European Review for Medical and Pharmacological Sciences 2012; 16: 902-907

Prevalence and severity of sensorineural hearing loss in patients with exfoliation syndrome

T.A. PAPADOPOULOS[1], M. CHARALABOPOULOU[3], I. VATHYLAKIS[3], P. GOUMAS[2], S. GARTAGANIS[1], S. NAXAKIS[2]

[1]Department of Ophthalmology, University of Patras, Patras (Greece)
[2]Department of Otolaryngology, University of Patras, Patras (Greece)
[3]Department of Audiology-Neurotology, "Korgialenio-Benakio" Red Cross General Hospital, Athens (Greece)

Abstract. – BACKGROUND AND OBJECTIVES, Exfoliation syndrome is characterized by the production and accumulation of abnormal extracellular material in many ocular and extraocular tissues. The aim of the present prospective case-control clinical study was to evaluate the effect of exfoliation syndrome on prevalence and severity of sensorineural hearing loss.

MATERIALS AND METHODS, In the study participated 94 ears of patients with unilateral or bilateral ocular exfoliation syndrome (study group) and 44 ears of individuals without the syndrome (control group). Subjects with a history of conditions affecting hearing function and patients with conductive or mixed hearing loss, glaucoma or ocular hypertension were excluded from the study. All participants underwent pure-tone audiometry with air and bone conduction. During audiometry, the eventual sensorineural hearing loss and its severity was determined for each ear, at frequencies of 250, 500, 1000, 2000, 4000 and 8000 Hz (Hertz).

RESULTS, The mean age of participants was 74.7 years in both groups. Differences in age and gender distribution between the two groups were not statistically significant. Compared to control group, study group displayed: (1) Significantly higher prevalence rates of hearing loss at frequencies of 1000, 2000, 4000 and 8000 Hz ($p = 0.007$). (2) More severe hearing loss at frequencies of 4000 and 8000 Hz ($p < 0.001$).

CONCLUSIONS, The above results demonstrate an effect of exfoliation syndrome on prevalence and severity of sensorineural hearing loss. These findings verify the theory that this syndrome is not only an ocular disease, but also a systemic disorder with potential otological complications.

Key Words:

Exfoliation syndrome, Glaucoma, Hearing loss, Audiometry, Presbyacusis.

Introduction

Exfoliation syndrome is an age-related disorder, characterized by the production and the progressive accumulation of abnormal fibrillar extracellular material in many ocular and extraocular tissues[1]. Ocular manifestations of the syndrome involve almost all structures of the anterior eye segment (cornea, iris, pupillary border, lens, ciliary body, zonules, anterior chamber angle, trabecular meshwork), but even the conjunctiva and the orbita[2]. Ocular exfoliation-like deposits have also been discovered in the skin, the cerebral meninges and in various visceral organs, such as heart, lung, liver, gall bladder and kidney[3-5].

The diffuse localization of exfoliative material has been considered as a cause of numerous ocular and extraocular complications, such as open-angle and angle-closure glaucoma, lens opacification, complications in cataract surgery, retinal vascular occlusion, age-related macular degeneration, Alzheimer's dementia, arterial hypertension, stroke, abdominal aortic aneurysm and coronary artery disease[6-14].

The prevalence of exfoliation syndrome increases with age[2] and geographic prevalence rates vary in different regions, from 5% in France[15] to 30% in Iceland[16]. An association of the syndrome with multiple inheritance patterns has been reported[17].

Sensorineural hearing loss is associated with pathologies of the inner ear, cochlear nerve and auditory cortex[18]. Possible causes include age (presbyacusis), noise (occupational hearing loss), oto-toxic drugs, chemical substances, trauma, vascular, neurological and systemic diseases, congenital, autoimmune and metabolic syndromes, infections, tumours, Menière's disease, perilymph fistula etc[19]. Sensorineural hearing loss may also occur in combination with ophthalmic diseases in cases of various syndromes (ex. Usher, Alport and Stickler's syndrome), infections during pregnancy (ex. congenital syphilis and rubella), retinitis pigmentosa, Peters' anomaly and Behçet's disease[20,21].

Corresponding Author: Stephanos Naxakis, Ph.D.; e-mail: naste@in.gr

Patients and Methods

Selection and Exclusion Criteria

The present prospective case-control clinical study was conducted to evaluate the effect of the exfoliation syndrome on the prevalence and severity of sensorineural hearing loss. The study sample was collected from candidates for cataract surgery, in the out-patients section of 1st Department of Ophthalmology, at Red Cross General Hospital, Athens. Study group subjects manifested exfoliation syndrome in one or both eyes, whereas control group subjects did not manifest any clinical signs of the syndrome in either eye. Both groups were chosen to have similar demographic characteristics. Medical history and informed consent were obtained from all participants. The study was approved by the Hospital's Ethics Committee and was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Exclusion criteria from the study were history of congenital or acquired hearing loss, previous ear surgery, acute or chronic ear diseases, ear or head trauma, noise exposure, intake of oto-toxic drugs, concurrent infection of upper respiratory system, glaucoma, ocular hypertension without antiglaucoma medication and various vascular and systemic diseases or autoimmune and metabolic syndromes that may be related to sensorineural hearing loss (ex.uncontrolled diabetes mellitus or hypertension, coronary artery disease, stroke, sarcoidosis, sickle-cell disease, lupus erythematosus, Behçet's disease, hypothyroidism).

Examinations

All participants in the study underwent a complete ophthalmologic and otologic assessment.

The ophthalmologic assessment was performed by the same examiner (TP) and included measurement of Snellen best-corrected visual acuity, slit-lamp biomicroscopy, Goldmann applanation tonometry, gonioscopy, dilated fundoscopy with a +90 dioptre non-contact lens and selectively visual field testing. Exfoliation syndrome was diagnosed on presence of exfoliative material on the iris surface, the corneal endothelium, the trabecular meshwork and/or on the central area of the anterior lens capsule after pupil dilation, in either eye. These findings were confirmed by an ophthalmologist not participating in the study. The diagnosis of ocular hypertension was based on measurement of intraocular pressure >21mmHg. The diagnosis of glaucoma was based on the observation of typical glaucomatous optic nerve head damage during fundoscopy and in cases of ambiguous findings, on the presence of glaucomatous visual field defects. Visual field testing was performed using the central 30-2 program of the Humphrey 740 automated perimeter (Humphrey Systems, Dublin, CA, USA).

The otologic assessment was also performed by the same examiner (MC) and included ear inspection and palpation, otoscopy, nasopharyngeal examination, tuning fork testing and pure-tone audiometry. Pure-tone audiometry was performed using the Orbiter 922-2 clinical audiometer (Madsen Otometrics, Copenhagen, Denmark). During audiometry, air and bone method of sound conduction was applied, in order to differentiate between sensorineural hearing loss and conductive or mixed hearing loss. Subjects with conductive or mixed hearing loss were excluded. Consequently, the hearing threshold (minimal intensity of perceptible sound) was calculated for every ear, using air and bone conduction, at frequencies of 250, 500, 1000, 2000, 4000 and 8000 Hz (Hertz). Testing began approximately 40 dB (Decibel) above the expected threshold at each frequency, continued with 10 dB descending steps below threshold and was completed with 5 dB ascending steps until 2 of 4 sounds were heard.

To investigate the prevalence and severity of sensorineural hearing loss, the above frequencies were divided into 3 groups of low (250 & 500 Hz), medium (1000 & 2000 Hz) and high (4000 & 8000 Hz). Ears with average hearing thresholds >25dB HL (Decibel hearing level) in each frequency group were classified as having sensorineural hearing loss at the respective frequencies. The severity of sensorineural hearing loss was assessed according to the scale of the American national standards institute (ANSI) 1969, as follows: 0-25dB HL=normal hearing, 26-40dB HL=mild sensorineural hearing loss, 41-55dB HL=moderate, 56-70dB HL=moderately severe, 71-90dB HL=severe and >90dB HL=profound[22].

Statistical Analysis

Statistical analysis was performed with SPSS statistical software (SPSS for Windows, version 15.0, SPSS Inc., Chicago, IL, USA). Normality of data distribution was checked by Kolmogorov-Smirnov's test. Differences in age and gender distribution between study and control groups were examined using unpaired Student's t-test and Pearson's x^2-test respectively. Audiometry data for prevalence and severity of hearing loss were

analysed by Pearson's x^2-test. A p-value <0.05 was considered to indicate statistical significance. Study power analysis yielded an adequate power of 84% for the detection of significant differences between study and control groups.

Results

138 ears of 69 subjects participated in the study, that included 94 ears of 47 patients (23 males, 49%) with exfoliation syndrome constituting the study group and 44 ears of 22 individuals (9 males, 41%) without the syndrome constituting the control group. All study group patients manifested the syndrome in at least one eye. The mean age of participants was 74.7 years in both groups. The median age was 76 years in the study group and 75 years in the control group. Differences in age and gender distribution between the two groups were not statistically significant ($p = 0.985$ and $p = 0.378$ for age and gender distribution respectively).

Results from Kolmogorov-Smirnov's test demonstrated that distribution of audiometry data was normal at all examined frequencies ($p > 0.05$). Age distribution of the examined subjects was also normal ($p = 0.133$). Hearing thresholds were identical for both air and bone conduction audiometry, in all examined subjects at each frequency, signifying pure sensorineural hearing loss or normal hearing. No clinically significant differences were found between the hearing thresholds of left and right ear in any of the 69 subjects.

Prevalence of sensorineural hearing loss was studied at 3 different frequency groups (as described in methods) and calculated in number and percentage of ears with average hearing thresholds >25dB HL in each group. Depending on the tested frequencies, sensorineural hearing loss was found in 54-92 of 94 ears (57-98%) in the study group and in 18-38 of 44 ears (41-86%) in the control group. Study group subjects displayed significantly higher prevalence rates compared to control group subjects at medium and high frequencies of 1000, 2000, 4000 and 8000 Hz ($p = 0.007$), but not at low frequencies of 200 and 500 Hz (Table I, Figure 1).

Severity of sensorineural hearing loss was also studied at 3 different frequency groups. In the study group 5-36 of 94 ears (5-38%) had mild sensorineural hearing loss, 16-33 (17-35%) moderate, 1-33 (1-35%) moderately severe and 1-35 (1-37%) severe, depending on the tested frequencies. In the control group 10-14 of 44 ears (23-32%) had mild sensorineural hearing loss, 4-14 (9-32%) moderate, 0-14 (0-32%) moderately severe and 0-5 (0-11%) severe, depending on the tested frequencies. Study group subjects displayed more severe sensorineural hearing loss compared to control group subjects at high frequencies of 4000 and 8000 Hz ($p < 0.001$), but not at low and medium frequencies of 250, 500, 1000 and 2000 Hz (Table II, Figure 2).

Discussion

The above results advocate for an effect of exfoliation syndrome on both prevalence and severity of sensorineural hearing loss.

Higher prevalence of sensorineural hearing loss in patients with exfoliation syndrome has already been reported in some previous studies[23-25]. However, only one study has assessed the severity of sensorineural hearing loss, reporting no association with exfoliation syndrome[23].

Table I. Prevalence of sensorineural hearing loss in study and control groups at different frequencies, calculated in number and percentage of ears.

Frequencies	Study group	Control group	Statistics (χ^2-test)
Low 250 & 500 Hz	54 (57%)	18 (41%)	$p = 0.070$ OR = 1.950 95% CI = (0.943-4.034)
Medium 1000 & 2000 Hz	76 (81%)	26 (59%)	$p = 0.007$ OR = 2.923 95% CI = (1.326-6.445)
High 4000 & 8000 Hz	92 (98%)	38 (86%)	$p = 0.007$ OR = 7.263 95% CI = (1.403-37.605)

Hz = hertz, OR = odd's ratio, CI = confidence interval.

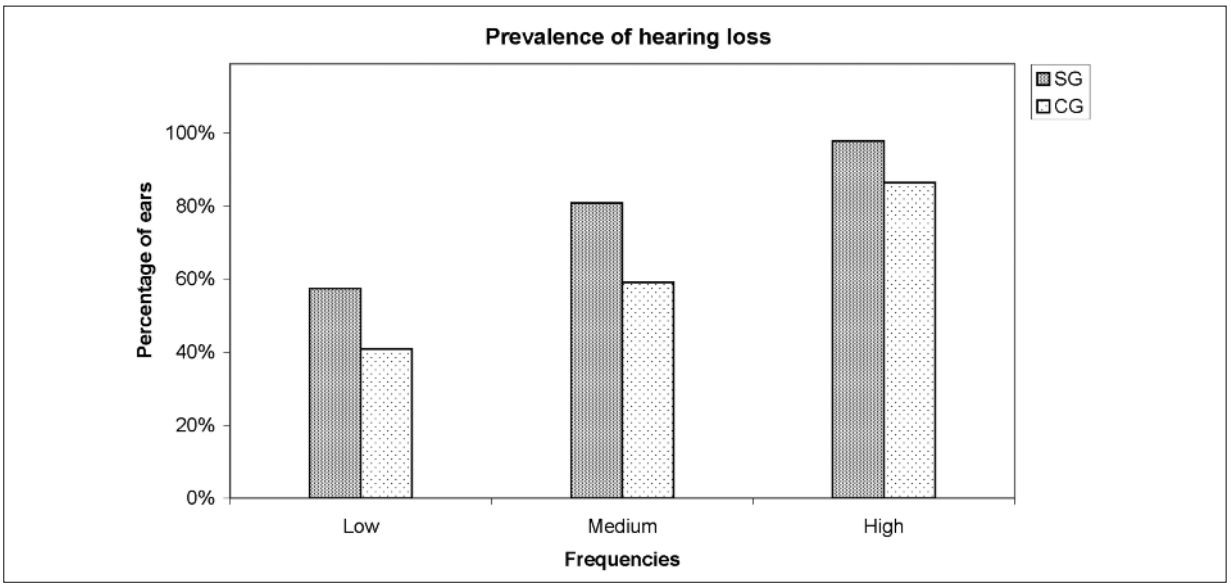

Figure 1. Prevalence of sensorineural hearing loss at different frequencies. SG = study group, CG = control group.

Our findings support evidence from previous research on the prevalence of sensorineural hearing loss in exfoliation syndrome. However, they provide a totally new finding, that is the statistically significant effect of the syndrome on the severity of sensorineural hearing loss at high frequencies.

Compared to previous investigations, the present study referred the effect of exfoliation syndrome on the prevalence and severity of sensorineural hearing loss in a more thorough manner, focusing into 3 different frequency groups, instead of considering only 1 group with all tested frequencies. Additionally, the study methodology has advantages, because the candidate exclusion criteria were more detailed and the audiometric testing involved a greater number of frequencies, covering the entire audible frequency range. In conclusion, an important feature differentiating the study from all previous ones was the exclusion of glaucomatous patients, in order the effect of exfoliation syndrome on hearing loss to be isolated and to be examined in a more objective way.

The relationship between glaucoma and hearing loss is not clear, according to the contradicting results from various reports. Some studies did not demonstrate any association of glaucoma or optic nerve ischemic disorders with hearing loss[26,27]. Exception though was found for normal tension glaucoma[28] and glaucoma combined with specific congenital syndromes and degenerative diseases, such as Stickler's syndrome, abdominal aortic aneurysm-deafness syndrome and familial deafness with iris degeneration[21,29,30].

The pathogenesis of sensorineural hearing loss in exfoliation syndrome may be explained by the following hypotheses:

Table II. Severity of sensorineural hearing loss in study and control groups at different frequencies, calculated in number and percentage of ears.

Frequencies	Sensorineural hearing loss										Statistics (χ^2-test)
	Study group					Control group					
	MI	MO	MS	SE	PR	MI	MO	MS	SE	PR	
Low 250 & 500 Hz	36	16	1	1	0	14	4	0	0	0	$p = 0.367$
	38%	17%	1%	1%	0%	32%	9%	0%	0%	0%	
Medium 1000 & 2000 Hz	30	33	12	1	0	10	14	2	0	0	$p = 0.064$
	32%	35%	13%	1%	0%	23%	32%	4%	0%	0%	
High 4000 & 8000 Hz	5	19	33	35	0	10	9	14	5	0	$p < 0.001$
	5%	20%	35%	37%	0%	23%	20%	32%	11%	0%	

Hz = hertz, MI = mild, MO = moderate, MS = moderately severe, SE = severe, PR = profound.

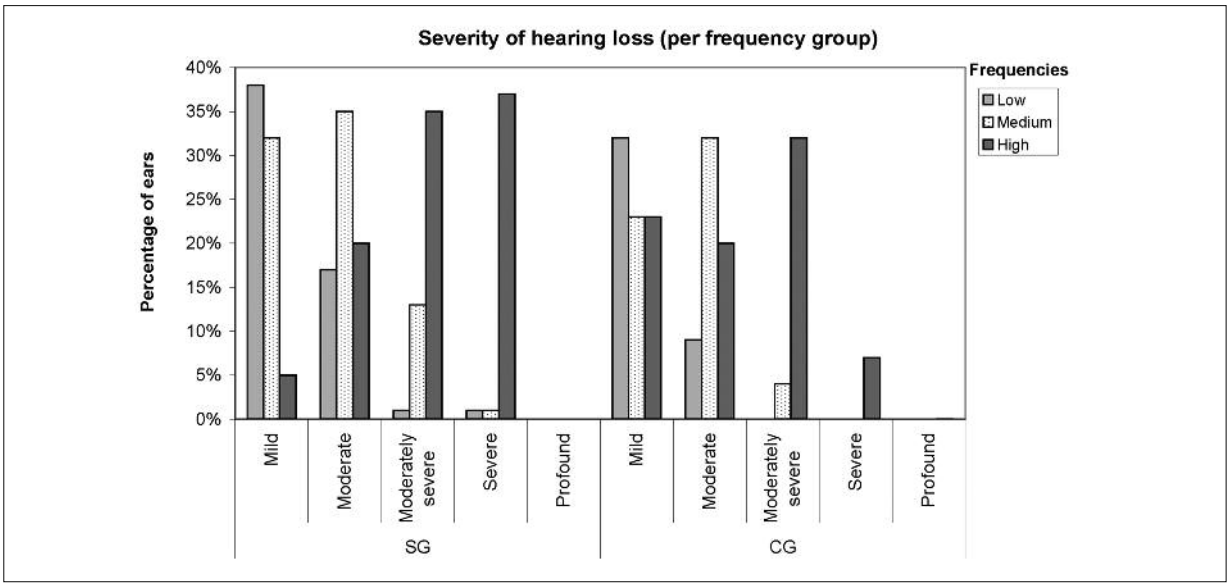

Figure 2. Severity of sensorineural hearing loss at different frequencies. SG = study group, CG = control group.

- The deposition of exfoliative material in the organ of Corti of the inner ear may affect the transmission of vibration energy to the neurosensory hair cells and induce alterations in the chemical composition of the surrounding environment[31]. This hypothesis is supported by the common embryological derivation of the anterior segment structures of the eye affected by exfoliation syndrome and the tectorial and basilar membranes of the organ of Corti[32].
- The relationship between exfoliation syndrome and age-related hearing loss (presbyacusis) may be attributed to similarities in the pathologic and biochemical findings of these conditions or to common predisposing factors, such as age, cellular stress (oxidation, ischemia-hypoxia) and insufficiency of cellular protection mechanisms[23,33-36].
- The deposition of exfoliative material on the vascular walls may impair the blood supply to the inner ear and the temporal lobe, resulting in a dysfunction of the acoustic receptors and the auditory cortex[24]. It has been reported that disorders in the blood supply to the brain and the inner ear (ex. due to migraine, hyperviscosity or vertebrobasilar occlusion) are possible causes of sensorineural hearing loss[37-39].

Conclusions

The effect of exfoliation syndrome on prevalence and severity of sensorineural hearing loss demonstrated by the data of the present study and evidence from previous researches, verify the theory that this syndrome is not only an ocular disease, but also a systemic disorder with potential otological complications. Consequently, we recommend an evaluation of hearing ability with audiometric testing in patients with exfoliation syndrome, besides the routine ophthalmologic examination.

Acknowledgements

The authors are grateful to 1st Department of Ophthalmology "Korgialenio-Benakio" Red Cross General Hospital, Athens, Greece and to Christos T. Nakas, PhD, biostatistician, for his assistance with data analysis.

References

1) Schlötzer-Schrehardt U, Naumann GO. Ocular and systemic pseudoexfoliation syndrome. Am J Ophthalmol 2006; 141: 921-937.
2) Ritch R, Schlötzer-Schrehardt U. Exfoliation syndrome. Surv Ophthalmol 2001; 45: 265-315.
3) Streeten BW, Dark AJ, Wallace RN, Li ZY, Hoepner JA. Pseudoexfoliative fibrillopathy in the skin of patients with ocular pseudoexfoliation. Am J Ophthalmol 1990; 110: 490-499.
4) Naumann GO, Schlötzer-Schrehardt U, Küchle M. Pseudoexfoliation syndrome for the comprehensive ophthalmologist. Intraocular and systemic manifestations. Ophthalmology 1998; 105: 951-968.
5) Streeten BW, Li ZY, Wallace RN, Eagle RC Jr, Keshgegian AA. Pseudoexfoliative fibrillopathy in visceral organs of a patient with pseudoexfoliation syndrome. Arch Ophthalmol 1992; 110: 1757-1762.

6) Ritch R. Exfoliation syndrome-the most common identifiable cause of open-angle glaucoma. J Glaucoma 1994; 3: 176-177.
7) Puska P, Tarkkanen A. Exfoliation syndrome as a risk factor for cataract development: five-year follow-up of lens opacities in exfoliation syndrome. J Cataract Refract Surg 2001; 27: 1992-1998.
8) Shastri L, Vasavada A. Phacoemulsification in Indian eyes with pseudoexfoliation syndrome. J Cataract Refract Surg 2001; 27: 1629-1637.
9) Gillies WE, Brooks AM. Central retinal vein occlusion in pseudoexfoliation of the lens capsule. Clin Experiment Ophthalmol 2002; 30: 176-187.
10) Kling F, Colin J. [Potential association of pseudoexfoliation syndrome (PEX) with age-related macular degeneration (ARMD)]. J Fr Ophtalmol 2001; 24: 7-12.
11) Linnér E, Popovic V, Gottfries CG, Jonsson M, Sjögren M, Wallin A. The exfoliation syndrome in cognitive impairment of cerebrovascular or Alzheimer's type. Acta Ophthalmol Scand 2001; 79: 283-285.
12) Mitchell P, Wang JJ, Smith W. Association of pseudoexfoliation syndrome with increased vascular risk. Am J Ophthalmol 1997; 124: 685-687.
13) Schumacher S, Schlötzer-Schrehardt U, Martus P, Lang W, Naumann GO. Pseudoexfoliation syndrome and aneurysms of the abdominal aorta. Lancet 2001; 357: 359-360.
14) Andrikopoulos GK, Mela EK, Georgakopoulos CD, Papadopoulos GE, Damelou AN, Alexopoulos DK, Gartaganis SP. Pseudoexfoliation syndrome prevalence in Greek patients with cataract and its association to glaucoma and coronary artery disease. Eye 2009; 23: 442-447.
15) Colin J, Le Gall G, Le Jeune B, Cambrai MD. The prevalence of exfoliation syndrome in different areas of France. Acta Ophthalmol Suppl 1988; 184: 86-89.
16) Allingham RR, Loftsdottir M, Gottfredsdottir MS, Thorgeirsson E, Jonasson F, Sverisson T, Hodge WG, Damji KF, Stefánsson E. Pseudoexfoliation syndrome in Icelandic families. Br J Ophthalmol 2001; 85: 702-707.
17) Challa P. Genetics of pseudoexfoliation syndrome. Curr Opin Ophthalmol 2009; 20: 88-91.
18) Schuller DE, Schleuning AJ. Hearing loss. In: Schuller DE, Schleuning AJ, eds. De Weese and Saunder's Otolaryngology-Head and Neck Surgery. 8th ed. St. Louis: Mosby; 1994: pp. 453-468.
19) Nadol JB Jr. Hearing loss. N Engl J Med 1993; 329: 1092-1102.
20) Bayazit YA, Yilmaz M. An overview of hereditary hearing loss. ORL J Otorhinolaryngol Relat Spec 2006; 68: 57-63.
21) Gorlin RJ. Genetic hearing loss associated with eye disorders. In: Gorlin RJ, Toriello HV, Cohen MM, eds. Hereditary Hearing Loss and Its Syndromes. New York: Oxford University Press; 1995: pp. 105-118.
22) Kileny PR, Zwolan TA. Diagnostic and rehabilitative audiology. In: Cummings CW, Flint PV, Schuller DE, Thomas JR, Robbins KT, Harker LA, Haughey BH, Richardson MA, eds. Otolaryngology, Head & Neck Surgery, IV. 4th ed. St.Louis: Mosby; 2004: pp. 3483-3487.
23) Aydogan, Ozkan B, Yüksel N, Keskin G, Altintas O, Karabas VL, Caglar Y, Almaç A. Homocysteine levels in plasma and sensorineural hearing loss in patients with pseudoexfoliation syndrome. Eur J Ophthalmol 2006; 16: 542-547.
24) Turacli ME, Özdemir FA, Tekeli O, Gökcan K, Gerçeker M, Dürük K. Sensorineural hearing loss in pseudoexfoliation. Can J Ophthalmol 2007; 42: 56-59.
25) Yazdani S, Tousi A, Pakravan M, Faghihi AR. Sensorineural hearing loss in pseudoexfoliation syndrome. Ophthalmology 2008; 115: 425- 429.
26) Shapiro A, Siglock TJ, Ritch R, Malinoff R. Lack of association between hearing loss and glaucoma. Am J Otol 1997; 18: 172-174.
27) Hayreh SS, Podhajsky P, Zimmerman B. Ocular and optic nerve head ischemic disorders and hearing loss. Am J Ophthalmol 1999; 128: 606-611.
28) Kremmer S, Kreuzfelder E, Bachor E, Jahnke K, Selbach JM, Seidahmadi S. Coincidence of normal tension glaucoma, progressive sensorineural hearing loss, and elevated antiphosphatidylserine antibodies. Br J Ophthalmol 2004; 88: 1259-1262.
29) Adoki II, Stoodley BJ. Abdominal aortic aneurysm, glaucoma and deafness: a new familial syndrome. Br J Surg 1992; 79: 637-638.
30) Rundle P, Lotery AJ, Archer DB, McGinnity FG. Familial deafness associated with iris degeneration and glaucoma. Eye (Lond) 1997; 11(Pt 4): 476-478.
31) Cahill M, Early A, Stack S, Blayney AW, Eustace P. Pseudoexfoliation and sensorineural hearing loss. Eye 2002; 16: 261-266.
32) Larsen WJ. Essentials of Human Embryology. New York: Churchill-Livingstone; 1998: pp. 229-272.
33) Seidman MD, Ahmad N, Bai U. Molecular mechanisms of age-related hearing loss. Ageing Res Rev 2002; 1: 331-343.
34) Liu XZ, Yan D. Ageing and hearing loss. J Pathol 2007; 211: 188-197.
35) Schlötzer-Schrehardt U. [Oxidative stress and pseudoexfoliation glaucoma]. Klin Monbl Augenheilkd 2010; 227: 108-113.
36) Zenkel M, Kruse FE, Naumann GO, Schlötzer-Schrehardt U. Impaired cytoprotective mechanisms in eyes with pseudoexfoliation syndrome/glaucoma. Invest Ophthalmol Vis Sci 2007; 48: 5558-5566.
37) Olsson JE. Neurotologic findings in basilar migraine. Laryngoscope 1991; 101(1 Pt 2 Suppl 52): 1-41.
38) Hildesheimer M, Bloch F, Muchnik C, Rubinstein M. Blood viscosity and sensorineural hearing loss. Arch Otolaryngol Head Neck Surg 1990; 116: 820-823.
39) Sauvaget E, Kici S, Petelle B, Kania R, Chabriat H, Herman P, Tran Ba Huy P. Vertebrobasilar occlusive disorders presenting as sudden sensorineural hearing loss. Laryngoscope 2004; 114: 327-332.