Optic Neuritis in African Americans

Paul H. Phillips, MD; Nancy J. Newman, MD; Michael J. Lynn, MS

Objective: To describe the clinical profile of demyelinating optic neuritis in African Americans.

Methods: The medical records of all patients with a diagnosis of optic neuritis examined at the Neuro-Ophthalmology Unit at the Emory University Eye Center (Emory) and at the Grady Memorial Hospital Eye Clinic (Grady), Atlanta, Ga, between 1989 and 1996 were retrospectively reviewed.

Patients: African American and white patients, aged 15 through 55 years, with a single initial episode of acute optic neuritis of unknown or demyelinating origin were included in the study. Study patients included 23 African American patients and 56 white patients examined at Emory as well as 10 African American patients examined at Grady.

Results: There were no significant differences among the African American study patients, the white study patients, and patients from the Optic Neuritis Treatment Trial (ONTT) regarding sex (P = .36), age (P = .73), or the presence of disc edema (P = .40), lesions found on magnetic resonance imaging (P = .43), or multiple sclerosis (P = .54) at the onset of an initial episode of optic neuritis. The Emory African American patients presented with more frequent severe visual loss (13 [93%] of 14 patients with a visual acuity ≤20/200) compared with Emory white patients (12 [39%] of 31 patients; P = .002) and with ONTT patients (161 [36%] of 448 patients; P < .001). At follow-up examination of at least 1 year, Emory African American patients had worse vision (9 [39%] of 23 patients <20/40, and 4 [17%] of 23 patients ≤20/200) compared with Emory white patients (5 [8%] of 63 patients <20/40, P = .001; 3 [5%] of 63 patients ≤20/200, P = .08), and with ONTT patients (29 [7%] of 409 patients <20/40, P = .0001; 12 [3%] of 409 patients ≤20/200, P = .01). Compared with ONTT patients, the Emory African American patients combined with the Grady African American patients had more frequent severe visual loss (visual acuity ≤20/200) at presentation (18 [90%] of 20 patients vs 161 [36%] of 448 patients; P < .001) and at follow-up examination of at least 1 year (6 [18%] of 33 patients vs 12 [3%] of 409 patients; P = .002). Seven (58%) of 12 African American patients with multiple sclerosis had a “neuromyelitis optica” presentation defined by the presence of neurological deficits limited to the optic nerves and spinal cord.

Conclusions: The African American study patients with a single episode of demyelinating optic neuritis had visual acuities more severely affected at onset and after 1 year of follow-up compared with the white study patients and with patients in the ONTT. In the African American patients, multiple sclerosis occurred most frequently in a “neuromyelitis optica” form.

Arch Neurol. 1998;55:186-192

Demyelinating optic neuritis most frequently occurs in whites. The clinical profile of optic neuritis in African Americans has received little attention. Racial effects on the clinical profile of optic neuritis and demyelinating disease have been suggested in other countries. Although demyelinating optic neuritis is rare in South African blacks, when it occurs in this group it is frequently associated with severe visual loss. Similarly, demyelinating disease occurs infrequently in Japan. However, Japanese patients with multiple sclerosis (MS) frequently have severe involvement of the optic nerves at presentation and during the course of the disease.

The clinical profile of demyelinating optic neuritis specifically in African Americans is unknown. In the Optic Neuritis Treatment Trial (ONTT) there were 68 nonwhite patients, and within this group, 59 patients were African American (R. Beck, MD, written communication, November 8, 1995). The visual acuities of the white and nonwhite patients were not significantly different at the 6-month follow-up examination. No other
PATIENTS AND METHODS

The medical records of all patients with a diagnosis of optic neuritis examined at the Neuro-Ophthalmology Unit at the Emory University Eye Center (Emory) and at the Grady Memorial Hospital Eye Clinic (Grady), Atlanta, Ga, between 1989 and 1996 were reviewed. Inclusion criteria for further analysis included the presence of an acute optic neuritis of unknown or demyelinating origin; age range of 15 through 55 years; and the presence of decreased visual acuity, a visual field deficit, or a relative afferent pupillary defect either alone or in combination. Patients were excluded from further analysis if they had any ocular or systemic disease that would cause visual loss other than MS, ocular findings suggestive of a nondemyelinating cause of optic neuritis, positive results of a syphilis serological test, or an angiotensin-converting enzyme level above 60 U/L.

Age at onset of symptoms, ocular symptoms, visual acuity with best refractive correction, color vision, optic nerve appearance, and treatment interventions at presentation and for all follow-up visits were recorded for each initial attack of optic neuritis within a given eye. Data were collected for both eyes in patients with bilateral nonsimultaneous optic neuritis but not for recurrent episodes of optic neuritis within the same eye.

Eighteen African American patients examined at Grady between 1989 and 1996 were diagnosed as having optic neuritis. Eight patients were discontinued from further analyses because of the concurrent presence of the acquired immunodeficiency syndrome (n=2), neurosyphilis (n=1), sarcoidosis (n=1), elevated intracranial pressure (n=1), an orbital mass (n=1), a pituitary mass (n=1), and an angiotensin-converting enzyme level of 93 U/L (n=1). The 10 remaining patients had 20 episodes of optic neuritis, including 14 initial episodes and 6 recurrent episodes of optic neuritis. Four of the 10 patients had bilateral nonsimultaneous episodes of optic neuritis.

Thirty-two African American patients examined at Emory between 1989 and 1996 were diagnosed as having optic neuritis. Nine patients were discontinued from further analyses because of the concurrent presence of severe uveitis (n=2), glaucoma (n=2), herpes zoster ophthalmicus (n=1), functional visual loss (n=1), sarcoidosis (n=1), recent sinus surgery (n=1), and an angiotensin-converting enzyme level of 84 U/L (n=1). The 23 remaining patients had 39 episodes of optic neuritis, including 30 initial episodes and 9 recurrent episodes of optic neuritis. Seven of the 23 patients had bilateral nonsimultaneous episodes of optic neuritis.

Eighty-two white patients examined at Emory between 1989 and 1996 were diagnosed as having optic neuritis. Twenty-six patients were discontinued from further analyses because of the concurrent presence of severe uveitis (n=8), ocular trauma (n=1), systemic lupus erythematosus (n=4), elevated intracranial pressure (n=1), sarcoidosis (n=1), mononucleosis (n=1), meningitis (n=1), and an age outside the acceptable range (n=9). The remaining 56 patients had 97 episodes of optic neuritis, including 76 initial episodes and 21 recurrent episodes of optic neuritis. Twenty of these 56 patients had bilateral nonsimultaneous episodes of optic neuritis.

Table 1 shows patient demographics and clinical characteristics of our study patients compared with patients in the ONTT. There were no significant differences in patient characteristics among the groups except for the presence of ocular pain. Although the 4 groups showed significant differences regarding ocular pain when analyzed together, there was no statistically significant difference in the percentage of patients with ocular pain when the Emory African American patients were compared with the Emory white patients (P=.32) or with patients in the ONTT (P=.10) separately.

Figure 1 shows the distribution of visual acuities at onset of an initial episode of optic neuritis for our 3 study groups. Table 2 shows that the Emory African American patients presented with significantly more frequent severe visual loss (visual acuity ≤20/200) compared with Emory white patients (93% vs 39%; P=.002) or patients in the ONTT (93% vs 36%; P=.0001). The Emory African American patients combined with the Grady African American patients presented with significantly more frequent severe visual loss compared with patients in the ONTT (90% vs 36%; P<.0001).
By our selection criteria, results of syphilis serological tests were negative and the angiotensin-converting enzyme level was lower than 60 U/L when these tests were performed. Results of syphilis serological tests were obtained in 28 (85%) of 33 African American study patients and in 44 (79%) of 56 Emory white patients) were either normal or revealed lesions consistent with MS. Among patients with a final visual acuity of less than 20/40, MRI was performed in 9 (90%) of 10 African American study patients and in 4 (80%) of 5 Emory white patients.

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zyme level was obtained in 19 (58%) of 33 African American study patients and in 8 (14%) of 56 Emory white patients. Among patients with a final visual acuity of less than 20/40, an angiotensin-converting enzyme level was obtained in 8 (80%) of 10 African American study patients and in 1 (20%) of 5 Emory white patients.

Chest radiographs always showed no abnormalities and were performed in 21 (64%) of 33 African American study patients and in 6 (11%) of 56 Emory white patients. Among patients with a final visual acuity of less than 20/40, chest radiographs were obtained in 6 (60%) of 10 African American study patients and in 1 (20%) of 5 Emory white patients.

Results of lumbar punctures were either normal or revealed abnormalities consistent with demyelinating disease, such as increased protein levels, elevated immunoglobulin levels, oligoclonal bands, or a lymphocytic cellular response. A lumbar puncture was obtained in 12 (36%) of 33 African American study patients and in 10 (18%) of 56 Emory white patients. Among patients with a final visual acuity of less than 20/40, a lumbar puncture was performed in 4 (40%) of 10 African American study patients and in none of the Emory white patients.

An antinuclear antibody (ANA) titer was obtained in 17 (52%) of 33 African American study patients. Eight of these patients had positive titers. The highest titer was 1:160. These 8 patients had no clinical evidence of a collagen-vascular disease and 7 of them had further rheumatological workup results that were unremarkable. Among patients with a final visual acuity of less than 20/40, an ANA titer was obtained in 5 (50%) of 10 patients. The ANA titer was normal in 4 of these patients and 1 patient had positive titers of 1:80. This patient had no clinical evidence of collagen-vascular disease and further results of rheumatological workup were unremarkable.

An ANA titer was obtained in 23 (41%) of 56 Emory white patients. Four of these patients had positive titers. The highest titer was 1:160. These 4 patients had no clinical evidence of a collagen-vascular disease and 1 of them had further rheumatological test results that were unremarkable. Among patients with a final visual acuity of less than 20/40, an ANA titer was obtained in 2 (40%) of 5 patients and was normal in both patients.

An ANA titer was obtained in 3 (43%) of 7 African American study patients with a Devics-like presenta-

tion. Two of these patients had positive titers measuring 1:40. Neither patient had clinical evidence of a collagen-vascular disease and results of further rheumatological workup were unremarkable for both patients. Among all the study patients, positive ANA titers did not significantly correlate with severe vision loss (visual acuity ≤20/200) either at presentation (P = .42) or at 1 year of follow-up (P = .36).

The study patients were observed either with no treatment or treated with oral or intravenous steroids. None of the study patients had a steroid-dependent optic neuropathy with a decrease in visual acuity as use of steroids was discontinued.

**Comment**

The clinical profile of demyelinating optic neuritis in African Americans has received little attention. Racial effects on the clinical profile of demyelinating optic neuritis have been suggested in several groups from other countries. Although demyelinating optic neuritis is rarely described in South African blacks, optic neuritis in this group is often associated with severe visual loss. Dean et al described 12 black patients with MS from South Africa and Zimbabwe. Six of these patients became bilaterally “blind, or nearly so, from severe optic neuritis.” Ames and Louw reported 7 black South African patients with MS. All 7 patients had a history of optic neu-
White groups did not differ significantly at the 6-month presentation compared with northern-born African Americans.

Few studies have examined the clinical profile of MS in African Americans. Haerer15 performed a retrospective analysis of the natural history of MS in Mississippi blacks and whites. He reported that Mississippi black patients with MS had increased disability, increased mortality rates, more frequent chronic progressive disease, and fewer years from onset of disease to death compared with Mississippi white patients. Retrospective studies by Morariu and Linden16 and Alter17 both conclude that, overall, the clinical profile of MS in African Americans is not significantly different from that of whites. However, southern-born African Americans had more frequent chronic progressive disease and were older at presentation compared with northern-born African Americans.

Compared with ONTT1,7 patients and with white patients in our practice, the African American patients with optic neuritis in our study had significantly worse visual acuities at onset and after at least 1 year of follow-up from a single initial episode of optic neuritis. The

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### Table 3. Visual Acuity at 1 Year or More After Presentation

<table>
<thead>
<tr>
<th>Visual Acuity</th>
<th>Emory Blacks, % (n=409)</th>
<th>Emory Whites, % (n=44)</th>
<th>ONTT, % (n=409)</th>
<th>Emory Blacks and Grady Blacks, % (n=33)</th>
<th>ONTT, % (n=409)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20/40</td>
<td>39 (P=.001)†</td>
<td>8 (P=.001)†</td>
<td>7 (P=.001)†</td>
<td>36</td>
<td>7 (P=.001)§</td>
</tr>
<tr>
<td>≤20/200</td>
<td>17 (P=.001)†</td>
<td>5 (P=.001)†</td>
<td>3 (P=.01)†</td>
<td>18</td>
<td>3 (P=.002)§</td>
</tr>
</tbody>
</table>

* Emory indicates the Neuro-Ophthalmology Unit at the Emory University Eye Center and Grady, the Grady Memorial Hospital Eye Clinic in Atlanta, Ga; ONTT, data from the Optic Neuritis Treatment Trial; and n, number of eyes.
†P value comparing ONTT patients with white patients.
‡P value comparing ONTT patients with Emory blacks.
§P value comparing ONTT patients with Emory blacks.

### Table 4. Visual Acuity at 1 Year or More After Presentation Assuming a Visual Acuity of 20/20 for Black Patients Without Follow-up

<table>
<thead>
<tr>
<th>Visual Acuity</th>
<th>ONTT, % (n=409)</th>
<th>Emory Blacks and Grady Blacks, % (n=30)</th>
<th>Emory Blacks, % (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20/40</td>
<td>7 (P=.001)†</td>
<td>27 (P=.001)†</td>
<td>30 (P=.001)†</td>
</tr>
<tr>
<td>≤20/200</td>
<td>3 (P=.03)‡</td>
<td>14 (P=.008)†</td>
<td>13 (P=.03)‡</td>
</tr>
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* ONTT indicates data from the Optic Neuritis Treatment Trial; Emory, the Neuro-Ophthalmology Unit at the Emory University Eye Center and Grady, the Grady Memorial Hospital Eye Clinic in Atlanta, Ga; and n, number of eyes.
†P value comparing ONTT patients with Emory blacks and Grady blacks.
‡P value comparing ONTT patients with Emory blacks.

### Table 5. Patients With Neuromyelitis Optica—Clinical Data

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>VA (OD)*</th>
<th>VA (OS)*</th>
<th>MRI (Head)</th>
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<tbody>
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<td>1</td>
<td>NLP</td>
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</tr>
<tr>
<td>2</td>
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<td>ND</td>
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<td>4</td>
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<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>5</td>
<td>NA</td>
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* Final visual acuities (VAs) are shown. OD indicates right eye; OS, left eye; MRI, magnetic resonance imaging; NLP, no light perception; NA, eye not affected; ND, not done; LP, light perception; and HM, hand motion.
†An MRI with lesions consistent with demyelination.

A similar racial effect on the clinical course of demyelinating optic neuritis has been demonstrated in Japanese patients with MS, another group with a low prevalence of demyelinating disease. Kuroiwa et al4 analyzed 1084 Japanese patients with MS in a nationwide survey. These patients had more frequent visual impairment, especially bilaterally, at the onset of the illness, and more frequent and severe involvement of the optic nerves during the course of their illness compared with patients with MS in western countries.

The only source of published data on demyelinating optic neuritis in African Americans is the ONTT.1 The ONTT patients included 68 nonwhites of whom 59 were African American (R. Beck, written communication, November 8, 1995). The visual acuities of the nonwhite and African American (R. Beck, written communication, November 8, 1995). The visual acuities of the nonwhite and African American (R. Beck, written communication, November 8, 1995). The visual acuities of the nonwhite and Asian populations have lower rates of MS than whites. Oh and Calhoun11 also showed that African Americans had decreased prevalence rates of MS compared with whites within the same city.

In South African black, MS frequently occurs in the form of neuromyelitis optica, accounting for up to 98% of cases.12-14 Ames and Louw3 described 4 black South African patients with MS with severe optic nerve and spinal cord involvement. Cosnett13 described 6 African blacks with neuromyelitis optica. A similar pattern occurs in Japanese patients. In the nationwide survey by Kuroiwa et al10 of MS in Japan, Japanese patients had frequent involvement of the optic nerves and spinal cord during the course of their illness, with neuromyelitis optica occurring in 7.6% of these patients.

More has been written on the effects of race on the clinical profile of MS. Most of this information reports the effect of race on the prevalence of the disease. Within a given location, the black population generally has a lower prevalence of MS compared with the white population.18-11. This has been demonstrated in South Africa8,9 and in North America10. The extensive epidemiological study by Kurtzke et al11 and by Kurtzke18 on US veterans showed that, in America, African Americans and Asians have lower rates of MS than whites. Oh and Calhoun11 also showed that African Americans had decreased prevalence rates of MS compared with whites within the same city.

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achieved a final visual acuity of 20/20, the African
episode of optic neuritis or had a recurrent attack of
were either not yet 1 year out from the onset of their
was not a significant source of bias in this study. Most
patients who are doing well may not follow up,
most of these patients had either definite clinical
evidence of a collagen-vascular disease, extremely el-
evident ANA titers, or other results of serological tests
indicative of a collagen vascular disease, or a steroid-
dependent optic neuropathy with decreased vision with
tapering of steroid therapy. Although several of our study
patients had positive ANA titers, none had clinical evi-
cence of a collagen-vascular disease, the titers were low,
results of further rheumatological and serological workup
were unremarkable, and none of the study patients had
a steroid-dependent optic neuropathy. Furthermore, the
presence of positive ANA titers was not significantly cor-
related with poor vision. Similarly, the ONTT patients
with positive ANA test results (16%) did not have a worse
visual outcome.5 The ONTT authors concluded that “this
clinical profile of optic neuritis among all the groups was
otherwise similar. This difference in our results from those
of the ONTT may be the result of a variety of factors, in-
cluding genetic or environmental influences and referral bias.

THE AFRICAN AMERICAN patients in our
study were derived from 2 medical cen-
ters within a single southern American
city, whereas the African American pa-
tients in the ONTT were derived from
multiple centers throughout the United States. The Af-
rican American patients in our study may represent a
subgroup of patients genetically at risk for severe optic
neuritis. Several reports16-25 suggest a genetic influence
on the prevalence and expression of MS. Kira et al24
showed immunogenetic differences between Japanese
patients with MS with disseminated central nervous system involvement and those with selective involve-
ment of the optic nerve and spinal cord.

Alternatively, environmental factors may account for
the different results. Many of the ONTT patients were
from the northern United States. As noted earlier,
Morariu and Linden16 and Alter17 described differences in
the clinical expression of MS in northern vs southern
African Americans, with the latter having more severe,
chronic progressive disease.

Referral bias may account for the worse visual acu-
ities observed in our African American patients. The Af-
rican American patients in our study were derived from
2 different sources. One group was from Emory, a pri-
ate neuro-ophthalmology referral practice. The other
group was from Grady, an inner-city facility with pri-
mary eye care. Patients with severely affected vision may
be more likely referred to a tertiary care center such as
Emory. Alternatively, patients of low socioeconomic
means may not seek medical care unless they are devas-
tated by their disease. In general, African American pa-
tients seen at Emory are not socioeconomically differ-
ent from whites seen at this center. However, the Emory
African American patients had significantly worse vi-
sion compared with the Emory white patients. Since both
these groups are governed by similar referral patterns,
referral bias is an unlikely explanation for the differ-
ences observed between these 2 groups. In addition, the
visual acuities were significantly worse in our African
American patients when the Emory and Grady patients
together were compared with the ONTT patients. The
inclusion of African American patients from the pri-
mary care eye clinic at Grady should reduce the amount
of referral bias.

One of the problems with retrospective studies is
that patients who are doing well may not follow up,
thus biasing the results toward a worse outcome. This
was not a significant source of bias in this study. Most
of the patients without 1 year follow-up visual acuities
were either not yet 1 year out from the onset of their
episode of optic neuritis or had a recurrent attack of
optic neuritis before the 1 year follow-up visit. In addi-
tion, even if it is assumed that all these patients had
achieved a final visual acuity of 20/20, the African
American study patients still had significantly worse
vision at 1-year follow-up compared with the ONTT7
patients (Table 4).

Finally, the inadvertent inclusion of nondemyelin-
ating optic neuritis secondary to diseases such as sar-
coidosis, syphilis, or systemic lupus erythematosus could
account for the worse visual acuities observed in the Af-
rican American study patients. This is unlikely since most
of the study patients with poor visual acuity underwent
an extensive workup to rule out other causes of optic neu-
ritis. Furthermore, except for age, all the study patients
would have fulfilled the rigorous inclusion criteria of the
ONTT. Several reports26-31 have described patients with
an “autoimmune retrobulbar optic neuritis” with a poor
visual outcome. Some of these reported patients had se-
vere optic neuritis associated with a transverse myelitis
similar to our African American study patients.26-35 How-
ever, most of these patients had either definite clinical
evidence of a collagen-vascular disease, extremely el-

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Accepted for publication July 2, 1997.

This work was supported in part by a departmental grant (ophthalmology) from the Research to Prevent Blindness Inc, New York, NY, and grant P30EY06360 from the National Eye Institute, Bethesda, Md.

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REFERENCES