

Is pseudoexfoliation associated with sensorineural hearing loss?

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ABSTRACT

الأهداف: يعتقد أن الفطريات الزائفة (بي اس اكس) عبارة عن اضطراب جهازى. تهدف الدراسة إلى تحديد العلاقة المحتملة بين الفطريات الزائفة وفقدان السمع الحسى العصبى.

الطريقة: أجريت هذه الدراسة بجامعة أفيون كوساتيب في الفترة ما بين يوليو ٢٠٠٢م و يونيو ٢٠٠٥م. تم فحص ٦٣ مريضاً بالفحص المجهري الروتيني تبين أنهم يعانون من وجود فطريات زائفة وتم تقييم ٣٨ شخصاً عمرهم متطابق كمجموعة التحكم من وجود دليل على إصابتهم بتشوه سمعي. تم مقارنة قياس مجموعة مدى سمع النبرة - الصافية عند ٢٥٠-٢٠٠٠ هرتز، ٢٠٠٠-٦٠٠٠ هرتز و ٢٥٠-٦٠٠٠ هرتز في كل أذن مع مجموعة التحكم لنفس الترددات.

النتائج: بلغ متوسط عمر المرضى ٦٨,٤ + ١٠,٣ عاماً وتؤثر الفطريات الزائفة على عينا واحدة على الأقل. تبين أن خمسين مريضاً (٧٩,٤٪) مصاباً بالفطريات الزائفة و ١٠ مريضاً (٢٦,٣٪) من مجموعة التحكم يعانون من فقدان السمع (نسبة الخطأ: ٠,٠٠٠ مربع - تشي). من بين الخمسين مريضاً المصابين بفطريات زائفة والذين يعانون من فقدان السمع، ٣٤ مريضاً يعانون من وجود فطريات زائفة على الجانبين و ١٦ مريضاً يعانون من وجود فطريات زائفة ولكن ليست على الجانبين. أصيب ٢٩ مريضاً بفقدان للسمع للترددات العالية بينما أصيب ٢٠ مريضاً بفقدان للسمع في جميع الترددات. أصيب ٤٨ مريضاً يعاني من وجود فطريات زائفة و ٧ مريضاً من مجموعة التحكم بفقدان السمع الحسى العصبى (نسبة الخطأ: ٠,٠٣٠).

خاتمة: تبين وجود فقدان السمع الحسى العصبى بشكل متكرر بشكل أكثر لدى المرضى الذين يعانون من وجود فطريات زائفة بالمقارنة مع الأشخاص ذو العمر المتطابق من مجموعة التحكم.

Objective: To determine the possible relation between pseudoexfoliation (PSX) and sensorineural hearing loss.

Methods: This study was carried out in Afyon Kocatepe University, Afyon, Turkey between July 2002 and June 2005. Sixty-three patients who were found to have ocular PSX on routine biomicroscopic examination, and 38 age-matched control subjects were evaluated

for evidence of audiometric abnormality. The sum of pure-tone hearing threshold measured at 250-2000 Hz, 2000-6000 Hz, and 250-6000 Hz in each ear was compared with controls for the same frequencies.

Results: The mean age of the patients was 68.4±10.3 years. All patients had PSX affecting at least one eye. Fifty (79.4%) patients with PSX, and 10 (26.3%) control subjects were found to have hearing loss ($p=0.00$, chi-square). From the 50 patients with PSX who had hearing loss, 34 patients had bilateral PSX, and 16 patients had unilateral PSX. Twenty-nine patients had high frequency hearing loss, while 20 patients had hearing loss in all frequencies. Forty-eight patients with PSX and 7 controls had bilateral sensorineural hearing loss ($p=0.030$).

Conclusion: Sensorineural hearing loss was seen more frequently in patients with PSX in comparison with age-matched control subjects.

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Pseudoexfoliation syndrome (PSX) has been considered a systemic disorder. The ocular manifestation of this syndrome is diagnosed with ophthalmic examination as deposits in the margins of the pupils or on the anterior lens capsule. Pseudoexfoliative material can also settle on the trabecular meshwork, ciliary body, zonules, and conjunctiva.¹ The documentation of exfoliative fibrillar material in the basement membrane of extraocular orbital tissues, the skin, visceral organs, vessel walls, and cardiac structures has led to a suggestion that exfoliative material may be deposited in many organs. Fibrillar pseudoexfoliative material has been demonstrated to contain complex glycoprotein/proteoglycan

structures.²⁻⁴ A possible deposition of exfoliative material on the cochlear structures may cause hearing loss. An association between ocular PSX and hearing loss has been suggested.⁵⁻⁷ In our study, an audiometric abnormality was investigated in patients with ocular PSX to further assess a possible relationship between PSX and sensorineural hearing loss.

Methods. Patients attending the eye clinic of Afyon Kocatepe University, Afyon, Turkey for routine ophthalmic examination between July 2002 and June 2005 were screened for diagnosis of ocular PSX. Sixty-three consecutive patients who were found to have PSX were included in the study. The age of the patients was 68.4 ± 10.3 years; 35 patients were male and 28 were female. Patients with a history of diabetes mellitus or otological diseases were excluded from the study. As a control group, 38 consecutive age-matched subjects without ocular PSX were selected from the population consulted for routine ophthalmic examination. The age of controls was 65.2 ± 12.3 years (20 female and 18 male). Among the control subjects, those with ophthalmological, otological diseases, or systemic disorders were excluded from the study. All the control and study subjects gave their consent before their inclusion in the study. The study was performed in accordance with the ethical standards of the Declaration of Helsinki, and ethical approval was obtained from the institutional review board. Full ophthalmic examination, including Snellen visual acuity, biomicroscopy, gonioscopy, applanation tonometry, and retinal examination after pupil dilation was performed in all patients. Identification of PSX was made by observation of existence of material of PSX on the pupil margins, in the anterior chamber angle gonioscopically, and on the anterior lens capsule after pupil dilatation. All patients were evaluated in the Department of Ear, Nose, and Throat by one physician masked to the study groups. Otoscopic examination was performed and patients with a history of previous ear surgery or tympanic membrane perforation, chronic otitis media, conductive hearing loss, middle ear pathology, history of noise exposure such as working in a noisy environment, use of ototoxic medicines, and acute infection of upper respiratory system were excluded from the study. Pure tone audiometry was carried out in all patients with ocular PSX and control subjects. Pure tone hearing threshold of both air conduction and bone conduction were obtained at 250, 500, 1000, 2000, 3000, 4000, and 6000 Hz using an audiometer (Interacustics AD 229 audiometer, Denmark). Hearing loss was classified in low (250-2000 Hz), high (2000-6000 Hz) and all (250-6000 Hz) frequency loss. All conductive hearing losses were not included in the study group. Presence of hearing loss was accepted when hearing threshold was higher than 25 dB at all frequencies.

Statistical analysis was performed using SPSS program version 13.0. Pearson chi-square test was used and a p -value < 0.05 was considered significant.

Results. Fifty of 63 (79%) patients were found to have hearing loss, whereas 13 (21%) patients were normal. In the control group, 10 (26%) subjects had hearing loss and 28 (74%) subjects had normal hearing thresholds ($p=0.000$). Hearing loss was bilateral in 48 patients with ocular PSX, and 2 of 50 had unilateral hearing loss. In the control group, 7 of 10 subjects with hearing loss had bilateral hearing loss, while 3 subjects had unilateral hearing loss ($p=0.03$). In the PSX group, hearing loss at a frequency of 250-2000 Hz was found in one case, hearing loss at 2000-6000 Hz was found in 29 patients, hearing loss at 250-6000 Hz was found in 20 patients. In the control group, there were 3 cases with hearing loss at 250-1000 Hz, 3 subjects at 2000-6000 Hz, and 4 subjects at 250-6000 Hz frequency. Table 1 illustrates the relation of hearing loss and laterality in the PSX patients.

Discussion. Although PSX has been recognized as deposition of fibrillar material in ocular structures, an identical fibrilopathy such as PSX has been demonstrated in the basement membranes and extracellular matrices of extraocular orbital tissues, the skin, and visceral organs.¹⁻⁴ The existence of PSX material in the vessel walls of patients with PSX has been suggested to increase the risk of vascular diseases.^{6,8-10} Central retinal vein occlusions have been occasionally seen.¹¹ The relationship between hearing loss and ocular disease has been a subject of interest for several investigators. In our study, we determined that sensorineural hearing loss was seen more frequently in subjects with PSX compared to control subjects. In patients with hearing loss, this finding was largely bilateral, and indicated that PSX was a systemic disease. The most frequent hearing loss was found in the high frequencies, while the second most frequent was observed in all frequencies. Hearing loss in the low frequency was rare.

Table 1 - The relation of hearing loss and laterality in pseudoexfoliation syndrome patients.

Hearing loss (frequency)	Unilateral	Bilateral	Total
		n (%)	
250-2000 Hz	1 (2)	-	1 (2)
2000-6000 Hz	9 (18)	20 (40)	29 (58)
250-6000 Hz	6 (12)	14 (28)	20 (40)
Total	16 (32)	34 (68)	50 (100)

Cahill et al⁵ reported that a large proportion of patients with PSX had sensorineural hearing loss in comparison with age-matched controls, regardless of whether or not this is associated with glaucoma. Shaban and Asfour⁶ reported their results supporting the previous study. Both studies used "ISO 7029" and "National Study of Hearing" standards for control instead of separate control subjects. In our study, we used age-matched control subjects and found findings consistent with previous reports. The high proportion of hearing loss in patients with PSX implicates that ocular PSX has a systemic variety and distributes in different organs like the ears. The association of hearing loss and glaucoma has been investigated previously, and no distinct relationship has been reported.¹²⁻¹⁶ However, in these studies, patients with PSX have not been a separate group. Fibrilopathy like PSX has histologically been demonstrated in the skin, visceral organs, and extraocular orbital tissues. Postmortem autopsy studies revealed electron microscopically deposition of exfoliative material in the heart, kidney, liver, lungs and meninges of patients with PSX.^{2-4,8,9}

The possible accumulation of pseudoexfoliative material in the basilar or tectorial membrane of the organ of Corti in the inner ear may explain the association between ocular PSX and hearing loss. Both the anterior segment structures of the eye, which are affected by PSX, and the basilar and tectorial membranes in the inner ear originate embryologically from the neural ectoderm.¹⁷ Tectorial and basilar membrane contain type II collagen and proteoglycan-glycoproteins.¹⁸ Type IV collagen, present in the crystalline lens has also been demonstrated in the tectorial and basilar membrane.¹⁹ The organ of Corti contains the auditory hair cells, or sound receptors, which are mechanoreceptors characterized by organized stereocilia, and sit on a number of support cells that rest on the basilar membrane.^{20,21} The tectorial membrane covers the stereocilia. The tectorial membrane is characterized by a hydrated matrix stabilized by collagen fibers.²¹ The existence of pseudoexfoliative material in the organ of Corti may result in increase in the hearing threshold. The structural changes in the organ of Corti caused by deposition of fibrillar PSX in the basilar and tectorial membranes may affect conversion of the mechanical energy produced by a sound wave to bioelectrical energy resulting in sensorineural hearing loss. Another mechanism may involve changes in the pathophysiology of the vascular supply of the inner ear.⁸⁻¹¹ Demonstration of fibrillar PSX in the vessel walls of patients with ocular PSX may suggest that deposition of PSX in the vascular structures supplying the inner ear causes a decrease in nourishment of the inner ear and worsening in the metabolism of stria vascularis, which has an important

role in the regulation of ion balance of endolymph and perilymph.^{8,9} Besides, basophilic deposits, eosinophilic hyaline matter or mucopolysaccharides accumulated in the stria vascularis have been demonstrated to be associated with hearing loss.^{22,23} However, exact mechanisms explaining pathophysiologic developmental fundamentals of hearing loss in patients with PSX are not known and remain to be clarified. Up to now, there has not been a study demonstrating the presence of pseudoexfoliative material in the inner ear. This seems to be the main limitation of our and other studies.

In conclusion, patients who have ocular PSX showed significantly more frequent sensorineural hearing loss compared to age-matched control subjects. The PSX syndrome, which is thought to be a systemic disease, seems to affect the ear and further studies dealing with the presence of PSX material in the inner ear are needed.

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