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ORIGINAL ARTICLE

Investigation of Hearing and Outer Hair Cell Function of Cochlea in Patients with Psoriasis

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Objective: Psoriasis is a chronic, papulo-squamous skin disease characterized by circumscribed, erythematous, scaling, thickened plaques. The primary cause of psoriasis is unknown; however recent genetic and immunological researches have increased understanding of the pathogenesis of psoriasis as a chronic, immune mediated, inflammatory disorder. Some research groups have implicated CD8+ T cells as predominant in psoriatic epidermis and find that reduction in this subset during treatment of psoriasis correlates most closely with disease resolution. Many studies have been published about hearing in autoimmune diseases, however studies about hearing loss in psoriasis have been very limited. The aim of this study was to investigate cochlear functions and hearing evaluation in patients with psoriasis.

Study design: Prospective, case control study

Materials and Methods: Pure-tone audiometry at 250, 500, 1,000, 2,000, 4,000, 6,000 Hz and immittance measures including tympanometry and acoustic reflex and DPOAE (Distortion Product Otoacoustic Emission) testing were performed in the patients and controls. Totally, 42 psoriasis patients (84 ears) and 60 healthy control subjects (120 ears) were included in the study.

Result: Mean age of patients with psoriasis was 36.1 years (range 13-71 years) and control group was 38.8 years (range 11-69 years). There was no statistically significant difference between the pure-tone thresholds and levels of noise floor, DPOAE responses and signal noise ratio of the patients and controls in all frequencies ($P > 0.05$).

Conclusion: In our study, based on the DPOAE and audiological findings, we did not find any damage of outer hair cells of cochlea and hearing loss in patients with psoriasis.

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Introduction

Psoriasis is a chronic, papulo-squamous skin disease characterized by circumscribed, erythematous, scaling, thickened plaques situated over scalp, sacrum and extensor surfaces of knees and elbows. Acute clinical manifestations include small guttate lesions, erythroderma, psoriatic arthritis and nail involvement. It occurs worldwide, but the incidence is lower in warmer climates[1,2]. Psoriasis commonly presents before the age of 35 years, although any age group may be affected. It affects approximately 2% of the general population, and sex incidence is equal[3]. The primary cause of psoriasis is unknown; however recent genetic and immunological researches have increased understanding of the pathogenesis of Psoriasis as a chronic, immune mediated, inflammatory disorder[4-8].

The inner ear is subject to the target of an autoimmune attack, and sensorineural hearing loss can occur in complication of various non–organ-specific autoimmune diseases; however, the inner ear can also represent the primary focus of an autoimmune inner ear disease. Since the first description of autoimmune sensorineural hearing loss by McCabe[9] in 1979, many studies have been published about hearing in autoimmune diseases such as rheumatoid arthritis, ankylosing spondilitis, Behçet's disease, Sjögren's syndrome, polyarteritis nodosa and systemic lupus erytematosus [10-16].

However studies about hearing loss in psoriasis have been very limited. We have found 6 case reports in literature research by entering hearing and psoriasis keywords in PubMed website, but we could not find any clinical study about hearing in psoriasis.

Srikumar reported a case of sudden-onset sensorineural hearing loss in association with psoriatic arthritis[17]. A case of psoriasis presented with sudden

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simultaneous bilateral sensorineural hearing loss after taking oral acitretin[18]. Basavaraj et. al reported two patients with psoriasis who underwent cochlear implant surgery, discussing the risk of surgical site infection and treatment options to minimise infection[19]. A 13-year-old girl, affected by juvenile psoriatic arthritis, who was treated with etanercept developed a bilateral and asymmetric sensorineural deafness[20].

There were also two case of toxic iner ear damage in topical treatment of psoriasis with salisilates[21,22].

Therefore, this study was performed to investigate hearing and cochlear functions in patients with psoriasis.

Materials and Methods

Patients

Totally, 42 psoriasis patients (84 ears) who were diagnosed and treated in our Dermatology department and 60 healthy control subjects (120 ears) were included in the study. The diagnosis of psoriasis was done according to clinical and histopatological findings. Disease severity was evaluated by the PASI (Psoriasis Area and Severity Index)[23,24]. Informed consent was obtained from all participants. Detailed information was obtained about possible etiological factors leading to hearing loss (ototoxic drugs, noise exposure, ear surgery, perforated tympanic membrane, Meniere's disease, cranial trauma, metabolic diseases). There were no patients who have had a history of these factors. Participants were excluded from the study if they had any of following: (1) otoscopic evidence of a perforated tympanic membrane or other middle ear pathology, (2) presence of a flat tympanogram or absence of acoustic reflexes at 1 kHz with contralateral stimulation, (3) an air-bone gap of 5 dB at any frequency.

Audiometry

The initial hearing examination included otoscopy, tympanogram and complete audiologic evaluation including pure-tone air- and bone-conduction audiometry and speech audiometry. Pure-tone audiometry was performed at the frequencies 250, 500, 1,000, 2,000, 4,000, 8,000 Hz using a diagnostic audiometer (Madsen Orbiter 922-2 Clinical Audiometer, Denmark) in a sound-treated cabin. Normal middle ear function was defined by immitance and acoustic reflex results using a Middle Ear Analyzer (Tympstar GSI, Grason-Stadler Inc., Milford, USA)

The patients and controls who had normal peak compliance, peak pressure, gradient, ear canal volume and acoustic reflexes as defined by American Speech Language and Hearing Association[25,26] were included in the study.

DPOAE testing

Distortion Product Otoacoustic Emission (DPOAE) were measured using a Otodynamics ILO 292 Echoport USB II version 6 equipment (Otodynamics Ltd., London, UK) with ILO-OAE software installed on the computer. Primary tones f1 and f2 were fixed at f1/f2 = 1.22, and f2 frequencies ranged from 1,000 to 6,000 Hz in 1/2 octave steps. Stimulus intensities were L1 =65, L2 = 55. The individuals were seated in a soundproof room to remain as quiet as possible during the test. Once the probe was placed with a good seal in the ear canal, the level of the two frequencies was set according to our protocol.

The statistical analyses were performed using SPSS 13.0 for Windows. p value of <0.05 was considered significant. For overall group comparisons (patients with psoriasis and controls), Independent Samples T test was performed. For comparison of gender of patients and controls, chi-square test and for comparison of ages of patients and controls, Independent Samples T test were used.

Results

Mean age of patients with psoriasis was 36.1 years (range 13-71 years). There were 28 female and 14 male patients. Mean age of control group was 38.8 years (range 11-69 years). There were 35 female and 15 male subjects. Otoscopic examination was normal in all participants. There was no statistically significant difference between the ages and genders of the patient and control groups ($p > 0.05$).

Psoriasis patients with plaque, guttate and palmoplantar lesion types were included in the study, and lesions were 32 (78.6%) plaque, 7 (16.7%) guttate and 2 (4.7%) palmoplantar type. There were 9 (21.4%) joint and 7 (16.7%) nail involvements in patients. Disease severity was evaluated by the PASI, and mean PASI score was 5.7±3.2 (range 2.4-14.4).

Normal peak compliance, peak pressure, gradient, ear canal volume and acoustic reflexes obtained by immitance measures in the patients and controls. Because there was no air-bone gap in the participant, only bone conduction thresholds were taken into consideration.

Pure-tone audiometry findings of the patients and controls are shown in Table 1. There was no statistically significant difference between pure-tone thresholds of the patients and controls at all frequencies ($p > 0.05$).

The DPOAE signal, and noise floor findings of the patient and controls are shown in Table 2, and SNR (Signal Noise Ratio) findings of the patient and controls are shown in Figure 1. There was no statistically significant difference in levels of noise floor, DPOAE responses and signal noise ratios between the patients and controls at all frequencies ($p > 0.05$).

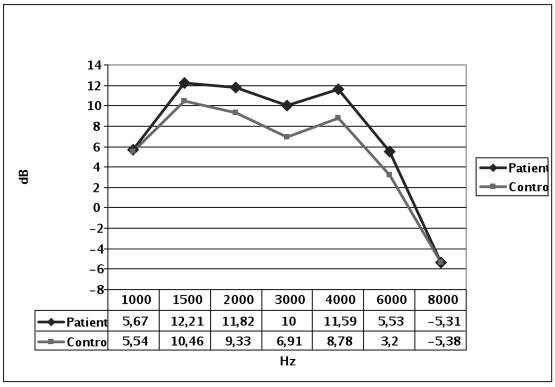

Figure 1. SNR Findings.

Discussion

Otoacoustic emissions are sounds found in the external auditory canal that originates from mechanical activity in the cochlea transmitted in a reversed direction through the middle ear and the tympanic membrane. These emissions arise from the vibratory motion of the outer hair cells. Attachment of the outer hair cells to the basilar membrane allows for a wave to be transmitted toward the stapedial footplate and ultimately into the external auditory canal[27]. Specifically, measurements of DPOAE corresponds closely to the physiological state of outer hair cells of the cochlea. Their main applications are the assessment of cochlear function to determine the site of pathological conditions associated with sensorineural hearing loss. DPOAE, if normal, provides extremely strong evidence of normal cochlear function, regardless of audiometric data. The function of outer hair cells is integral to the overall sensitivity and frequency-selectivity of the auditory system. The auditory system can function without outer hair cells, but thresholds raise roughly 50 dB and frequency-selectivity decreases dramatically when the cochlea contains only inner hair cells[28].

Psoriasis is a chronic and lifelong disease of unknown etiology, but current opinion is in favor of the disease immunologically-mediated and possibly autoimmune in nature[1,3]. Autoimmune diseases are the result of an

Table 1. Air-conduction thresholds of patient and control group

Frequency Hz	Patient's Right Ear Range(dB HL)	Mean(dB HL)	SD	Patient's Left ear Range(dB HL)	Mean(dB HL)	SD
250	0-25	13.1	5.7	5-20	11.8	4.8
500	5-30	9.4	5.7	0-20	10.0	4.8
1,000	0-30	9.8	5.6	0-25	9.5	5.8
2,000	0-30	10.5	7.1	0-30	11.6	7.0
4,000	0-45	15.5	11.1	0-45	16.5	11.3
8,000	5-60	23.4	11.9	10-55	23.1	9.8
PTA	3-30	9.9	5.5	2-25	10.5	5.1
SDS %	10-100	93.9	16.4	84-100	97.3	3.6
Frequency Hz	**Contr Right Ear Range(dB HL)**	**Mean(dB HL)**	**SD**	**Contr Left ear Range(dB HL)**	**Mean(dB HL)**	**SD**
250	0-25	11.6	5.2	0-35	11.7	6.9
500	0-25	9.9	5.6	0-20	11.2	5.1
1,000	0-20	9.2	5.6	0-25	9.7	6.4
2,000	0-25	9.2	7.1	0-25	10.1	6.7
4,000	0-45	12.8	11.0	0-45	13.6	10.9
8,000	5-55	22.4	14.1	0-50	22.1	13.1
PTA	0-22	9.5	5.2	0-20	10.4	4.8
SDS %	5-100	94.6	14.4	88-100	96.9	3.2

Hz (Hertz), dB HL (Decibel Hearing Level), PTA (Pure Tone Average), SDS (Speech Discrimination Score), SD(Standard Deviation)

Table 2. DPOAE signal, and noise floor findings of groups

	Patient Group					Control Group				
Frequency (Hz)	**N**	**Minimum (dB SPL)**	**Maximum (dB SPL)**	**Mean (dB SPL)**	**SD (dB SPL)**	**N**	**Minimum (dB SPL)**	**Maximum (dB SPL)**	**Mean (dB SPL)**	**SD (dB SPL)**
1.000 DPOAE	84	-19.7	22.1	4.66	9.22	120	-18.5	22.5	4.71	7.39
1.000 Noise Floor	84	-11.5	15	-2.47	4.91	120	-13.7	8.9	-3.49	5.47
1.500 DPOAE	84	-15.8	23.9	8.91	8.64	120	-15.8	26.2	7.14	8.41
1.500 Noise Floor	84	-14.8	5.6	-6.9	4.4	120	-18.4	1.3	-8.12	4.21
2.000 DPOAE	84	-42.9	20.5	5.64	10.32	120	-30	21	3.18	9.71
2.000 Noise Floor	84	-16.8	5.1	-10.57	3.87	120	-16.9	0.6	-10.63	3.87
3.000 DPOAE	84	-27.7	23.2	1.37	10.27	120	-30	17.5	-1.14	9.51
3.000 Noise Floor	84	-18	4.3	-13.05	3.15	120	-19.2	0.2	-13.39	3.27
4.000 DPOAE	84	-30	24.2	3.22	12.01	120	-30	22.2	1.24	9.53
4.000 Noise Floor	84	-19.4	5	-12.97	3.01	120	-17.4	-2.9	-12.8	2.68
6.000 DPOAE	84	-31.1	23.1	-2.86	12.63	120	-35.8	22.3	-5.96	13.31
6.000 Noise Floor	84	-16.7	-8.3	-12.92	1.79	120	-18.9	10.9	-12.99	3.11
8.000 DPOAE	84	-37.2	10.7	-19.95	11.41	120	-48	2.1	-19.21	9.51
8.000 Noise Floor	84	-20.9	-12.2	-16.11	1.83	120	-20.9	16.5	-15.82	3.53

dB(decibel). SPL(Sound Pressure Level). SD(Standard Deviation)

interaction between predisposing genes and triggering environmental factors, leading to loss of self-tolerance and an immune-mediated destruction of autologous cells and tissues[3]. Genes in the HLA complex are among the strongest predisposing genetic factors. The HLA complex genes primarily involved are most often those encoding the peptide-presenting HLA class I or II molecules. A probable mechanism is preferential presentation by the disease-associated HLA molecules of peptides from autoantigens to T cells[29].

The pathophysiology of Psoriasis is characterized by chronic T-cell stimulation by antigen presenting cells in the skin. However, overall evidences in pathophysiology of the disease hinge on several interacting components including: T cells; cytokine profiles; antigen-presentation; superantigens; epidermal stem cells, and major histocompatibility complex (MHC) associations[3]. T cells appear central to the immune-mediated hypothesis, and the epidermal and dermal inflammatory cell infiltration in psoriasis is comprised predominantly of T cells. Furthermore, most psoriasis pathogenesis investigators would agree that T cells are integral to the initiation and maintenance of epidermal keratinocyte proliferation observed in psoriasis. Disease initiation may be dependent on influx of activated CD4+ T cells and its maintenance dependent on CD8+ T cells, thereby providing the link to both MHC class I and class II associations[3-8]. Valdimarsson et al. studied the immunology of evolving cutaneous lesions of acute guttate psoriasis and observed that an intraepidermal influx of activated, HLA-DR+, CD4+ T cells was one of the earliest events[30]. In comparison resolving plaques of psoriasis exhibit a relative reduction in activated CD4+ T cells within the epidermis. Undoubtedly CD4± T cells are an important component of the dermal infiltrate but there are controversial issues regarding the predominant phenotype of the intraepidermal T cells observed in psoriasis[3].

Some research groups have implicated CD8+ T cells as predominant in psoriatic epidermis and find that reduction in this subset during treatment of psoriasis correlates most closely with disease resolution. It is unusual for an autoimmune disease to be strongly linked to MHC class I although this may indicate that MHC class I-associated CD8+ T-lymphocytes are of integral importance to maintenance of psoriasis lesions[4-8].

While CD4+ T cells are essential for initiating and maintaining the pathogenic process, CD8+ T-cells are the principle effector cells in the pathogenesis of psoriasis[4,5]. Sensorineural hearing loss or inner ear involvement have been widely reported in autoimmune diseases such as rheumatoid arthritis, ankylosing spondilitis, Behçet's disease, polyarteritis nodosa and systemic lupus erythematosus[10-17,31].

Two studies showed that the significantly increased CCR4 expression on circulating CD4+ T cells in their

study supported a crucial role for CCR4 in CD4+ T cell migration in ankylosing spondilitis, rheumatoid arthritis and systemic lupus erythematosus patients[32], and pro-inflammatory CD4+ T cells specific for inner ear peptides were capable of mediating experimental autoimmune hearing loss in mice[33].

The central role of the endolymphatic sac for the immunologic activity within the inner ear was definitively confirmed and reported by numerous studies. Several studies demonstrated that the inner ear was the source of the antibody, and the endolymphatic sac was capable of both processing antigen and producing a local antibody response[34-36]

The study of the distribution and anatomical localization of immunocompetent cells in normal mouse endolymphatic sac, by an immnohistochemical method, showed CD4 cells in the epithelial perisaccular region, whereas CD8 cells were rarely present31. Another immunohistochemical study of the extraosseous part of the endolymphatic sac from an otopsy revealed that T-helper cells (CD4 cells) predominate in the ES. CD8 cells are present in small numbers, but B cells as well as macrophages are detected in the lumen and perisaccular region[31].

We did not find sensorineural hearing loss or outer hair cell damage in patients with psoriasis in our study, because it may be related to predominance of CD8+ T cells proposed in the pathogenesis of psoriasis.

Conclusion

In our study, based on the DPOAE and audiological findings, we did not find any damage of outer hair cells of cochlea and hearing loss in the patients with psoriasis.

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