/a	0.6	n/a	96	n/a	0.625	normal	n/a
						0.63		0.8		91		0.5	normal	
3-F	ADEM-ON	10.8	BE	1	23	1.0	1.0	0.8	1.0	66	64	0.25	normal	temporal pale
						1.0	1.0	1.0	1.0	44	43	0.25	normal	temporal pale
4-F	NMOSD-ON	6.5	BE[a]	5	62	0.5	0.8	0.6	0.9	n/a	59	−0.125	swollen	temporal pale
						1.0	0.9	1.0	0.8		57	0.375	normal	temporal pale
5-M	ON	13.3	RE	1	12	n/a	n/a	0.1	1.6	113	84	1.0	normal	temporal pale
								1.25	1.6	110	110	0.875	normal	normal
6-F	ON	6.1	RE	1	0	n/a	n/a	0.014	n/a	n/a	n/a	4.625	swollen	n/a
								0.8				3.5	normal	
7-F	ADEM-ON	6.1	BE[a]	2	32	1.0	1.0	1.0	1.0	107	77	0.125	normal	normal
						0.1	1.0	0.005	1.0	315	79	1.375	swollen	normal
8-F	ADEM	8.1	BE	1	12	1.0	n/a	1.0	n/a	n/a	n/a	1.625	normal	n/a
						1.0		1.0				1.625	normal	
9-M	ADEM-ON	5.1	BE[a]	3	18	n/a	1.0	0.8	1.0	146	61	n/a	swollen	temporal pale
						0.1	0.9	0.005	1.0	153	54		swollen	temporal pale
10-M	ADEM-TM	8.0	n/a	1	6	1.0	n/a	1.25	n/a	112	n/a	n/a	normal	n/a
										106			normal	

[a] Patients initially diagnosed with unilateral ON but progressed to bilateral involvement as the disease progressed.

Table 2
Overview of data for near visual acuity in Snellen.

PN	Eye	0	1	2	6	12	18	24	30	36	42	48	54	60
P1	RE	0.6	1.0	0.9	1.0	1.0	1.25	n/a	1.0					
	LE	0.014	0.1	0.7	0.8	0.8	1.25	n/a	1.0					
P2	RE	0.5												
	LE	0.63												
P3	RE	1.0	n/a	n/a	n/a	1.0								
	LE	1.0	n/a	n/a	n/a	1.0								
P4	RE	0.5	0.3	0.4	n/a	0.8	0.8	0.8	1.0	1.0	n/a	n/a	1.0	1.0
	LE	1.0	0.9	0.5	0.7	0.9	0.8	0.8	1.0	1.0	n/a	n/a	1.0	1.0
P5	RE	n/a	1.0											
	LE	n/a	0.6											
P6	RE	n/a												
	LE	n/a												
P7	RE	1.0	1.0	0.8	1.0	1.0	n/a	1.0	1.0	1.0				
	LE	0.1	1.25	1.0	1.0	1.0	n/a	1.0	1.0	1.0				
P8	RE	1.0	n/a	1.0										
	LE	1.0	n/a	1.0										
P9	RE	n/a	0.3	0.7	0.8	1.0	1.0							
	LE	0.1	0.3	0.7	0.9	0.9	1.0							
P10	RE	1.0	n/a	1.25										
	LE	1.0	n/a	1.25										

LE, Left eye; RE, Right eye; X-axis: disease duration in months; Y-axis: PN, Patient number.

Table 3
Overview of data for distance visual acuity in Snellen.

PN	Eye	0	1	2	6	12	18	24	30	36	42	48	54	60
P1	RE	1.25	1.25	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0		
	LE	0.01	0.2	0.6	0.8	1.0	1.0	1.0	1.0	1.0	1.0	1.0		
P2	RE	0.6												
	LE	0.8												
P3	RE	0.8	n/a	n/a	n/a	1.0	n/a	1.0						
	LE	1.0	n/a	n/a	n/a	1.0	n/a	1.0						
P4	RE	0.6	0.5	0.8	0.9	0.9	0.8	1.0	1.0	1.0	1.0	1.0	1.0	1.0
	LE	1.0	1.0	0.8	0.9	0.8	0.8	1.0	1.0	1.0	1.0	1.0	1.0	1.0
P5	RE	0.1	1.0	n/a	1.0	1.6								
	LE	1.25	1.6	n/a	1.3	1.6								
P6	RE	0.01	0.01											
	LE	0.8	1.0											
P7	RE	1.0	0.8	1.0	1.0	1.0	n/a	1.0	1.0	1.0				
	LE	0.01	0.8	1.0	1.0	1.0	n/a	1.0	1.0	1.0				
P8	RE	1.0	n/a	1.0										
	LE	1.0	n/a	1.0										
P9	RE	0.8	0.05	1.0	1.0	1.0	1.3							
	LE	0.01	0.3	1.0	1.0	1.0	1.3							
P10	RE	1.0	n/a	1.3										
	LE	1.0	n/a	1.3										

LE, Left eye; RE, Right eye; X-axis: disease duration in months; Y-axis: PN, Patient number.

3.4. Effect of a relapsing disease course on individual outcome measures

The progression of VA and pRNFL of patient 4 with a relapsing disease course is displayed in Fig. 2. Note that the initial global pRNFL thickness was not included in the graph due to insufficient OCT quality resulting from optic disc edema.

The patient had 4 NMOSD-ON relapses over a period of 62 months that resulted in fluctuations in both near and distance VA. Initially only the right eye was affected, but during the relapsing disease course the left eye was also involved. Although each relapse caused a drop in VA, the patient recovered each time and reached a visual acuity of ≥1.0 after the last documented relapse. Following the resolution of the initial optic disc swelling, the global pRNFL thickness remained stable at reduced levels during the first two relapses. Following the third relapse, the global pRNFL thickness further decreased and remained at low levels. The fourth relapse had little or no effect on the global pRNFL thickness. In this patient, MOG antibodies titers remained high during the disease course despite immunosuppressive therapy with high-dose methylprednisolone, azathioprine, rituximab, and intravenous immunoglobulins.

4. Discussion

This retrospective study analyzes the progression and impact of MOGAD on the visual system of pediatric patients by analyzing the global thickness of the pRNFL and the near and distance visual acuity. In our cohort of 10 MOG-IgG-positive pediatric patients with a median age of 7.7 years, most patients presented with a combined manifestation of ON with ADEM, ADEM with TM or ADEM alone. This observation aligns with previous research suggesting that clinical manifestations vary depending on the patient's age, with pediatric patients <10 years old more likely to present with ADEM [2,3,9]. The high co-occurrence of ADEM and ON raises the question of whether regular pediatric neuro-ophthalmological examinations should be integrated into standard clinical practice for pediatric patients with encephalopathy. Children under 10 years old may not verbalize visual deterioration, emphasizing the need for proactive assessment. This may have been the reason why one ADEM-ON patient (P3) showed no acute manifestations of ON, despite presenting with reduced pRNFL thickness at initial hospital visit (right eye: 66 µm, left eye: 44 µm). Another contributing factor could have been the timing of the ophthalmologic examinations, which

Table 4
Overview of data for the global pRNFL thickness in micrometers.

PN	Eye	0	1	2	6	12	18	24	30	36	42	48	54	60
P1	RE	n/a	73	72	75	75	72	n/a	71	74	72	73		
	LE	n/a	77	61	55	52	50	n/a	51	50	47	50		
P2	RE	96												
	LE	91												
P3	RE	66	n/a	n/a	n/a	64	n/a	64						
	LE	44	n/a	n/a	n/a	43	n/a	42						
P4	RE	n/a	n/a	n/a	64	59	59	57	56	55	58	57	55	57
	LE	n/a	n/a	n/a	74	57	56	51	53	45	48	46	45	44
P5	RE	113	n/a	n/a	n/a	84								
	LE	110	n/a	n/a	n/a	110								
P6	RE	n/a												
	LE	n/a												
P7	RE	107	192	116	82	77	n/a	77	77	76				
	LE	315	101	95	84	79	n/a	81	83	n/a				
P8	RE	n/a												
	LE	n/a												
P9	RE	146	221	101	62	61	59							
	LE	153	100	67	56	54	52							
P10	RE	112	n/a	112										
	LE	106	n/a	109										

LE, Left eye; RE, Right eye; X-axis: disease duration in months; Y-axis: PN, Patient number.

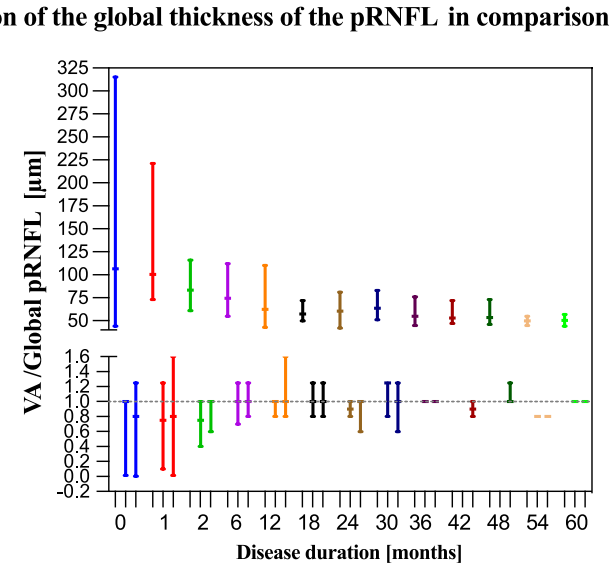

Fig. 1. Progression of the global thickness of the pRNFL in comparison with visual acuity of 10 pediatric patients. Near visual acuity is included as a sensitive measure of amblyopia development at follow up.
The X-axis shows the disease duration in months. Each month has its own color and shows the value of three parameters in the following order: global pRNFL thickness (upper panel, µm), near visual acuity (second line, Snellen decimal), distance visual acuity (third line, Snellen decimal).
The Y-axis is divided into two sections: The upper axis shows the global pRNFL thickness in µm, the lower axis demonstrates the visual acuity values in Snellen decimal.
The grey area shows the reference range for global pRNFL thickness (age range: 4–10 years, 103.8 ± 9.879 µm [24] and the dashed grey line indicates a visual acuity of 1.0 Snellen.
The graph shows increased but variable thickness of the pRNFL at onset with subsequent reduction and stabilization at low levels by 12 months. The visual acuity is reduced but variable at onset and then increases to normal to slightly reduced levels over the follow up period. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

may have occurred after the edema had subsided. Furthermore, frequent neuro-ophthalmologic re-assessments in pediatric MOGAD patients play a critical role in the early detection of additional amblyopia after ON, enabling prompt initiation of necessary treatments [14].

The remaining patients exhibited diverse manifestations including isolated ON and NMOSD-like phenotype highlighting the heterogeneous nature of MOGAD disease that has been described in previous literature [4].

We observed a female predominance of 70 % (7/10), greater than that documented by other authors who observed only a slight female predominance [9,25–31]. A possible explanation for the discrepancy with previous studies may be our small sample size.

In our cohort, most patients had a bilateral disease course, of whom the majority were first diagnosed with unilateral ON that progressed to both eyes as the patients suffered from a relapse despite initial steroid treatment. The higher frequency of bilateral ON, and especially the sequential disease course over time, is also seen in previous studies and is specific to the pediatric population [23,32–35].

In recent years, more studies have been conducted to investigate the disease course and prognosis of MOGAD patients, especially in

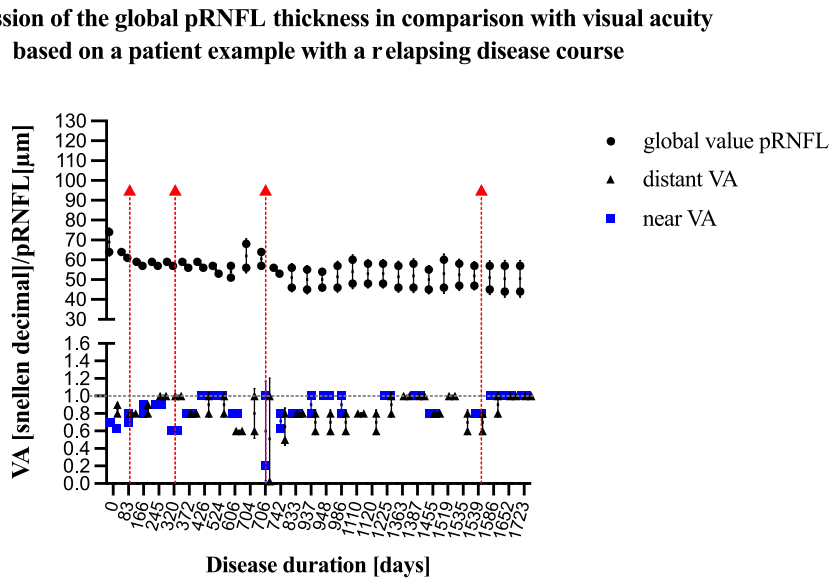

Fig. 2. Progression of global pRNFL thickness and VA in P4 (female; relapsing disease course; each relapse is indicated by a red arrow). The X-axis shows follow-up time in days. The Y-axis is divided into two sections: The upper axis shows global pRNFL thickness in µm (black dots), the lower axis VA in Snellen decimal (distance: black triangles; near: blue squares).
The grey area shows the reference range for global pRNFL thickness (age range: 4–10 years, 103.8 ± 9.879 µm [24] and the dashed grey line indicates a visual acuity of 1.0 Snellen.
VA declined with each relapse, but ultimately improved to a visual acuity of ≥1.0 after recovering from the final relapse. Following the initial swelling, pRNFL initially decreased to lower levels and remained stable until the third relapse, where it further decreased but eventually stabilized. In this patient, MOG antibody titers remained high during the disease course despite immunosuppressive therapy with azathioprine and rituximab. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

comparison with ON experienced in the context of multiple sclerosis (MS) and other demyelinating diseases [4,9,12,20,36,37]. However, due to the rarity of the disease, there is little data on the disease course and structural changes to the retina of pediatric patients. The European Union pediatric MOG consortium consensus has described the clinical characteristics of an acute MOGAD-ON attack as severe vision loss at onset (VA≤0.1) with optic disc edema in 60–90 % of cases [9]. During the phase of acute inflammation, most pediatric patients in our cohort experienced severe visual impairment with a visual acuity ≤0.1 and optic disc edema. During and following the initial presentation, both visual acuity and pRNFL thickness show high variability which may be due to insufficient scan quality (due to optic disc edema) and varying time points of undertaking the scans.

At 6 months, consistent with previous studies [2,9,37,38], significant improvement in VA was observed in our pediatric patients, which continued to progress until complete visual recovery was achieved for all patients. Meanwhile, the overall pRNFL thickness exhibited a continuous decrease over several months after the swelling subsided. In our cohort, pRNFL thickness stabilized at reduced levels around 12 months from the initial presentation (median: 61 µm (43–84 µm)), provided no further relapses occurred. None of the patients without previous ON in our cohort experienced a deterioration of visual acuity and, if evaluated, a reduction of the pRNFL, which are known as possible signs of a non-symptomatic ON in patients with MS [39].

Wendel et al. (2022) have conducted research regarding the factors able to predict the occurrence of relapses. They have found that while initial MOG-IgG titers are similar in both monophasic and relapsing patients, there is a significant difference in titers between these groups during the first and second years after the onset of the disease. Patients whose MOG-IgG titers decline, particularly those who convert to MOG-IgG-negative status, have a significantly lower risk of relapse [40]. In addition, recent research has recorded that the occurrence of relapses within 12 months of the initial presentation increases the long-term risk of relapsing disease [41]. In our cohort, one patient exhibited relapsing ON with 4 relapses during a follow-up of 62 months, with the occurring 5 months after disease onset. Consistent with these previous findings, the patient remained anti-MOG-positive for 55 months despite immunosuppressive therapy, as opposed to monophasic patients whose MOG-IgG-titers showed a decline.

Around a third of our cohort experienced progression of the disease to the fellow eye over a median period of one month, which we interpreted as fluctuation during tapering of steroids in the acute phase or as a relapse following a longer asymptomatic period.

The small patient number in our cohort does not permit us to draw conclusions as to whether a longer treatment with steroids is recommended to prevent progression. Further longitudinal large-scale studies are necessary to address this question.

In terms of the long-term impact of relapses on VA, studies conducted in adult MOGAD patients concluded that the increasing structural damage caused by the increasing number of relapses leads to a lasting deterioration of visual acuity [2,4,18,21]. In pediatric patients however, this may not be the case. In our cohort, all patients showed a complete recovery of both near and distance visual acuity (VA≥0.8) by the 12-month-analysis following the last relapse. Our result is consistent with those of other studies of pediatric patients that recorded no correlation between the number of relapses and the visual outcome [2,12,23]. In terms of neuroaxonal retinal atrophy however, the relapses were associated with a continuation of the pRNFL thinning in our cohort.

Havla et al. compared age-dependent effects on the visual system of a pediatric and adult MOGAD cohort in a prospective study [2]. They found, along with other studies, that the severity of neuroaxonal retinal atrophy does not differ between adult and pediatric MOGAD patients [2,10,37,42] but visual acuity recovery does. The age-dependent neuroplasticity of the visual system has been proposed as a possible explanation [43,44]. Havla et al. concluded that pediatric patients show better visual recovery independent of neuroaxonal retinal atrophy and number of relapses [2], which is consistent with our findings. However, additional development of amblyopia should always be considered and monitored/treated if apparent.

Our study has limitations. As MOGAD is a rare disease, the sample

size of pediatric patients is small. Furthermore, the retrospective nature of the study had an impact on the analyzed outcome parameters. Both near and distance VA were not always measured together, which made direct comparison of the values more challenging.

Future multicentric and/or prospective study designs with testing of additional outcome parameters such as high and low contrast VA, perimetry, retinal ganglion cell layer thickness measurement, color vision, or visual evoked potentials, may be desirable.

In conclusion, this study identified that pediatric patients with ON showed VA deterioration and optic disc edema in most patients. Following resolution of the optic disc edema, VA showed continuous improvement, leading to complete visual recovery in all patients, irrespective of the number of relapses or the severity of initial visual acuity loss. The thickness of the pRNFL decreased for several months after initial presentation and stabilized at reduced levels by the 12-month-analysis if no further relapses occurred. Patients without a history of ON showed no decline in VA or, if evaluated, a reduction in pRNFL thickness. This may indicate that the visual system is not affected in MOGAD patients without previous ON. Further investigations are necessary to explore the functional relevance of these findings and determine the optimal examination methods for patients with MOGAD. We would recommend standardized ophthalmologic follow-ups for these patients for at least two years after disease onset. Moreover, future prospective and multicenter studies, involving larger sample sizes, are crucial to comprehensively understand the impact of MOGAD on a larger scale and to investigate additional outcome parameters.

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Declaration of competing interest

There is no conflict of interest in the paper being submitted to the journal.

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