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Original Article

The Clinical Characteristics of Optic Neuritis in Korean Children

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Purpose: To study the clinical characteristics of optic neuritis in Korean children.

Methods: A retrospective review of the medical charts of 20 patients who were diagnosed with optic neuritis before age 10 was conducted in this study. Data were collected on the demographics, clinical features, use of intravenous corticosteroids, neuroimaging, and diagnosis of multiple sclerosis.

Results: The mean age at diagnosis was 6.5 ± 1.8 years (range, 3 to 9 years). Seventeen patients (85%) were female, and 13 patients (65%) exhibited bilateral diseases. Visual acuity had decreased to ≤20 / 200 in 16 of the 20 patients, and recovered to ≥20 / 40 in 16 of the 20 patients. The mean duration between the worst visual acuity and 20 / 40 was 2.30 ± 2.91 months. Intravenous corticosteroid treatment was performed in 15 patients and exerted a beneficial effect on the visual outcomes. Disc swelling was observed in 75.8% of the affected eyes. Multiple sclerosis was diagnosed in five patients with a mean follow-up period of 21.9 ± 20.3 months. The presence of lesions in brain magnetic resonance images was identified as the most significant factor with regards to the occurrence of multiple sclerosis.

Conclusions: In children with optic neuritis, a profound decrease in initial visual acuity and rapid recovery of visual acuity were confirmed. Corticosteroid treatment resulted in a beneficial effect on visual outcomes, but had no effect on the risk of multiple sclerosis.

Key Words: Corticosteroid, Multiple sclerosis, Optic neuritis

Anterior and bilateral types of optic neuritis are more common in children than adults [1]. Many cases have been reported to have occurred within one or two weeks after viral infection or vaccination [2-4]. The relationship between optic neuritis and multiple sclerosis (MS) has been well-established, and several articles have noted a lower incidence of MS in children with optic neuritis [3,5-11]. Since there have been no studies of childhood optic neuritis comparable to the Optic Neuritis Treatment Trial (ONTT), a multi-center, randomized, placebo-controlled trial for adult optic neuritis, the previous results regarding childhood optic neuritis cannot be viewed as complete or definitive.

In previous studies on childhood optic neuritis, the study populations were heterogeneous in nature, owing to the broad age distributions of the subject children. Some previous reports have suggested that hormonal effects and puberty affected the clinical manifestations of the condition [4,6,12]. Working from this perspective, several authors have focused on prepubertal patients, however, the number of study patients was small [12,13].

In this study, we describe the clinical characteristics of optic neuritis in young children who were diagnosed before the age of 10. This age group was chosen in order to exclude postpubertal adolescents who might exhibit characteristics of adulthood.

Materials and Methods

Our study reviewed patients younger than 10 years of age

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that visited the Seoul National University Children's Hospital and were diagnosed with optic neuritis between November 1st, 1996 and October 31st, 2008. Optic neuritis was diagnosed on the basis of the following clinical symptoms and signs: acute loss of visual acuity or visual field lasting 8 days or less, relative afferent pupillary defect, and abnormal color vision. Additionally, bilateral disease was defined as a loss of vision in the other eye occurring within two weeks after the initial attack. All cases were confirmed by an experienced neuro-ophthalmologist (SJK).

Patients who had a history of corticosteroid treatment, neurological disorders at the initial examination, and other ocular or systemic diseases were excluded. Among the patients who fulfilled these criteria, 6 patients were excluded for the following exclusion criteria: 1 for a previous history of steroid treatment to treat suspicious optic neuritis, 2 for diagnosis of neuromyelitis optica, and 3 for too brief of a follow-up period (less than 6 months). After these exclusions, 20 patients were identified for our study.

The following data were recorded: demographics (age at diagnosis, sex), clinical profiles (laterality, initial visual acuity, worst visual acuity, final visual acuity, duration between initial symptom and recovery), ophthalmologic characteristics (disc swelling, visual evoked potential, results of color vision test and visual field test), presumed or definite viral infection or vaccination preceding visual loss, findings in brain magnetic resonance images (MRI), development of MS, and the use of steroid treatment. We considered 20 / 40 as functionally good visual acuity, and the duration of visual recovery to 20 / 40 was checked. Diagnosis of clinically definite MS was confirmed by an experienced pediatric neurologist (JHC) on the basis of the criteria developed by McDonald et al. [14] and revised by Polman et al. [15].

For the statistical analysis for visual outcomes and the risk of MS according to the use of corticosteroid treatment and other clinical features, the Mann-Whitney *U*-test and the crossover tabulation test were conducted, respectively. We used SPSS ver. 17.0 (SPSS Inc., Chicago, IL, USA) for the analysis, and regarded the result as statistically significant when the *p*-value was less than 0.05.

Results

We identified 20 patients, 17 of whom were girls (85%) and the remaining 3, boys. Mean age at diagnosis was 6.5 ± 1.8 years (range, 3 to 9 years). Thirteen patients were diagnosed with bilateral diseases (65%). The mean initial and worst visual acuity were both approximately 20 / 2000 (logarithm of the minimum angle of resolution [logMAR] scale, 1.89 ± 0.91 and 1.91 ± 0.91, respectively). Sixteen patients (80%) exhibited visual acuity worse than 20 / 200. However, 16 patients (80%) recovered to a visual acuity level better than 20 / 40, and the mean final visual acuity was 20 / 25 (logMAR scale, 0.07 ± 0.10). The duration between the worst visual acuity and 20 / 40 was 2.30 ± 2.80 months (6 days to 8 months). The time between the worst visual acuity and final visual acuity was 5.51 ± 6.12 months (6 days to 22 months). Four patients showed no recovery of visual acuity, 3 patients

Table 1. Demographic findings and treatment options of the study patients

No.	Age (yr)	Sex	Laterality	Presence of visual recovery	Development of multiple sclerosis	Intravenous corticosteroid treatment
1	3	F	B	Y	N	Y
2	7	F	B	Y	N	Y
3	7	F	U	Y	N	Y
4	7	F	B	N	Y	N
5	9	F	U	Y	N	Y
6	9	M	B	Y	N	Y
7	6	F	B	Y	Y	Y
8	9	F	B	N	N	N
9	8	F	U	Y	N	Y
10	5	F	U	N	N	N
11	5	M	B	Y	Y	N
12	6	F	B	Y	N	N
13	6	F	B	N	N	Y
14	5	F	B	Y	Y	Y
15	6	F	B	Y	N	Y
16	9	F	U	Y	Y	Y
17	7	F	U	Y	N	Y
18	6	M	U	Y	N	Y
19	5	F	B	Y	N	Y
20	4	F	B	Y	N	Y

Age = age at diagnosis; F = female; M = male; B = bilateral; U = unilateral; Y = yes; N = no.

Table 2. Clinical profiles of young children with optic neuritis

Characteristics	Data
Age (yr)	6.5 ± 1.82 (3-9)
Follow-up period (mon)	21.9 ± 20.3 (6-69)
Initial VA (logMAR)*	1.89 ± 0.91 (0.40-3.50)
Worst VA (logMAR)*	1.91 ± 0.91 (0.40-3.50)
VA better than 0.5 (% of eyes)	81.8
Duration between worst VA and 0.5 (mon)	2.30 ± 2.84 (0.2-8)
Recovery VA (logMAR)*	0.07 ± 0.10 (-0.08-2.5)
Duration between worst VA and recovery VA (mon)	5.51 ± 6.12 (0.2-22)
Disc swelling (% of eyes)	75.8
Preceding febrile illness (% of patients)	40
Preceding vaccination (% of patients)	10

VA = visual acuity; logMAR = logarithm of the minimum angle of resolution.
*For statistical analysis, the visual acuities were transformed as follows: finger count to 2.5 logMAR, hand motion to 3 logMAR, and light perception to 3.5 logMAR visual acuities.

showed bilateral disease, and 3 patients did not receive corticosteroid treatment.

We administered a regimen of 10 to 30 milligrams of methylprednisolone per kilogram per day with 15 patients receiving this treatment. Based on previous reports of corticosteroid treatment on favorable visual outcomes in childhood optic neuritis, we recommended the treatment to every parent. However, 5 patients refused the therapy and underwent a follow-up. Compared to the non-treated subjects, patients who received intravenous corticosteroid treatment resulted in better visual outcomes ($p = 0.043$). There has been no complication regarding the treatment; the minimum age of the treated subjects was 3 years.

Disc swelling was observed in 75.8% of eyes (25 eyes). Visual evoked potential test was performed in 13 patients, and all of them showed abnormal responses, reduced amplitude, or delayed latency. Color vision tests were done on 12 eligible patients. Ten patients did not even notice the demo plates, while the other 2 patients showed nonspecific red-green and mild red-green defects, respectively. Goldmann perimetry was conducted with the same 12 patients. Six of the patients experienced central and paracentral scotomas, 4 patients reported diffuse decreased central sensitivity, 1 patient exhibited a paracentral island, and the other patient reported no generalized depression.

Eight patients reported suffering from febrile illnesses before the onset of acute visual loss, and 2 patients had received the vaccine for measles, mumps, and rubella prior to the attack.

With the exception of 2 patients, all children had a baseline brain MRI. Seven of the patients exhibited no abnormalities. There were 3 and 5 patients in this study who exhibited optic nerve enhancement and high signal lesions in the white matter, respectively. On the MRI of the other 3 patients, both high signals in the optic nerve and white matter lesions in the brain were observed.

The mean follow-up period was 21.9 ± 20.3 months (range, 6 to 69 months). During that time, five patients developed multiple sclerosis. Four of the patients were female, and 2 of them did not initially receive intravenous corticosteroid treatment for optic neuritis. We conducted a crossover tabulation test for all discrete variables with the risk of MS: age at diagnosis, sex, corticosteroid treatment, febrile illness or vaccination, and brain white matter lesions on the MRI. Only the presence of MRI lesions in the brain was identified as a risk factor for MS ($p = 0.008$). The use of corticosteroid treatment did not affect the risk of MS (Tables 1 and 2).

Discussion

According to the ONTT, female predominance was observed in adulthood optic neuritis, that is, 77% of the enrolled patients were female [16]. With regards to its dominance in childhood, there has been some controversy regarding a female predilection for the condition, and the ratio of females to males affected was 2:3 to 4:1 [2,6,7,17]. Some authors reported that no sex preponderance was found in prepubescent children, but the female-to-male ratio increased to 2:1 after puberty [4,6,12]. In a previous study conducted in Thailand, the proportions of females were 59% and 71% of patients with optic neuritis age under 10 and between 10 and 12, respectively [13]. However, in this study, a female predominance was detected with 85% of the patients being female. Factors other than hormonal effects may be attributed to female preponderance, but they have yet to be discovered.

Childhood optic neuritis was considered to be bilateral in nature. Contrary to the inclusion criteria of the ONTT, which covers only patients with unilateral visual acuity loss [16], some authors have recruited children with bilateral optic neuritis [18], while other authors did not attempt to exclusively include bilateral diseases, but exclusively reported cases in which the conditions were bilateral [11,19]. There were 13 cases of bilateral disease among our 20 patients, which was consistent with previous articles where bilateral disease was

reported in the range of 42% to 87% [2,6,20].

Initial profound visual loss occurred more commonly in children than adults. The authors reported that 84% to 100% of childhood patients experienced visual acuity of 20 / 200 or worse upon presentation [6,10]. According to the ONTT, initial visual acuity was better than 20 / 200 in 64.1% of the 454 patients [21]. In our study, the mean initial visual acuity was about 20 / 2,000, and 80% of patients experienced visual acuity less than 20 / 200. Despite severe visual loss at the initial phase, visual prognosis was good to excellent in the childhood optic neuritis patients. Previous articles reported that 53% to 92% of patients recovered visual acuity better than 20 / 40 [2,12,17]. The ONTT provided long-term follow-up results of visual prognosis: 72% of the affected eyes had a visual acuity of 20 / 20 or better, and 66% of patients had a visual acuity of 20 / 20 or better in both eyes at 15-years' follow-up [22]. In this study, with the exception of 4 patients who exhibited no recovery of their visual acuity, the mean final visual acuity was approximately 20 / 25 in 16 patients, all of whom showed a visual acuity better than 20 / 40, the visual acuity which could be regarded as functionally sound. The durations between the worst visual acuity and 20 / 40 were 2.30 ± 2.80 months.

This study was not a controlled study, and the number of study patients was small. However, we were able to identify significant beneficial effects of intravenous corticosteroid therapy on the visual outcomes. We employed the regimen of 10 to 30 milligrams of methylprednisolone per kilogram per day, which was consistent with previous articles that reported satisfactory visual outcomes with corticosteroid therapy [2,4]. Of course, there have also been reports showing no correlation between the use of steroids and the final visual outcomes, making the decision of corticosteroid treatment on young children difficult and controversial [6,12]. However, it is both logical and ethical to treat optic neuritis patients with corticosteroids when taking the suspected autoimmune mechanism underlying the pathogenesis of optic neuritis into account [1].

Many reports have focused on the association between optic neuritis and MS, because MS affects both the quality of life of the patients and the overall prognosis. According to the ONTT, the aggregate cumulative probabilities of developing MS were 30%, 38%, and 50% with 5-year, 10-year, and 15-year follow-ups, respectively [23]. In a study of childhood optic neuritis, Lucchinetti et al. [5] estimated the risk of MS to be 13%, 19%, 22%, and 26% after 10, 20, 30, and 40 years from the onset of optic neuritis. In another case series, the risk of developing MS was estimated to be 8% to 50% [3,7-11]. Meadows [18] reported no cases of MS over a follow-up period of 3 to 18 years. In our study, during the mean follow-up period of 21.9 ± 20.3 months, 5 patients (20%) were diagnosed with MS. After the ONTT reports, it became commonly accepted that steroid therapy did not alter the visual outcomes or the risk of MS in adults. In addition, we find no significance in corticosteroids preventing MS. Only the presence of MRI lesions, the most important risk factor in the ONTT, affected the risk of MS. In our study, only patients who showed abnormalities in the baseline MRI developed MS. This finding was comparable to the findings of the ONTT, which reported the risk of MS after 15 years increasing 25% to 72% in cases where the baseline MRI showed one or more lesions [23], and the findings of the study on patients were younger than 18 years of age [24].

This study has the same disadvantage as other studies concerning childhood optic neuritis: the study population is too small to fully analyze the prognosis depending on the treatment and risk factors of multiple sclerosis. The prevalence of optic neuritis in children is known to be less than in adults, and thus the possibility of studying large population of patients is considered fairly low. Nevertheless, we found that steroid treatment exerted a significant effect on visual outcomes, and the presence of MRI lesions had a statistically significant effect on the risk of MS.

Additionally, the patients in this study were all Koreans, and thus the differences between previous reports and this study might be based on the ethnic background. Some authors have reported that the incidence of multiple sclerosis was low in cases of childhood optic neuritis among Asians [2,13]. However, this study recruited a large number of patients who were younger than 10 years when diagnosed with optic neuritis, and thus created a distinction between our results and the previous articles. Previous reports regarding childhood optic neuritis that studied such a broad age group or such a small study population exhibited insignificant results.

In this study, we demonstrated the clinical characteristics of optic neuritis in young children, reaffirmed some aspects of previous studies, and clarified the attributes of the specific age group under age 10. In particular, the patients in this age group tended to be female, have bilateral disease, and despite initial deep visual loss, recovered their visual acuity within a few months. Corticosteroid treatment appeared to exert a helpful effect on the visual outcomes, and in cases involving MRI lesions at baseline, the risk of developing MS tended to be higher.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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