Pediatric Optic Neuritis

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Objective: *Describe the clinical characteristics of pediatric optic neuritis.*
Material and Method: *Retrospective observational case series was performed on patients ≤ 12years of age with optic neuritis at Childrens Hospital Los Angeles.*
Results: *Thirty-one patients (48 eyes) were identified. Mean follow-up was 2.7 years. There were 17 pre-adolescents (< 10 years old) in group I, and 14 adolescents (10-12 years old) in group II. Females comprised 59% of group I, and 71% of group II. Bilateral cases comprised 65% from group I, and 43% from group II. Five patients from group I had acute disseminated encephalomyelitis (ADEM). Two patients from group II had multiple sclerosis (MS). No other patients developed MS. There was no difference in initial or final vision for the eyes with or without steroid treatment.*
Conclusion: *Pediatric optic neuritis has no gender or racial predilection, is usually bilateral, and is associated with ADEM rather than MS.*

Keywords: *Optic neuritis, Pediatric, Acute disseminated encephalomyelitis, Multiple sclerosis, Steroids*

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Kennedy and Carroll first brought the unique features of pediatric optic neuritis to public attention in 1960[1]. Since that time at least ten reports of series of cases have generally supported Kennedy and Carroll's findings that this condition is usually bilateral, associated with disc edema, has a good visual outcome, and is not a harbinger of multiple sclerosis[1-19]. There has been considerable variability in these reports of the actual prevalence of these findings in pediatric optic neuritis as well as the prevalence of other associations such as sexual predilection, prodromal illness, and encephalomyelitis. Much of the variability in prevalence of these outcomes and associations may be attributed to the relatively few patients in most of the reports, heterogeneous populations, and incomplete data. The authors feel, however, that the biggest problem with previous reports of pediatric optic neuritis is that all of the case series included adolescents, and therefore represented admixtures of pediatric and adult optic neuritis.

The authors hypothesized that the outcomes and associations of pediatric optic neuritis are even more distinct from adult optic neuritis than previously reported and that this distinction would be apparent in a study that divided pre-pubertal from adolescent children. The purpose of the present study was to retrospectively review the presented cases of optic neuritis presenting at less than ten years of age and compare the outcomes and associations with those cases presenting at age 10-12 years. The authors also reviewed the literature on pediatric optic neuritis and, where possible, gleaned the reported differences among those cases presenting in similar, and older, age groups.

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Design

This is a retrospective observational case series.

Material and Method

All medical records of patients with a diagnosis of optic neuritis during the period 1979- July 2003 at Children's Hospital of Los Angeles were retrospectively reviewed. These were identified from a diagnosis database maintained in the Division of Ophthalmology. The Committee on Clinical Investigations (IRB) at Children's Hospital Los Angeles approved this survey. All records reviewed were for patients aged 12 years or younger at the onset of their vision loss. The diagnosis of optic neuritis was made clinically on the basis of acute or subacute vision loss in one or both eyes with or without optic nerve swelling, and no other identifiable cause such as tumor, retinal lesion, vasculitis, or infection. Ocular pain on eye movement, afferent pupillary defect, dyschromatopsia, pre-chiasmal visual field defect, or neuro-imaging results may have been used to support the diagnosis.

The authors collected the following information for each patient: age at onset, sex, ethnicity, best-corrected initial visual acuity, prodromal symptoms, preceding illnesses, eye examination, laboratory findings, cerebrospinal fluid (CSF) findings, perimetry, neuro-imaging, treatment, and follow-up data. Bilateral optic neuritis was defined as both eyes involved simultaneously or within one month of each other, and recurrent optic neuritis when repeated attacks affected one or both eyes over an interval greater than one month.

Acute disseminated encephalomyelitis (ADEM) and multiple sclerosis were diagnosed on clinical grounds by pediatric neurologists. ADEM is a monophasic multifocal neurologic disease with multiple bilateral lesions at the gray-white matter interface on MRI scan and CSF pleocytosis usually following a viral syndrome. Multiple sclerosis, on the other hand, has multifocal recurrences of neurologic signs and symptoms over time.

Patients were divided in two groups according to the age of onset of optic neuritis. The first group comprised patients who were younger than 10 years of age at onset and the second group comprised patients who were 10 to 12 years of age at onset.

Table 1. Clinical characteristic in patients younger than 10 years at age of onset (Group I) (n = 17)

Pt. No./Sex/ Age (yr)	Eye	Initial VA	Initial disc appearance	Recovery time	Final VA	Final disc appearance	F/U	Associated neurological disease
1/F/5	OD	10/200	Pallor	4.7 mos	20/20	Pallor	7.7 yrs	ADEM
	OS	3/200	Pallor	4.7 mos	20/20	Pallor		
2/M/5	OD	1/30	Edema	5.8 mos	20/30	Pallor	7.5 yrs	ADEM
	OS	10/30	Hyperemia	5.8 mos	20/30	Normal		
3/M/5	OD	HM	Edema	3 mos	20/30	Pallor	8.7 yrs	
	OS	6/200	Edema	3 mos	20/20	Pallor		
4/F/6	OS	NLP	Edema	2.5 mos	20/20	Normal	2.5 mos	
5/F/7	OS	HM	Edema	1 mo	CF	Normal	1 mo	
6/M/2	OD	LP	Edema	19 days	1/30	Pallor	3 mos	
	OS	NLP	Edema	19 days	1/30	Pallor		
7/M/8	OD	20/50	Normal	5.7 mos	20/25	Pallor	4.2 yrs	
8/M/8	OD	3/400	Hyperemia	1.2 mo	20/20	Pallor	4.3 yrs	
9/F/3	OD	0.5/30	Edema	9.2 mos	20/40	Pallor	1 yrs	
	OS	1.5/30	Pallor	6.3 mos	20/30	Pallor		
10/F/4	OD	20/30	Normal	2 mos	20/20	Normal	8 yrs	
	OS	10/100	Normal	2 mos	20/25	Normal		
11/F/4	OD	4/30	Edema	3.9 mos	10/30	Normal	3.9 mos	ADEM
	OS	4/30	Edema	3.9 mos	11/30	Normal		
12/F/5	OD	NLP	Edema	8 days	20/20	Edema	3 mos	ADEM
	OS	NLP	Edema	8 days	20/30	Edema		
13/M/3	OD	NLP	Normal	2.6 mos	20/30	Normal	2.6 mos	
	OS	1/30	Normal	2.6 mos	20/30	Normal		
14/F/6	OD	NLP	Edema	2.9 mos	20/20	Normal	2.4 yrs	
15/F/8	OD	3/100	Edema	8.8 mos	20/20	Pallor	7.6 yrs	
	OS	10/100	Edema	8.8 mos	20/40	Pallor		
16/M/5	OD	3/200	Normal	1.8 mos	20/30	Normal	13.5 yrs	ADEM
	OS	13/100	Normal	1.8 mos	20/30	Normal		
17/F/7	OD	20/80	edema	2.2 mos	20/50	Pallor	2 mos	

Results

A total of 31 patients with optic neuritis was identified, 20 (64.5%) were girls and 11 (35.5%) were boys. Their ages at onset of optic neuritis ranged from 2 to12 years (average 7.9 years). Thirteen patients (42%) were Hispanic, eight (26%) were white, three (10%) were Asian, two (6%) were black and five (16%) were mixed race or unknown.

Patients underwent follow-up for a mean of 2.7 years (range: 1 week – 13.5 years). Only one patient (#20) had a recurrence of optic neuritis during the period of follow-up, and another (#22) presented with recurrence of an attack from the previous year diagnosed at another institution. Both of these patients were older than 10 years of age at onset of their first attacks. Neither of these patients developed clinical multiple sclerosis during the period of follow-up (1 year and 2.2 months).

There were 17 patients younger than 10 years old in group I and 14 patients between 10-12 years old in group II. (Table 1, 2) Females comprised 10 of 17 (58.8%) in group I and 10 of 14 (71.4%) in group II. Mean age at onset was 5.4 years in group I, and 11 years in group II. There were 11 (64.7%) patients with bilateral optic neuritis in group I and six (42.9%) patients in group II. Five patients from group I had ADEM at the time of their attacks. None from group I developed multiple sclerosis with a mean follow-up of 4.2 years (range 1 month to 13.5 years). Two patients from group II had a diagnosis of multiple sclerosis preceding their optic neuritis attacks. No other patients in group II developed multiple sclerosis over an average follow-up of 1.3 years (range 1 week to 5.3 years). These and other clinical characteristics are summarized in Table 3.

Optic disc swelling was present on initial examination in 57% of affected eyes from group I and in 75% from group II. Optic atrophy supervened in half of the affected eyes from group I and in one-quarter from group II. Nearly half of the affected eyes had normal disc appearance after resolution of optic neuritis.

Vision improved in all patients. The mean initial visual acuity of the affected eyes (log MAR calculation[20]) was counting fingers in both age groups. The mean final visual acuity was 20/40 in both age groups. The mean time to maximum visual recovery was 105 days (range 8-277 days) for group I and 32 days (range 7-105 days) for group II. Visual acuity at presentation, final visual acuity, duration from onset to final visual acuity is summarized for each group in Tables 1 and 2.

Ten patients (15 eyes) were treated with intravenous prednisolone, seven patients (12 eyes) were

Table 2. Clinical characteristic in patients 10-12 years at age of onset (Group II) (n = 14)

Pt. No./Sex/ Age (yr)	Eye	Initial VA	Initial disc appearance	Recovery time	Final VA	Final disc appearance	F/U	Associated neurological disease
18/F/11	OD	LP	Normal	3 wks	20/800	Pallor	3 wks	MS
19/F/11	OS	NPL	Edema	1.2 mos	20/30	Normal	1.1 yr	
20/F/11	OD	7/200	Edema	8 days	20/20	Normal	1 yr	
21/F/12	OS	LP	Edema	3 days	20/20	Pallor	3 mos	
22/F/10	OD	LP	Edema	2.2 mos	20/25	Pallor	2.2 mos	
23/M/11	OD	LP	Edema	7 days	20/30	Hyperemia	5.3 yrs	
	OS	NLP	Edema	7 days	20/25	Hyperemia		
24/M/12	OS	20/100	Normal	7 days	20/30	Pallor	5 mos	MS
25/F/10	OD	20/50	Edema	3.5 mos	20/20	Normal	7 mos	
	OS	LP	Edema	3.5 mos	20/70	Pallor		
26/F/11	OD	8/200	Edema	1.8 mos	20/20	Normal	5.3 yrs	
	OS	20/200	Edema	1.8 mos	20/20	Normal		
27/M/11	OD	LP	Edema	1 mo	20/20	Normal	3.7 yrs	
28/F/10	OD	HM	Edema	7 days	5/200	Edema	1 wk	
	OS	20/50	Hyperemia	7 days	20/50	Hyperemia		
29/F/11	OD	10/200	Hyperemia	13 days	20/20	Normal	1 mos	
	OS	10/200	Hyperemia	13 days	20/30	Normal		
30/F/11	OD	14/100	Edema	1.2 mos	20/20	Normal	1.2 mos	
	OS	20/40	Edema	1.2 mos	20/20	Normal		
31/M/12	OD	CF	Edema	1.2 mos	20/50	Normal	1.2 mos	

Table 3. Summary of characteristic of patients group I and II

	Group 1 (younger than 10 years of age)	Group 2 (10-12 years of age)	Total
n	17	14	31
Female	10 (58.8%)	10 (71.4%)	20 (64.5%)
Mean age (year)	5.4	11	7.9
Range (year)	2-8	10-12	2-12
Bilateral	11 (64.7%)	6 (42.9%)	17 (54.8%)
Preceding illness*	9 (52.9%)	6 (42.9%)	15 (48.4%)
Eye pain	3 (17.7%)	6 (42.9%)	9 (29.0%)
Headache	4 (23.5%)	6 (42.9%)	10 (32.3%)
Multiple sclerosis	0	2 (14.3%)	2 (6.5%)
Encephalomyelitis	5 (29.4%)	0	5 (16.1%)

* Viral infection, sinusitis, or other within 2 weeks of onset

treated with oral prednisone, and 14 patients (20 eyes) received no steroids treatment. There was no difference in initial or final vision for the eyes in any of these treatment groups.

Forty percent of affected eyes developed optic disc pallor. Of these, 73% recovered vision to 20/40 or better.

Reliable Goldmann perimetry was obtained on nine patients (13 eyes) after maximum recovery of vision had been achieved. All of the tested eyes had visual acuity of 20/40 or better. Eight eyes of six patients had field defects consisting of paracentral scotomas or diffuse field constriction. All but one of these eyes had disc pallor on direct ophthalmoscopic examination. The eyes with normal visual fields all had normal appearing optic discs.

Spinal fluid examinations were performed in eight patients from group I. Four of these had lymphocytic pleocytosis. Three of them had ADEM; one had tonsillitis with a viral exanthema. CSF protein and IgG levels were normal in all eight patients and no oligoclonal bands were found. From group II, CSF was examined in six patients; four of these revealed lymphocytic pleocytosis. CSF protein levels were normal in all. Elevated IgG level and oligoclonal bands were found only in the two patients with multiple sclerosis.

In group I, 14 patients underwent computed tomographic (CT) evaluation. Thirteen patients had normal-appearing CT of the brain and orbit. In another patient CT demonstrated irregular thickening of the optic nerve from mid portion within the orbit to the apex which correlated with the patient's magnetic resonance imaging (MRI) scan. MRI scans were performed in six patients from group I; two of these were normal. Two others demonstrated abnormal enhancement along the optic nerve with extension to chiasm. The last two patients had bilateral white matter lesions consistent with their diagnosis of ADEM.

From group II, CT scans performed on two patients were normal. MRI performed on eight patients was abnormal in four patients. Multiple white matter lesions were identified in both cases with multiple sclerosis. One patient had a single white matter lesion, and another showed three ill-defined areas of abnormal signal within the centrum ovale. Neither of these patients has developed multiple sclerosis after 1.3 and 5.5 years of follow-up.

Discussion

The largest reported series of cases of pediatric optic neuritis are summarized in Table 4[1-7,9,12,13,17,18,21-23]. This table includes the presumably idiopathic cases and excludes those reportedly due to infection, neoplastic disease, and vasculitis. It also combines cases that are reported in more than one series[12,18,21]. A total of 346 cases are reported in these series with a mean age of 9.8 years (range: 1-17 years). 61% of the reported cases were female, but female prevalence varied from 41% to 81% in these series. In the present series 65% were female, but female prevalence was higher (71%) in the 10-12 year old age group than in those less than age 10 years (59%). This is consistent with the known female predominance in adult optic neuritis[24,25], suggesting that some of the presented cases in the 10-12 year-old age group may have had the adult form of the disease.

If one divides (where possible from the reported information)[3,5,6,13,23] the previously reported

Table 4. Summary of demographic and clinical characteristic in children with optic neuritis

Author	#	Age range	Meanage	Follow-up range	Mean follow-up	Female < 10 yr	Female 10-12 yr	Female > 12 yr	Female/ total	Eye pain	Prodromal illness
Kennedy & Carrol[1]	30	4-16 yrs	9.5	1-20 yrs	8 yr				19/30	14/30	13/30
Hierons & Lyle[21]; Meadows[12]; Parkin[18]	44	2-17 yrs		2-32 yrs□	18 yr						7/24
de Leersnyder, et al[23]	14	4.5-15 yrs	9.3	3 mos-3 yrs	1 yr	4/8	3/3	2/3	9/14		
Kriss, et al[9]	39	3-15 yrs	8.6	3 mos -29 yrs	8.8 yrs				29/39		18/39
Riikonen[2,7,22]*	18	5.2-14.5 yrs	10.8	1-13 yrs	6 yrs				13/16		10/18
Visudhiphan, et al[4]	22	1-12 yrs	7.1	6-20 yrs					12/22		6/22
Lucchinetti, et al[17]	94	2-16 yrs	11□	2.7-43 yrs□	22 yrs				58/94	35/94	34/94
Brady, et al[5]	22	1.75-15 yrs	8.7	0.5-56 mos	11 mos	4/12	3/5	4/5	11/22		
Morales, et al[3]*	13	4-15 yrs	9.8		17.5 mos	2/5	1/5	3/3	6/13		
Lana-Peixoto, et al[13]	27	3-16 yrs	10.9	0-41 mos	13 mos	4/8	6/8	1/11	11/27	10/27	10/27
Hwang JM, et al[6]	23	3-15 yrs	8.9	2-40 mos	14 mos	8/14	3/7	2/2	13/23		9/23
Chirapapaisan & Borchert	31	2-12 yrs	7.9	1 wk-13.5 yrs	2.7 yrs	10/17	10/14		20/31	9/31	15/31
Total	346			0.5 mos-43 yrs		32/64	26/42	12/24	201/331	68/182	122/308
%						50	62	50	61	37	40

* Cases secondary to infectious, degeneration, or neoplastic diseases were excluded, □ Median, □17 subjects, □79 subjects

Table 5. Summary of initial and final vision in children with optic neuritis

Author	Initial vision ≥ 20/40			Initial vision ≤ 20/200			Final vision ≥ 20/40			Final vision ≤ 20/200		
	< 10 yrs	10-12 yrs	Total	< 10 yrs	10-12 yrs	Total	< 10 yrs	10-12 yrs	Total	< 10 yrs	10-12 yrs	Total
de Leersnyder, et al[23]	1/9	0/3	1/12	7/9	2/3	9/12						
Visudhiphan, et al[4]			0/22			22/22						
Brady, et al[5]	0/21	1/8	1/29	15/21	7/8	22/29	13/21	6/8	19/29	1/21	2/8	3/29
Morales, et al[3]	1/10	3/7	4/17	9/10	3/7	12/17	7/10	3/7	10/17	1/10	3/7	4/17
Lana-Peixoto, et al[13]	1/13	1/11	2/24	10/13	9/11	19/24						
Hwang JM, et al[6]	6/27	7/17	13/44	10/27	4/17	14/44	23/27	12/17	35/44	4/27	1/17	5/44
Total	9/80	12/46	21/148	51/80	25/46	98/148	43/58	21/32	64/90	6/58	6/32	12/90
%	11	27	15	64	57	66	74	66	71	10	19	13
Chirapapaisan & Borchert	1/28	1/20	2/48	21/28	15/20	36/48	22/28	15/20	37/48	5/28	1/20	6/48
%	4	5	4	75	75	75	79	75	77	18	5	13

cases into three age groups (< 10years; 10-12 years; > 12 years), there is no apparent increase in female pre-disposition with increasing age (Table 4). However, in one of the reported series, 10 of 11 patients older than 12 years were male[13]. If this anomalous group is excluded, there is a clear increase in reported female prevalence with age: 50% female in cases < 10 years; 62% female in cases 10-12 years; 85% female in cases > 12 years.

In a prior series of pediatric optic neuritis, 217 (66%) of 325 patients had bilateral involvement. Patients less than 10 years of age had a higher prevalence of bilateral involvement (83%) than patients 10-12 years old (36%) or those greater than 12 years (44%). Disc edema was found in 199 (56%) of 355 eyes in the previously reported series. The present series supports these previous observations, with 65% of patients bilaterally affected and 57% with papillitis if less than ten years of age. In the 10-12 year-old age group, 43% were bilaterally affected and 75% had papillitis. This is in contradistinction to adults in whom bilateral optic neuritis is rare and papillitis is present in 28-35%[25,26].

Prevalence of eye pain and prodromal illness was similar in the presented patients to previously published series (Table 4).

The initial and final vision was similar in the presented patients less than ten years of age and those 10-12 years of age. The initial visual acuity from the presented patients in these age groups is worse than in those abstracted from the literature for pediatric optic neuritis. However, final visual acuity is similar to previous reports (Table 5). In contrast, both initial and final visual acuity are better in adults with optic neuritis[27,28].

None of the presented patients younger than 10 years old developed multiple sclerosis with mean follow up of 4.2 years. This compares to an incidence of 30% multiple sclerosis in adults after five years of follow up[29].

Information abstracted from the literature supports the authors' finding of an increasing rate of multiple sclerosis in pediatric optic neuritis presenting after puberty. 58 (18%) of 317 analyzable patients in prior series had developed multiple sclerosis[1-7,9,12,13,17,18,21-23]. The risk of developing multiple sclerosis during the reported period of follow-up was higher in children older than 12 years of age (11 of 29 patients, 38%) than in the patients10-12 years of age (four of 29 patients, 14%) or in the patients younger than 10 years (four of 53 patients, 8%)[2,3,5-7,22,23]. Multiple sclerosis developed in 33% (17 of 52 patients) of reported cases with unilateral pediatric optic neuritis compared to 17% (26 of 153 patients) of those with bilateral involvement[2,3,5-7,9,17,22,23].

Five (29%) of presented 17 patients less than 10 years of age had ADEM. This compares with 17 (19%) of 90 analyzable patients (of all ages) in the literature with pediatric optic neuritis and ADEM. However, one cannot distinguish pre-pubertal from adolescent patients in these previous reports.

The presented data showed no difference in final visual acuity between bilaterally and unilaterally affected patients, consistent with a previous report[6]. This is in contrast to another report indicating that patients with bilateral involvement had a much worse visual outcome[3].

The present report significantly increases the number of documented cases of pediatric optic neuritis affecting children aged 12 years or less. Several conclusions can be drawn from these cases that suggest that pediatric optic neuritis is a different disease than adult optic neuritis, confirming the impressions of Kennedy and Carroll from 1960[1]. In contrast to adult optic neuritis[25], pediatric optic neuritis does not have a sexual or racial predilection. It is usually bilateral and associated with optic disc swelling. The initial vision is usually very poor and no light perception is common. Visual recovery is usually good, but residual poor vision and optic atrophy are more common than in adult optic neuritis. Visual recovery takes longer than in adult optic neuritis and steroids do not seem to improve the outcome. Optic atrophy does not preclude good visual acuity, but visual field defects are usually associated with optic atrophy.

Most importantly, the risk of multiple sclerosis following pediatric optic neuritis is very low especially when it occurs in a child less than ten years of age with bilateral disc swelling. On the other hand, associated ADEM is very common in such children suggesting that, just as adult optic neuritis is a forme fruste of multiple sclerosis, pediatric optic neuritis should be considered a forme fruste of ADEM.

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โรคเส้นประสาทตาอักเสบในเด็ก

นิพนธ์ จิรภาไพศาล, *Mark S Borchert*

วัตถุประสงค์: *เพื่อศึกษาลักษณะทางคลินิกของโรคเส้นประสาทตาอักเสบในเด็ก*
วัสดุและวิธีการ: *ทำการศึกษาย้อนหลังในผู้ป่วยเด็ก อายุน้อยกว่าหรือเท่ากับ12 ปี ที่เป็นโรคเส้นประสาทตาอักเสบที่โรงพยาบาล Childrens Hospital Los Angeles*
ผลการวิจัย: *พบผู้ป่วยเด็กจำนวน 31 คน (48 ตา) โดยมีค่าเฉลี่ยการติดตามผลการรักษา 2.7 ปี ผู้ป่วยเด็กกลุ่มที่ 1 อายุน้อยกว่า 10 ปี จำนวน 17 คน เป็นผู้หญิง 59% และเป็นโรคเส้นประสาทตาอักเสบทั้ง 2 ข้าง 65% โดยมีเด็ก 5 คน เป็นโรค acute disseminated encephalomyelitis (ADEM) ผู้ป่วยกลุ่มที่ 2 เป็นเด็กย่างเข้าวัยรุ่น อายุ 10-12 ปี จำนวน 14 คน เป็นผู้หญิง 71% และเป็นโรคทั้ง 2 ตา 43% มีเด็ก 2 คน เป็นโรค multiple sclerosis โดยเด็กคนอื่นทั้ง 2 กลุ่ม ไม่มีใครเกิดเป็น โรค multiple sclerosis ตามมา การรักษาด้วยสเตียรอยด์ไม่มีผลต่อการมองเห็น*
สรุป: *ผู้ป่วยเด็กที่เป็นโรคเส้นประสาทตาอักเสบ พบในเพศชายและหญิงได้ไม่ต่างกัน มักเป็น 2 ตา และมักสัมพันธ์กับ ADEM มากกว่า multiple sclerosis*