EXTENDED REPORT

Peripapillary atrophy after acute primary angle closure

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Aim: To determine the changes in peripapillary atrophy after episodes of acute primary angle closure (APAC).

Methods: Prospective observational study of 40 eyes in 38 patients of predominantly Chinese ethnicity. The mean (SD) intraocular pressure at the time of presentation was 51.7 (12) mm Hg (median, 55 mm Hg) and the mean duration of the symptoms was 37.7 (69.4) hours. A laser iridotomy was undertaken 3.2 (8.4) days after the APAC episode, leading to normalisation of intraocular pressure in all cases. Colour optic disc photographs taken at 2 and 16 weeks after APAC were examined morphometrically. Peripapillary atrophy was divided into α and β zones.

Results: Comparing measurements at baseline with week 16, the minimum width of the α zone (0.013 (0.056) v 0.016 (0.001) arbitrary units; $p=0.23$), the maximum width of the α zone (1.11 (1.31) v 1.31 (0.79) arbitrary units; $p=0.22$), the minimum width of the β zone (0.030 (0.122) v 0.033 (0.166) arbitrary units; $p=0.93$), and the maximum width of the β zone (0.62 (0.94) v 0.73 (0.98) arbitrary units; $p=0.42$) did not vary significantly. The mean cup to disc ratio increased from 0.56 (0.05) to 0.62 (0.07) ($p<0.0001$) at the end of follow up.

Conclusions: The α and β zones of peripapillary atrophy did not enlarge markedly in patients after APAC, despite an enlargement of the optic cup during a follow up of four months.

About 100 years ago, ophthalmologists such as Elschnig and Bücklers described an association between glaucoma and peripapillary chorioretinal atrophy.^{1,2} It was called "halo glaucomatosus" when it totally encircled the optic disc in eyes with end stage glaucoma. Later, other investigators confirmed these observations, describing the occurrence of peripapillary atrophy in eyes with glaucoma.^{3–11} Heijl and Samander found a spatial correlation between peripapillary atrophy and the location of the most marked visual field loss.⁵ Nevarez *et al* found that the presence or extent of peripapillary atrophy correlated with glaucomatous disc damage.⁷ Ophthalmoscopically, peripapillary atrophy was divided into a central β zone and a peripheral α zone.⁹ The α zone was characterised by an irregular hypopigmentation and hyperpigmentation, and intimated thinning of the chorioretinal tissue layer. Features of the inner β zone were marked atrophy of the retinal pigment epithelium and the choriocapillaris, good visibility of the large choroidal vessels and the sclera, thinning of the chorioretinal tissues, and round borders with the adjacent α zone on its peripheral side and with the peripapillary scleral ring on its central side.

Both α and β zones were larger and the β zone occurred more often in eyes with primary open angle glaucoma (POAG) than in normal eyes.⁹ In POAG, the size of both zones and the frequency of the β zone were significantly correlated with variables reflecting the severity of the glaucomatous optic nerve damage, such as neuroretinal rim loss, decrease in retinal vessel diameter, reduced visibility of the retinal nerve fibre bundles, and perimetric defects.² It was larger in that sector with the most marked loss of neuroretinal rim, and largest in the quadrant that had the longest distance to the exit of the central retinal vessel trunk on the lamina cribrosa.² The decreased choroidal filling in the β zone on fluorescein angiography was considered to indicate that the optic nerve head had a compromised blood supply and hence was more susceptible to damage from glaucoma.¹¹ Interestingly, closure of the

choriocapillaris and a decreased thickness of the choroid in the region of the β zone was seen on histological slides.^{12,13}

Primary angle closure glaucoma is a major form of glaucoma in Asia.¹⁴ In eyes with primary angle closure glaucoma, peripapillary atrophy has been postulated to have a different relation to the structural and functional optic disc changes compared with POAG, and it has been proposed that different mechanisms are involved in development of the optic disc damage in the two types of glaucoma.¹⁵ A recent study found structural changes in the neuroretinal rim and optic cup after an episode of acute primary angle closure (APAC).¹⁶ Our aim in the present study was to assess whether there were also changes in peripapillary atrophy after APAC.

METHODS

This prospective observational study included patients aged 21 years and over who were diagnosed with APAC. Diagnostic criteria were as follows:

- the presence of at least two of the following symptoms: ocular or periocular pain, nausea or vomiting or both, and an antecedent history of intermittent blurring of vision with haloes;
- a presenting intraocular pressure of more than 28 mm Hg on Goldmann applanation tonometry;
- the presence of at least three of the following signs: conjunctival injection, corneal epithelial oedema, mid-dilated unreactive pupil, and shallow anterior chamber;
- the presence of an occluded angle in the affected eye on gonioscopy.

The study was approved by the ethics committee of the Singapore National Eye Research Institute and was carried out

Abbreviations: APAC, acute primary angle closure; POAG, primary open angle glaucoma

according to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all patients.

For each patient, the demographic characteristics, previous medical history, and ophthalmic data on the APAC episode were recorded at presentation. The APAC attack was managed with medical treatment followed by peripheral laser iridotomy within a few days of presentation. A stereoscopic optic disc photograph was taken at 2 weeks and 16 weeks after the APAC episode.

Subjects were excluded from the study for the following reasons: patients who did not meet the above criteria; patients diagnosed with secondary angle closure, such as lens induced glaucoma, neovascular glaucoma, or uveitic glaucoma; patients whose Snellen visual acuity of the affected eye was worse than 6/12 after the APAC attack had resolved; patients who had corneal abnormalities, media opacities, or retinal abnormalities that would affect stereoscopic optic disc photography; and patients who had cataract or trabeculectomy surgery between the study visits.

The stereoscopic colour optic disc photographs were analysed morphometrically. Slides of each eye were projected in masked fashion without knowledge as to which was the first slide or the last slide taken, and the structures of the optic disc, optic cup, peripapillary scleral ring, and α and β zones of the peripapillary atrophy were plotted on paper by trained examiners (JBJ and FR). As already defined in previous morphometric studies on the appearance of the optic nerve head, the border of the optic disc—and by that the outer margin of the neuroretinal rim—was identical with the inner margin of the peripapillary scleral ring. The inner border of the neuroretinal rim—and by that the outer margin of the optic cup—was defined by contour and not by pallor.² The minimum and maximum widths of the α and β zones and the horizontal diameters of the optic disc and the optic cup were measured and recorded. To compare the measurements of the slide taken at the end of the follow up with the measurements taken shortly after the APAC episode, the horizontal disc diameter was considered to be constant. The measurements of the follow up examination were then divided by the quotient of the horizontal disc diameter of the second examination divided by the horizontal disc diameter of the first examination.

In a second step of the examination, the slides of each eye were again mixed and projected in a randomised masked order so that the examiner did not know which slide was the first taken. The examiner had to determine whether there was a difference between the two slides.

Statistics

Statistical analysis was carried out using a commercially available statistical software package (SPSS for Windows, version 13.0, SPSS, Chicago, Illinois, USA). To assess the statistical significance of a difference between the baseline and follow up examinations, we use the Student *t* test for paired samples. The 95% confidence intervals (CI) were calculated.

RESULTS

The inclusion criteria were fulfilled by 40 eyes (20 right, 20 left) in 38 patients (25 female, 13 male). The mean (SD) age of the patients at presentation was 59.7 (8.8) years; median, 59 years; range 45 to 91). Of the 38 patients, 34 (89.5%) were of Chinese ethnicity. The disease was unilateral in 36 patients (95%), with two patients having both eyes affected. The intraocular pressure at the time when the patients presented was 51.7 (12) mm Hg (median, 55 mm Hg; range 30 to 74). The mean duration of the symptoms ranged between one hour and 336 hours (mean (SD), 37.7 (69.4) hours; median 16 hours). Laser iridotomy was done 3.2 (8.4) days after the APAC episode (median, 1 day;

range 0 to 48 days). Seven patients (of 34) were myopic (−1.00 or worse). The mean refractive error, spherical equivalent, was +0.67 (1.68) dioptres (D) (range −2.50 D to +3.75 D). The APAC attack was successfully managed and intraocular pressure was normal after the laser iridotomy throughout the follow up period. The mean cup to disc ratio increased from 0.56 (0.05) to 0.62 (0.07) ($p < 0.0001$). As reported previously, the neuroretinal rim was significantly smaller at follow up compared with the baseline values.¹⁵

Comparing the baseline measurements with the measurements made 16 weeks after the APAC episode, the minimum width of the α zone (0.013 (0.056) ν 0.016 (0.001) arbitrary units (95% CI, −0.01 to 0.03), $p = 0.23$); the maximum width of the α zone (1.11 (1.31) ν 1.31 (0.79) arbitrary units (95% CI, −0.42 to −0.04), $p = 0.02$); the minimum width of the β zone (0.030 (0.122) ν 0.033 (0.166) arbitrary units (95% CI, −0.021 to 0.019), $p = 0.93$), and the maximum width of the β zone (0.62 (0.94) ν 0.73 (0.98) arbitrary units (95% CI, −0.29 to 0.12), $p = 0.42$) did not vary significantly (fig 1, fig 2) after carrying out Bonferroni's correction for multiple statistical comparisons. The locations of the minimum and maximum width of peripapillary atrophy at baseline did not differ from the locations at follow up, so the measurements of baseline ν follow up were taken at the same locations.

In the qualitative assessment of a difference between the two slides of the same eye, for 24 eyes, no difference was detected. For 16 eyes (40%), it was thought that there was a slight difference, with seemingly larger peripapillary atrophy in the last slide in seven eyes (18%) and seemingly larger peripapillary atrophy in the first slide in nine eyes (23%).

DISCUSSION

In previous studies, the presence and amount of peripapillary atrophy varied between the various types of POAG. The β zone of peripapillary atrophy was significantly larger in eyes with highly myopic POAG than in eyes with the age related atrophic type.² The β zone in the latter was larger than in eyes with secondary open angle glaucoma caused by pseudoexfoliation of the lens (pseudoexfoliative glaucoma), primary melanin dispersion syndrome (pigmentary glaucoma), and non-highly myopic POAG.² The β zone was the smallest in juvenile onset POAG. The substantial peripapillary atrophy in eyes with the highly myopic type of POAG may be explained by the myopic stretching of the optic nerve head, with thinning of the lamina cribrosa and peripapillary sclera leading to an increased glaucoma susceptibility and loss of choroid in the peripapillary

Figure 1 Box plots showing the maximum diameter of the α zone (arbitrary units) at two weeks after an acute angle closure episode ("baseline") and at 16 weeks after the episode ("end of follow up"), with no significant difference detected.

Figure 2 Box plots showing the maximum diameter of the β zone (arbitrary units) at two weeks after an acute angle closure episode ("baseline") and at 16 weeks after the episode ("end of follow up"), with no significant difference detected.

region.^{17 18} For the non-highly-myopic types of POAG, there was a tendency for an inverse relation between the amount of peripapillary atrophy, particularly of the β zone, and the intraocular pressure rise, with the largest β zone occurring in eyes with a relatively small elevation of intraocular pressure.

In our series, a short term elevation of intraocular pressure to rather high levels (up to 74 mm Hg) and normalisation of the pressure after 37.7 (69.4) hours did not result in a detectable enlargement of peripapillary atrophy over a follow up period of 16 weeks, despite a noticeable enlargement of the optic cup. We suggest two possible reasons for this: either the short term marked elevation of intraocular pressure leads to a change in the appearance of the optic nerve head as in vascular induced optic neuropathy (for example, non-arteritic anterior ischaemic optic neuropathy, in which the size of the peripapillary atrophy and of the optic cup do not change after the event¹⁹; or the enlargement of the peripapillary atrophy may take place over a longer period than the enlargement of the optic cup, as has been shown in monkeys. Thus in a previous study on experimental glaucoma with a relatively short follow up of 11.1 (56.6) months, peripapillary atrophy did not change markedly,²⁰ while in another investigation on experimental glaucoma in monkeys with a follow up of 25.5 (13.4) months, it showed a marked increase.²¹ As in the present investigation the optic cup was significantly enlarged, we favour the hypothesis that the development of peripapillary atrophy needs a longer time to develop compared with the intrapapillary changes.

There are limitations of the present study. In addition to the measurement of the smallest and longest width of peripapillary atrophy, planimetric measurements of the area of peripapillary atrophy might have given additional information. To overcome this potential weakness, a qualitative assessment of the differences between baseline and follow up of the study was carried out, but showed no significant differences. A blinded qualitative examination of differences between the baseline slides and the slides taken at follow up might even be more sensitive for detecting slight differences than planimetric measurements, in which the examination technique is accompanied by unavoidable noise.

Conclusions

Our study shows that after a pronounced and short term elevation of intraocular pressure, peripapillary atrophy did not increase markedly within four months after the episode of

acute angle closure, despite morphological changes in the intrapapillary region. From a clinical point of view, this suggests that after a short period of high intraocular pressure, the lack of increased peripapillary atrophy does not rule out glaucomatous optic nerve damage, as demonstrated by a loss of the neuroretinal rim.

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