

Original Article

Evaluation of Asymptomatic Cardiac Disease in Patients with Ocular Pseudoexfoliation

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Abstract

Purpose: To evaluate asymptomatic cardiac disease in patients with ocular pseudoexfoliation.

Patients and Method: Forty-two patients with ocular pseudoexfoliation (with or without glaucoma) and 40 patients without pseudoexfoliation, who had no positive signs or symptoms of cardiac diseases, were enrolled in this study. For each participant a standard treadmill exercise test, as a noninvasive and reliable method for detecting ischemic heart disease, was performed under supervision of a cardiologist. The prevalence of ischemic heart disease was compared in the case and control groups.

Results: The mean age of participants was 68.38 ± 8.10 years in the case and 62.45 ± 8.40 years in the control group. There was no statistically significant difference between the two groups in terms of diabetes mellitus, hyperlipidemia, smoking, and family history of ischemic heart disease. Twenty patients (47.6 %) with pseudoexfoliation and 9 participants (22.5 %) without pseudoexfoliation had hypertension ($P = 0.02$). There were 10 (23.8 %) positive exercise tests in the pseudoexfoliation group and 8 (20 %) positive exercise tests in participants without pseudoexfoliation ($P = 0.78$).

Conclusion: Based on our findings ocular pseudoexfoliation was not associated with increased risk of asymptomatic ischemic heart disease as evaluated by the treadmill exercise test.

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Introduction

Pseudoexfoliation (PEX) syndrome, first described by Lindberg, is an age related fibrillopathy, which is caused by deposition of fibrillar material in the anterior segment of the eye, specially the anterior lens capsule¹. PEX is reported to be the most common identifiable cause of open angle glaucoma². However, not all patients with PEX develop glaucoma. The proportion of people worldwide affected by this syndrome ranges from 0.5 % in those younger than 60 years to 15 % in people aged 60 years and older^{3,4}. In addition to ocular involvement, pseudoexfoliative fibrils have been found in many organs such as heart, lung, liver, kidney, and meninges by electron microscopy; therefore PEX syndrome has been known as a generalized disorder involving various visceral organs^{5,6}. Elevated serum antiphospholipid antibodies, a known risk factor for cardiovascular and cerebrovascular disease, are also more common in patients with PEX⁷. Although deposition of pseudoexfoliative fibers in the cardiovascular system has been documented, the studies regarding the relation between PEX and coronary artery disease (CAD) have produced conflicting results with some studies proposing that PEX might be related to cardiovascular mortality⁸⁻¹¹, while others indicating the opposite¹²⁻¹⁴. The aim of the present study was to evaluate the relationship between asymptomatic CAD discovered in treadmill exercise test and PEX.

Patients and Methods

In this prospective case control study a total of 42 patients with ocular PEX with or without glaucoma and 40 participants without PEX were enrolled. Signed informed consent was obtained from all patients, and the ethical

committee of the Iran University of Medical Sciences, Tehran, Iran, approved the study. PEX was diagnosed based on observing the deposition of pseudoexfoliative material in pupillary margin, lens capsule, or angle in at least one eye before or after pupillary dilation under slit lamp examination and gonioscopy. None of study participants had a positive history of cardiac diseases or was under treatment for cardiac diseases. A comprehensive eye examination including IOP measurement by calibrated Goldmann applanation tonometer, Snellen chart best corrected visual acuity (BCVA), Sussman gonioscopy, slit lamp examination, and hand held + 78 lens funduscopy was performed in all participants. Risk factors of ischemic heart disease including age, sex, diabetes mellitus, hypertension, hyperlipidemia, smoking, and family history of ischemic heart disease (first degree family) was recorded based on the interviews with participants and from their available medical records. Inclusion criteria for the case group included the presence of PEX disease and age between 50 and 85 years. The exclusion criteria included any other kinds of glaucoma, history of chest pain or dyspnea, CCU admission, medical treatment for cardiac disease, or disability to perform exercise tests such as in patients with osteoarthritis. The inclusion and exclusion criteria for the control group were similar to the case group except for the presence of PEX.

For detection of asymptomatic ischemic heart disease, a treadmill exercise test, which is a noninvasive test with sensitivity of about 68 % to 78 %¹⁵⁻¹⁷, was performed for all participants under supervision of a cardiologist. The test period was determined depending on the age of the participant and the test was ended in the case of cardiac symptoms appearing. Detection of ST depression during the test

was reported as a positive exercise test. A test was considered negative only when a subject had achieved 85 % of the maximum heart rate predicted and did not have positive ST-T changes.

A sample size of 40 participants in each group was calculated to detect a difference of 20 % in ST-T changes with a confidence of 95 % and statistical power of 80 %¹⁸. Data analysis was performed using SPSS version 20 (Armonk, NY: IBM Corp.), and chi-square and Student's t-test were used for comparing proportions and means between the two groups. Logistic regression backward method was used for multivariate analysis. P values less than 0.05 were considered statistically significant.

Results

The mean age of patients was 68.38 ± 8.10 years (range 50 to 82 years) in the PEX group and 62.45 ± 8.40 years (range 50 to 85 years) in participants without PEX ($P = 0.07$). Nine patients in the case and 7 participants in the control group had diabetes ($P = 0.54$). There were twenty patients with PEX and 9 participants without PEX showing hypertension ($P = 0.02$). Thirteen patients in the case group and 6 participants in the control group had hyperlipidemia ($P = 0.11$). None of the patients with PEX and 4 participants without PEX had a family history of ischemic heart disease ($P = 0.91$). Four patients in the control group and 3 participants in the case group were smokers ($P = 0.48$). There were 10 (23.8 %) positive exercise tests in the PEX group and 8 (20 %) positive exercise tests among participants without PEX ($P = 0.78$).

In a logistic regression analysis using the treadmill test as the outcome and PEX and other risk factors as the predictors, only sex and hypertension showed correlation with treadmill results.

Discussion

PEX is a systemic disorder with a particularly high prevalence in Scandinavian countries¹⁹. The disease is characterized by deposition of extracellular material, which in most cases is easily detectable in the anterior segment of the eye and might also be found in other tissues, such as blood vessels, skin, gallbladder, kidneys, lungs, cerebral meninges, and heart^{5,6,20,21}. These findings have led to the hypothesis that PEX is more likely a systemic disorder with multiple clinical manifestations. In our study, we found that although patients with ocular PEX had a higher chance of having hypertension, there was no statistically significant difference in standard treadmill exercise test results as a sign of asymptomatic ischemic heart disease, between patients with ocular PEX and participants without PEX. In line with our finding Shrum et al.,¹² in their study including 472 patients who were diagnosed with PEX syndrome or pseudoexfoliative glaucoma at the Mayo Clinic, from 1976 to 1995, found no association between ocular PEX and cardiovascular or cerebrovascular mortality. Also Brajkovic et al.,¹⁴ investigated the relationship between PEX and hypertension, CAD, arrhythmia, diabetes, and cerebrovascular accidents, and only arrhythmia was found to be higher in PEX patients. No relationship was found between PEX and mortality or other risk factors¹⁴.

Contrary to our results several previous studies have reported an association between ocular PEX and CAD^{8,10,22,23}, asymptomatic myocardial diastolic dysfunction²⁴, peripheral vascular disease²⁵, abdominal aortic aneurysm²⁰, heart failure²⁶, and subclinical myocardial ischemia²⁷.

Wang et al.,²⁸ reported that PEX is associated with an increased risk of vascular disease, and Ciçek Yılmaz et al.,²⁹ study showed that

decreased left ventricular diastolic functions correlated with plasma B-type natriuretic peptide levels in PEX patients. Mitchell et al.,⁸ suggested that PEX might be associated with a history of angina or hypertension, acute myocardial infarction, or stroke. In another study designed to investigate the prevalence of glaucoma and CAD in patients with cataract and PEX, Andrikopoulos et al.,¹⁰ reported a positive association between PEX and the risk of CAD among subjects 50 years or older. Our study had some limitations including the small number of study subjects and the use of a low sensitivity test (treadmill exercise test) for detection of ischemic heart disease. Another limitation of the present study was that the information regarding the risk factors of ischemic heart disease was obtained from patient interviews and medical records, and

was not checked by the authors.

Using tests other than exercise test to increase the sensitivity of diagnosis and including a larger number of study participants might provide more information about the possible association between PEX and ischemic heart disease.

Conclusion

Based on our findings ocular PEX was not associated with increased risk of asymptomatic ischemic heart disease as evaluated by the treadmill exercise test.

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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.