· Original article ·

Sensory-neural hearing loss in pseudoexfoliation syndrome

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Abstract

• AIM: To evaluate relationship between ocular pseudoexfoliation syndrome (PXF) and sensory-neural hearing loss (SNHL).

• METHODS: This prospective case-control study was designed on patients who referred to a general ophthalmic clinic at Imam Khomeini Medical Center, Urmia, Iran (March 2010 through November 2010). On routine ophthalmic examination, patients diagnosed with ocular PXF were referred to the ENT department and, selected cases (after evaluating inclusion and exclusion criteria) were referred to Audiometric Department. Pure tone hearing threshold level(HTL) was measured at 1, 2, 3 kHz for each ear and was compared with International Standard (ISO 7029) median age associated hearing loss (AAHL) at 1, 2, 3 kHz.

• RESULTS: Overall 21 (42.0%) of 50 patients had a higher HTL than the ISO 7029 median AAHL at 1, 2 and 3kHz, which included 14 ears of 9 patients in the male group and 21 ears of 12 patients in the female group. Approximately 12.0% of patients had glaucoma at the same time, however; no significant correlation was found in SNHL prevalence and severity between PXF patients and patients with simultaneous glaucoma. SNHL was more common in patients with ocular PXF compared to their age-sex matched controls (P<0.05).

• CONCLUSION: Most of patients with ocular PXF had SNHL compared to their age-sex matched controls, which could be due to PXF fibrils in the inner ear. These findings suggest PXF could be a systemic disease.

• KEYWORDS: pseudoexfoliation; sensory-neural hearing loss, glaucoma
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INTRODUCTION

Pseuoexfoliation syndrome (PXF) is characterized by grey-white fibrillogranular extra cellular deposits in ocular structure such as anterior capsule, iris, anterior chamber angle, zonules, ciliary body, anterior vitreous face, and conjunctiva. It is an accidental finding most of the times, and seems to be unilateral 2/3 of cases[1]. In addition to intraocular deposits, PXF material found in the heart, lung, liver, gallbladder and arteries, which cause systemic vascular disorders including systemic hypertension, abdominal aortic aneurysms, ischemic heart disease, Alzheimer's disease, retinal vascular disorders and age-related macular degeneration[2], Also there are some reports about finding PXF fibrils in the basement membrane of extraocular and orbital tissues, which are documented pathologically[3,4]. In immunologic studies, aggregates stained positively for elastin and human amyloid P protein[5]. In recent studies, there are evidences and traces of PXF fibrils in multiple organs (such as lung, heart, liver, gallbladder and *etc.*) of autopsy tissues which suggest systemic process[5]. The organ of corti is a complex structure in the inner ear which contains hair cells that are located on the basilar membrane and are overlaid by the tectorial membrane. There are 2 types of hair cells in the cochlea: the inner hair cells and outer hair cells. One row of inner cells spirals up the cochlea near the central axis, while 3-4 rows of adjacent outer hair cells spiral up the cochlea further from the central axis. The tectorial and basilar membranes are connected centrally. Sound moves these structures differentially and produces a shear force that bends the steriocelia. The tectorial membrane covers the steriocilia. The conversion of the mechanical energy produced by a sound wave to electrical energy (resulting in hearing) requires deflection of steriocilia, induced by a shearing motion between the reticular lamina and the tectorial membrane. This shearing motion is produced by the basilar membrane moving as a result of the traveling sound wave[6-8]. Any dysfunction in this process will cause sensory-neural hearing loss(SNHL)[9]. SNHL and presbycusis may be attributed to various etiologies such as toxic agents, acoustic trauma, or the aging process; however, the exact mechanism is unknown [10,11]. SNHL in PXF syndrome may be caused by deposits of its material in inner ear structures (organ of corti), it may cause slight alterations in fine vibrations induced by sound analogous[2] and also inhibits the conversion of the vibration energy to bioelectric energy by depositing in tectorial and basilar

membranes [9].

Glaucoma is a condition characterized by raised intraocular pressure, typical glaucomatous optic nerve head damage and presence of glaucomatous visual field defects. PXF syndrome is relatively common but an easily overlooked cause of chronic open angle glaucoma. They are found at the same eye most of the time, but few studies demonstrated the relationship between PXF and SNHL[1]. The goal of our study is to evaluate correlation between PXF and SNHL and to assess the possible systemic nature of this syndrome.

MATERIALS AND METHODS

Subjects Patients attending a general ophthalmic clinic in Imam Khomeini medical center (Urmia, Iran, March to November 2010) were interviewed and underwent a complete ophthalmologic examination including determination of best-corrected Snellen visual acuity, slit-lamp examination, Goldmann applanation tonometry, gonioscopy, and dilated ophthalmoscopy using a 90D noncontact lens.

Methods The presence of pseudoexfoliation substance on the iris, lens capsule, angle, or corneal endothelium was observed and confirmed by one of the investigators. Patients were classified into groups according to their age and gender and matched controls were selected and screened for absence of pseudoexfoliation substance by the same investigator. Glaucoma was diagnosed based on presence of at least 2 of the 3 following criteria: (1) intraocular pressure > 22mmHg without anti-glaucoma medications; (2) typical glaucomatous damage of optic nerve's head and (3) presence of glaucomatous visual field defects. Visual field defects were defined on the basis of Anderson's criteria [12]. In order to prevent any misinterpretation related to glaucoma diagnosis and terminology, only patients with at least one definite glaucomatous eye and those who were non-glaucomatous were enrolled in this study and glaucoma suspects (subjects with only one of the above diagnostic criteria) were not entered in the study.

Any subject with manifestations of pseudoexfoliation or with evidence of glaucoma in either eye was considered a case of PXF or glaucoma, respectively. Patients were excluded if there was a history of acute or chronic ear disease, head trauma, long-term exposure to heavy noise or gunfire, and intake of ototoxic agents such as gentamicin or streptomycin. All subjects were referred to an otolaryngologist who examined them and excluded cases with evidence of upper respiratory tract infection and external or middle ear abnormalities. One masked operator performed standard bilateral pure-tone audiometery using the same device for all subjects. Hearing thresholds was determined using pure-tone audiometery using air and bone conduction at 1, 2, and 3 kilohertz (kHz) frequencies, which are thought to be important for speech comprehension. The sum of these thresholds was compared with the ISO 7029 standard [13] which is the result of a meta-analysis of large community-based studies to determine the normal distribution of hearing thresholds at different frequencies in otologically normal white subjects. Hearing loss was diagnosed if HTLs 1, 2, and 3 were higher than the sum of corresponding normal median thresholds as defined by the ISO 7029 standard. The level of hearing loss in one or both ears was compared between cases and controls; furthermore, average hearing thresholds at each frequency were compared between cases and controls.

Table 1 Demographic characteristics of study and control groups

Age(a)	Control group(n)		Study group(n)	
	Female	Male	Female	Male
50-54	3	3	3	2
55-59	4	5	5	5
60-64	13	7	12	5
65-69	9	6	7	10
≥70	0	0	0	1
Total	29	21	27	23

According to ISO 7029 data, males aged (in terms of years old) 18-30, 31-40, 41-50, 51-60, 61-70 and 71-80 had median $AAHL_{1,2,3}$ of 0-5kHz, 5-10kHz, 10-25kHz, 25-40kHz, 40-60kHz and 60-85kHz, respectively. Similarly, females aged (in terms of years old) 18-30, 31-40, 41-50, 51-60, 61-70 and 71-80 had median $AAHL_{1,2,3}$ of 0kHz, 5-10kHz, 10-25kHz, 25-30kHz, 30-45kHz and 50-65kHz, respectively[14].

RESULTS

Overall 50 patients (23 males with mean age of 61 years, range 52-70 years and 27 females with mean age of 60.5 years, range 52-69 years) were included in the study group. 3 males and 3 females had unilateral glaucoma at the same time; 41 of them had bilateral PXF. After evaluating inclusion and exclusion criteria, cases of both genders were allocated into 5-year age strata (Table 1). Control group consisted of 50 patients (21 males with mean age of 59.2 years, range 51-69 years and 29 females with mean age of 61.5 years, range 53-69 years). Similar to the case group, they were classified into 5-year age strata and none of them were glaucomatous (Table 1).

In audiometric studies, mean hearing thresholds in PXF patients were obtained 40.6db and 41.2db in the right and left ear, respectively. In patients with simultaneous glaucoma, mean hearing thresholds were 57.5db and 60.8db in the right and left ear, respectively, which was higher than ISO 7029 standard(Table 2).

In control group 6 out of 50 patients (12.0%) had hearing loss in one or both ears and 44 out of 50 controls (88.0%) had normal hearing thresholds. 9/100 studied ears in control group were found to have SNHL. Also in the study group 21/50 patients(42.0%) including 9 males and 12 females had unilateral or bilateral hearing loss, which included 35/100 ears(Table 3).

Only 4/21 of patients with SNHL had glaucoma too in study group . Prevalence of glaucoma in study group was 12.0% in our study (Table 4).

Table 2 Mean hearing thresholds in study and control groups

Frequency	Control group(db)		Study group(db)			
	Right ear	Left ear	PXF		PXF and glaucoma	
			Right ear	Left ear	Right ear	Left ear
1kHz	5.66	5.41	7.24	7.48	9.16	8.35
2kHz	8.65	8.89	12.32	13.48	18.33	21.33
3kHz	14.32	15.52	20.56	21.31	23.34	30.33
[1]$HTL_{1,2,3}$kHzs	28.58	30	40.59	41.20	57.5	60.83

db: decibel; [1]Sum of hearing thresholds at 1, 2, and 3 kHz.

Table 3 Number of patients in control and study groups with and without hearing loss classified by their gender

Groups	Control group(n)		Study group(n)	
	Male	Female	Male	Female
With SNHL	2	4	9	12
Without SNHL	19	25	14	15
Total	21	29	23	27

Table 4 SNHL in glaucomatous and non-glaucomatous patients in study group

Groups	Male(n)		Female(n)	
	With SNHL	Without SNHL	With SNHL	Without SNHL
PXF	8	12	9	15
PXF and Glaucoma	1	2	3	0
Total	9	14	12	15

DISCUSSION

This study was conducted to evaluate correlation between PXF and SNHL and to find the possible systemic nature of this syndrome. The results of this study showed that SNHL is more common in study group with PXF than age-sex matched control group (P = 0.001). This finding is based on comparison to ISO 7029 standard, which is consistent with recent studies and confirms the systemic nature of the PXF disease. In this study, severity and prevalence of SNHL were also studied between PXF patients and patients with concomitant PXF and glaucoma. The results demonstrated that difference was not statistically significant (P=0.118) and (P=0.193) respectively (in both sides ears at HTL1, 2, 3kHzs).

In the study by Cahill *et al*[14] sum of pure-tone hearing thresholds was measured at 1, 2 and 3kHz ($HTL_{1,2,3}$) in each ear and compared with the ISO 7029 standard. Sixty-nine patients were studied. 101 ears (73.7%) had a higher $HTL_{1,2,3}$ than the ISO 7029 median $AAHL_{1,2,3}$. There was no significant difference between the proportion of ears with SNHL on the same side as eyes without PXF, with PXF but not glaucoma and with PXF and glaucoma, in either male or female group. A large proportion of patients with PXF had SNHL in comparison to age-matched controls, regardless of whether or not there is associated glaucoma.

Similarly in our study there was no significant difference between the proportion of SNHL, in either male or female group. SNHL prevalence was more common in patients with PXF and concomitant glaucoma contrary to PXF patients but it was not statistically significant in either ear at $HTL_{1,2,3}$ kHzs (P=0.193).

The significant difference between this study and previous studies is that the mean age of under study patients in this article were lower than previous studies[1,2,4,9,15,16]. We selected PXF patients at younger ages therefore it was possible for us to reduce the presbycusis effect in patients. Also it is obvious that prevalence of SNHL in PXF patients is lower in our study in comparison to other articles.

In the study by Yazdani *et al*[2] on 166 subjects which included 83 patients with PXF and 83 age-gender matched controls, equal numbers of male and female subjects were allocated into each of the study groups. Prevalence of SNHL (in one or both ears) was 94.0% in case group and 69.5% in control group which demonstrated a significant difference.

Detorakis *et al*[16] evaluated the acoustic function in PXF and exfoliation glaucoma. Tympanometric peak values were significantly lower in study compared with control group (P=0.04). The reduced tympanometric peak values in cases imply impairment in the elastic properties of the middle ear in PXF syndrome . Finally it is concluded that SNHL is more common in frequencies important for speech in patients affected by ocular PXF than in single frequency in comparison to age-sex matched controls, which is irrelevant to simultaneous glaucoma. Similar to Detorakis's study, in our study also, hearing thresholds were evaluated at 1, 2 and 3kHzs; but results did not show a statistically significant difference between study and control ears at both sides (P=0.333 for all frequencies).

Correlation and association of SNHL with PXF syndrome have been demonstrated in several studies. We also choose studying SNHL associated with PXF like, because it was easy and

cheap way to evaluate the systemic character of this syndrome. more studies like biopsy and specific staining are needed to evaluate other organs such as ears in order to understand the necessity of additional tests in PXF patients. The findings of this study support presence of pseudoexfoliative material in ear tissues and imply that this disorder may truly a systemic condition with envolvment of multiple organs. More research on visceral complications of PXF is required to pronounce it as a systemic disease, and to prevent more complications.

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假性剥脱综合征中感觉神经性听力丧失

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摘要

目的:评估眼部假性剥脱综合征(pseudoexfoliation syndrome, PXF)与感觉神经性听力丧失(sensory-neural hearing loss, SNHL)之间的关系。

方法:该前瞻性病例对照研究选取2010-03/12在伊朗乌尔米耶,伊玛何梅尼医疗中心普通眼科门诊就诊的患者。常规眼科检查后,确诊为PXF的患者建议去耳鼻喉科,被选病例(纳入排除标准评估后)被推荐到听力检测科。分别在1, 2, 3 kHz对每只耳进行了纯音听阈级检测(Pure tone hearing threshold level, HTL),并将检测结果与国际标准(International Standard,ISO 7029)在1, 2, 3 kHz平均年龄相关性听力丧失(age associated hearing loss, AAHL)进行比较。

结果:在1, 2, 3kHz,50例患者中21例(42.0%)HTL高于ISO 7029平均AAHL,包括男性组9例14耳,女性组12例21耳。大约12.0%的患者同时伴有青光眼,不过,PXF患者和同时伴有青光眼的患者在SNHL的患病率和严重程度上无明显差别。同年龄-性别匹配对照组相比,眼部PXF的患者SNHL更普遍($P<0.05$)。

结论:大部分眼部PXF患者有SNHL,与年龄-性别匹配对照组相比,可能是由于其内耳的PXF纤维造成。这些发现表明PXF可能是一个系统性疾病。

关键词:假性剥脱综合征;感觉神经性听力丧失;青光眼