Parapapillary Atrophy and Retinal Vessel Diameter in Nonglaucomatous Optic Nerve Damage

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Parapapillary chorioretinal atrophy and decreased retinal vessel diameter occur in glaucomatous eyes. To evaluate the frequency and degree of these signs in nonglaucomatous optic neuropathy, the authors evaluated morphometrically and compared 47 patients with nonglaucomatous optic nerve atrophy from extraocular causes with 292 patients with primary open-angle glaucoma and 179 normal subjects. Eyes with anterior ischemic optic neuropathy were excluded. The parapapillary atrophy was differentiated into a central zone (beta) with sclera and large choroidal vessels visible by ophthalmoscopy and a peripheral zone (alpha) with irregular pigmentation. Both zones did not differ significantly in the eyes with nonglaucomatous optic neuropathy and the normal eyes. In the glaucomatous eyes, they were significantly larger and occurred more frequently. The retinal vessel diameter was significantly smaller in both groups with optic nerve atrophy than in the normal group. It was concluded that decreased retinal vessel diameters unspecifically suggest optic nerve atrophy. Evaluation of parapapillary chorioretinal atrophy can be helpful in differentiating nonglaucomatous from glaucomatous optic neuropathy.


The abnormalities of parapapillary chorioretinal atrophy were reported to be more common and marked in eyes with glaucomatous optic nerve damage than in normal eyes or eyes with ocular hypertension. Some authors described a spatial correlation between the location of the parapapillary chorioretinal atrophy and the most pronounced glaucomatous damage in the intrapapillary region of the optic disc and the most marked perimetric defect in the visual field. In an indirect histomorphometric investigation, the parapapillary changes corresponded with irregular pigmentation or complete loss of retinal pigment epithelium cells and a decreased count of retinal photoreceptors.

Another feature of the parapapillary region, retinal vessel diameter, was found to be smaller in glaucomatous eyes compared with normal ones. It is unclear whether the vessel diameter reduction was secondary to retinal ganglion cell loss or the primary event leading to ganglion cell death.

In this study, we considered to what degree parapapillary chorioretinal alterations and a reduction of the retinal vessel caliber occur in eyes with nonglaucomatous optic nerve atrophy. This might be helpful to differentiate eyes with glaucomatous and nonglaucomatous optic neuropathy and could provide hints for the pathogenesis. With these objectives in mind, we evaluated morphometrically and compared serial photographs of the optic discs of patients with nonglaucomatous and glaucomatous optic neuropathy and of normal subjects.

Materials and Methods

Patients

Nonglaucomatous optic neuropathy (Figs. 1–4) was documented in 92 eyes (48 right eyes and 44 left eyes) of 23 men and 24 women with a mean age of 38.8 ± 15.7 years (mean ± standard deviation; range, 9–77 years) and a mean refractive error of −1.11 ± 2.41 diopters (range, −7.50–+2.0 diopters). Selection criteria were neuroophthalmologic diseases affecting the optic nerve directly, such as optic nerve gliomas, intracranial meningiomas, pituitary gland adenomas, and earlier inflammations of the optic nerve; visual field defects; a decreased visibility of the retinal nerve fiber bundles; normal intraocular pressure less than 22 mm Hg; and a negative history of glaucoma. To pre-
vent influences of the ciliary circulation and the optic disc size, patients with nonarteritic or arteritic anterior ischemic optic neuropathy or optic disc drusen were excluded.

The primary open-angle glaucoma group (Figs. 5–7) included 528 eyes (277 right eyes and 251 left eyes) of 292 patients (140 men and 152 women) with a mean age of 64.7 ± 12.4 years (range, 23–94 years) and an average refractive error of −0.62 ± 2.42 (range, −7.50–7.00 diopters). Selection criteria were an open anterior chamber angle, intraocular pressure readings of at least 22 mm Hg, “idiopathic” origin of the elevated intraocular pressure, no other reason for optic nerve damage than glaucoma, glaucomatous changes in the intrapapillary region such as abnormal area and configuration of the neuroretinal rim, decreased visibility of the retinal nerve fiber bundles, and glaucomatous visual field loss. This included nasal steps of at least 10° and Bjerrum scotomas.

The control group (Fig. 8) was composed of 290 normal optic nerve heads (138 right eyes and 152 left eyes) of 102 men and 77 women with a mean age of 49.0 ± 16.9 years (range, 7–82 years) and a mean refractive error of 0.09 ± 1.92 diopters (range, −7.25–+6.50 diopters). The subjects came to the eye clinic for a checkup, or for treatment of diseases in the contralateral eyes not included in the study. These diseases, such as perforating corneal injuries and retinal detachments, did not affect the optic nerve primarily. Intraocular pressure in this group was less than 22 mm Hg.

Some of the glaucoma patients and normal subjects had been examined in previous investigations, and others were included for the first time in a biomorphometric study of the optic disc. If both eyes of the same individual had been examined, only one randomly selected eye was taken for statistical analysis. High myopic subjects with a myopic refractive error of more than −8 diopters generally were excluded to avoid the altered characteristic of the optic disc morphology influencing the results. The patients with nonglaucomatous optic nerve atrophy were significantly younger than the normal subjects and the glaucoma patients. For this reason, two subgroups of the control and glaucoma group were formed. They were age matched with the patients with nonglaucomatous optic nerve damage (Table 1).

Methods

For all eyes, 15° color stereo optic disc diapositives were taken using the Allen stereo separator and a telecentric fundus camera. For morphometric analysis, the slides were projected onto a screen, and the outline of the optic disc, peripapillary scleral ring, parapapillary chorioretinal atrophy, and inferior temporal and superior temporal retinal artery and vein at the optic disc border were plotted manually. The outer border of the optic disc was identical with the inner border of the parapapillary scleral ring. The parapapillary chorioretinal atrophy was divided into a peripheral zone (Zone alpha), characterized by irregular hypopigmentation and hyperpigmentation, and a second zone (Zone beta), located close to the parapapillary scleral ring with sclera or denuded Bruch’s membrane and large choroidal vessels visible by ophthalmoscopy (Figs. 5–7). The retinal vessel caliber was determined as the diameter of the superior temporal and inferior temporal retinal artery and vein at the optic disc border. To correct the ocular and camera magnification, Littmann’s method was used after considering the anterior corneal curvature and the refractive error.

The nonparametric test Mann-Whitney test was used to analyze the significance of differences between the groups.

Results

The area and frequency of both zones of parapapillary chorioretinal atrophy taken separately or as a sum did not vary significantly between the normal eyes and the eyes with nonglaucomatous optic neuropathy matched or unmatched for age (P > 0.40, Table 1). Ophthalmoscopically, both zones were more detectable but not larger in the eyes with nonglaucomatous optic nerve atrophy than in the control group (Figs. 1–4, 8).

In the glaucomatous eyes, Zones alpha and beta were significantly larger than in the normal eyes (P < 0.001 and P < 0.001, respectively) and the eyes with nonglaucomatous optic neuropathy matched or unmatched for age (P > 0.007 and P < 0.001, respectively). Additionally, Zone beta occurred significantly more often in the glaucoma group than in the two other groups (P < 0.001, by chi-square test). The frequency of Zone alpha did not vary significantly among the three groups. The differences in the groups was significant after they had been matched for age (Table 1). Zone beta was smaller in the age-matched glaucoma subgroup than in the total glaucoma group (Table 1). The reason for this was that the younger glaucoma patients in the age-matched glaucoma subgroup had less severe glaucomatous optic nerve damage (neuroretinal rim area, 1.18 ± 0.58 mm²) than the patients of the total glaucoma group with a higher mean age (neuroretinal rim area, 0.98 ± 0.55 mm²).
For calculating the sensitivity and specificity of the parapapillary chorioretinal atrophy to differentiate among the three groups examined, the parapapillary atrophy was considered to be abnormal if Zone alpha was larger than 0.71 mm² (mean plus one standard deviation in the control group) or if Zone beta was present. Using this arbitrary definition of an abnormal Zone alpha (beta), the eyes of 15.6% (18.4%) of the normal subjects, 39.7% (68.2%) of the glaucoma patients, and 8.9% (17.8%) of the patients with nonglaucomatous optic nerve atrophy were pathologic. We defined sensitivity as the ratio of the true-positive glaucoma diagnoses to the total number of glaucoma patients and specificity as the percentage of the true-negative diagnoses of nonglaucomatous optic nerve atrophy divided by the total count of patients with this disease. Using this terminology, Zones alpha and beta had a sensitivity of 39.7% and 68.2%, respectively, and a specificity of 91.1% and 82.2%, respectively, to differentiate between the eyes with glaucomatous and nonglaucomatous optic nerve damage. Because the normal subjects and the patients with nonglaucomatous optic nerve atrophy did not vary significantly in size and frequency of the two zones, the latter parameters did not have a sensitivity and specificity able to differentiate between these two groups.

The retinal vessel diameter did not vary significantly between the eyes with glaucomatous and nonglaucomatous optic nerve atrophy (0.26 < P < 0.80). The vessel caliber was significantly smaller in the eyes with optic nerve damage than in the normal ones (P < 0.001, Table 1). An exception was the caliber of the inferior retinal vein. The area of the optic disc was not significantly different (P > 0.26) among the three groups.

Discussion

Parapapillary Chorioretinal Atrophy

Morphologic differentiation of nonglaucomatous and glaucomatous optic nerve atrophy usually was based on intrapapillary features such as rim pallor and depth of the optic cup. In glaucomatous eyes, the neuroretinal rim characteristically shows a loss of area and a change of form with a secondary increase of cup area and cup-to-disc ratios. The same, however, was described for eyes with nonglaucomatous optic nerve damage. Using the parameters “neuroretinal rim pallor” and “rim obliteration,” it is difficult to differentiate between eyes with glaucomatous and nonglaucomatous optic nerve atrophy.

With exception of changes in the retinal nerve fiber layer, the parapapillary region has not been consid-

| Table 1. Papillomorphometric data (figures given in percent values indicate frequency) |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Parapapillary chorioretinal atrophy | Group 1: patients with nonglaucomatous optic nerve atrophy (n = 47) | Group 2: patients with primary open-angle glaucoma (POAG) (n = 292) | Group 3: patients with POAG age-matched with group 1 (n = 32) | Group 4: normal subjects (n = 179) | Group 5: normal subjects age-matched with groups 1 and 3 (n = 103) |
| Zone alpha (mm²) | 0.45 ± 0.27 (93%) | 0.62 ± 0.48 (87.3%) | 0.68 ± 0.53 (93.8%) | 0.41 ± 0.30 (82.1%) | 0.37 ± 0.49 (82.5%) |
| Zone beta (mm²) | 0.16 ± 0.45 (17.8%) | 0.78 ± 1.08 (68.2%) | 0.48 ± 0.55 (75.0%) | 0.17 ± 0.56 (18.4%) | 0.15 ± 0.54 (19.4%) |
| Total (mm²) | 0.61 ± 0.48 | 1.41 ± 1.13 | 1.12 ± 0.66 | 0.57 ± 0.65 | 0.53 ± 0.59 |
| Diameter retinal vessels (mm) | | | | | |
| Temporal superior artery | 0.095 ± 0.014 | 0.091 ± 0.021 | 0.085 ± 0.025 | 0.110 ± 0.022 | 0.109 ± 0.022 |
| Temporal inferior artery | 0.096 ± 0.021 | 0.095 ± 0.022 | 0.097 ± 0.024 | 0.114 ± 0.023 | 0.115 ± 0.025 |
| Temporal superior vein | 0.132 ± 0.023 | 0.130 ± 0.027 | 0.132 ± 0.025 | 0.143 ± 0.032 | 0.143 ± 0.035 |
| Temporal inferior vein | 0.141 ± 0.020 | 0.132 ± 0.027 | 0.126 ± 0.033 | 0.145 ± 0.028 | 0.146 ± 0.030 |
| Optic disc area (mm²) | 2.54 ± 0.40 | 2.66 ± 0.58 | 2.61 ± 0.54 | 2.71 ± 0.69 | 2.71 ± 0.73 |
erated routinely. The chorioretinal atrophy in the parapapillary region of glaucomatous eyes can be interpreted as a precursor to halo glaucomatous and therefore deserves attention in glaucomatous eyes. In this study, parapapillary chorioretinal abnormalities were found to occur less often and to be less marked in eyes with nonglaucomatous optic neuropathy than in glaucomatous eyes (Table 1). The differences were more pronounced for Zone beta with sclera or denuded Bruch’s membrane and large choroidal vessels visible by ophthalmoscopy than for Zone alpha characterized by irregular pigmentation (Figs. 5–7). This shows that, in eyes with decreased visibility of retinal nerve fiber bundles and visual field defects, the presence of Zone beta or an unusually large Zone alpha suggest glaucomatous optic neuropathy; a normal appearance of the parapapillary region in respect to the chorioretinal atrophy is more likely to indicate the nonglaucomatous type of optic nerve atrophy. It must be remembered, however, that Zones alpha and beta were normal in 60.3% and 31.8% of the glaucomatous eyes, respectively, and abnormal in 8.9% and 17.8% of the eyes with nonglaucomatous optic nerve atrophy, respectively. This indicates that evaluation of the parapapillary chorioretinal atrophy may be helpful but not sufficient by itself to separate eyes with glaucomatous and nonglaucomatous optic nerve atrophy.

Pathogenetically, we may infer that presence of the parapapillary chorioretinal atrophy in glaucoma does not depend entirely or at all on the nerve fiber loss, but that other factors may be responsible. One of these factors may be that the depth of the optic cup is more shallow in glaucoma eyes with marked parapapillary chorioretinal atrophy than in glaucomatous eyes with little or no parapapillary chorioretinal atrophy.17

Retinal Vessel Diameter

Retinal vessel diameter was significantly smaller in both groups with optic nerve atrophy than in the normal eyes (Table 1). This agrees with a previous morphologic study20 and investigations of retinal blood flow.31 It suggests that the decreased vessel caliber in glaucomatous eyes is not primary to the ganglion cell loss; it occurs secondarily as a consequence of a diminished retinal ganglion cell population. This indicates autoregulation of the retinal blood circulation. From a clinical point of view, in eyes with abnormally small retinal vessels, optic nerve atrophy should be excluded diagnostically.

Key words: optic disc morphometry, optic nerve atrophy, parapapillary atrophy, retinal vessel caliber, glaucoma

References