The Neurologic Evaluation of Patients with Low-Tension Glaucoma

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One hypothesized cause of low-tension glaucoma is chronic or intermittent ischemia of the optic nerve. Since the optic nerve and brain are both parts of the central nervous system and share a common blood supply, the authors wondered if patients with low-tension glaucoma might also have clinical or radiographic evidence of cerebral atrophy. In this study, 27 patients with low-tension glaucoma were examined using neurobehavioral testing, electroencephalography, computerized tomographic scan, neurological history, and physical examination. In only a small number of patients were these tests abnormal. However, 12 of the 27 patients gave a history of common or classic migraine. This unexpected finding raises the possibility that migraine-related ischemia might be the pathogenic mechanism in some cases of low-tension glaucoma. Invest Ophthalmol Vis Sci 26:1101-1104, 1985

Low-tension glaucoma is an ocular disorder of the elderly characterized by glaucomatous cupping and atrophy of the optic nervehead and nerve-fiber bundle defects in the visual field. Although the optic nerve cupping and visual field loss in low-tension glaucoma are identical to that caused by high intraocular pressure in other forms of glaucoma, the intraocular pressure in low-tension glaucoma is consistently normal.

The cause or causes of low-tension glaucoma are not known with certainty. A history of shock, blood loss, or low blood pressure is more common in patients with low-tension glaucoma than in controls.1 This suggests that ischemia may cause the optic nerve damage in some cases. The common occurrence of optic disc hemorrhages in low-tension glaucoma is also consistent with an ischemic process.

In 1946, Sjogren3 drew attention to the histologic resemblance of cavernous optic atrophy, which Schnabel4,5 described in low-tension glaucoma as well as in high-pressure glaucoma, to lacunar infarcts of the brain, a condition that is usually due to hypertensive vaso-occlusive disease of small cerebral blood vessels.6 Sjogren suggested that cerebral atrophy and low-tension glaucoma may occur together in the same patient because of a "vasomotor disturbance." As evidence for this theory, he described four cases of low-tension glaucoma in which pneumoencephalography had disclosed cerebral atrophy. He also observed slight dementia in two cases, severe headaches in two cases, and neurologic abnormalities in four cases.

These historical studies have to be interpreted with caution. There are no modern reports of the histopathology of the optic nerveheads in eyes with low-tension glaucoma. Schnabel's work was done before the availability of accurate tonometers. Thus, we cannot be certain that his patients truly had low-tension glaucoma. Sjogren defined low-tension glaucoma as an intraocular pressure less than 30 mmHg using the old calibration scale of the Schiotz tonometer. Using the 1955 scale, his upper limit would have been considerably lower, but here again it is difficult to be sure that all of his patients would today be classified as low-tension glaucoma.

Nevertheless, Sjögren's hypothesis of an association between low-tension glaucoma and cerebral atrophy or central nervous system dysfunction has a certain intuitive appeal. The optic nerve and brain are both central nervous system tissues and share a common blood supply. However, Sjögren's hypothesis has never been critically tested. In the present study we performed comprehensive neurologic evaluations on 27 patients with well-documented low-tension glaucoma. The neurologic evaluation included neurologic history, neurologic examination, computerized axial tomography, electroencephalography, and neurobehavioral testing.
Table 1. Area of ventricles as a percent of the total area of intracranial cavity at the same level (mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Third ventricle</th>
<th>Body of ventricles</th>
<th>Frontal horns</th>
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<tbody>
<tr>
<td>LTG</td>
<td>0.69 ± 0.28</td>
<td>7.46 ± 4.19</td>
<td>2.75 ± 1.09</td>
</tr>
<tr>
<td>Control</td>
<td>0.64 ± 0.24</td>
<td>7.68 ± 2.92</td>
<td>2.44 ± 0.98</td>
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The controls were age- and sex-matched, selected from the group of normal subjects studied by Damasio H et al. The ratios were derived from measuring the area of the ventricles and dividing that by the area within the internal circumference skull at the same level.

Materials and Methods

Twenty-seven patients, 22 women and five men, with low-tension glaucoma were entered into the study. The average age was 70.4 yr with a range of 48–84 yr. Only two patients were less than 60 yr old. Educational level varied between 7 and 19 yr of schooling with a mean of 12.2 yr. All but one patient were right-handed. All had glaucomatous optic disc cupping and characteristic nerve fiber bundle visual field defects in one or both eyes. All had intraocular pressures consistently less than 22 mmHg on repeated measurements, even when receiving no medications to lower intraocular pressure. Each patient had at least one series of “around-the-clock” measurements when pressures were taken at 7 AM, 10 AM, 1 PM, 4 PM, 7 PM, and 10 PM. We included only patients who were reliable subjects for visual field testing and who had no other lenticular, retinal, optic nerve, or cerebral cause of visual field loss. Most patients were referred by other physicians for low-tension glaucoma evaluation. Loss of vision brought 13 of the patients to medical attention; the remainder were asymptomatic and had been detected when glaucomatous cupping was noted during a routine ophthalmoscopic examination.

Informed consent was obtained from each patient after the nature of the tests was explained fully.

The neurologic history included detailed questions about neurologic symptoms, especially focal motor deficits, double vision, or sensory loss. It also included questions regarding headaches: family history of headache, personal history of unilateral headache, nausea, vomiting, and preceding visual symptoms (fortification specters), sensory or motor symptoms, blurred vision, somnolence, and postheadache diuresis.

Computed tomographic scans of the head were performed on a Picker 1600 Scanner. After the scans were masked and arranged in random order, they were magnified using an Omega D-5 photographic enlarger (Omega Division, Berkey Marketing, Woodside, NY) with a Rodenstock Rodagon 150-mm flat-field projection lens (Optische Werke G. Rodenstock; Munich, West Germany). Using the method of Damasio et al., we traced the outline of the bodies of the lateral ventricles, the frontal horns at their widest point, the third ventricle, and the internal circumference of the skull at each level where the ventricles were traced. The ratio of the area of ventricle to the area of the internal cross section of the skull at the same level was calculated and multiplied by 100 to determine the percent of total cross-sectional area represented by ventricular area. The ratios obtained from the low-tension glaucoma patients were compared to those of elderly normal subjects. The control group was age- and sex-matched and was drawn from a pool of subjects examined during a previous study at this hospital. These elderly normal subjects had undergone similar clinical neurologic examinations, behavioral assessment, and electroencephalography as well as computerized tomographic scan. Because the previous study did not include younger subjects, we matched the two youngest low-tension glaucoma patients with two patients of similar age who had undergone computerized tomography for hysterical hemiparesis.

Electroencephalography was performed on a Grass Model 8, 16 channel recorder (Grass, Quincy, MA) using International 10-20 montages and was done with the patient awake.

Neurobehavior studies included tests for assessment of temporal orientation, intelligence, short-term verbal memory, visual-perceptual discrimination of unfamiliar faces, speech and associative word fluency (controlled oral word association), and visual memory for geometric designs. The test results were compared to standard scores for subjects of similar age.

Results

Neurological history and examination disclosed no episodes of stroke or transient ischemic episodes. One patient had benign essential tremor. There was a history of migraine in 12 (48%) of the 27 patients. Eleven patients with migraine were women. These patients had headache with two or more of the following migraine features: unilaterality of the headache, accompanying nausea, and visual prodromata. Two of the migraine patients had classic migraine with fortification specters; the other ten had common migraine (unilateral headache with nausea and vomiting).

Electroencephalography was normal in 23 of the patients, disclosed nonspecific age-related slowing in
three patients, and disclosed focal abnormalities in one patient. This patient had no corresponding clinical, historical, or radiologic abnormality.

The computed tomographic scans were normal in 26 patients and abnormal in one. The one abnormality was a small low density cortical lesion in the right frontal area in a patient who had no history or signs of neurologic disorder, no electroencephalographic abnormality, and no disturbance of mental function. The nature of the lesion, while presumably vascular, remains unknown.

The ventricular:skull area ratios in the low-tension glaucoma patients were comparable to the normal controls \( (P > 0.05, \text{paired } t\text{-test}) \) (Table 1).

Neurobehavior testing did not reveal any consistent patterns of intellectual, memory, perceptual, or linguistic impairment. Twenty patients (74%) had completely normal examinations. Five patients exhibited a mild decrease in attention or concentration but no clear evidence of abnormal mental decline or lateralized brain dysfunction. Only two patients showed a deficit that was serious enough to suggest a drop in function from previously attained abilities. Both of these patients had large ventricles but no focal neurologic deficits; neither was seriously demented.

**Discussion**

We found no evidence to support the hypothesis that neurologic disease, as manifested by an abnormal neurologic history or abnormalities in the neurologic examination, computed tomographic scan, electroencephalography, or neurobehavior testing, is consistently associated with low-tension glaucoma. The neurologic status of our patients, with few exceptions, was normal.

In one respect our study was biased against finding any such neurologic association since we included only low-tension glaucoma patients who could reliably perform visual field testing and whose general health allowed them to participate. During the time we recruited patients for the study we excluded only three patients who failed to meet these criteria. Had they been included, and had they been found to have cerebral atrophy, they would still constitute only a small fraction of the low-tension glaucoma population.

Thus, Sjögren's hypothesis of a common lacunar atrophy that affects both the brain and optic nervehead is unlikely to be correct. This speaks neither for nor against a vascular pathogenic mechanism in low-tension glaucoma, but it implies that the pathogenic process, whatever the mechanism, is localized to the optic nervehead and is not a more generalized central nervous system disorder.

We did not anticipate finding that nearly half of the low-tension glaucoma patients in this study had migraine. This prevalence was higher than we would have expected in a normal group of people of this age range. A possible association between migraine and low-tension glaucoma has potentially important pathogenic implications. Migraine is associated with transient alterations of cerebral or meningeal blood flow.\(^{15}\) Other investigators have found associations between migraine, Prinzmetal's angina, and Raynaud's phenomenon.\(^{16-18}\) Migraine attacks have also been associated with infarctions of cerebral cortex,\(^{19}\) retina,\(^{20}\) or optic nerve.\(^{21}\) Could some cases of low-tension glaucoma represent ischemic optic atrophy due to migraine?

This is an important question because the symptoms of migraine can be alleviated in most patients by prophylactic treatment with systemic beta-adrenergic blocking drugs.\(^{22}\) Perhaps further visual loss in some patients with low-tension glaucoma might be prevented by such treatment.

To further investigate the possible association of migraine with low-tension glaucoma, we recently have conducted a case-control study. This is the subject of a companion article.\(^{23}\)

**Key words:** computerized tomography (CT) scan, electroencephalography, low-tension glaucoma, migraine, neurobehavioral testing

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**References**