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Acute Peripapillary Retinal Pigment Epithelium Changes Associated with Acute Intraocular Pressure Elevation

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Purpose: To assess changes in the peripapillary retinal pigment epithelium (RPE) in association with an acute intraocular pressure (IOP) elevation provoked by a dark room prone provocative test (DRPPT).

Design: Prospective, comparative clinical observational study.

Participants: Nineteen study group eyes (14 individuals) and 26 control eyes (21 patients).

Methods: Individuals with normal optic nerve heads (ONHs) underwent a DRPPT in a standardized manner. They were stratified into a study group with an IOP rise of more than 15 mmHg at the end of the DRPPT and a control group with an IOP rise between 2 and 4 mmHg. Before and at the end of the test, the ONH was imaged by spectral-domain optical coherence tomography (OCT).

Main Outcome Measures: Morphologic features of the RPE at the peripapillary end of Bruch's membrane.

Results: After a mean IOP rise by 32.1±9.5 mmHg (range, 17−47 mmHg), 18 (95%) eyes in the study group showed a folding or a centrifugal sliding, or both, of the end of the RPE layer on the peripapillary Bruch's membrane. The RPE changes were located most often at the temporal pole of the ONH (16 eyes [89%]), followed by the nasal pole (2 eyes [11%]). The RPE changes were not detected at the inferior or superior disc poles. Some eyes with marked RPE changes showed corresponding changes in peripapillary β zone on infrared ONH photographs. In 7 eyes of 7 participants with OCT images obtained on the day after the PRPPT, the RPE end moved back to the end of peripapillary Bruch's membrane. The single eye of the study group without exhibiting IOP rise−associated RPE changes showed an interdigitation zone line indistinguishable from Bruch's membrane line on OCT images. None of the control eyes showed RPE changes. The difference in frequency of RPE changes between study and control groups was significant ($P < 0.001$).

Conclusions: Eyes with an acute rise in IOP (>15 mmHg) showed a folding and centrifugal sliding of the peripapillary RPE and, after IOP reduction, centripetal RPE movement. These observations may be of interest to elucidate the pathogenesis of peripapillary atrophy in glaucoma. *Ophthalmology 2015;■:1−7 © 2015 by the American Academy of Ophthalmology.*

Peripapillary atrophy has been shown to be associated with glaucomatous optic neuropathy.[1−4] Previously, peripapillary atrophy was differentiated into 2 ophthalmoscopically defined zones.[1,2] The α-zone was characterized by an irregular hypopigmentation and hyperpigmentation and occurred in almost all eyes. The β-zone was distinguished by the visibility of large choroidal vessels and sclera, and it was located between the optic disc border and α-zone. Hospital-based and population-based investigations and experimental studies reveal that β-zone occurs more often and is larger in glaucomatous eyes than in normal eyes, and that progression of glaucomatous optic neuropathy is associated with presence and size of β-zone at baseline and with its enlargement.[5−11] Interestingly, β-zone is associated only with the glaucomatous type of optic nerve damage, whereas nonglaucomatous optic neuropathy resulting from various nonglaucomatous causes does not differ from normal eyes in prevalence and size of β-zone.[12] With the introduction of high-resolution optical coherent tomography (OCT), the ophthalmoscopic β-zone has been further differentiated into an OCT-defined β-zone that is characterized by the presence of Bruch's membrane without retinal pigment epithelium (RPE) covering it and into a γ-zone located between β-zone and the optic disc border and that is characterized by the absence of Bruch's membrane.[13−16] Although the OCT-defined β-zone is associated mainly with glaucoma and, to a markedly lower degree—or not all—with axial myopia, the γ-zone is associated mostly with axial elongation of the globe, but to a minor degree, or not at all, with glaucoma.[13,14] Although clinical and population-based studies and experimental investigations on monkeys with artificially induced glaucoma clearly show the association between β-zone and glaucoma, the cause of the development and enlargement of β-zone in association with glaucoma has remained elusive so far. The purpose of this study was to demonstrate changes in the peripapillary RPE observed in eyes with an acute rise in intraocular pressure (IOP) and that may be of interest for the discussion of the pathogenesis of peripapillary atrophy.

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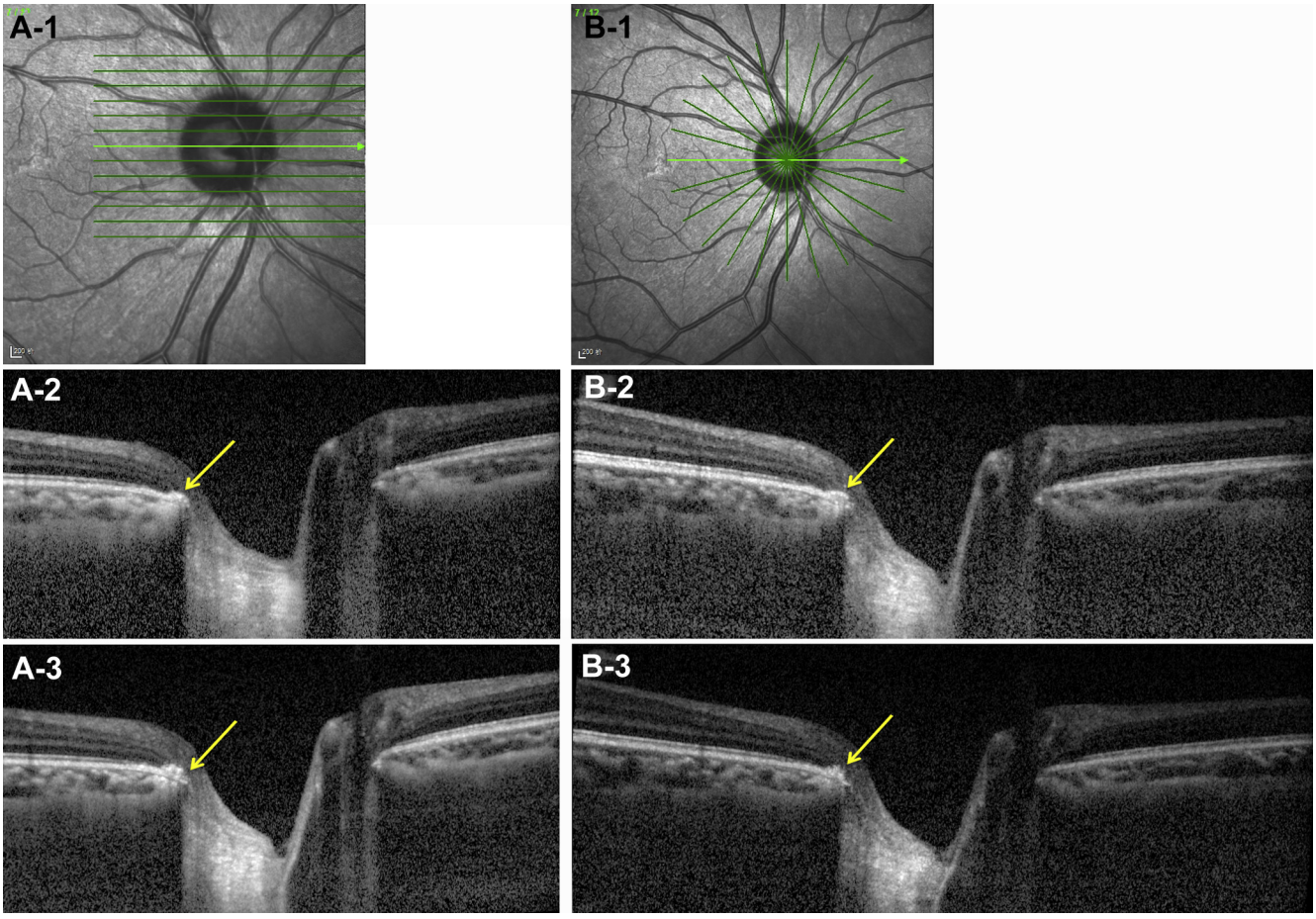

Figure 1. Images showing the change in the peripapillary retinal pigment epithelium (arrows) detected (**A-2**, **B-2**) before and (**A-3**, **B-3**) after rise in intraocular pressure (IOP) from 22 to 50 mmHg after a 2-hour dark room prone provocative test, imaged in (**A-1** to **A-3**) the line scan mode and (**B-1** to **B-3**) the star scan mode in the same eye.

Methods

This prospective, comparative study included all individuals who routinely and consecutively underwent a dark room prone provocative test (DRPPT) from February 2013 through September 2013 and who showed an elevation in IOP of more than 2 mmHg in the DRPPT.[17] The Ethical Review Committee of Beijing Tongren Hospital approved the study and confirmed that it adhered to the provisions of the Declaration of Helsinki for research involving human subjects. All study participants gave written informed consent. We divided the eligible study participants into a study group including all eyes with a rise in IOP of more than 15 mmHg and a control group consisting of all eyes with an elevation in IOP between 2 and 4 mmHg. Exclusion criteria were any disorder of the optic nerve including glaucoma, any ocular disorder that might have affected the quality of fundus images, and age younger than 18 years.

The DRPPT was performed routinely in the Beijing Tongren Hospital for the examination of individuals suspected for acute primary angle closure. The patients were asked to sit in a chair in a dark room for 2 hours and to rest the forehead on a pillow placed on a desk. The patients wore a plastic eye patch with space between the patch and the eye, and they were asked to keep their eyes open for the entire period of the test. Shortly before the test and at 1 and 2 hours after the start of the test, IOP was measured by noncontact tonometry (Topcon CT-60; Topcon Ltd, Tokyo, Japan). All tonometric measurements were performed 3 times, and the mean value of the 3 measurements was used in further statistical analysis.

The optic nerve head (ONH) was imaged by spectral-domain OCT (Spectralis; Heidelberg Engineering GmbH, Heidelberg, Germany) with the enhanced depth imaging mode, which was performed shortly before the start of the DRPPT and within 5 minutes after the end of the test. All the examinations were carried out by an experienced technician. The head position was checked carefully before each examination. Using the matrix scanning mode, we performed 13 horizontal B-scans in a rectangular area of $15^\circ \times 10^\circ$ which was centered on the optic disc. Additionally, the star-scan mode was applied. Each B-scan consisted of 25 OCT frames. We additionally obtained a 360° peripapillary circle scan with a diameter of 3.4 mm. The follow-up mode was used for the examination carried out after the end of the DRPPT to ensure the positional agreement of both scans. The OCT examination immediately was repeated when the quality of the initial scan was regarded as insufficient.

In addition, ocular biometry (optical low-coherence reflectometry; Lensstar 900 Optical Biometer; Haag-Streit, Koeniz, Switzerland) was carried out on the day after the test, when the IOP had returned to normal values. Some eyes additionally underwent an OCT examination on the next day.

Using the Heidelberg Eye Explorer software (version 1.6.4.0; Heidelberg Engineering Co, Heidelberg, Germany), the OCT