Clinical Profile of Non-Arteritic Anterior Ischaemic Optic Neuropathy in India and Factors Predictive of Visual Outcome

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Received: April 09, 2016; Published: May 14, 2016

Abstract

Purpose: To evaluate the clinical profile of non arteritic anterior ischemic optic neuropathy (NA-AION) in India and examine factors predictive of visual recovery.

Design: Prospective observational case control study of 40 NA-AION patients and 40 age and gender matched controls conducted at an apex eye care centre.

Methods: Demographic data of 40 consecutive NA-AION patients and age matched controls was recorded. Comprehensive ophthalmic evaluation including detailed history with emphasis on systemic diseases was performed and ophthalmic investigations (colour vision, contrast sensitivity, visual fields, VER and OCT) were done at presentation and over 3 months follow up.

Results: The mean age of patients was 51.2 ± 7.8 years with a male predominance (60%) and the mean presenting visual acuity was 1.5 ± 1 LogMAR units. While 16 patients (40%) had no systemic associations, the remaining had diabetes mellitus (20%), hypertension (20%) or multiple risk factors (20%). Visual acuity, colour vision and contrast sensitivity improved significantly at 1 month follow up (p value <0.001, 0.05 and 0.05 respectively) with no further improvement at 3 months. Eighteen patients (45%) showed spontaneous visual recovery on follow up. Mean baseline visual acuity parameters were similar in patients with or without systemic disease (P= 0.2), but the latter improved more on follow up (P= 0.03). Patients with a central involvement on visual fields showed insignificant improvement (P= 0.12). Presenting visual acuity, age, VER or OCT parameters did not affect the final visual outcome.

Conclusion: NA-AION patients in India are younger than the west and show significant spontaneous visual recovery. Presence of a systemic risk factor and a centre involving visual field loss predicts a poorer visual recovery.

Keywords: Optic neuropathy; Visual prognosis; OCT; NAION; Ischemic optic neuropathy

Introduction

Non arteritic anterior ischemic optic neuropathy (NA-AION) is an important cause of vision loss in the elderly and is believed to result from small vessel disease of the optic nerve causing transient non-perfusion or hypo perfusion of the optic nerve head. Risk factors for NA-AION include hypertension, diabetes mellitus, hyperlipidemia and hypercholesterolemia among many others [1]. While vision improves in 41-43% of patients within 2 weeks of onset of visual loss, no definite prognostic factors have been identified to predict the same [2,3]. The profile of NA-AION in Indian patients has never been studied and it likely differs from the west. This study evaluates the clinical profile of NA-AION patients in the Indian scenario including the demographic details and course of illness while attempting to define parameters which may predict visual recovery and prognosis.

Methods

A prospective case control study was conducted at a tertiary level eye care institution after prior approval from the ethics committee.

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The study recruited 40 consecutive patients of acute NA-AION (cases) who were diagnosed in the neuro-ophthalmology clinic based on predetermined criteria (given below). A control group of 40 age and gender matched individuals with no ocular pathology was included in the study for comparison of risk factor profile. The cases were followed up for a period of 3 months to document the course of recovery. A written informed consent for participation in the study was obtained from all patients and subjects.

Cases were diagnosed to have acute NA-AION if they (1) presented with sudden loss of vision within the preceding month, (2) had sectoral or diffuse disc edema (hyperaemic or pallid), (3) had field defects corresponding with the disc changes (4) demonstrated delayed choroidal filling in the prelaminar and peripapillary region on fundus fluorescein angiography and (4) had no other ocular or systemic conditions explaining the clinical findings. In addition, the presence of a small crowded disc in the fellow eye was documented as a secondary marker to ascertain the diagnosis [1-4].

Patients having symptoms suggestive of an arteritic anterior ischemic optic neuropathy including scalp tenderness, jaw claudication or temporal headaches along with presence of an elevated erythrocyte sedimentation rate (ESR) and high C-reactive protein levels were excluded, as were those with a bilateral presentation. Exclusion criteria for subjects in the control group included presence of an ocular or systemic pathology (including diabetic or hypertensive retinopathy) likely to cause visual deficit and confound ocular findings.

Demographic data of the cases and controls was recorded. A detailed ophthalmic and medical history was obtained from the patients at the first visit. In specific, the history focussed upon potential systemic illnesses (diabetes mellitus, hypertension and hyperlipidemia) and details of the ocular presentation. A systemic examination focussing on possible risk factors was performed including a complete cardiovascular examination. Systemic investigations including blood sugar and lipid profile were done in all patients. A comprehensive ophthalmic examination was performed to ascertain the diagnosis and record baseline values of visual acuity (Snellen’s acuity and Log MAR). Specific investigations performed among all cases and controls included colour vision (using Ishihara pseudo isochromatic plates), contrast sensitivity (using Pelli Robson chart), visual evoked potential (Nikoledt Ganzfeld stimulator), visual fields (Goldmann kinetic perimetry), optical coherence tomography (optic nerve head analysis protocol of the Cirrus HD-OCT, Carl Zeiss Meditec) and fundus fluorescein angiography. To avoid observational bias, specific parameters for improvement or worsening were established for subjective investigations like Goldman kinetic perimetry where a change of 10 degree or more of field was considered significant.

All investigations except fundus fluorescein angiography were repeated at 1 month and 3 month follow-up. Apart from control of risk factors and a multivitamin tablets, no specific therapy was given to any of the cases. The data was collected by a blinded observer and recorded in a prescribed format and statistical analysis was done using SPSS software (IBM Inc, Chicago, Il, USA) using appropriate parametric and nonparametric tests. P value of < 0.05 was taken as significant.

Results

The mean age for cases was 51.2 +/- 7.8 years while that for controls was 55.2 +/- 6.3 years, (T Test, p= 0.56) with both groups having an age range from 31-80 years. There was a slight male preponderance in both groups with 24 males: 16 females among the cases and 22 males: 18 females among the controls. (Mc Nemar; p= 0.5).

Among the cases, a systemic disease was seen in 24 patients [diabetes mellitus (8), hypertension (8), diabetes with associated hypertension and/or hyperlipidemia (8), isolated hyperlipidemia (0)], while 16 had no identifiable systemic vascular risk factor (Table 1).

The median presenting visual acuity of cases was 1.5 LogMAR units as against 0.2 LogMAR units for controls (Mann Whitney U, p= 0.02). Final visual acuity at three months improved to 0.8 LogMAR units. (Mann Whitney U, p < 0.05). The most common field defect seen was the inferonasal field defect (12 patients), followed by a centre involving field loss (10 patients) and a superior altitudinal defect (6 patients). Five patients presented with a generalised visual field depression while 4 had a pure altitudinal defect and 2 had a combination of two of these defects mentioned above (Table 1).

The VER showed increased mean latency and a normal mean amplitude (t Test, P= 0.001 and 0.13 respectively) (Table 2).

Clinical Profile of Non-Arteritic Anterior Ischaemic Optic Neuropathy in India and Factors Predictive of Visual Outcome

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Total (% Total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>40</td>
</tr>
<tr>
<td>Gender ratio: Male(M): Female(F)</td>
<td>24 (60%): 16 (40%)</td>
</tr>
<tr>
<td>Age at presentation</td>
<td>51.2 +/- 7.8 years (range: 30-80 years)</td>
</tr>
</tbody>
</table>

Associated Systemic Illness

- Diabetes mellitus: 8 (20%)
- Hypertension: 8 (20%)
- Diabetes and hypertension: 6 (15%)
- Diabetes and hypertension and hyperlipidemia: 2 (5%)
- Hyperlipidemia: 0 (0%)
- None: 16 (40%)

Mean visual acuity: 1.5 ± 1.1 log MAR units (range: No PL to 6/9)
Mean colour vision (no. of plates read): 5.4 ± 6
Mean contrast sensitivity: 0.0 ± 0.4

Visual Fields

- Inferonasal field defect: 12 (30%)
- Central involving field loss: 10 (25%)
- Superior altitudinal defect: 06 (15%)
- Generalised depression: 05 (12.5%)
- Inferior altitudinal: 04 (10%)
- Inferonasal and centre involving field defectscotoma: 02 (5%)
- Non-documentable: 01 (2.5%)

### Table 1: Clinical Features of NA-AION Patients at Presentation.

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Affected Eye</th>
<th>Fellow Eye</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Affected Eye v/s Control</td>
</tr>
<tr>
<td>Visual Acuity (Log MAR)</td>
<td>0.2 ± 0.1</td>
<td>1.5 ± 1.1</td>
<td>0.2 ± 0.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No. of Ishihara plates read</td>
<td>26 ± 3</td>
<td>3 ± 6</td>
<td>18 ± 6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Contrast sensitivity</td>
<td>1.5 ± 0.2</td>
<td>0.0 ± 0.4</td>
<td>1.2 ± 0.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>VER latency</td>
<td>96.2 ± 6.8</td>
<td>118.8 ± 15.8</td>
<td>100.6 ± 15.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>VER amplitude</td>
<td>4.8 ± 1.2</td>
<td>4.9 ± 2.8</td>
<td>5.0 ± 3.0</td>
<td>0.3</td>
</tr>
<tr>
<td>Average RNFLT</td>
<td>88.2 ± 8.2</td>
<td>114.1 ± 60.2</td>
<td>85.2 ± 20.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Superior RNFLT</td>
<td>121.1 ± 108.0</td>
<td>124.2 ± 94.3</td>
<td>116.6 ± 110</td>
<td>0.5</td>
</tr>
<tr>
<td>Inferior RNFLT</td>
<td>122.2 ± 146.6</td>
<td>144.8 ± 88.6</td>
<td>116.2 ± 28</td>
<td>0.1</td>
</tr>
<tr>
<td>Nasal RNFLT</td>
<td>69.0 ± 11.2</td>
<td>102.8 ± 66.4</td>
<td>66.1 ± 16.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Temporal RNFLT</td>
<td>62.8 ± 12.2</td>
<td>72.2 ± 51.9</td>
<td>58.4 ± 10.8</td>
<td>0.3</td>
</tr>
</tbody>
</table>

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Rim area in mm² | 1.6 ± 0.2 | 2.0 ± 0.4 | 1.47 ± 0.41 | 0.2 | 0.6
Disc area in mm² | 2.4 ± 0.5 | 2.3 ± 0.6 | 2.1 ± 0.4 | 0.8 | 0.048
Vertical cup: disc ratio | 0.4 ± 0.6 | 0.4 ± 0.3 | 0.4 ± 0.2 | 0.01 | 0.01
Cup volume (mm³) | 0.4 ± 0.8 | 0.08 ± 0.2 | 0.2 ± 0.03 | < 0.001 | 0.3

Table 2: Baseline Visual, Optic Disc, RNFL and Electrophysiological Parameters in Patients of NA-AION and Controls.

Eighteen patients (45%) showed a significant visual recovery (defined as an improvement of at least 3 lines on Snellen's acuity chart, representing a LogMAR change of 0.3) on follow up [4]. Visual acuity, colour vision and contrast sensitivity improved significantly at 1 month (p < 0.001, 0.05 and 0.05 respectively) with no further improvement at the three month follow up visit (p= 0.08, 1.0 and 0.16 respectively). VER amplitude and latency did not show any significant change on follow up (Paired t Test, p= 0.1 and 0.5 respectively). Ten patients (25%) had an improvement in visual fields on follow up. None of the patients reported a deterioration of visual acuity during the follow up.

The mean RNFL was thickened in all quadrants in the affected eyes, however statistical significance was found only in the nasal quadrant (t Test, p= 0.03). The RNFL thinned over time and was significantly thinner than controls in all quadrants after 3 months of acute vision loss (p= 0.02 for temporal and < 0.001 for all other quadrants). The disc area and cup to disc ratio of the fellow NA-AION eyes were significantly smaller than controls (Mann Whitney; P= 0.048 and 0.01). (Table 2) The mean RNFL was thin in all quadrants at the final follow up and while it apparently seemed to be more affected in the hemifield corresponding to visual field loss, this difference did not achieve statistical significance (p= 0.07).

Among the cases, a subgroup analysis was conducted wherein the patients were divided into two groups, one with systemic disease and the other without any systemic disease. The baseline visual acuity was similar between the two groups (P= 0.2), but the group with associated disease showed significantly lesser improvement on follow up (P= 0.03) (Table 3). Likewise, the systemic disease group apparently had a poorer recovery of colour vision and contrast sensitivity though it did not achieve statistical significance (p= 0.3/0.07, 0.1/0.02 and 0.1/0.03 at 0, 1 and 3 months respectively). Also, significantly lesser number of patients with systemic illness showed spontaneous recovery (P= 0.02) (Table 4).

Subgroup analysis based on different clinical parameters revealed that while presenting visual acuity did not have a bearing on final outcome (baseline vision < 6/60 v/s baseline vision ≥ 6/60; p= 0.1), presence of a central field loss on the visual field resulted in a significantly poorer baseline visual acuity and insignificant improvement (p= 0.01 and 0.12 respectively) (Table 3 and 4). Patients with age above or below 50 years showed similar improvement (P= 0.7). There was no significant bearing of VER amplitude, VER latency and OCT optic nerve head parameters on visual recovery.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Systemic Illness (a)</th>
<th>No Systemic Illness (b)</th>
<th>P value (a vs b)</th>
<th>Centre involving field defect (c)</th>
<th>Non centre involving field defect (d)</th>
<th>P value (a vs b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1.7 ± 1.2</td>
<td>1.1 ± 0.6</td>
<td>0.2</td>
<td>1.9 ± 0.9</td>
<td>0.9 ± 0.6</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>1 month follow up</td>
<td>1.6 ± 1.0</td>
<td>0.7 ± 0.6</td>
<td>0.046</td>
<td>1.8 ± 0.7</td>
<td>0.8 ± 0.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>3 month follow up</td>
<td>1.4 ± 1.1</td>
<td>0.7 ± 0.2</td>
<td>0.03</td>
<td>1.7 ± 0.3</td>
<td>0.7 ± 0.6</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Table 3: Visual Acuity Changes in Subgroup Analysis.

<table>
<thead>
<tr>
<th>Age ≤ 50 years</th>
<th>Patients Who Improved</th>
<th>Patients Who Did Not Improve</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≤ 50 years</td>
<td>7/18</td>
<td>11/22</td>
<td>0.69</td>
</tr>
<tr>
<td>Male gender</td>
<td>10/18</td>
<td>14/22</td>
<td>0.76</td>
</tr>
</tbody>
</table>

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| Table 4: Comparison of Visual Parameters in Patients with and without Improvement (Pearson Chi Square, Mann Whitney and Fischer’s Exact Test). |
|--------------------------------------------------|-----------------|-----------------|-----------------|
| Systemic disease | 6/18 | 20/22 | 0.01 |
| Vn < 6/60 | 6/18 | 14/22 | 0.14 |
| Centre involving field defect | 4/18 | 12/22 | 0.12 |
| Colour vision (No. of plates) | 7/24 | 5/24 | 0.50 |
| Contrast sensitivity | 0.4 ± 0.04 | 0.2 ± 0.08 | 0.5 |
| VER latency | 118.5 ± 14.7 | 118.2 ± 16.8 | 0.8 |
| VER amplitude | 4.9 ± 2.6 | 5.0 ± 2.2 | 0.4 |
| Average RNFL thickness | 104.8 ± 42.2 | 132.6 ± 82.8 | 0.5 |
| Superior RNFL thickness | 124 ± 48.6 | 160.6 ± 48.2 | 0.1 |
| Inferior RNFL thickness | 146.4 ± 70.2 | 148.6 ± 102.6 | 0.9 |
| Nasal RNFL thickness | 89.1 ± 32.5 | 122.1 ± 82.9 | 0.5 |
| Temporal RNFL thickness | 68.1 ± 42.0 | 73.4 ± 52.7 | 0.7 |
| Rim area in mm² | 2.1 ± 0.8 | 2.1 ± 0.7 | 0.7 |
| Disc area in mm² | 2.4 ± 0.2 | 2.8 ± 0.9 | 0.2 |
| Vertical cup to disc ratio | 0.4 ± 0.02 | 0.36 ± 0.02 | 0.6 |
| Cup volume in mm³ | 0.08 ± 0.2 | 0.13 ± 0.07 | 0.4 |

Discussion

This study aimed at defining a clinical profile for Indian patients with NA-AION and examines factors likely to predict visual recovery. The first aspect of the clinical profile which holds importance is the age group of patient affected. In our study, the mean age of NA-AION patients was 51.2 +/- 7.8 years which are lesser than reported in the other populations [2,5,6,8-11]. Literature has various instances of NA-AION developing in the young and age ranges varying from the second to third decade or even 11-91 years have been published [5,6]. However even large case series have shown only about 10.5% and 38.7% of patients below 45 and 50 years of age respectively as against 15% and 45% in our study [6,7]. This indicates a possible tendency for NA-AION to develop at a younger age in Indians. It could be linked to increasing incidence of microvascular diseases (hypertension and diabetes mellitus) in the young. The similar incidence of systemic disease in the younger and the elderly group of our study patients supports the above findings and reports in literature have shown strong associations of NA-AION with systemic diseases in the younger population [12].

The presenting visual acuity is known to vary from 6/9 to no PL [4,6]. There are conflicting results with regard to visual improvement though our study showed a clear but incomplete improvement in most cases [4,5,13,14]. Maximum improvement occurred within the first couple of months of the acute attack.

The commonest visual field defect which found was the inferonasal defect and the same has been previously described in literature [15]. However, we observed a significant number of cases having a centre involving field defect which is the cause for poor vision in these cases. These central defects were demonstrable on the full field kinetic perimetry and would probably present as a generalised field depression on standard static perimetry testing and get mislabelled into that category.

Studies have reported a significant thickening of the RNFL on OCT in the acute stage of NA-AION and our study concurs though it was essentially the nasal quadrant which showed significant thickening [16,17]. The fact that other quadrants of the RNFL though thickened did not show statistical significance could be related to the limited sample size of the study but also highlights the well described sectoral edema in NA-AION cases. This thickening is due to the swollen axons secondary to axoplasmic stasis manifesting as optic disc edema.

In addition, OCT revealed a significantly lower mean cup volume in the fellow eye indicative of a sub clinical parameter predictive of a greater compression of smaller vessels and a subsequent risk for clinical NA-AION. This strengthens the existing knowledge about the pathogenesis of NA-AION though not all studies in literature concur [18-24].

The eventual appearance of an optic atrophy in the natural course of NA-AION was documented by the progressive RNFL thinning and reductions in rim and disc area on follow up. Probably, the reduction in disc area may be explained by the initial over estimation of the disc area due to masking of the retinal pigment epithelium (RPE) near the ONH consequent to the initially edematous optic nerve head. These findings and differential thinning on RNFL corresponding to the affected visual hemifield also find support in literature [17,24-26]. As in literature, optic Nerve head parameters did not hold any significant predictive value for recovery and were not related to final visual outcome [27].

In concordance to our study, one scientific study also noted a better improvement in cases without systemic illness than those with [28]. However most other studies found a similar outcome in the two groups [29,30]. While our study found better improvement in visual acuity in patients without systemic illness, other visual function parameters were similar in both groups. In addition our study revealed those cases where the ischemic insult affected the papillomacular bundle showed least recovery which was indicated by the persistence of the centre involving field defect in the follow up.

Certain limitations of the study which merit mention include the small sample size and heterogeneous nature of systemic illnesses among the cases. While the study had adequate statistical strength, subgroup analysis among different systemic illness groups was not possible. In addition, an observational bias is likely in view of certain parameters investigations having a subjective/qualitative nature including Goldmann kinetic perimetry, however this was mitigated by defining standard parameters to document improvement or worsening and data collection by a blinded observer.

To conclude, the clinical profile of NA-AION in India patients is similar to that reported from the west albeit a slightly younger age of presentation. Nearly half the patient show significant recovery most of which occurs within the first two months of the acute attack. Presence of systemic illness and involvement of the papillomacular bundle tend to predict a poorer visual prognosis. None of the other structural or functional parameter studies hold any predictive value for the visual outcome.

Bibliography


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