Retinal Nerve Fiber Layer Changes and Visual Field Loss in Idiopathic Intracranial Hypertension

Thomas R. Hedges III, MD,1,2 Richard H. Legge, MD,1 Eli Peli, OD,1 Christine J. Yardley, COA1

Purpose: The authors retrospectively analyzed changes in the retinal nerve fiber layer in patients with idiopathic intracranial hypertension and studied their relation to visual field loss to determine the clinical usefulness of retinal nerve fiber analysis in the clinical management of patients with papilledema.

Methods: Retinal nerve fiber layer photographs and visual fields from 36 eyes of 21 patients with papilledema due to idiopathic intracranial hypertension were analyzed for abnormalities in a masked fashion.

Results: Nerve fiber layer changes were found in 67% of eyes studied. Superior areas within the nerve fiber layer were affected 5.4 times more frequently than inferior regions. Visual field loss was more prevalent in eyes with diffuse nerve fiber layer loss (89%) than in eyes with slit defects (29%). The location of the nerve fiber layer changes correlated with corresponding areas of visual field loss. Nerve fiber layer changes were as common in mild to moderate as in atrophic papilledema; however, slit defects predominated in patients with mild to moderate papilledema, and diffuse loss predominated in atrophic papilledema.

Conclusions: Changes in the retinal nerve fiber layer observed in patients with idiopathic intracranial hypertension provide objective information regarding the status of their optic nerve and may improve their clinical management.

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Long-term loss of visual acuity or visual field is sustained in 10% to 49% of patients with idiopathic intracranial hypertension.1-4 Indices of visual function, including perimetry, visual acuity, contrast sensitivity, and color vision1-4 used in these patients are limited by their subjective, psychophysical nature. Electrophysiologic testing has been used only on a limited basis for assessing papilledema.5 Red-free fundus photography, which demonstrates reflected striations of the retinal nerve fiber layer,5-7 has been shown to be useful in managing glaucoma. Although retinal nerve fiber layer abnormalities have been described in a variety of neurologic conditions,8 they rarely have been reported in patients with papilledema.10

We observed changes found in the retinal nerve fiber layer of patients with idiopathic intracranial hypertension and studied their relation to visual field loss. If retinal nerve fiber layer analysis can provide an objective index of damage to the optic nerve, it may improve the methods by which patients with idiopathic intracranial hypertension are monitored.

Methods

Photographs of 36 eyes in 21 patients with papilledema due to idiopathic intracranial hypertension were taken:
red-free, black and white slides of the superotemporal and inferotemporal retinal nerve fiber layer, color slides of the optic disc, and Goldmann or Octopus 2000 (Interzeag, Schlieren, Switzerland) automated visual fields (programs 32 and 24). The most temporally related set of photographs and visual fields were selected in each patient. Photographs and visual fields were collected from 41 consecutive patients seen by one of us (TRH) over a 6-year period. Patients were eliminated if the diagnostic information was not available, including spinal fluid pressure and constituents, and if computed tomography or magnetic resonance imaging were not able to be viewed by us. Other patients were eliminated if the photographs or visual fields were considered unreliable (see below). Forty-three red-free fundus photographs from 40 eyes of 27 control subjects were selected randomly.

Retinal nerve fiber layer photographs were taken with a Zeiss FK 30 (Carl Zeiss, Munich, Germany) or a Canon CF-60Z fundus camera (Canon, Inc, Lake Success, NJ) using an SE-40 blue fluorescein exciter filter in patients with fair pigmentation and hair color and a green spectrotech 540-µm green filter in subjects with darker pigmentation.³ Kodak Panatomic-X (Eastman Kodak Co, Rochester, NY) or Ilford Pan F135/ISO 50 film (Ilford, Paramus, NJ) was used and exposed to Kodalith film (Eastman Kodak) for projection. Eyes with red-free photographs of only one temporal quadrant and eyes with photographs that did not clearly show nerve fiber striations or small branch retinal arteries and veins throughout more than half of the image were eliminated. Slides of the superotemporal and inferotemporal retinal nerve fiber layer were projected in a masked, randomized fashion. The optic disc was obscured up to its margin, and the slides were oriented so that the disc was always in the lower, left quadrant, thus making whether the slide was of the superior or inferior temporal retinal nerve fiber layer. Two observers (TRH and EP) classified each slide as normal or abnormal on two separate occasions. The presence of diffuse atrophy, slits, etching, or wedges was tabulated from the slides with an abnormal reading. Diffuse retinal nerve fiber layer drop out was determined by loss of visible striations with baring of the retinal blood vessels over an entire quadrant (Fig 1). Slit defects were identified by loss of striations within an area less than the width of a large retinal blood vessel (200 µm), extending more than 2 disc diameters in length, and extending to the disc margin without branching. Etching was defined as more than four thin slits (<100 µm) divided by striations of similar width present throughout more than one half of a quadrant (Fig 2). Wedge defects were identified as slits greater than the width of two large retinal blood vessels (400 µm). The same observer evaluated the slides on a second occasion, after 80 patient slides had been mixed randomly with 43 slides from the control subjects.

Corresponding color slides of the optic discs were taken with the same fundus cameras using Kodacolor (Eastman Kodak) and Fujichrome RF 135/ISO 50 slide film (Fujifilm USA, Carlstadt, NJ). These were projected in a masked, randomized fashion to one observer (TRH). The papilledema was classified as mild, moderate, or atrophic.

Mild papilledema was determined by blurring of the disc margins with hyperemia and venous engorgement. Moderate papilledema was defined as circumferential blurring of the retinal nerve fiber layer and optic disc elevation. Atrophic papilledema was identified by loss of superficial capillaries and pallor of the optic disc, gliotic sheathing, and narrowing of blood vessels at the disc margins.

Visual fields done on the same day of each photographic session (except for 3 patients who had visual fields and photographs 10, 12, and 43 days apart) were read in a masked, randomized fashion by one observer (TRH). Octopus 2000 (program 24) was used to test 27 eyes. Automated field tests were considered reliable if fewer than five false-negative or false-positive answers were present. The Goldmann perimeter was used to test nine eyes by an experienced neuro-ophthalmologist (TRH). They were determined to be reliable if consistent responses were obtained with good fixation using IV-4e, I-4e, and I-2e test objects. Visual fields were classified as normal or abnormal for each quadrant. Goldmann visual fields were considered abnormal if there was a scotoma or if there was peripheral depression extending into the central 30° with an I-4e or larger isopter. Automated visual fields were considered abnormal if there was a scotoma greater than 5 decibels below normal, or if there was peripheral depression extending into the central 30° with at least three test points 5 decibels or more below normal.

**Results**

The patients' ages ranged from 14 to 53 years (median, 29 years). Female:Male ratio was 19:2. Best-corrected visual acuity was 20/20 in 34 eyes, 20/30 in 1 eye, and 20/40 in 1 eye. All patients had documented increased intracranial pressure with normal spinal fluid and normal computed tomography or magnetic resonance imaging. Associated conditions, other than obesity, included weight...
lifting in one patient and previous history of possible postviral meningitis in another. Control subjects ranged in age from 20 to 52 years (median, 33 years).

The distribution and type of nerve fiber layer abnormalities are listed in Table 1. One observer (TRH) found that 67% (24/36 [11 right eyes and 13 left eyes]) of eyes had retinal nerve fiber layer abnormalities. The second observer (EP) found 25/36 eyes had abnormalities. A second reading by the first observer (TRH) showed 21/36 patient eyes had abnormalities and 4/27 control eyes had abnormalities. Agreement concordance between the two observers for review of all patient slides was 0.754 (kappa = 0.53). When review of 121 photographs from patients was compared with that of 43 control photographs, the odds ratio for patients:controls was 7.62 (95% confidence interval, 2.26–28.23) (P < 0.001).

There was a predominance of diffuse loss and slits. Etching also was observed. Superotemporal findings (92%) were 5.4 times as frequent as inferotemporal findings (17%) (Figs 1 and 2). The prevalence of abnormal visual fields by type of retinal nerve fiber layer finding is shown in Table 1. Abnormal visual fields were found more often in eyes with diffuse loss (89%) than in those eyes with etching (60%) or slits (29%).

Visual fields were classified as abnormal in 19 (53%) of 36 eyes. Blind-spot enlargement occurred in 24 (67%)

Table 1. Distribution and Type of Retinal Nerve Fiber Layer Abnormalities

<table>
<thead>
<tr>
<th>Abnormalities</th>
<th>RNFL Abnormalities*</th>
<th>Visual Fields</th>
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<tbody>
<tr>
<td></td>
<td>Superior-temporal</td>
<td>Inferior-temporal</td>
</tr>
<tr>
<td>Diffuse loss</td>
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<td>2</td>
</tr>
<tr>
<td>Slits</td>
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<td>1</td>
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<td>Etching</td>
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<td>0</td>
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<tr>
<td>Etching and wedge</td>
<td>1</td>
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RNFL = retinal nerve fiber layer.

* Two eyes with both superior- and inferior-temporal abnormalities. Abnormal RNFL in total study eyes, 24/36 (67%).
of 36 eyes, but was not considered abnormal in this study. Correlation of the status of the retinal nerve fiber layer with the visual field status is shown in Table 2. Eyes with normal retinal nerve fiber layer and/or normal visual fields were not analyzed further. All others were classified into three groups:

Group 1 included 13 eyes in which both retinal nerve fiber layer and visual fields were abnormal. The locations of retinal nerve fiber layer abnormalities correlated with retinotopically appropriate visual field abnormalities in 10 of 12 eyes (Table 3) (Fig 3). The visual field was found to be tubular (constricted to all isopters without appropriate variability at various test distances) in one patient and was excluded from analysis.

Group 2 included 11 eyes with abnormal retinal nerve fiber layer and normal visual fields. The type of retinal nerve fiber layer defects found in this group included slits, diffuse loss, wedges, and etching (Table 1). Two separate readings of these retinal nerve fiber layers confirmed that diffuse loss was found less commonly (2/12 or 17% of eyes) than were slits (7/12 or 58% of eyes).

Group 3 included six eyes with normal retinal nerve fiber layer but abnormal visual fields. Of these fields, three were found to be fictitiously tubular, two demonstrated depression of less than 5 decibels in the most peripheral test points of Octopus program 24, and 1 eye demonstrated 5- to 20-decibel losses in several inferonasal test points.

The number of eyes classified as having mild, moderate, or atrophic papilledema; the prevalence of abnormal retinal nerve fiber layer; and abnormal visual fields in each of these classes is shown in Table 4. The prevalence of abnormal retinal nerve fiber layer was approximately equal between those eyes with mild (77%) and atrophic (70%) papilledema. In the moderate papilledema group, two of six eyes showed retinal nerve fiber layer changes. To analyze this further, the prevalence of diffuse loss and slit defects within the mild and atrophic groups was tabulated (Table 4). This showed slit defects predominating over diffuse loss in mild papilledema, and the converse was shown in atrophic papilledema.

**Comments**

Retinal nerve fiber layer changes were found in 67% of 36 eyes of 21 patients with papilledema due to idiopathic intracranial hypertension. In these 36 eyes, diffuse loss...
was found in 10 (28%), slits in 9 (25%), and etching in 5 (14%) (Table 1). The different types of retinal nerve fiber layer abnormalities may be related to the severity and, perhaps, the duration of papilledema. Visual field abnormalities were more common in eyes with atrophic (65%) compared with mild (38%) and moderate (50%) papilledema. Of those eyes with atrophic papilledema and visual field loss, diffuse loss predominated, whereas in those eyes with mild to moderate papilledema and visual field loss, slits predominated. In addition, slits also predominated in eyes with retinal nerve fiber layer defects and normal visual fields (Table 1). This suggests that slit defects may precede the occurrence of diffuse retinal nerve fiber layer loss and visual field loss. A similar type of progression appears to occur in glaucoma, wherein nerve fiber layer changes have been reported to be present before visual field loss in 60% of ten glaucomatous eyes. 11

Blind-spot enlargement was found in 67% of eyes, which is in agreement with the 33% to 93% prevalence reported by others. 1-4 We agree with Orcutt et al 9 and Corbett et al 10 that enlargement of the blind spot is a relatively unimportant index of visual dysfunction, which can be monitored more precisely by measuring peripheral isopters in the visual field.

Excluding blind-spot enlargement, abnormal visual fields were found in 53% of eyes in the current study. Although our visual field results must be interpreted with caution because two different types of perimeter were used, our findings agree with the 14% to 58% reported by those using a Goldmann perimeter or a tangent screen. 1,4 This is less than the 83% to 98% incidence of abnormalities reported in a study, wherein the central 30° was analyzed by automated perimetry, 4 perhaps because Goldmann perimetry or a 60° automated visual field test was used predominantly in our study. Although this reduces the likelihood of false-positive visual field findings, we agree that peripheral visual field testing may miss more significant central visual field abnormalities and recommend that automated visual field testing within 30° of fixation should be used in monitoring patients with papilledema.

Changes in the superotemporal retinal nerve fiber layer were 5.4 times more prevalent than in the inferotemporal retinal nerve fiber layer. Observer bias was unlikely as an explanation for this, because all slides were projected with the retinal nerve fiber layer oriented relative to the optic disc. The basis for the increased prevalence of retinal nerve fiber layer changes in the superotemporal region may be anatomic. Nerve fibers from the peripheral retina which enter the periphery of the optic disc, especially from the temporal periphery, 12,13 have been found histopathologically to be preferentially damaged in patients who died with papilledema. 14,15 An experimental study of papilledema showed a predisposition of superior and inferior optic nerve rims to damage from axonal swelling. 16

The dissimilarity of nerve fiber layer diameters in different regions of the retina 17 and a decreased amount of glial support for nerve fiber layer bundles above and below the optic disc 18 also may play a role in the distribution of retinal nerve fiber layer damage in papilledema. The neuroretinal rim of the inferior pole of the optic disc has been determined to be slightly thicker than the superior pole. 19

This disparity may explain the predominance of superior retinal nerve fiber layer changes if the superior nerve fiber layer has less reserve and may be the first portion of the retinal nerve fiber layer to manifest the effects of a generalized process. Variations in structure of the optic nerve head with respect to the lamina cribrosa 20,21 and vascular supply 22-24 may be important. Ischemic damage to the optic nerve has been shown to occur preferentially in the periphery of the optic nerve head, 14 and inferior altitudinal visual field defects predominate in patients with anterior ischemic optic neuropathy, 25 suggesting a vascular factor in the pathogenesis of retinal nerve fiber layer loss in papilledema.

The clinical usefulness of retinal nerve fiber layer monitoring in patients with idiopathic intracranial hypertension can be found in those patients with tubular visual fields, equivocal visual fields, and normal visual fields. Longstanding papilledema, normal visual acuity, and constricted visual fields in a patient can pose a management dilemma. In this case, relying on the visual fields to determine therapy can be misleading. Corbett et al 1 described a patient who underwent several surgical procedures to control elevated intracranial pressure for what later proved to be hysterical visual loss. If the retinal nerve fiber layer appears normal in such a case, the examiner should suspect that the visual field is spurious and should manage the patient more conservatively. However, if retinal nerve fiber layer abnormalities, especially diffuse loss, are apparent, the clinician has evidence of a destructive process, which may warrant a more aggressive approach. The patient with equivocal or fluctuating visual fields can be approached in a similar manner. Because retinal nerve fiber layer changes represent permanent neuronal loss, 14 serial examinations of the retinal nerve fiber layer over time may demonstrate a stable or declining course, adding valuable information for further management.

Interpretation of retinal nerve fiber layer changes in the absence of visual field loss must be viewed with reservation. Twelve of 17 study eyes with normal visual fields showed retinal nerve fiber layer abnormalities, with slit defects predominating (Table 1). Whether this means that retinal nerve fiber layer changes in papilledema precede the onset of visual field loss, as in glaucoma, 11 is unknown. Some retinal nerve fiber layer changes, especially slit defects, may be normal variants and only coincidentally related. In cynomolgus monkeys, the ophthalmoscopic detection of retinal nerve fiber layer loss occurred only after 50% of the axons were lost, 18 suggesting that retinal nerve fiber layer loss may be detected only shortly before visual field loss ensues. Retinal nerve fiber layer changes in the setting of normal visual fields are most likely a sign of neuronal loss, warranting closer follow-up than in the absence of such changes.

The retinal nerve fiber layer is commonly abnormal in patients with papilledema due to idiopathic intracranial hypertension. Retinal nerve fiber layer abnormalities may precede and eventually correlate with the location and type of visual field loss. Analysis of the retinal nerve fiber layer provides objective, clinical information, which can
assist in managing patients with papilledema due to idiopathic intracranial hypertension.

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References