Evaluation of the Risk Factors for Developing Demyelinating Disease after Optic Neuritis in Children: A Single Center Experience

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Introduction:

Optic neuritis (ON), an inflammatory disorder of the optic nerve, constitutes 25% of acute demyelinating diseases (DDs) in childhood (1).

It may be isolated (ION), or a manifestation of other DDs such as multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), myelin oligodendrocyte glycoprotein-associated disease (MOGAD), and acute disseminated encephalomyelitis (ADEM) (1). The risk of developing MS after ON in children is reported to be up to 40%. (2).

Objective:

We aimed to determine the risk factors for developing DDs after ON.

Materials and methods:

The data of 43 children (21 boys, 22 girls) presented with ON, between 2008 and 2018, were analyzed. The history, clinical and visual findings, and visual evoked potentials (VEP), optical coherence tomography (OCT), and neuroimaging findings were evaluated in the patients.

The ION group was compared with the groups of other DDs (DD group) and MS. The patients with ADEM, considering its distinct features, were excluded from the statistical comparison.

Inclusion criteria for the study: • Acute vision loss, decreased visual acuity with or without pain in eye movements; • Presence of at least one relative afferent pupillary defect, abnormal VEP, or visual field defect

Exclusion criteria: • Presence of a retinal lesion or other eye disease; •Vascular, toxic, metabolic, infiltrative, compressive, hereditary optic nerve damage.

Statistical analysis: Chi-square test was used to compare categorical variables, and Kolmogorov-Smirnov test was used to determine whether the distribution of data was normal. In the comparison of the two groups, Student-T test was used in case of normal distribution and Mann-Whitney U test was used in case of non-normal distribution.

Variables	Number of patients (n)	Percentage (%)
Gender		
Male	21	48.8
Female	22	51.2
Final diagnosis		
Idiopathic optic neuritis	26	60.5
ADEM	3	7
MS	9	20.9
NMO	2	4.7
Anti-MOG disease	1	2.3
Unidentified	2	4.7
Season at presentation		
Winter	15	34.9
Autumn	10	23.3
Summer	7	16.3
Spring	11	25.6
History of a recent infection		
No	8	18.6
Upper respiratory tract	10	23.3
HSV	2	4.7
Pneumococcal meningitis	1	2.3
Unspecified	16	37.2
The side of involvement		
Right	14	32.6
Left	14	32.6
Bilateral	15	34.9
Visual acuity ≥0.5 (20/40) in the worst eye at baseline	16/29	55.2
Final visual acuity in the worst eye ≥ 0.5 (20/40)	20/26	76.9
Improvement in visual acuity at follow-up		
Complete	7/15	46.7
Partial	6/15	40
No	2/15	13.3
Recurrence of ON	7/43	16.3

Table 1. Demographic and clinical characteristics of the patients.

Variable (mean±SD or n/total,%)	ADEM group	DD group	ION group	p value (Comparison of the DD and ION groups)
n	3	14	26	-
Age at first episode (years)	6.25±2.2	13.5±4.7	12.28±2.9	>0.05
Follow-up period (years)	3.16±2.14	3.95±3.23	2.05±2.5	0.049
Visual acuity at onset (%)				
Left	0.53±0.6	0.82±0.3	0.55±0.4	>0.05
Right	0.13±0.1	0.48±0.4	0.64±0.4	>0.05
Final visual acuity (%)				
Left	1 (n=1)	1±0	0.84±0.3	>0.05
Right	1 (n=1)	0.63±0.5	0.62±0.4	>0.05
RNFL (µm)				
Left	97.8 (n=1)	103±20.4	103.9±20.5	>0.05
Right	51.6 (n=1)	100.7±17.6	106.4±11	>0.05
Bilateral involvement (n/total)	2/3	2/14 (14.3%)	11/26 (42.3%)	>0.05
Number of ON episodes	-	2.1±1.6	1±0	0.027
Female gender (n/total)	2/3	10/14 (71.4%)	10/26 (38.5%)	0.047
Motor symptom (n/total)	2/3	3 /13	0 /24	0.037
Brain MRI lesion (n/total)	3/3	10 /13 (76.9%)	2 /25 (0.08%)	0.000
New demyelinating lesion in follow-up (n/total)	0/3	6 /12 (50%)	0 /7	0.000
Spinal lesion (n/total)	1/3	10/13 (76.9%)	0/24	0.000
Presence of oligoclonal bands in CSF (n/total)	0/2	4/11 (36.4%)	1/8 (12.5%)	>0.05
Recurrence of ON (n/total)	0/3	6/14 (42.9%)	0/26	0.001

Table 2. Findings of the patients in the groups of isolated ON (ION), ADEM, and diagnosed with demyelinating disease (DD) at follow-up; and statistical comparison results of ION and DD groups.

Variable (mean±SD or n/total,%)	ION group	MS group	p value
n (number of patients)	26	8	
Age at first episode (years)	12.28±2.9	15.82±1.8	0.003
Follow-up period (years)	24.6±30.8	49±41.7	0.047
Number of ON episodes	1±0.0	1.75±1.16	0.001
Age of >12 years at onset	10/26	8/8	0.002
Brain MRI lesion (n/total)	2/25	7/8	0.000
Demyelinating lesion in follow-up (n/total)	0/7	5/8	0.019
Spinal lesion (n/total)	0/24	7/8	0.000
Presence of oligoclonal bands in CSF (n/total)	1/8	4/6	0.063
Recurrence of ON (n/total)	0/26	3/8	0.009

Table 3. Comparison of the MS and ION groups.

Variable (n/total, %)	≤12 years	>12 years	*p* value
n	19	21	
Presentation in the autumn-winter seasons	14/19 (73.7%)	9/21 (42.9%)	0.049
Female gender	9/19 (47.4%)	11/21 (52.4%)	>0.05
Bilateral optic nerve involvement	11/19 (58%)	2/21 (9.5%)	0.001
Developing demyelinating disease	3/19 (15.8%)	11/21 (52.4%)	0.015
Brain MRI lesion	1/18 (5.6%)	11/20 (55%)	0.001
Spinal lesion	1/17 (5.9%)	9/20 (45%)	0.009

Table 4. Statistical comparison of the patient groups with an age of older and younger than 12 years at presentation.

Variable (n/total, %)	ION group	DD group	Odds ratio	95% confidence interval
Brain MRI lesion at onset	2/25 (8%)	10/14 (71.4%)	28.75	4.509-183.327
Enhancing lesion in optic nerve	4/19 (21%)	5/9 (55.6%)	6.25	1.026-38.076
Age of >12 years at presentation	10/26 (38.5%)	11/14 (78.6%)	5.867	1.307-26.327
Unilateral involvement	15/26 (57.7%)	12/14 (85.7%)	4.4	0.814-23.776
Female gender	10/26 (38.5%)	10/14 (71.4%)	4	0.983-16.271

Table 5. Risk factors for the development of demyelinating disease in ON patients during follow-up.

Conclusions:

In our study, the highest risk factor for the development of a demyelinating disease was the presence of a brain MRI lesion. Similar results have been reported in other studies (3). Additionally, in our study, the frequency of spinal and optic nerve lesions on MRI were significantly higher in the group that developed DDs.

Other risk factors for the development of DDs after ON, determined in our study, were the presentation of ON after the age of twelve, female gender, and unilateral optic nerve involvement.

The fact that bilateral involvement was more common in the prepubertal period and unilateral involvement was associated with demyelinating disease in our study is consistent with previous studies (4). However, there are also studies reporting that bilateral involvement increases the risk of MS (5).

In our study, the outcome visual acuity showed a close relationship with the severity in the loss of visual acuity at presentation.

Results:

The final diagnoses were ION (n=26), ADEM (n=3), MS (n=9), NMOSD (n=2), and MOGAD (n=1). The demographic and clinical characteristics of the patients were summarized in Table 1.

In the DD group, the number of ON episodes was higher (p=0.027); and the female gender (p= 0.047), presence of a T2-lesion on brain or spinal cord (p<0.001), and autoimmune antibody positivity (p=0.023) were more common (Table 2). The comparison of ION and MS groups was similar. Additionally, the age at first episode was greater in MS (p=0.003) (Table 3).

In the patients greater than 12-years old at the first episode, unilateral involvement of the optic nerve (p=0.001) and developing DDs (p=0.015) were more common (Table 4).

The highest risk factor for DDs was the presence of a brain T2-lesion (OR=28.75) (Table 5).

Patients with a final visual acuity less than 20/40 in at least one eye had a higher rate of visual acuity deterioration at presentation (p=0.003).

References:

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