Nonarteritic anterior ischemic optic neuropathy in young patients

Neuropathie optique ischémique antérieure non artéritique chez les jeunes patients

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Summary

Purpose. — To determine and report the demographic and clinical features of patients younger than 50 years with nonarteritic anterior ischemic optic neuropathy (NAION).

Material and methods. — In this comparative study, we retrospectively reviewed the medical records of 120 patients with NAION. Patients were divided into two groups according to their age: in group I, 44 patients were younger than 50 years, and in group II, 76 patients were older than 50 years.

Results. — The gender distribution was similar in both main groups. Involvement was bilateral in 50% and 26.3% of patients, respectively ($P < 0.0001$). Diabetes mellitus was present in 63.6% of patients in group I and 47.3% of patients in group II ($P = 0.009$). We found hypertension as a frequent risk factor in group II ($P = 0.019$). There was no significant difference in the initial and final visual acuities of patients between the two groups. Both groups had a significantly thinner peripapillary nerve fiber layer (RNFL) in every quadrant. The relative loss was greatest in the superior quadrant in both groups. We generally observed inferior altitudinal defect and superior RNFL thinning in two groups. In group I, 30 eyes (68.1%) demonstrated angiographically diffuse optic disc filling delay of $\geq 5$ seconds after choroidal filling confirming ischemia, and 14 (31.8%) eyes with segmental optic disc filling delay. In group II, diffuse optic disc filling delay was seen in 56 of 76 (73.6%) eyes. Segmental optic disc filling delay was present in 20 eyes (26.3%). There was no significant difference in angiographic findings between the two groups ($P = 0.67$).

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Conclusion. — We observed that age did not play a significant role in prognosis of NAION. Diabetes is an increased risk for NAION in the young age group, and HT for NAION in the older group. Fellow eye involvement is more frequent in young patients. These patients should be followed closely.

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Introduction

Non-arteritic anterior ischemic optic neuropathy (NAION) is an acute optic neuropathy characterized by the sudden onset of visual loss with optic disc edema [1–3]. The most common risk factors are vascular disorders such as diabetes mellitus (DM), systemic hypertension (HT), hyperlipidemia and smoking [4–6]. For this reason, it frequently occurs in the elderly. In the endurance studies, the mean age at onset ranges from 55 to 68 years [4,6,7]. Until now, Deramo et al. reported 43 cases with NAION under the age of 50, and compared them with a control group without NAION [8]. Preechawat et al. identified the demographic and clinical features of 169 patients with NAION younger than 50 years [9]. However, previous studies have not directly compared comorbid conditions, clinical presentation, ophthalmic findings including ancillary testing such as fundus fluorescein angiography (FFA) and optic coherence tomography (OCT), and outcomes between the young and older groups [8,9].

In this comparative study, we aimed to report the demographic, clinical features, and evaluation of FFA, OCT, perimetry of patients younger than 50 years with NAION.

Material and methods

We retrospectively reviewed the medical records of 120 patients with NAION seen at the Department of Ophthalmology, Akdeniz University since 2009. The study was approved by the ethics committees of the institution and was conducted in accordance with the Declaration of Helsinki. Patients who had sudden visual loss, edematous optic disc appearance and characteristic visual field defects were included in the study. Patients who had any disorder which might affect visual acuity such as...
cataract, glaucoma, retinal or optic nerve diseases were excluded. When giant cell arteritis was suspected, complete blood cell count, erythrocyte sedimentation rate and C-reactive protein analysis were obtained to rule out arteritic type of anterior ischemic optic neuropathy. Particularly in patients younger than 50 years were differentiated from other neuro-ophthalmologic conditions (e.g. demyelinating optic neuritis, vasculitic or infectious optic nerve inflammation) with magnetic resonance imaging.

Patients were divided into two groups according to their age; in group I (NAIONy), 44 of patients were younger than 50 years and in group II (NAIONo), 76 patients were older than 50 years. At the initial examination, a detailed history was taken about other systemic diseases and medications. The eye examination included initial and final visual acuity with Snellen charts, pneumatic tonometry, slit-lamp biomicroscopy, fundus examination, color vision evaluation with Ishihara color plates, Humphrey’s automated perimetry (30-2 central threshold test) (Model 750 Humphrey Field Analyzer II, Carl Zeiss Meditec, USA), retinal nerve fiber layer thickness (RNFLT) analysis with OCT (Topcon Medical Systems, Paramus, NJ) and angiography. Age, sex, etiology and laterality of first episode were recorded. Outcome measures were visual acuity, visual field defects, color vision, relative afferent pupillary defect (RAPD), RNFLT, and angiographic findings.

Statistical analysis was performed using the SPSS 17.0 program (SPSS Inc., Chicago, IL). To compare the demographic and clinical variables between two groups, the Pearson χ² test was used. Wilcoxon rank-sum test was used to compare the visual acuity, RNFL thinning and visual field defect between the groups. P-values less than 0.05 were considered as statistically significant.

**Results**

The demographic and clinical characteristics of patients and risk factors were summarized in Table 1. The gender distribution was similar in both main groups. There was DM in 63.6% of patients in group I and 47.3% of patients in group II. There was statistically significant difference between the two groups (P = 0.009). We found frequently HT as a risk factor in group II (P = 0.019). The rate of fellow eye involvement in NAION is higher (50%) in group I (P < 0.0001). The time to fellow eye involvement is shorter (2.6 years) in young patients than olds. But there was not significant difference (P = 0.264).

The initial and final visual acuities of patients were summarized in Table 2. There was no significant difference in visual acuities between the two groups.

Visual field defects and RNFL thickness loss at final visit were summarized in Table 3. The both groups had a significantly thinner peripapillary nerve fiber layer in every quadrant. The relative loss was greatest in the superior quadrant. In both groups, we generally observed inferior altitudinal defect and superior RNFL thinning.

At initial examination in group I, 30 eyes (68.1%) with FFA demonstrated diffuse optic disc filling delay of ≥5 seconds after choroidal filling confirming an ischemia, and 14 (31.8%) eyes with segmental optic disc filling delay (Fig. 1A and B). In group II, diffuse optic disc filling delay was seen in 56 of 76 (73.6%) eyes. Segmental optic disc filling delay was present in 20 eyes (26.3%). There was no significant difference in angiographic findings between the two groups (P = 0.67) (Fig. 2).

**Discussion**

The aim of our study was to investigate the demographic and clinical features of patients younger than 50 years with NAION. And we observed that they have a higher rate of fellow eye involvement; and more associated with DM as a risk factor than NAION age 50 or older. There were no significant differences in clinical findings (visual field defects, OCT and FFA findings) and prognosis of disease (visual acuity).

We observed NAION in 44 (36.6%) patients under age of 50. Preechawat et al. reviewed 727 patients with NAION, finding 169 (23.2%) in young patients [9]. Arnold et al. found NAION in 12.7% of their patients under age of 50 [4]. All these data confirm that NAION is not rare under age of 50. Generally, NAION was diagnosed in younger patients as optic neuritis. For this reason, NAION in patients under age 50 was known as rare. Non-arteritic anterior ischemic optic neuropathy, among young patients, must be differentiated from demyelinating, vasculitic or infectious optic nerve inflammation, and optic nerve compression. Neuroimaging usually is adequate for excluding other diseases.

The exact pathophysiology of disease is unclear. Diseases such as DM, HT and hyperlipidemia may predispose to occlusion of the vascular supplement of the optic nerve head [10,11]. We attempted to identify which risk factors were more frequent in the NAIONy group. In our study, we found frequently DM as a risk factor in NAION under age 50 and HT in older group. In previous studies, DM is the major risk factor in all age groups and is present in approximately 1 in 4 patients [8–12]. Deramo et al. identified 43 (7.5%) of 577 cases of NAION under age 50, comparing them with regard to vasculopathic risk factors to a control group of age- and gender-matched patients without NAION [8]. Hyperlipidemia and DM were significantly more frequent in the NAION patients than controls. In the study of Arnold et al., DM was present in 15 of 108 (14%), hyperlipidemia in 34 of 108 (47%), smoking in 27 of 108 (27%), anemia in 8 of 108 (9%), and HT in 35 of 108 (32%). They observed that NAIONy was significantly more frequently associated with hyperlipidemia and HT but not with DM. Similarly with our study, the NAIONy group demonstrated unusually high rates of both HT (55/108, 50.9%) and hyperlipidemia (36/57, 63.2%) [4].

In NAIONy, bilateral involvement occurred in 38–42% patients of the previous series [9,12,13]. Fellow eye involvement was associated with diabetes, but no other vasculopathic risk factors in the NAION [14–18]. In the study of Arnold et al., bilateral involvement occurred in 46 (42.6%) of 108 patients with NAIONy, compared to 32 (29.6%) of 108 patients with NAIONo (P = 0.047), a statistically significant difference [4]. They also suggested that DM is a more important risk factor for fellow eye involvement in NAIONy than in NAIONo. In our study, the rate of fellow eye involvement in NAION is higher (50%) and time to fellow eye involvement is shorter (2.6 years) in young patients than olds. Our higher results may be associated with the higher prevalence of DM in NAIONy.
Table 1  The demographic and clinical characteristics of patients.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>P-value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male (%)</strong></td>
<td>24 (55%)</td>
<td>46 (60%)</td>
<td>0.625</td>
</tr>
<tr>
<td><strong>Mean age (years)</strong></td>
<td>46 ± 12.9 (range 38—49)</td>
<td>64.1 ± 13.1 (range 51—84)</td>
<td>0.810</td>
</tr>
<tr>
<td><strong>Follow-up time (month)</strong></td>
<td>30.1 ± 17.2 (range 2—60)</td>
<td>32.8 ± 18.6 (range 2—52)</td>
<td>0.168</td>
</tr>
<tr>
<td><strong>Laterality</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral involvement</td>
<td>22 (50%)</td>
<td>56 (73.6%)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Bilateral involvement</td>
<td>22 (50%)</td>
<td>20 (26.3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Time to involvement of second eye (year)</strong></td>
<td>2.6 ± 5.2 (range 1.5—7)</td>
<td>3.8 ± 8.2 (range 1.3—11.2)</td>
<td>0.264</td>
</tr>
<tr>
<td><strong>Etiology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>28 (63.6%)</td>
<td>36 (47.3%)</td>
<td>0.009</td>
</tr>
<tr>
<td>Hypertension</td>
<td>16 (36.3%)</td>
<td>40 (52.6%)</td>
<td>0.019</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>24 (54.5%)</td>
<td>44 (57.8%)</td>
<td>0.733</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>6 (13.6%)</td>
<td>16 (21.05%)</td>
<td>0.165</td>
</tr>
<tr>
<td>TIA/CVA</td>
<td>4 (9.09%)</td>
<td>2 (12%)</td>
<td>0.820</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>1 (2.3%)</td>
<td>2 (2.6%)</td>
<td>0.880</td>
</tr>
<tr>
<td>Hypercoagulable disorders</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>16 (36.3%)</td>
<td>28 (36.8%)</td>
<td>0.990</td>
</tr>
<tr>
<td>Crowded disc</td>
<td>38 (86.3%)</td>
<td>62 (81.5%)</td>
<td>0.760</td>
</tr>
<tr>
<td><strong>Color vision</strong></td>
<td>3.6 ± 3.2/12</td>
<td>3.9 ± 3.6/12</td>
<td>0.230</td>
</tr>
<tr>
<td><strong>RAPD</strong></td>
<td>24 (54.5%)</td>
<td>36 (47.3%)</td>
<td>0.450</td>
</tr>
</tbody>
</table>

RAPD: relative afferent pupillary defect.
\(^a\) Chi\(^2\) test.

Table 2  The initial and final visual acuities.

<table>
<thead>
<tr>
<th>Visual acuity</th>
<th>Group I</th>
<th>Group II</th>
<th>P-value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 20/200</td>
<td>12 (27.2%)</td>
<td>26 (34.2%)</td>
<td>0.276</td>
</tr>
<tr>
<td>20/50-20/100</td>
<td>24 (54.5%)</td>
<td>38 (50%)</td>
<td>0.310</td>
</tr>
<tr>
<td>≥ 20/40</td>
<td>8 (18.1%)</td>
<td>12 (15.7%)</td>
<td>0.810</td>
</tr>
<tr>
<td><strong>Final</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 20/200</td>
<td>12 (27.2%)</td>
<td>20 (26.3%)</td>
<td>0.760</td>
</tr>
<tr>
<td>20/50-20/100</td>
<td>12 (27.2%)</td>
<td>18 (23.6%)</td>
<td>0.540</td>
</tr>
<tr>
<td>≥ 20/40</td>
<td>20 (45.4%)</td>
<td>38 (50%)</td>
<td>0.480</td>
</tr>
</tbody>
</table>

\(^a\) Wilcoxon rank-sum test.

Table 3  Visual field defects and retinal nerve fiber layer thinning in groups.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>P-value</th>
</tr>
</thead>
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<tr>
<td><strong>Visual field defects</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior altitudinal defect</td>
<td>20 (45.4%)</td>
<td>32 (42.1%)</td>
<td>0.450</td>
</tr>
<tr>
<td>Diffuse visual field defect</td>
<td>16 (36.3%)</td>
<td>24 (31.5%)</td>
<td>0.310</td>
</tr>
<tr>
<td>Peripheric defects</td>
<td>6 (13.6%)</td>
<td>12 (15.7%)</td>
<td>0.660</td>
</tr>
<tr>
<td>Superior altitudinal defect</td>
<td>2 (4.5%)</td>
<td>6 (7.8%)</td>
<td>0.272</td>
</tr>
<tr>
<td>Central scotoma</td>
<td>—</td>
<td>2 (2.6%)</td>
<td>0.184</td>
</tr>
<tr>
<td><strong>RNFL thinning</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior</td>
<td>32 (72.7%)</td>
<td>48 (63.1%)</td>
<td>0.275</td>
</tr>
<tr>
<td>Inferior</td>
<td>16 (36.3%)</td>
<td>28 (36.8%)</td>
<td>0.810</td>
</tr>
<tr>
<td>Temporal</td>
<td>28 (63.6%)</td>
<td>40 (52.6%)</td>
<td>0.196</td>
</tr>
<tr>
<td>Nasal</td>
<td>20 (45.4%)</td>
<td>32 (42.1%)</td>
<td>0.672</td>
</tr>
</tbody>
</table>
In our study, both groups had similar visual acuity and visual field improvement. Similarly, the authors suggested that age did not play a significant role in prognosis of NAION in their studies [3,4,9].

The relatively small number of subjects is a limitation to this study. However, the low incidence of NAION, makes a study with more patients very difficult. Also, the retrospective nature of our study limits the strength of our conclusions. Unlike the previous studies, the advantage of this study, a cohort of patients aged 50 or older with NAION was included.

In conclusion, we have compared the demographic and clinical features of NAION in younger and older patients than 50 years. We observed that age did not play a significant role in prognosis of NAION. Diabetes is an increase risk for the NAION in young patients and HT for the NAION in old patients. Fellow eye involvement is more frequent in young patients. For this reason, these patients should be followed closely.

Disclosure of interest
The authors declare that they have no conflict of interest concerning this article.

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[4] Arnold AC, Costa RMS, Dumitrascu OM. The spectrum of optic disc ischemia in patients younger than 50 years (an American


