Investigation of the Association Between Pseudoexfoliation and Herpes Simplex Virus

Psödoeksfolyasyon ve Herpes Simplex Virüs Arasındaki İlişkinin Araştırılması

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ABSTRACT

Purpose: To investigate the relation between pseudoexfoliation (PEX) and Herpes simplex virus (HSV).

Materials and Methods: This prospective study included 50 patients with PEX glaucoma and cataract (Group 1) and 40 cataract patients without glaucoma and PEX (Group 2). All participants underwent a complete ophthalmic examination. HSV was evaluated in all anterior lens capsule specimens with polymerase chain reaction.

Results: HSV DNA was not detected in the anterior lens capsule specimens of group1 and 2.

Conclusions: The results of this study showed that HSV was not associated with PEX.

Key Words: Pseudoexfoliation, infection, herpes simplex virus.

ÖZ

Amaç: Herpes simplex (HSV) virüs ile psödoeksfolyasyon arasındaki ilişkiyi araştırmak.

Gereç ve Yöntem: Prospektif olarak yapılan bu çalışmada psödoeksfolyasyon (PEX) glokomu ve kataraktı olan 50 (Grup 1) , PEX ve glokomu olmayan 40 katarakt hastası (Grup 2) yer aldı. Tüm olgulara tam bir oftalmik muayene yapıldı. HSV ön kapsül materyalinde polimeraz zincir reaksiyonu ile değerlendirildi.

Bulgular: Grup 1 ve 2'de ön kapsül materyallerinde HSVDNA saptanmadı.

Sonuç: Bu çalışmanın sonuçları HSV'nin PEX ile birlikte olmadığını gösterdi.

Anahtar Kelimeler: Psödoeksfolyasyon, infeksiyon, herpes simplex virus.

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INTRODUCTION

Pseudoexfoliation (PEX) syndrome is a generalized systemic disorder. Deposits of white material on the anterior lens surface are the most consistent and important diagnostic feature of PEX.[1] The exact etiopathogenesis of PEX is not known. An infection, is one of the proposed pathogenetic mechanismsb[2] Herpes simplex virus type 1 (HSV-1) infects 70-90% of any given population. There is a high rate of clinically silent primary infection.[3] The objective of this study was to test the hypothesis of infection.

MATERIALS AND METHODS

This prospective study included 50 patients with PEX glaucoma and cataract who underwent combined cataract-glaucoma surgery (Group 1), and 40 cataract patients without glaucoma and PEX who underwent cataract surgery (Phacoemulsification-intraocular lens implantation) (Group 2). All of the patients and control subjects were Turkish. Informed consent was obtained from each patient and control. The study was conducted in accordance with the principles of the Declaration of Helsinki. On ophthalmological examination, the anterior and posterior segments of all the cases were evaluated and intraocular pressures (IOP) were measured with Goldman applanation tonometry. Criteria for inclusion in group 2 were IOP<22 mmHg, no evidence of glaucomatous changes in optic disk, and no history of POAG or ocular hypertension in first-degree relatives. These controls had no pseudoexfoliative material at the anterior lens capsule or pupillary margin. The corneal endothelium, iris, and iris margins were evaluated for pseudoexfoliative material before and after dilation; the anterior lens surface was examined. To evaluate the angle for pseudoexfoliative material and increased pigmentation, we used gonioprisms. PEX glaucoma was diagnosed by the presence of IOP>21 mmHg and typical glaucomatous cupping and visual field loss in at least one eye. HSV was investigated in all anterior lens capsule specimens with polymerase chain reaction. Tissue specimens were stored at -80 ° after surgery . Inclusion criteria included; no ophthalmic infection with a HSV, no patient and controls were receiving systemic or topical steroids.

Deoxyribonucleic acid (DNA) extraction: DNA extraction was performed using "Genomic DNA from tissue-NucleoSpin Tissue" kit (Macherey-Nagel) with the manufacturers recommendations. To avoid/reduce the possible inhibitors, the samples were stored at 4°C before DNA extraction and also diluted at a ratio of 1:10.

Polimerase chain reaction (PCR)

PCR was performed in 50 μl final volume. The reaction consisted of 1 U of Taq polymerase (Bioron GmbH9), 50pmol primer 1ml each, 200 mmol dNTP mix, and 3 mmol of MgCl2. Amplification was performed at Techgene thermal cycler (Techne FTGENE 5D) with initial denaturation at 940C for 5 minutes followed by 40 cycles at 940C for 30 sec, 580C for 30 sec, 720C for 35 sec and final extention 5 minutes at 720C. For HSV detection, DNA extracted from Hep-2 cell line cultures infected with HSV-1 and HSV-2 were used as positive controls. Primer sequences used for identification and differentiation of HSV and length of expected PCR product sizes are shown in table.

Screening

Samples were electrophoresed with 1.5% agarose gel containing 0.5mg ml-1 ethidium bromide and were exposed to 100 V in 0.5XTBE (tris borate buffer- pH 8) and visualized with UV transilluminator.

RESULTS

There were no significant differences in age (P=0.078, T test), and sex (p=0.924, Chi-Square tests) between the study groups. Group 1 (PEX) consisted of 28 male and 22 female (mean age: 62.76±6.03 years), Group 2 (control) involved 22 male and 18 female (mean age: 60.55±5.60 years). No evidence of herpetic viral etiology was found in this study. Herpes simplex virus DNA was not detected in group 1 and 2.

DISCUSSION

PEX is associated with the excessive synthesis and deposition of an abnormal elastic microfibrillar material in all tissues of the anterior segment of the eyes and systemic tissues.[4] Although recent studies showed that lysil oxidase-like 1 gene polymorphism were highly associated with PEX[5,6] the pathogenesis of PEX is still uncertain.

The prevalence of PEX in both partners of married couples was found to be significantly higher than one would expect.[2] A striking morphologic similarity was detected between the fibrillar material of scraping and the exfoliation fibers, suggesting the possibility of a viral disorder.[7] There are further evidence for the possibility of an infectious agent in the etiopathogenesis of PEX. In a few studies, the authors described that PEX have developed in younger patients after intraocular surgery or trauma with iris surgery in infancy and childhood.[8-11] In litera-

Table: The primer sequences used in the determination of HSV.

Microorganism		Primer sequences (Sequence 5′-3′)	PCR yield size
HSV (General)	Forward primer	5′-CAGTACGGCCCCGAGTTCGTGA-3′	476 bp
	Reverse primer	5′-GTAGATGGTGCGGGTGATGTT-3′	
HSV-1	Forward primer	5′-GTAGATGGTGCGGGTGATGTT-3′	110 bp
	Reverse primer	5′-ATACCGACGATATGCGACCT-3′	
HSV-2	Forward primer	5′-GGGTTTGTCCGCTTCGTAAC-3′	93 bp
	Reverse primer	5′-GGGAAGAAGAGAGGCGAGAA-3′	

ture, there are several reports of younger patients developing PEX after penetrating keratoplasty from elderly donors.[8,10,12,13]

Most of the human population is infected with HSV type.[1] HSV establishes a latent infection in sensory neurons that persists for the life of the individual.[3] The detection of viral genomic DNA would not be expected in the ocular tissues in the absence of an active infection. However, experimental studies showed that HSV genome is retained in non-neuronal ocular tissues such as cornea, choroid, retina, and sclera during quiescent HSV infection. These results support the concept of extraneuronal latency and reactivation.[14,15]

Detorakis, et al.[16] investigated the presence of HSV and varicella-zoster virus (VZV) in iris and anterior capsule specimens of patients with PEX and controls. HSV-I from iris specimens was detected in thirteen percent of PEX patients and 1.75% of control participants. VZV DNA was not detected in any of the examined specimens. They concluded that a possible relationship between HSV-I and PEX existed . Luntz et al failed to detect any correlation between circulating anti-HSV antibodies and PEX.[17]

In our study, we investigated the possible role of Herpes viruses in the etiology of PEX. PCR was performed in the anterior lens capsule of the participants. HSV was not detected in the samples. In conclusion, our study does not suggest the possibility of any relationship between patients with PEX and HSV.

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