BRITISH JOURNAL OF HOSPITAL MEDICINE

ARTICLE

Evaluating the Clinical Characteristics and Ophthalmic Manifestations in Children and Adolescents with Acquired Demyelinating Disorders in China

Si-Yuan Li[1], Chun-Xia Peng[1], Hua-Xin Zuo[1], Qi Lin[1], Ji-Feng Yu[1], Wen Liu[1], Li Li[1], Wei Shi[1,*]

[1]Department of Ophthalmology, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Beijing, China

*Correspondence: Weishi1666@163.com (Wei Shi)

Abstract

Aims/Background Pediatric acquired demyelinating disorders (ADS) include various monophasic and recurrent inflammatory conditions of the central nervous system (CNS). Optic neuritis (ON) is a demyelinating disease primarily affecting the optic nerve axons due to autoimmune inflammation. To investigate the clinical characteristics, ophthalmic manifestations, laboratory test results, and prognostic indicators of Chinese children and adolescents with ADS.

Methods The clinical data of 57 patients with ADS treated in the Beijing Children's Hospital from March 2021 to December 2023, were retrospectively collected and analyzed. The primary outcomes include best-corrected visual acuity (BCVA) at onset, peripapillary retinal nerve fiber layers (RNFL) thickness, serum myelin oligodendrocyte glycoprotein (MOG) antibody level, aquaporin-4 (AQP4) antibody level, and final BCVA after hormone therapy.

Results The analyses included 57 children and adolescents in the study, including 38 optic neuritis (ON), 12 neuromyelitis optica spectrum disorder (NMOSD), 5 acute disseminated encephalomyelitis (ADEM), and 2 multiple sclerosis (MS) patients. The median age of patients facing the initial attack of ON was 9 years (3–15 years), with 23 children and adolescents (40.4%) aged eight years or younger, and 37 patients (64.9%) were bilaterally affected. Half of the children and adolescents (15/30) were MOG-Ab seropositive, and 19.4% (6/31) were AQP4-Ab seropositive. Children and adolescents with NMOSD were more likely to have severe visual impairment at acute onset ($p < 0.05$), with 84.2% of them having low vision acuity (BCVA worse than 0.1), as compared with 64.9% in the ON group. The RNFL thickness of affected eye was thinner than unaffected eyes (median 72.0 μm vs. median 102.0 μm, $p < 0.05$). Patients with NMOSD exhibited lower RNFL thickness across all measured sectors compared to those with ON. Significant differences were noted in the average RNFL and in each specific region of the retina, including the temporal RNFL, nasal RNFL, nasal superior RNFL, nasal inferior RNFL, temporal superior RNFL, and temporal inferior RNFL (all $p < 0.05$). After the treatment with intravenous methylprednisolone, both patients with ON (52 eyes; 86.7%) or NMOSD (20 eyes; 90.9%) group had functional visual recovery (BCVA better or equal 0.4).

Conclusion This study shows that Chinese children and adolescents with ADS present distinctive clinical features, including earlier onset and more bilateral involvement. Furthermore, NMOSD patients experience more severe visual acuity impairment and thinner peripapillary RNFL. All children and adolescents of ON or NMOSD respond well to methylprednisolone treatment.

Key words: acquired demyelinating disorders; optic neuritis; neuromyelitis optica spectrum disorder; acute disseminated encephalomyelitis; multiple sclerosis; peripapillary retinal nerve fiber layers; myelin oligodendrocyte glycoprotein

Submitted: 20 August 2024 Revised: 15 October 2024 Accepted: 18 October 2024

How to cite this article:
Li S, Peng C, Zuo H, Lin Q, Yu J, Liu W, Li L, Shi W. Evaluating the Clinical Characteristics and Ophthalmic Manifestations in Children and Adolescents with Acquired Demyelinating Disorders in China. Br J Hosp Med. 2025. https://doi.org/10.12968/hmed.2024.0555

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Introduction

Pediatric acquired demyelinating disorders (ADS) comprise a spectrum of monophasic and recurrent inflammatory conditions of the central nervous system (CNS). Optic neuritis (ON) is a demyelinating disease caused by an autoimmune inflammatory course mainly involving optic nerve axons. Monophasic conditions include isolated ON and acute disseminated encephalomyelitis (ADEM), while recurrent disorders of ADS encompass multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD).

The incidence of ADS ranges from 0.06 to 0.34 per 100,000 children in Asia (Lin et al, 2020; Yamaguchi et al, 2016). Children and adolescents with early-onset ADS often exhibit distinctive clinical features, manifested during the critical period of neurological, endocrine, and immune system development. Due to the variety of symptoms and possible recurrent episodes, differential diagnosis often presents challenges. Myelin oligodendrocyte glycoprotein (MOG)-associated disease (MOGAD) is more prevalent in ADS children than in adults (Peng et al, 2017). To date, there have been few pediatric ADS studies in Asia.

The aim of this study was to assess the clinical features and eye-related symptoms in children and adolescents with ADS to provide further support for future multicenter prospective studies.

Methods

Participants

57 participants presenting to the Beijing Children's Hospital between March 2021 and December 2023 were considered for this retrospective study. This study protocol was approved by the Ethics Committee at the Beijing Children's Hospital (Ethical approval number: [2023]-E-116-Y) and adhered to the Declaration of Helsinki's tenets as well as the relevant Chinese laws and regulations. Written informed consent was obtained from the guardians of participants. All patients with acute stage of ADS were treated with intravenous methylprednisolone (10 mg/kg/day) for five days, followed by a taper of oral prednisone (starting dose 1 mg/kg/day) with varying durations, based on their age and recovery time from ON attack. During their return visits at the ophthalmology center, clinical examination data were collected. All ADS patients were followed up for at least six months.

Inclusion criteria for this study are as follows: (1) age $<$18 years; (2) at least one episode of clinical optic neuritis, with a history of acute loss of visual acuity (VA) or visual field irrespective of eye pain; and (3) diagnosis of acquired demyelinating syndrome of the CNS including the following phenotypes: ON (unilateral or bilateral), ADEM, NMOSD, and MS, and then divided into corresponding diagnostic subgroups. All diagnoses were confirmed by an experienced pediatric neurologist and neuro-ophthalmologist based on diagnostic criteria defined by the International Pediatric Multiple Sclerosis Study Group (Krupp et al, 2013; Wingerchuk et al, 2015). Patients with other ocular diseases, or any other types of optic neuropathy, such as those of vascular, hereditary, toxic, metabolic, and infiltrative

nature, and individuals with incomplete data, were excluded. The final VA was determined based on the best VA recorded during the last available follow-up.

Laboratory Examinations

Serum samples were tested for the presence of myelin oligodendrocyte glycoprotein (MOG) and aquaporin-4 (AQP4) antibodies using the myelin oligodendrocyte glycoprotein-immunoglobulin G (MOG-IgG) detection kit (indirect immunofluorescence method; EUROIMMUN, Lübeck, Germany) and the AQP4-IgG detection kit (RSR, Cardiff, UK), respectively. The AQP4-IgG detection kit is a cell-based assay following the immunofluorescence of fixed cells that had been transfected with recombinantly AQP4 M23 isoform. Considering the need to manage healthcare costs effectively, our examination was limited to patients who were suspected of having NMOSD, specifically for the presence of MOG and AQP4 antibodies. A total of 30 participants underwent both MOG and AQP4 antibody testing, while one participant underwent only AQP4 antibody testing without MOG testing.

Neuro-Ophthalmology Examinations

The primary outcome of this study was the thickness of peripapillary retinal nerve fiber layers (RNFL) after the acute phase of treatment. Optical coherence tomography (OCT) examination was performed using a Heidelberg OCT instrument (Heidelberg Engineering, Heidelberg, Germany) according to the standard protocols for obtaining peripapillary images. The RNFL was displayed in six sectors: nasal (N), nasal superior (NS), nasal inferior (NI), temporal (T), temporal superior (TS), and temporal inferior (TI). All OCT examinations were performed by an experienced technician.

Best-corrected visual acuity (BCVA) was another primary outcome studied to assess the visual function at onset and during the last recorded follow-up. Visual acuity (VA) assessment was performed using the standard protocol at 5 meters using a standard clinical Snellen eye chart with refractive correction. Those unable to read any letters at 1 meter were further examined through counting fingers (CF), hand movements (HM), light perception (LP), or no light perception (NLP). To better calculate the average VA during the correlation between RNFL thickness and VA, we transformed VA measurements from the Snellen assessment to the logarithm of the minimal angle resolution (logMAR) (Holladay, 1997; Miwa et al, 2013). Counting the number of fingers held was transformed as a logMAR value of 2.0, and hand movement as a logMAR value of 2.3, according to the previous study (Lange et al, 2009).

Statistical Analysis

Statistical analyses were performed using SPSS 18.0 software (IBM Corporation, Armonk, NY, USA). Kolmogorov-Smirnov tests were used to test the normality of data. Continuous variables that adhere to a normal distribution were represented as means accompanied by standard deviations (SD). The *t*-test served to assess differences in distribution between two independent groups. In contrast, continuous variables that do not conform to a normal distribution were illustrated as

medians and interquartile ranges. The Kruskal-Wallis test was applied to evaluate differences among three or more groups, while the Mann-Whitney U test was used to compare two independent groups. Categorical variables were expressed as frequencies and percentages. To analyze categorical data, we utilized the Pearson chi-square test, the Pearson chi-square test with continuity correction, and Fisher's exact test. The correlation between RNFL thickness and VA were analyzed using Spearman's rank correlation coefficient. *p*-value less than 0.05 were considered statistically significant.

Results

A total of 73 children and adolescents were recruited between March 2021 and December 2023. Sixteen children and adolescents were excluded, including 13 individuals with insufficient medical information and three with viral encephalitis. Final analyses included 57 children and adolescents in the study, including 38 ON, 12 NMOSD, 5 ADEM, and 2 MS patients. Table 1 summarizes the clinical and demographic characteristics of patients in this retrospective study. In all patients, the median age at onset of ON attack was 9 years (range 3–15 years), with 40.4% being younger children and 10.5% being teenagers (the younger child was defined as age $\leq$8 years, while the teenager was defined as age $>$13 years). At the initial attack, 37 patients (64.9%) were bilaterally affected. Serum tests of MOG-Ab and AQP4-Ab showed that 15 out of 30 patients (50%) who were tested for serum MOG-Ab were seropositive, while 6 individuals (19.4%) were seropositive for serum AQP4-Ab in 31 patients who were tested for the antibody. Furthermore, we found two patients who were seropositive for both MOG-Ab and AQP4-Ab. The median of disease duration in all patients was 6 months (range 0.3–36 months), with 6 patients (10.5%) experiencing the recurrent disease. The median length of VA recovery after treatment was 2 months. We found significant differences in age of onset (χ^2 = 9.82, p = 0.02), percentage of teenagers (χ^2 = 10.71, p = 0.01), and the seropositive AQP4-Ab in subgroups (χ^2 = 6.06, p = 0.048). Because of the few participants in the subgroup of ADEM and MS, we analyzed the comparison of subgroup ON and NMOSD. Although the bilateral predominance, longer disease duration, higher frequency of recurrent disease, and seropositive AQP4-Ab were more commonly observed in the NMOSD subgroup, significant differences were absent between the ON and NMOSD groups.

Table 2 compares the initial and follow-up visual outcomes in patients with ON and NMOSD. The BCVA at onset was statistically different among the two subgroups (χ^2 = 9.84, p = 0.03). Children and adolescents with NMOSD were more likely to suffer severe visual impairment at acute onset, with 84.2% of them having low VA (BCVA worse than 0.1), as compared to 64.9% in the ON group. After the treatment with intravenous methylprednisolone, both patients with ON (52 eyes; 86.7%) or NMOSD (20 eyes; 90.9%) group had functional visual recovery (BCVA better or equal 0.4). Moreover, there was no statistical difference between the two groups (χ^2 = 7.21, p = 0.08). The changes of BCVA at onset and follow-up are displayed in Fig. 1.

Table 1. Clinical and demographic characteristics of patients.

Variable	All patients (n = 57)	ON (n = 38)	NMOSD (n = 12)	ADEM (n = 5)	MS (n = 2)	p-value [a]	Statistics [a]	p-value [b]	Statistics [b]
Female-to-male ratio (% Female)	32:25 (56.1)	23:15 (60.5)	5:7 (41.7)	3:2 (60)	1:1 (50)	0.59 [e]	2.14 [e]	0.25 [d]	1.32 [d]
Median age of onset (range) in years	9 (3–15)	9 (4–14)	9 (3–12)	10 (5–15)	13 (13–14)	0.02 [g]	9.82 [g]	0.99 [c]	910.0 [c]
Younger child (%)	23/57 (40.4)	17/38 (44.7)	4/12 (33.3)	2/5 (40)	0/2 (0)	0.70 [e]	1.61 [e]	0.48 [d]	0.49 [d]
Teenager (%)	6/57 (10.5)	3/38 (7.9)	0/12 (0)	1/5 (25)	2/2 (100)	0.01 [e]	10.71 [e]	1.00 [e]	N/A
Bilateral-to-unilateral ratio (% Bilateral)	37:20 (64.9)	22:16 (57.9)	10:2 (83.3)	4:1 (80)	1:1 (50)	0.36 [e]	3.37 [e]	0.21 [f]	1.58 [f]
Frequency of recurrent diseases (%)	6/57 (10.5)	2/38 (5.3)	3/12 (25)	1/5 (20)	0/2 (0)	0.14 [e]	4.89 [e]	0.08 [e]	N/A
Median disease duration (range) in months	6 (0.3–36)	5 (1–36)	7 (0.3–31)	6.5 (2–12)	6 (6–8)	0.41 [g]	2.87 [g]	0.13 [c]	595.5 [c]
Median length of VA recovery (range) in months	2 (0.33–20)	2 (0.33–20)	2 (0.6–12)	5 (3–5)	N/A	0.11 [g]	4.34 [g]	0.25 [c]	350.0 [c]
Frequency of seropositive MOG-Ab detection (%)	15/30 (50.0)	8/17 (47.1)	3/9 (33.3)	3/3 (100)	1/1 (100)	0.17 [e]	4.58 [e]	0.68 [e]	N/A
Frequency of seropositive AQP4-Ab detection (%)	6/31 (19.4)	2/19 (10.5)	3/8 (37.5)	0/3 (0)	1/1 (100)	0.048 [e]	6.06 [e]	0.14 [e]	N/A

[a] p-value was based on the comparison of four subgroups; [b] p-value was based on the comparison between the ON and NMOSD groups; [c] p-value is derived from Mann-Whitney U tests; [d] p-value is derived from Pearson's chi-square test; [e] p-value is derived from Fisher's exact tests; [f] p-value is derived from Pearson's chi-square test with continuity correction; [g] p-value is derived from Kruskal-Wallis test.

Younger child was defined as age $\leq$8 years, whereas teenager was defined as age $>$13 years.

ON, optic neuritis; NMOSD, neuromyelitis optica spectrum disorder; ADEM, acute disseminated encephalomyelitis; MS, multiple sclerosis; VA, visual acuity; MOG, myelin oligodendrocyte glycoprotein; AQP4, aquaporin-4.

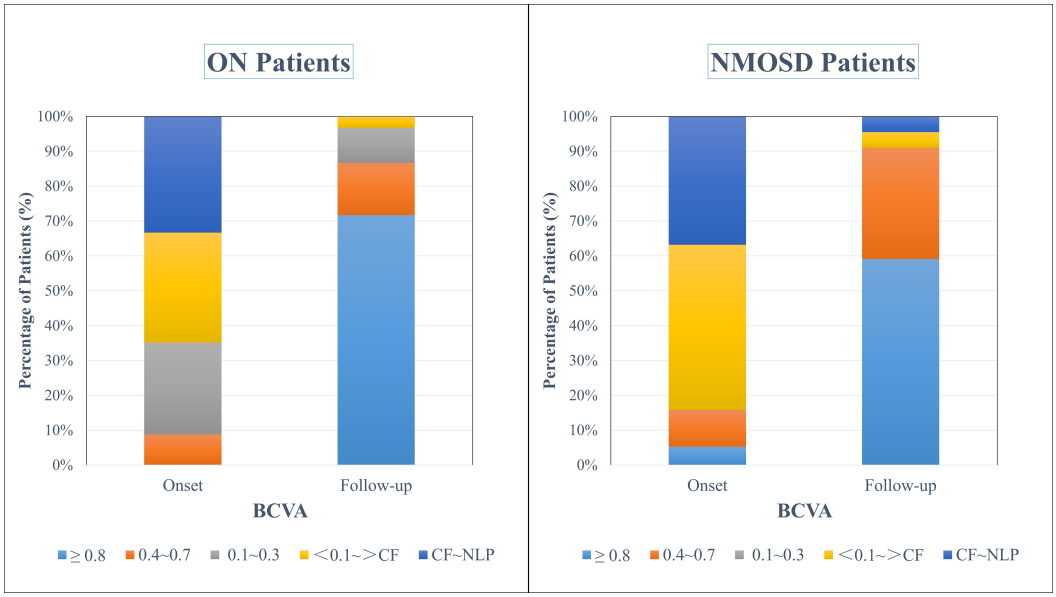

Fig. 1. Percentage of patients across various levels of BCVA at onset and follow-up. BCVA, best-corrected visual acuity; CF, counting fingers; NLP, no light perception.

OCT examination was performed in 114 eyes of 57 patients. Table 3 shows the comparisons of the RNFL thickness of affected and unaffected eyes. We found a significant difference in RNFL between affected and unaffected eyes in all patients (U = 464.5, $p < 0.01$) and the ON subgroup (U = 262.5, p = 0.01). Affected eyes of the patients in the ON subgroup suffered from more severe retinal damage with greater RNFL thinning than unaffected eyes (median 81.5 µm [40–125 µm] vs. median 102.5 µm [59–118 µm]). Moreover, there was no significant difference in average RNFL between affected and unaffected eyes of the NMOSD subgroup (U = 17.5, p = 0.65) due to the fewer eyes that were unaffected.

Furthermore, we analyzed the comparisons of the RNFL thickness of affected eyes in different sectors among patients with ON and NMOSD (Table 4). Patients with NMOSD exhibited lower RNFL thickness across all measured sectors compared to those with ON. Significant differences were noted in the average RNFL and in each specific region of the retina, including the temporal RNFL, nasal RNFL, nasal superior RNFL, nasal inferior RNFL, temporal superior RNFL, and temporal inferior RNFL (all $p < 0.05$). Unfortunately, we failed to determine a correlation between the mean RNFL thickness and visual impairment (logMAR) (r = –0.12, p = 0.29). After analyzing the RNFL thickness of affected eyes in different subgroups, we found a significant difference in RNFL thickness for children and adolescents with ON compared to patients with NMOSD. Patients with NMOSD had thinner average RNFL than patients with ON (81.95 µm vs. 62.27 µm, $p < 0.05$).

Discussion

Our retrospective study examined the clinical characteristics of ON in a Chinese children and adolescent sample with equal sex ratio, of which 40.4% experienced earlier onset (age is ≤8 years), 64.9% had bilateral involvement, and 50%

Table 2. Vision assessment at onset and follow-up in patients with ON and NMOSD.

Vision assessment	ON (n = 60)	NMOSD (n = 22)	p-value [a]	χ^2
BCVA at onset (number of affected eyes) [b]				
≥0.8	0/57 (0%)	1/19 (5.3%)		
0.4–0.7	5/57 (8.8%)	2/19 (10.5%)	0.03	9.84
0.1–0.3	15/57 (26.3%)	0/19 (0%)		
<0.1–>CF	18/57 (31.6%)	9/19 (47.4%)		
CF–NLP	19/57 (33.3%)	7/19 (36.8%)		
BCVA at last follow-up (number of affected eyes)				
≥0.8	43/60 (71.7%)	13/22 (59.1%)		
0.4–0.7	9/60 (15%)	7/22 (31.8%)	0.08	7.21
0.1–0.3	6/60 (10%)	0/22 (0%)		
<0.1–>CF	2/60 (3.3%)	1/22 (4.5%)		
CF–NLP	0/60 (0%)	1/22 (4.5%)		

[a] p-value is derived from Fisher's exact tests; [b] In each group, three eyes were documented as declined/unknown at onset.
BCVA, best-corrected visual acuity; ON, optic neuritis; NMOSD, neuromyelitis optica spectrum disorder.

Table 3. RNFL thickness in affected and unaffected eyes of patients with ON, NMOSD, ADEM, and MS.

Group	RNFL thickness (number of eyes)		p-value [a]	U
	Affected	Unaffected		
All patients, median (range) μm	72.0 (26–125) (n = 94)	102.0 (55–118) (n = 20)	<0.01	464.5
ON, median (range) μm	81.5 (40–125) (n = 60)	102.5 (59–118) (n = 16)	0.01	262.5
NMOSD, median (range) μm	57.5 (26–110) (n = 22)	72.0 (55–89) (n = 2)	0.65	17.5
ADEM, median (range) μm	64.0 (53–103) (n = 9)	102.0 (n = 1)	N/A	N/A
MS, median (range) μm	76.0 (57–83) (n = 3)	93.0 (n = 1)	N/A	N/A

[a] p-value is derived from Mann-Whitney U tests between the affected and unaffected eyes.
RNFL, retinal nerve fiber layer; ON, optic neuritis; NMOSD, neuromyelitis optica spectrum disorder; ADEM, acute disseminated encephalomyelitis; MS, multiple sclerosis.

were seropositive for MOG-Ab. Furthermore, NMOSD patients were more likely to have bilateral involvement, severe VA impairment, and thinner peripapillary RNFL. All children and adolescents of ON or NMOSD responded well to methylprednisolone treatment, and 71.7% of ON patients and 59.1% of NMOSD patients recovered with BCVA higher than 0.4.

Based on this study, we found that Chinese children and adolescents with ADS experienced earlier onset of ON, at a mean age of 9 years, compared with 10.3 years in Japan (Yamaguchi et al, 2016), 16 years in Denmark (Boesen et al, 2018), and 11.84 years in India (Ambika et al, 2018). Furthermore, ADS indiscriminately affects the both genders of the Chinese children and adolescents, with 56.1% of them

Table 4. Comparison of peripapillary RNFL thickness in affected eyes in different sectors between patients with ON and NMOSD.

Variables	ON group RNFL (μm) (n = 60)	NMOSD group RNFL (μm) (n = 22)	Statistics	95% confidence interval of the difference	p-value
Average	81.95 ± 22.05	62.27 ± 23.72	3.51 [a]	8.52–30.84	0.001 [a]
Nasal	50.32 ± 17.74	36.77 ± 17.52	3.07 [a]	4.78–22.32	0.003 [a]
NS	100.17 ± 30.66	74.36 ± 28.70	3.43 [a]	10.85–40.76	0.001 [a]
NI	93.98 ± 26.81	66.45 ± 33.47	3.85 [a]	13.29–41.77	0.000 [a]
Temporal	50.50 (35.25–97.75)	38.00 (32.50–54.0)	464.5 [b]	–0.74–25.11	0.041 [b]
TS	121.13 ± 32.36	93.77 ± 37.18	3.26 [a]	10.65–44.07	0.002 [a]
TI	119.00 (97.75–146.50)	86.00 (76.00–119.25)	390 [b]	6.50–46.00	0.005 [b]

RFNL data of average, nasal, NS, NI, TS are expressed as mean ± SD, and RFNL data of temporal, TI are expressed as median (range).
[a] p-value is derived from Student's t-tests, statistics value is t.
[b] p-value is derived from Mann-Whitney U tests, statistics value is U.
ON, optic neuritis; NMOSD, neuromyelitis optica spectrum disorder; NS, nasal superior; TS, temporal superior; NI, nasal inferior; TI, temporal inferior; SD, standard deviation.

being female. Among individuals with NMOSD, the female patients were not predominant (female:male = 5:7), a ratio different from those reported in other studies: Japan (4:1) (Yamaguchi et al, 2016) and German (2:1) (Lotze et al, 2008). These differences suggest that genetic or environmental factors may affect the pathogenic processes associated with ADS onset, with the extent of such influence subjected to ethnicity of the patients. Unilateral and bilateral ON occurred with equal frequency in the patients, whereas bilateral involvement in NMOSD patients (83.3%) has been confirmed in other series (Ambika et al, 2018).

We found half of the children and adolescents with seropositive AQP4-Ab had NMOSD, which is higher than those reported in a previous study (Hacohen et al, 2017) and lower than adults. To the best of our knowledge, MOG-Ab is more common in children (Hacohen et al, 2017; Lechner et al, 2016), which is confirmed in our study: half of the children and adolescents with ADS were seropositive for MOG-Ab, and 33.3% of the NMOSD patients were seropositive for MOG-Ab. Moreover, it is not surprising that the implementation of the latest diagnostic criteria for NMOSD (Wingerchuk et al, 2015) may bring about a surge in the number of NMOSD diagnoses, which raises the cases of MOG-Ab positivity. A recent research found that microglia contributes to the early-activated CNS-intrinsic complement, triggered by the binding of an AQP4-IgG water channel on astrocytes (Chen et al, 2020). On the other hand, the highest extent of microglial heterogeneity has been detected in young-age mice (Hammond et al, 2019). These molecular findings may account for the higher antibody seropositivity among children and adolescents than adults.

In the comparison of ON and NMOSD patients, we found that NMOSD patients had more severe VA impairment and thinner peripapillary RNFL. In our study, 84.2% of children and adolescents with NMOSD had BCVA under 0.1, and 36.8%

of them under CF, similar to the findings of a previous study (Song et al, 2019). The structure of retinal nerve layers has been widely analyzed for confirming its applicability as axonal loss marker in ON by means of OCT measurement (Fernandes et al, 2013; Eyre et al, 2018). Other studies demonstrated severe and diffuse retinal nerve fiber layer (RNFL) loss in the temporal and nasal section of the retina in NMOSD adults (Park et al, 2014; Peng et al, 2017). These pathological findings were shown in children and adolescents, as confirmed in this study. Furthermore, several studies have found a correlation between VA and RNFL, indicating the latter as a predictor of visual function (Eyre et al, 2018; Yeh et al, 2009). Despite the detection of more severe VA impairment and thinner peripapillary RNFL in children and adolescents with NMOSD, we failed to determine the correlation between BCVA and RNFL. This is likely due to the limitations of a small sample size and the transformation of Snellen VA to logMAR VA. The transformation of "manual or no light perception vision" into logMAR vision would disrupts data continuity. In a previous study, patients with deficient vision, such as those with LP and NLP conditions, belonged to the semi-quantitative categories with floor effect, and their conditions were not quantifiable (Lange et al, 2009). Furthermore, the calculation could also be impacted with the NMOSD patients suffering more severe vision damage.

In this study, all patients of ON or NMOSD responded well to intravenous methylprednisolone treatment. According to the latest VA assessments, both patient categories of ON and NMOSD showed functional visual recovery (BCVA $\geq$0.4), an improvement that surpassed that in adult patients with NMOSD (logMAR = 0.2) (Tewarie et al, 2012). In our study, recurrent disease occurred in 6 out of 57 patients (10.5%), with a higher rate of occurrence in those with NMOSD, at 3 out of 12 patients (25%). Importantly, persistently high serum MOG-Ab levels represent a crucial biomarker for predicting frequent ON relapses and are closely associated with final VA. It is worth noting that blindness occurs in 44% to 83% of ON cases after frequent remissions and relapses. Thus, we need to prioritize regular monitoring of BCVA in children for an extended period in order to enable prompt detection of recurrence.

Several limitations of this study should be acknowledged. Firstly, as a single-center observational study, this research is prone to selection bias, which has an impact on the cause-and-effect relationship. Secondly, the sample size was relatively small, potentially introducing bias. The findings of the present study need to be verified in studies with larger samples. Also, due to the small sample size, we did not consider analyzing disease duration for patients with MOG-associated disease. Thirdly, limited set of data were available for analysis in this retrospective study with elements of variable descriptions and follow-up, for example, only 30 out of 57 patients underwent serum tests of MOG-Ab (52.6%). It is possible that if a higher proportion of serum tests for MOG-Ab had been conducted, additional neurological diagnoses may have been identified. Lastly, the fact that serum MOG-Ab and AQP4-Ab are a set of more sensitive markers than their cerebrospinal fluid counterparts may magnify the bias.

Conclusion

In summary, this study demonstrates that Chinese children and adolescents with ADS exhibit diverse clinical features, including an earlier onset of disease and more bilateral involvement. Furthermore, NMOSD patients are affected with more severe VA impairment and thinner peripapillary RNFL. The study also shows that all children and adolescents of ON or NMOSD exhibits satisfactory response to methylprednisolone treatment.

Key Points

- This retrospective study examined the clinical characteristics of ON in a Chinese children and adolescent sample with an equal sex ratio, of which 40.4% experienced earlier onset (age is $\leq$8 years), 64.9% had bilateral involvement, and 50% were seropositive for MOG-Ab.
- NMOSD patients were more likely to have bilateral involvement, severe VA impairment, and thinner peripapillary RNFL.
- All children and adolescents of ON or NMOSD responded well to methylprednisolone treatment, and 71.7% of ON patients and 59.1% of NMOSD patients recovered with BCVA higher than 0.4.

Availability of Data and Materials

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

LL and WS were responsible for the study concept and design. CXP, SYL, HXZ, JFY, QL, and WL contributed to data collection and analysis. The manuscript was drafted by SYL and CXP and then critically reviewed and revised by all remaining authors. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee at the Beijing Children's Hospital (Ethical approval number: [2023]-E-116-Y) and adhered to the Declaration of Helsinki's tenets as well as the relevant Chinese laws and regulations. Written informed consent was obtained from the guardians of participants.

Acknowledgement

The authors would like to thank Lirong Tan and Ru Zhang for providing us with the OCT data. We also thank the pediatric ADS patients and their families for

their contribution to advancing our understanding of pediatric neuroimmunological disease.

Funding

This study was supported by the Beijing municipal cultivation plan project (NO. PX2023046), the Wu Zuze Foundation Fund, project "Key Technologies and Promotion of Visual Rehabilitation for Children with Low Vision Based on Expanded Reality" (WZZ20230202) and "Key Technologies for Safety Analysis of Electromagnetic Fields in 6G Terminal Equipment for 2024" (No: L233018).

Conflict of Interest

The authors declare no conflict of interest.

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