Anterior Ischemic Optic Neuropathy Is Not Associated With Carotid Artery Atherosclerosis

Constance L. Fry, MD; John E. Carter, MD; Merrill C. Kanter, MD; Charles H. Tegeler, MD; and Michael R. Tuley, PhD

Background and Purpose: The relation between anterior ischemic optic neuropa thy and carotid artery atherosclerotic disease is unclear. We studied patients with anterior ischemic optic neuropathy to determine if they had an increased occurrence of carotid artery stenosis.

Methods: Fifteen consecutive patients with anterior ischemic optic neuropathy were evaluated prospectively for cervical carotid artery stenosis and compared with 30 age- and sex-matched asymptomatic patients and also with 11 age- and sex-matched patients experiencing transient monocular blindness.

Results: There was no difference in the mean stenosis of the internal carotid artery between patients with anterior ischemic optic neuropathy (mean carotid stenosis, 19%) and asymptomatic patients (mean carotid stenosis, 9%; p > 0.05), whereas patients with transient monocular blindness had significantly more stenosis (mean, 77%) in the cervical carotid arteries than both control subjects (p < 0.0001) and patients with anterior ischemic optic neuropathy (p < 0.0001). There was also no difference in the percentage of patients with stenosis ≥30% in anterior ischemic optic neuropathy (two of 15) and asymptomatic patients (five of 30), whereas 10 of 11 patients with transient monocular blindness had stenoses ≥30%, significantly more than patients with anterior ischemic optic neuropathy (p < 0.0001) and asymptomatic patients (p < 0.0001).

Conclusions: Anterior ischemic optic neuropathy is not a marker for atherosclerotic carotid artery stenosis. The pathogenesis of nonarteritic anterior ischemic optic neuropathy does not involve carotid artery stenosis in most patients.

KEY WORDS • carotid artery diseases • cerebrovascular disorders • ultrasonics

Anterior ischemic optic neuropathy (AION) is an infarction of the optic nerve head caused by compromised blood flow in one or more of the posterior ciliary arteries. It is characterized by acute loss of vision, optic disc edema, an afferent pupillary defect, and monocular visual field abnormalities. AION may occasionally be due to temporal arteritis and other systemic inflammatory diseases, but the majority of cases occur in the elderly and are associated with hypertension (45%) and diabetes.1-3 Some other ocular syndromes such as transient monocular blindness (TMB) are generally recognized as being associated with ipsilateral carotid occlusive disease and with an increased risk of ipsilateral stroke. The relation between AION and carotid disease is controversial.4-8 Some authors have suggested that patients with idiopathic AION and AION associated with hypertension undergo a carotid evaluation.4 To determine the clinical utility of carotid evaluation in patients with AION, we performed a case-control study comparing carotid artery patency in patients with AION with neurologically asymptomatic patients and with patients with TMB. We believe this is the first attempt to quantify the degree of carotid stenosis in a consecutive series of patients with nonarteritic AION.

Subjects and Methods

Fifteen consecutive patients referred for evaluation by a neuro-ophthalmologist for an acute episode of nonarteritic AION were evaluated prospectively with carotid duplex scanning in the Neurosonology Research Laboratory at the University of Texas Health Science Center in San Antonio between 1987 and 1990. AION was defined as an abrupt loss of vision accompanied by optic disc edema, an afferent pupillary defect, and an appropriate visual field abnormality. No patients had recent ocular or other surgery. The carotid arteries were evaluated with high-resolution two-dimensional B-mode real-time imaging and duplex Doppler spectral analysis.

We compared AION patients with two groups of age- and sex-matched patients chosen retrospectively. The control group was randomly selected from patients with atrial fibrillation undergoing carotid duplex scanning as part of the Stroke Prevention in Atrial Fibrillation study9; two control subjects were chosen for each AION patient. No patient with atrial fibrillation had symptoms of cerebrovascular disease. The second group consisted
of consecutive patients with TMB seen at our institution by Neurology, Vascular Surgery, and Neurosurgery services. Each AION patient was age- and sex-matched with a single patient with TMB; there were insufficient numbers of female patients with TMB, leading to four AION patients unmatched with TMB patients. Angiography determined the degree of carotid stenosis in patients with TMB. In our institutions, clinical carotid ultrasonography is often done in laboratories other than the Neurosonology Research Laboratory, which provide only spectral analysis; patients with typical features of TMB were routinely studied by angiography because it was believed to be a more reliable measure of carotid stenosis. All patients with AION, however, were studied in the Department of Neurology Neurosonology Research Laboratory, which has an overall 90% sensitivity and specificity correlation with arteriography in our institution.

The maximum degree of carotid stenosis in the common carotid artery, bifurcation, or internal carotid artery on the symptomatic side of patients with AION was compared with the maximum stenosis of the carotid artery on the same side in the control group and the symptomatic side in the TMB group. The means of the maximum stenoses in the three groups were compared using Schefle's test. If the patient had experienced a prior episode of AION in the contralateral eye, only the acutely involved eye and the ipsilateral carotid artery were evaluated. In addition, the number of patients with ≥30% and ≥70% stenosis in each group was compared with Fisher's exact test.

Results

The 15 AION subjects were between the ages of 51 and 71 years (Table 1). All had normal Westergren sedimentation rates and lacked any history suggesting temporal arteritis. Forty percent had hypertension, and 33% were diabetic. Forty-seven percent had experienced a previous episode of AION in the contralateral eye.

Thirty age- and sex-matched patients with atrial fibrillation and no cerebrovascular symptoms served as control subjects (Table 1). Fifty-three percent were hypertensive, and 37% had diabetes. Eleven patients with AION were matched by age and sex with patients with TMB. We were unable to match by age four female patients with AION with patients with TMB. Patients with TMB had a similar frequency of hypertension, but there were fewer diabetics than in the AION group. No patient had bilateral TMB.

The degree of carotid artery stenosis ipsilateral and contralateral to the eye with AION and TMB and the degree of stenosis in the control carotid artery from patients with atrial fibrillation are shown in Table 2. The mean degree of carotid artery stenosis in patients with AION was not significantly different from that of control patients with atrial fibrillation (Table 3), whereas carotid artery stenosis in patients with TMB was significantly greater than that in either the control subjects (p<0.0001) or the patients with AION (p<0.0001). To estimate a worst-case scenario in regard to the four unmatched AION patients, the data were reanalyzed as if the four missing TMB patients had no stenosis; the difference remained highly significant (p<0.001).

Analyzing our data for the number of patients with either ≥30% or ≥70% stenosis resulted in a similar outcome; patients with AION and control patients with atrial fibrillation were not significantly different, whereas patients with TMB had more stenoses than either of these groups (p<0.0001 for both comparisons) (Table 4).

The degree of stenosis of ipsilateral and contralateral carotid arteries for the AION and TMB patients is shown in Table 2. The contralateral carotid artery showed similar stenotic characteristics in the AION

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean stenosis (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>9</td>
<td>(3.4, 14.8)</td>
</tr>
<tr>
<td>AION</td>
<td>19*</td>
<td>(8.3, 30.3)</td>
</tr>
<tr>
<td>TMB</td>
<td>77†</td>
<td>(62.2, 92.4)</td>
</tr>
</tbody>
</table>

CI, confidence interval; AION, anterior ischemic optic neuropathy; TMB, transient monocular blindness.

*p>0.05 AION vs. control.

†p<0.0001 TMB vs. AION or TMB vs. control.
patients with a high correlation between the percent stenosis of the two sides ($R^2=0.67$) in each group. Although there was a substantial degree of stenosis on the contralateral side in patients with TMB, there was no correlation between the degree of stenosis in ipsilateral and contralateral carotid arteries in patients with TMB.

**Discussion**

Our study indicates that carotid artery stenosis is uncommon in patients with AION. This is the first study, to our knowledge, to quantify the degree of carotid artery stenosis in a consecutive series of patients with AION. Our patients were quite representative of nonarteritic AION in the literature.\(^1\)-\(^3\) AION would not appear to be an indicator of greater risk for atherosclerotic stenosis in the territory of the ipsilateral carotid artery. At issue is whether AION is an indication of symptomatic carotid atherosclerosis with its implications for carotid endarterectomy, or a marker for systemic atherosclerotic disease such as an asymptomatic carotid bruit with implications for medical therapy but none for surgery. Although not addressed to the occurrence of stroke, our study suggests that extracranial carotid stenosis is not especially common in AION and, therefore, that any increase in stroke risk in patients with AION may not be due to carotid disease.

The relation between AION and cerebrovascular disease in general remains unclear. Studies by Boghen and Glaser,\(^1\) Ellenberger et al,\(^2\) and Repka et al\(^3\) did not find an increased frequency of cerebrovascular events in patients with AION. In 1985, however, Guyer et al documented an increased incidence of cerebrovascular events in patients with idiopathic AION and AION associated with hypertension. Based on their results, they suggested evaluating carotid artery patency in these patients, although the relation of stroke to carotid artery stenosis was not clear in this study. Our results suggest that the frequency of significant carotid stenosis will be no greater than in a group of age- and sex-matched asymptomatic patients. Only two of our 15 patients with AION had ipsilateral carotid stenosis $\geq 30\%$ and none $\geq 70\%$. In contrast, $>70\%$ of patients with TMB had severe carotid stenosis. It seems clear that the pathogenesis of these two forms of ocular ischemia is quite different.

Guyer et al\(^4\) divided their patients with nonarteritic AION into several subgroups: presumed atherosclerosis, diabetes, hypertension, both diabetes and hypertension, and idiopathic. In our small study such a subdivision is not possible. In the study by Guyer et al, only patients in the idiopathic and hypertensive groups had a significantly increased incidence of stroke. It is not clear why patients with hypertension but not patients with both diabetes and hypertension should have an increase in the frequency of stroke. Similarly, patients with a previous cerebrovascular or cardiovascular event, classified as “presumed atherosclerosis” by Guyer et al, have generally been found to be at substantially increased risk of experiencing further ischemic events,\(^10\)-\(^14\) a finding not present in the patients studied by Guyer et al. It seems unlikely that clinicians will evaluate or treat patients with AION in the setting of hypertension differently from those patients with AION and both hypertension and diabetes. We believe that patients aged $\geq 40$ years with AION not associated with arteritis or complicating ocular surgery probably represent a single group in terms of basic pathophysiology, i.e., occlusion of the posterior ciliary arteries, and they should be investigated as such when considering the relation of AION and cerebrovascular disease. Exceptions to this are patients with AION and associated focal clinical features such as transient ischemic attacks, TMB, and visible retinal emboli, features that are recognized by themselves not just as risk factors for stroke but as indicators of extracranial cerebrovascular disease. A few anecdotal reports document cases of AION associated with carotid occlusive disease based on these presentations;\(^15\)-\(^17\) almost all cases had the additional clinical features present at the time of the AION, providing the clinicians with the information necessary to adjust their diagnosis.

Whether AION is a marker for stroke and, if so, whether it is due to carotid disease, small-vessel disease, or merely a nonspecific marker for all types of stroke remain to be determined. Strokes in the patients studied by Guyer et al were equally likely to occur ipsilateral or contralateral to the involved eye. Also, they did not determine the number of strokes caused by extracranial cerebrovascular disease as opposed to lacunar infarction. Sawle et al\(^\text{18}\) also found an increase in the mortality of patients with AION from both myocardial infarction and stroke but did not provide data regarding the occurrence of nonfatal strokes or the type or location of strokes. Since the pathophysiology of both lacunar infarcts and AION involves occlusion of small arteries, AION might well be a marker for small-vessel atheromatous degeneration or lipohyalinosis and related lacunar stroke.\(^19\) In fact, studies of carotid artery stenosis and lacunar stroke indicate a degree of stenosis similar to that found in our patients with AION.\(^20\) AION is certainly a marker for AION in the contralateral eye; $30$–$45\%$ of patients with AION will eventually suffer a similar event in the fellow eye.\(^1\)-\(^3\) Our data indicate no significant increase in carotid artery stenosis either ipsilateral or contralateral to an eye with nonarteritic ischemic optic neuropathy, but we did find a high degree of stenosis of the ipsilateral carotid in TMB patients. Patients with TMB had a typical history and normal funduscopic exams; none had venous stasis retinopathy associated with ocular ischemic syndrome seen occasionally with severe, bilateral carotid occlusive disease. The degree of stenosis for our patients with TMB is comparable to that in some series\(^21\),\(^22\) even though it is higher than that in others.\(^23\) This increase in carotid

<table>
<thead>
<tr>
<th>Group (n)</th>
<th>Stenosis $\geq 30%$ No.</th>
<th>%</th>
<th>Stenosis $\geq 70%$ No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (30)</td>
<td>5</td>
<td>17</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AION (15)</td>
<td>2</td>
<td>13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TMB (11)</td>
<td>10</td>
<td>91</td>
<td>8</td>
<td>72</td>
</tr>
</tbody>
</table>

AION, anterior ischemic optic neuropathy; TMB, transient monocular blindness; NT, no test; both groups are 0.

Probability values are by Fisher's exact test.
artery stenosis correlates with the clinical finding in many studies that patients with TMB are at increased risk for cerebrovascular events in the ipsilateral carotid distribution. Therefore, if patients with AION, in the absence of other neurological symptoms and signs, do have a higher risk for future stroke, it may not be related to carotid disease.

Several limitations of this study are recognized. First, the definition of significant carotid stenosis is not agreed on by all, but with information from the ongoing carotid endarterectomy trial it may become standardized. We analyzed our data using both a moderate degree of stenosis (≥30%) and a more severe stenosis (≥70%). Either way the data were evaluated, a significant difference between asymptomatic patients or patients with AION and those with TMB persisted. Both comparison groups with atrial fibrillation and TMB were chosen retrospectively. Additionally, we compared angiographic results in patients with TMB with carotid Doppler results in the other two groups, because detailed Doppler analysis in the carotid artery was not always available in patients with TMB. Although this is not ideal, duplex carotid ultrasonography has an 85% sensitivity and a 90% specificity for detection of carotid stenosis overall. For detection of stenoses >50% there is a 90% sensitivity and specificity in comparison with arteriography. Duplex ultrasonography is currently the preferred initial test in the evaluation of the extracranial carotid system.

Because the number of participants in our study was small, it remains to be determined whether these results can be applied to AION patients in general; the possibility of a β error with this small sample is 60%. A larger, prospective study of patients with AION and their risk of stroke is needed and could also be designed to study therapeutic options aimed at diminishing the 40% incidence of bilaterality in patients seen with their first episode of AION.

References

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