Original Article

Pathological Manifestations of the Iris in Primary Chronic Open-Angle Glaucoma

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Abstract

Purpose: This study aims to assess the histopathological changes in the iris of patients diagnosed with primary chronic open-angle glaucoma (PCOAG) undergoing trabeculectomy surgery.
Patients and Methods: Conducted at the Imam Hossein Medical Center in Tehran, Iran, this study included 25 patients diagnosed with PCOAG scheduled for trabeculectomy. Exclusion criteria included patients with diabetes mellitus, systemic hypertension, uveitis, vascular lesions, central retinal vein occlusion, pseudoexfoliation, iris neovascularization, and previous prostaglandin usage. Following peripheral iridectomy, iris specimens were fixed in 10 % formalin, processed, and stained with hematoxylin and eosin for histopathological examination. The evaluation focused on vascular hyalinization, anterior border layer (ABL) thickness, stromal pigmentation, and pigmented epithelium characteristics.
Results: Twenty-five patients (mean age 64.4 ± 8.8 years) participated in the study. Notable findings included vascular hyalinization in 72 % of patients, ABL thickening in 48 %, severe stromal pigmentation in 40 %, and vacuolated or depigmented epithelium in 32 % and 4 % of patients, respectively. Intranuclear inclusions and nuclear invaginations were noted in 88 % of cases. The average number of glaucoma medications used per patient was 1.3 ± 1.1.
Conclusion: The present study results underscore the significant histopathological alterations in the iris among PCOAG patients. These changes are likely influenced by factors such as aging, patient ethnicity, and increased intraocular pressure. Gaining a deeper understanding of these changes is vital for advancing PCOAG management and treatment methodologies.

Keywords: Iris; Chronic; Open-Angle; Glaucoma; Manifestations.

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Introduction

The iris histopathologically consists of several layers, including the anterior border layer (ABL), stroma, muscle layer, and pigmented epithelial layer [1].

Diseases such as diabetes and systemic hypertension lead to changes in various layers of the iris and cause vascular abnormalities, including vascular hyalinization of the iris [2,3].

Glaucoma is one of the most common causes of irreversible blindness [4]. Glaucoma can lead to changes in various parts inside the eye. These changes may be secondary to increased intraocular pressure or may accompany the initial processes of the disease [5]. Glaucoma can also cause the occurrence of histopathological changes in the iris [6]. Since in glaucoma, intraocular pressure rises globally, the resulting pressure is transmitted to the iris tissue, affecting the blood vessels, with early-stage disease causing venous occlusion and later stages, along with disease progression, leading to arterial perfusion disturbances [7]. This perfusion disturbance may result in ischemic changes in tissue and an increase in vascular wall hyalinization [7].

Latanoprost, used in glaucoma treatment, increases the thickness of the ABL of the iris and melanin accumulation in this layer and stroma [8]. Iris darkening resulting from treatment with Latanoprost and other prostaglandin analogs has been reported in a high percentage of patients [8].

Numerous studies have investigated the effects of prostaglandin treatment on the iris among glaucoma patients, but research examining the histopathological changes in the iris caused by glaucoma itself without the influence of prostaglandins is limited. Given the importance of a more precise understanding of the mechanism of glaucoma effects on various eye tissues, including the iris, we aimed to investigate histopathological changes in the iris of patients with primary chronic open-angle glaucoma (PCOAG) who were candidates for trabeculectomy surgery and did not have a history of prostaglandin usage.

Patients and Methods

The present study was conducted at the Imam Hossein Medical Center in Tehran, Iran and included 25 patients diagnosed with PCOAG scheduled for trabeculectomy. The study protocol was approved by the ethics committee of Shahid Beheshti University of Medical Sciences and all participants gave written consent before entering the study. Exclusion criteria included patients with diabetes mellitus, systemic hypertension, uveitis, vascular lesions, central retinal vein occlusion, pseudoexfoliation, iris neovascularization, and a history of prostaglandin usage.

The trabeculectomy procedure was performed uniformly for all patients. Peripheral iridectomy was performed using the standard method during trabeculectomy. Following peripheral iridectomy, iris specimens were fixed in 10 % formalin. After tissue processing and embedding in paraffin, thin tissue sections were prepared and stained with hematoxylin and eosin. Then, the stained specimens were examined under a light microscope (Olympus BX41, Tokyo, Japan) by a collaborating eye pathologist focusing on vascular wall hyalinization, ABL thickness, stromal pigmentation, appearance of pigmented epithelium, and appearance of stromal melanocytes.

Results

In this study, 25 patients with a mean age

of 65 ± 8.8 years were examined, with the youngest being 50 and the oldest being 80 years old.

All patients had a cup-to-disc ratio greater than 0.7. Sixteen patients (64 %) had IOP between 20-30 mmHg and nine patients (36 %) had IOP between 30-40 mmHg. Twenty patients (80 %) were using diamox, 16 patients (64 %) were using timolol, nine patients (36 %) were using dorzolamide, and two patients (8 %) were using brimonidine. The mean number of medications used was 1.1 ± 3.1, ranging from 0 to 3.

In 18 patients (72 %), vascular wall hyalinization was observed. Thickening of the ABL was seen in one cell layer in 12 patients (48 %) and in two cell layers in 13 patients (52 %). Stromal pigmentation was severe in 10 patients (40 %), and moderate in the remaining 15 patients (60 %). Pigmented epithelium was normal in 16 patients (64 %), vacuolated in 8 patients (32 %), and depigmented in 1 patient (4 %). Melanocytic nuclear inclusions and invaginations were observed in 22 patients (88 %), but no evidence of nuclear pleomorphism was found in any case (Table 1).

Table 1: Distribution of iris changes in patients with primary chronic open-angle glaucoma entering the study

Iris Changes	Distribution Number (%)
Vascular wall hyalinization	18 (72)
Thickening of the ABL (one cell layer)	12 (48)
Thickening of the ABL (two cell layers)	13 (52)
Severe stromal pigmentation	10 (40)
Moderate stromal pigmentation	15 (60)
Normal pigmented epithelium	16 (64)
Vacuolated pigmented epithelium	8 (32)
Depigmented epithelium	1 (4)
Melanocytic nuclear inclusions and invaginations	22 (88)
Nuclear pleomorphism	0 (0)

Discussion

In our study, vascular wall hyalinization of the iris was observed in 18 patients (72 %). Vascular wall hyalinization of the iris is a phenomenon expected to be influenced by increasing age and associated atherosclerosis; however, the effect of increased intraocular pressure on its occurrence is noteworthy. Since our study did not include a control group, it was not possible to compare the pathological findings in the iris, including vascular hyalinization, between patients and individuals without glaucoma in the same age range.

In the present study, one cell layer thickening of the ABL was observed in 12 patients (48 %), while two cell layers thickening was observed in 13 patients (52 %). Grierson et al.,[10] have reported similar results regarding ABL thickening among glaucoma patients with a history of Latanoprost treatment. The theoretical explanation for this thickening is unclear; it is uncertain whether this thickening is due to long-term treatment with Latanoprost, or whether it occurs due to structural rearrangement or regional migration of stromal melanocytes to the ABL, or increased production of melanin granules. The presence of ABL thickening to the extent of two cell layers in approximately half of our study patients who had no history of Latanoprost usage or iris color changes raises a different

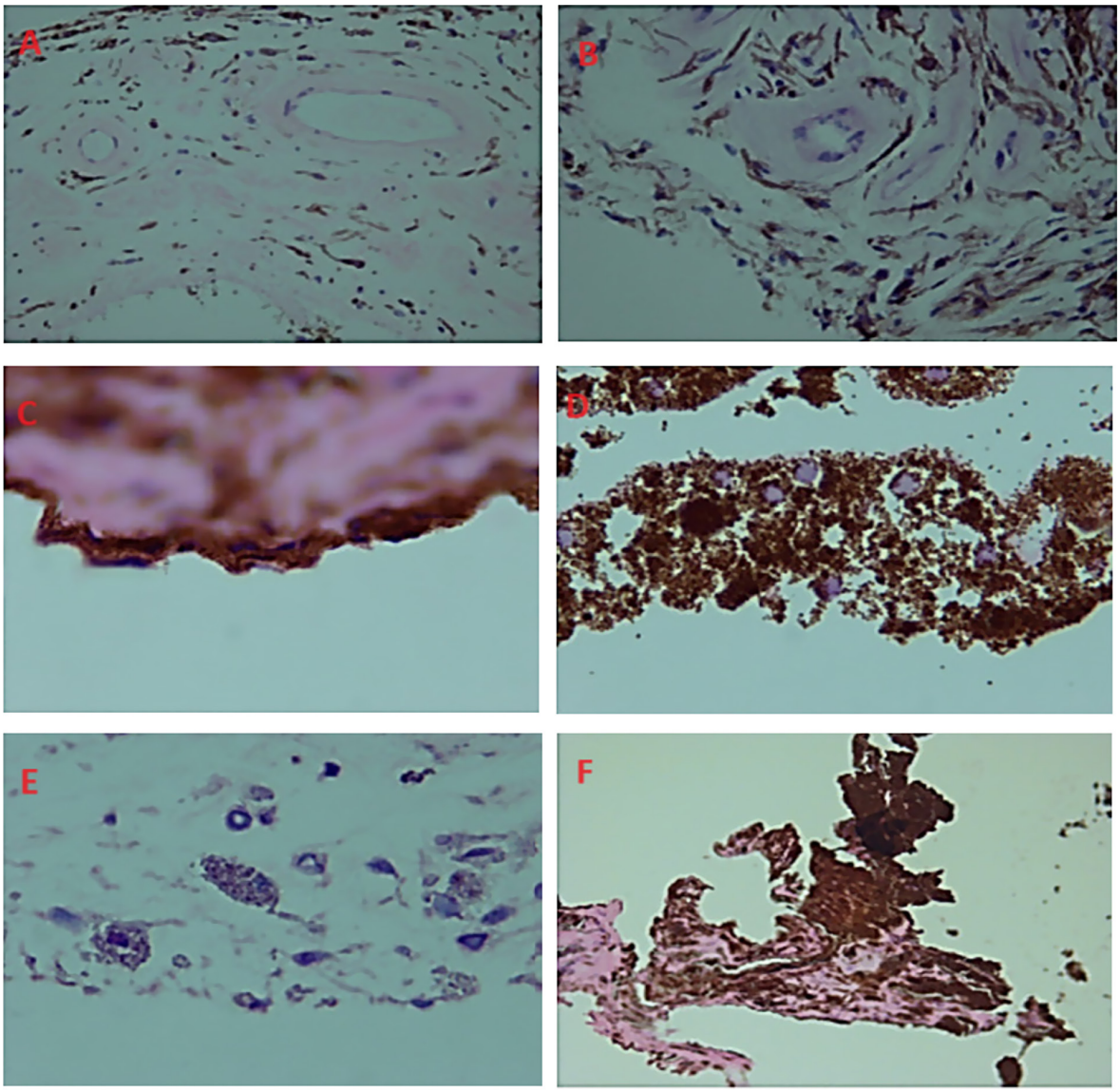

Figure 1: Histopathological changes in the iris of patients with primary chronic open-angle glaucoma. (A and B): Vascular wall hyalinization (H&E staining, × 400 magnification). C: Bilayer thickening of the anterior iris border (H&E staining, × 1000 magnification). D: Vacuolation of pigmented epithelial cells (H&E staining, × 1000 magnification). E: Nuclear inclusions (H&E staining, ×1000 magnification). F: Increase in iris stromal pigmentation (H&E staining, × 200 magnification)

explanation suggesting the thickening may be due to increased intraocular pressure.

In the present study, stromal pigmentation was severe in 10 patients (40 %) and moderate in the rest of the patients. Pigmented epithelium was normal in 16 patients (64 %), vacuolated in 8 patients (32 %), and depigmented in 1 patient (4 %). However, in a study by Teus et al., [11] 50 to 70 percent of cases had excessive pigmentation, which differs from the results of our study. The reason for this difference may be due to different methods of measuring the

amount of pigmentation. Since the level of stromal pigmentation is a qualitative variable, an appropriate definition of the various degrees of pigmentation should be made and used in different studies to ensure comparable results.

Previous studies have indicated that patients with higher pigmentation also tend to have a thicker ABL [12]. However, these findings are contentious due to the influence of other factors, such as racial disparities in melanocyte density. In some instances, this variation is observable within the same individual's eyes or across different regions of the same iris.

Stromal melanocytic changes, including the presence of nuclear inclusions and nuclear invaginations, as seen in other studies by Arranz-Marquez et al., [13] and Albert et al., [8] were also observed in this study, but there was no evidence of pleomorphism indicating precancerous changes. Some authors believe that these changes indicate increased nuclear activity and metabolism. However, these intranuclear bodies have also been seen in normal brown irises and in older individuals' irises. In other words, although these changes may also be seen in atypical melanocytes, their presence in the stroma of glaucomatous patients does not necessarily indicate pre-malignant iris changes.

Apart from patients' age and associated atherosclerosis, factors such as the unknown onset time of angle-closure glaucoma, the nature of the occurrence, and the sequence of changes over time were additional confounding factors that could not be eliminated in the present study due to the nature of the disease. To mitigate these confounders and draw more robust conclusions, it is advisable to conduct future case-control studies with an adequate sample size to investigate the histopathological changes induced by glaucoma in the iris with greater precision.

Conclusion

The present study results underscore the significant histopathological alterations in the iris in PCOAG patients. These changes are likely influenced by factors such as aging, patient ethnicity, and increased intraocular pressure. Gaining a deeper understanding of these changes is vital for advancing PCOAG management and treatment methodologies.

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Footnotes and Financial Disclosures

Conflict of Interest:

The authors have no conflict of interest with the subject matter of the present study.