Original Article

Clinical Profile of Patients with Nonarteritic Anterior Ischemic Optic Neuropathy Presented to a Referral Center from 2003 to 2008

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Background: We conducted this study to report the demographics and clinical profile of patients with nonarteritic anterior ischemic optic neuropathy referred to a referral neuro-ophthalmology center in Iran.

Methods: During a five-year period, 107 patients with nonarteritic anterior ischemic optic neuropathy were studied. A detailed history of previous or current systemic diseases was obtained and a complete ophthalmic evaluation including best corrected visual acuity, color vision testing, and computerized perimetry was performed.

Results: Sixty-six men and 41 women with a mean±SD age of 52.7±10.3 (range: 30 – 80) years were studied. Most (62.2%) of the patients aged more than 50 years. Twenty-two (20.5%) patients had had an episode of nonarteritic anterior ischemic optic neuropathy in the fellow eye. Overall, 51 (47.7%) patients had no evidence of a previous or current systemic disease. Diabetes mellitus and hypertension were reported in 40.1% and 26.1% of the patients, respectively.

The best corrected visual acuity was 20/200 or worse in 43 (40.1%) eyes and 20/40 or better in 43 (40.1%) eyes. The best corrected visual acuity was significantly better in nondiabetic patients (0.62±0.69 LogMAR) than diabetics (0.96±0.84, *P*=0.03). The visual field analysis of reliable fields (76 eyes) revealed that the mean deviation ranged from -32.6 to -1.3 dB with a mean±SD of -19.7±8.08 dB. Diffuse defect was the most prevalent defect detected on 36.8% of visual fields of the study eyes followed by inferior altitudinal defect (26.3%). In the fellow eyes, without any evidence of prior optic nerve problem, inferior and superior arcuate scotoma were found in 30% and 20% of the eyes, respectively.

Conclusion: Characteristics of nonarteritic anterior ischemic optic neuropathy patients in a population of Iranian patients were similar to nonarteritic anterior ischemic optic neuropathy as described in previous studies, with the exception of higher proportion of younger patients and a higher propensity for diabetes. Visual field defects were common in clinically normal fellow eyes.

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Introduction

Nonarteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in the elderly.[1,2] The annual incidence of NAION has been estimated from 2.3 to 10.2 per 100,000 for persons 50 years and older.[3,4]

NAION is presumably the result of circulatory insufficiency within the optic nerve head; however, the exact mechanism of the vasculopathy remains unknown.[5] Although several factors have been shown to be associated with NAION, it has been debated which factors, other than old age and a small cupless optic disc, predispose to the disease.[1,5–8] Sixty percent of all NAION patients had one or more risk factors thought to be associated with small-vessel cerebrovascular

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disease, including hypertension, diabetes mellitus, and cigarette smoking.[3,6,9] This does not assure that the disease is vascular; however, similar proportions might be observed in a comparable patient population without NAION.[10]

Although NAION is a worldwide problem, data on its characteristics and natural history come mainly from some developed countries.[1–11] They have been completely missing for the Iranian population. Considering the paucity of the reports on the characteristics of NAION patients in different geographic locations and ethnicity, in this study, we evaluated the demographics and clinical profile of NAION in Iran.

Materials and Methods

From August 2003 through June 2008, all patients who were referred to the Neuro-Ophthalmology Clinic of Rassoul-e Akram Hospital with typical symptoms and signs of NAION including acute loss of visual acuity, positive relative afferent pupillary defect, swelling of optic disc, blurring of disc margins with or without hemorrhage, and field defect on computerized perimetry were selected for the study. The exclusion criteria included any evidence suggestive of temporal arteritis such as history of scalp tenderness, Westergren sedimentation rate ≥40 mm/hr, or positive C-reactive protein. Also excluded were the patients with a history of multiple sclerosis with or without optic neuritis, collagen vascular disease, or any other systemic autoimmune diseases. Ophthalmologic exclusion criteria were any symptoms or signs suggestive of vitreous, retinal, or other optic nerve disease that could affect central vision or cause visual field defects (e.g., vitrous hemorrhage or organization, retinal detachment, hereditary vitreoretinal or retinochoroidal diseases, glaucoma, optic nerve head colobomatous diseases, and optic nerve head drusen). The study was approved by the institutional review board of the Eye Research Center.

A detailed ophthalmic and medical history was obtained; in the medical history, we took a detailed history of all previous or current systemic diseases, particularly of arterial hypertension, diabetes mellitus, ischemic heart disease, strokes, transient ischemic attacks, carotid artery disease, hyperlipidemia, and vasculitis. Those patients without a clinical examination for hypertension or laboratory examinations for diabetes and hyperlipidemia during past year were referred for appropriate related examinations, and final results were recorded. A comprehensive ophthalmic evaluation was performed. This included recording the best corrected visual acuity using the Snellen visual acuity chart, color vision testing with Ishihara pseudoisochromatic plates, computerized perimetry with a Humphrey Field Analyzer (Carl Zeiss, Jena, Germany) using the SITA standard program 24-II, intraocular pressure (IOP) using the Goldmann applanation tonometer, slit-lamp examination of the anterior segment, lens and vitreous, direct and indirect ophthalmoscopy, stereoscopic color fundus photography, and, in acute cases, stereoscopic fluorescein fundus angiography. Visual fields were classified according to the methods for computerized analysis of the visual fields which has been described elsewhere.[12]

Statistical analyses were performed by Student's *t*-test for paired and unpaired data, χ^2, and Fisher exact tests. Statistical significance was considered as $P<0.05$.

Results

One hundred and seven patients including 66 men (61.7%) and 41 women (38.3%) with a mean±SD age of 52.7±10.3 (range: 30 – 80) years were included in this study. Most (62.2%) of the patients aged more than 50 years. The symptoms were present for a median of 14.5 (mean±SD: 29.8±63.5) days. Laterality of the eye involved, gender distribution, and the prevalence of systemic disease in different age groups are given in Table 1. Twenty-two (20.5% of total) patients had had an episode of NAION in the fellow eye before presentation. Overall, 51 (47.7%) patients had no evidence of a previous or current systemic disease. Diabetes mellitus had a prevalence of 40.1%, followed by hypertension (26.1%), and hyperlipidemia (20.5%). Of 43 diabetic patients, 33 had no sign of diabetic retinopathy and 10 had background diabetic retinopathy without macular edema. Seven (6.5%) patients reported a history of ischemic heart disease and one (0.9%) reported a previous stroke. Fifteen (14%) patients currently smoked cigarettes or had discontinued the use of cigarette. NAION was developed following cataract surgery in two (1.9%) patients.

Visual acuities were 20/200 or worse in 43 (40.1%) eyes and 20/40 or better in 43 (40.1%)

Table 1. Patients' demographics and the prevalence of systemic disease.

	≤45 years	45 – 65 years	≥65 years	Total
Number of patients	27	67	13	107
Gender (male/female)	13/14 (48.1%/51.9%)	42/25 (62.7%/37.3%)	11/2 (84.6%/15.4%)	66/41 (61.7%/38.3%)
Eye affected (right/left/both)	12/10/5 (44.4%/37%/18.5%)	31/24/12 (46.2%/35.8%/11.2%)	4/4/5 (30.7%/30.7%/38.4%)	47/38/22 (43.9%/35.5%/20.5%)
Previous or current systemic disease	9 (33.3%)	39 (58.2%)	8 (61.5%)	56 (52.3%)
Diabetes mellitus	5 (18.5%)	31 (46.2%)	5 (38.4%)	43 (40.1%)
Hypertension	3 (11.1)	19 (28.3%)	6 (46.1%)	28 (26.1%)
Hyperlipidemia	6 (22.2%)	12 (17.9%)	4 (30.7%)	22 (20.5%)

eyes (Figure 1). The mean±SD of visual acuities was 0.78±0.8 LogMAR in the NAION eyes, 0.68±0.54 LogMAR in the fellow eyes with previous attack of NAION (P=0.8), and 0.1±0.35 LogMAR in the noninvolved fellow eyes (P<0.001). Visual acuity was significantly (P=0.03) better in nondiabetic patients (0.62±0.69 LogMAR) compared to diabetics (0.96±0.84). However, no significant difference was found between hypertensive and normotensive patients (P=0.7) and between hyperlipidemic and non-hyperlipidemic patients (P=0.1). Fellow eye involvement was not significantly different between diabetics and nondiabetics (P=0.8).

Refractive errors ranged from spherical equivalents of +7 to -4.1 diopters (D), with a median of -0.12 D. The median refractive error of the fellow eye was statistically the same (0.00, P=0.5). IOP ranged from 9 to 20 mm Hg, with a mean±SD of 15±2.3 mm Hg. The mean±SD IOP of the fellow eye was 15.1±2.4 mm Hg (P=0.9).

Color vision testing revealed a median of six (range: zero to 14) plates. There was a significant correlation between visual acuity and color vision plates were seen (r^2=0.4, P<0.001).

Reliable visual fields were found in 76 (71%) eyes. The visual field analysis revealed that the mean deviation (MD) ranged from -32.6 to -1.3 dB with a mean±SD of -19.7±8.08 dB. The mean±SD of pattern standard deviation (PSD) was 9.5±4.1 dB (range: 1.99 – 16.07). The mean±SD of the MD of the noninvolved fellow eyes was -7.5±5.5 dB (P=0.002), with a PSD mean±SD of 7.1±4.1 dB (P=0.03). Diffuse defect was the most prevalent defect detected on 36.8% of visual fields (28/76) of the study eyes followed by inferior altitudinal defect (26.3%) and inferior arcuate (19.7%). In the fellow eyes without any evidence of prior optic nerve problem, inferior and superior arcuate scotoma were found in 30% and 20% of eyes, respectively; 50% had normal visual fields. Other less common defects included superior altitudinal (7.8%), superior arcuate (7.8%), and absolute scotoma (1.3%). There was no significant difference between MD in diabetics and nondiabetics (P=0.8). The pattern of visual field defect was the same for both groups (P=0.3).

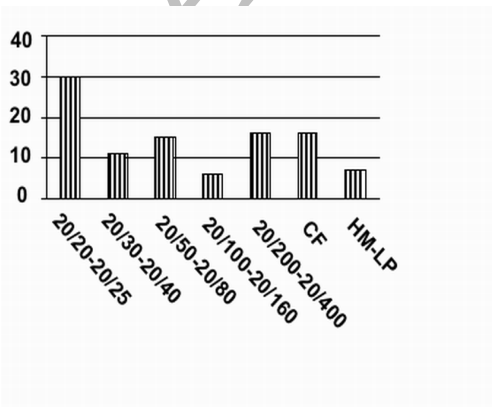

Figure 1. Number of the patients in different visual acuity categories.

Discussion

The classification of ischemic optic neuropathies distinguishes between the anterior and posterior type, with the latter being much rarer and characterized by the absence of optic disc edema, and arteritic and NAION. The casual definition of NAION is that of a sudden, painless, unilateral, and irreversible ischemic event of the intraocular optic nerve without associated systemic disease, which has no effective treatment.[8] Almost every aspect of the definition and characteristics of NAION has been the subject of intense, often heated discussion. In fact, there are numerous publications on NAION that directly and sharply contradict a previous, well-researched article in the literature.[5,8,10] The intent of this study was to provide an overview of the current status of NAION on clinical presentation and associated systemic diseases in an Iranian population.

NAION typically occurs after the age of 50 years, with most series reporting a mean age

between 60 and 70 years.[8,9,11] Although cases in younger patients, and even in children are well-documented, the prevalence of NAION in young population in our study (37.8% with an age of ≤50 years) is higher than those previously reported.[6,13,14] This may be due to the referral bias. Younger patients with NAION may refer more frequently than older patients for diagnostic and systemic evaluation. Nevertheless, we agree with Preechawat et al.[13] that NAION in younger patients is not uncommon. It has been proposed that when NAION occurs in a young patient, it is often the result of an underlying condition predisposing the patient to vascular insufficiency, such as diabetes mellitus, end-stage renal disease under treatment with dialysis, hypotension, or anemia.[6,13] However, the prevalence of systemic diseases in our study was lower in younger patients. This suggests that the ocular factors (i.e., optic disc structure) may be more important than systemic associations in the development of NAION in this age group. Even so, these patients require a thorough systemic evaluation for potentially treatable underlying vascular risk factors.

NAION in both eyes has been reported in as few as 10.5% and as many as 73% of patients.[15] Twenty-three percent of the patients in the Ischemic Optic Neuropathy Decompression Trial (IONDT) initially had contralateral optic disc pallor, which suggested possible previous NAION, although only 15% of patients reported a previous diagnosis of NAION.[9] In the present study, NAION in both eyes was detected in 20.5% of the patients.

The prevalence of systemic disease in our patients is similar to that reported by others.[3,6,9,11,14–18] Fifty-two percent of our patients had one or more risk factors thought to be associated with small-vessel cerebrovascular disease, including hypertension, diabetes mellitus, hyperlipidemia, and cigarette smoking. Twenty-six percent of our patients had systemic hypertension compared with 26% to 47% in other studies,[6,9,11,14] and 40% had a diagnosis of diabetes mellitus compared with 10% to 31%,[6,9,11,14,18] in other reports. We are not able to judge whether this percentage is higher than what would be found in the population in general, since our study was not designed to examine this association and did not include a control population. However, the prevalence of hypertension and diabetes in Iran has been reported to be 25% and 5.5%, respectively.[19,20] Although the prevalence of hypertension is nearly the same, diabetes was obviously more prevalent among our patients.

Among those studies that have provided visual acuity data from the initial appearance of symptoms, 43% to 47% of patients had an initial visual acuity better than 20/40. [9,11,19] Since visual loss in patients with NAION may progress throughout days or weeks from the onset, and spontaneous visual recovery of three lines or more occurs in approximately 43% of patients at six months,[9] some patients' visual acuities may have deteriorated or improved by the time of the reported measurement. The distribution of visual acuities among patients in our study was similar to that reported by other studies.[11,9,16,18] For example, 40% of our patients had baseline visual acuities of 20/200 or worse compared with 35% to 53% reported in other studies.

Eagling et al.[16] compared a subgroup of patients with NAION and no evidence of systemic or retinal vascular disorders with the entire cohort; they found 75% of the patients with "no related disease" had visual acuities better than 20/40 compared with 51% of the whole group. In contrast, Boghen and Glaser[17] reported no difference in the course of visual deficit in patients with or without hypertension who had NAION. In a large cohort of patients, Hayreh and Zimmerman[18] reported that the initial visual acuity did not differ significantly between diabetic and non-diabetic patients. Our results showed better visual acuities in nondiabetic patients compared to diabetics; however, no difference was noted in the visual acuities in patients with or without hypertension, and patients with or without hyperlipidemia.

Refractive error of patients with NAION has been reported within studies of other anatomic predispositions. Beck et al.[21] reported the role of cup to disc ratio in the pathogenesis of NAION. In their data, hyperopia was more prevalent in the NAION patients than the control group. Similarly, Katz and Spencer[22] reported that patients with NAION are less myopic than the control population. In contrast, the mean refractive error of our patients was not in the range of hyperopia.

The classic presentation of NAION often involves the sudden loss of lower or, less commonly, upper visual field. Central scotomas, arcuate defects, and quadrantic defects may also occur.[7] Repka and colleagues[11] tabulated the location and type of visual field defect by Goldmann perimetry and found that 46% of

NAION patients had an inferior altitudinal defect and 20% had isolated central scotomas. Hayreh and Podhajsky[23] reported inferior nasal or inferior altitudinal defects in 57% of NAION patients and central scotoma in 25%. Traustason and colleagues[24] quantitatively classified field defects performed by Octopus perimetry and found that, although 55% of AION patients demonstrated a significant altitudinal field loss, the "spared" hemifields routinely showed some loss of sensitivity. Hayreh and Zimmerman[25] reported a combination of relative inferior altitudinal defect with absolute inferior nasal defect as the most common pattern in the initial presentation in patients with NA-AION. Feldon[12] evaluated the pattern and within-pattern severity of field defects for study eyes included in IONDT at the baseline and six-month follow-up. He identified 14 different types of visual fields. Based on this report, the most common pattern of defect was a superior and inferior arcuate with central scotoma for randomized eyes (19.2%) and a superior and inferior arcuate for nonrandomized eyes (30.6%), and the field patterns at six months and baseline were not different. In the present study, a pure field defect confined to the upper or lower hemisphere was relatively unusual. This is consistent with prior observations that automated perimetry frequently demonstrates defects, even in asymptomatic hemifields.[12,24] The clinical perception that field involvement is primarily altitudinal is likely derived from differential severity of involvement in the upper and lower hemifields and by ignoring the presence of central scotoma.

One surprising result of this study was the high percentage of abnormal patterns of visual fields in eyes without optic neuropathy. This finding was also reflected in the depressed mean deviation for the group. The vast majority of anomalous patterns were mild superior or inferior arcuate defects. These may have been artifactual, owing to learning effects, or secondary to nonoptic nerve-related eye disease that differed from the age-matched normal population included in the Humphrey Visual Field normative data set. Our finding supports Feldon's report[12] that clinically normal fellow eyes may have abnormal field defects. He reported mild superior and/or inferior arcuate defects in about three-quarters of nonstudy eye visual fields and proposed that the crowding associated with a disk at risk may be capable of producing minimal, clinically unapparent, acute or chronic axonal loss, and corresponding field defect.

Several limitations of the present study should be addressed, most of which related to the nature of large retrospective analyses. Existing medical diagnoses occasionally were made based on the patient's report, not by strict assessment of medical data. Selection bias may reduce the precision of the results. Absence of age- and sex-matched control group precludes definitive conclusions. In addition, to describe the complete clinical profile, longterm follow-up of patients is needed.

In conclusion, we found NAION in a population of Iranian patients to be similar in many ways to NAION as described in previous studies, with the exception of higher proportion of younger patients and a higher propensity for diabetes. NAION should be considered in the differential diagnosis of younger patients with a painless optic neuropathy with disk edema at presentation. These patients require a thorough systemic evaluation for underlying vascular risk factors.

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