Chapter

Audiovestibular Dysfunction and Hearing Loss in Patients with Psoriasis and Psoriatic Arthritis

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Abstract

Psoriasis is now considered a T cell-mediated chronic systemic inflammatory disease rather than only a simple skin disease. The relationship and coexistence of this common disease with many other comorbidities have gained increasing attention in recent years. Although psoriatic skin lesions are seen frequently in the auricle and external auditory canal, there are not many studies evaluating the possible effect of psoriatic disease (psoriasis with or without joint involvement) on the auditory system. Hearing impairment detected in psoriasis patients is mostly seen as subclinical hearing loss at high frequencies, but it can also have a significant impact on patients' health and quality of life due to the possible risk of developing sudden sensorineural hearing loss. In this chapter, the frequency, pattern, and patient-related risk factors of hearing impairment and audiovestibular dysfunction in patients with psoriasis and psoriatic arthritis were extensively reviewed and discussed. In conclusion, it was emphasized that subclinical sensorineural hearing loss is a neglected but an important comorbidity in patients with psoriasis and psoriatic arthritis. The relationship between psoriatic disease and audiovestibular dysfunction supports the need for further studies aimed at better identification of the underlying pathogenic mechanisms, and accordingly to update diagnostic and even treatment approaches.

Keywords: psoriasis, psoriatic arthritis, hearing impairment, sensorineural hearing loss, deafness, audiovestibular dysfunction

1. Introduction

Psoriasis is a common erythemato-squamous disease which has a prevalence of 2–4% in the general population [1, 2]. Even though the precise etiology remains unknown, it is now considered an autoimmune, chronic, immune-mediated inflammatory disease (IMID) characterized by T cell mediated hyperproliferation of keratinocytes [3, 4]. There are multiple clinical types of psoriasis that can overlap in a spectrum from mild sebopsoriasis localized to the scalp to generalized pustular psoriasis. In the most common type of psoriasis vulgaris, the diameters of erythemato-squamous papular lesions can range from pinhead-size to plaques covering the larger skin surface. Besides typical skin involvement in psoriasis, significant deterioration of the nails and painful inflammatory joint involvement (psoriatic arthritis, PsA) can also be seen [1, 2]. PsA is a disease in the group of seronegative

spondyloarthropathies, such as ankylosing spondylitis and reactive arthritis. While its prevalence in the general population has been estimated between 0.02% and 0.42%, its frequency in people with psoriasis ranges from 6–42%. This inflammatory arthritis has different symptoms such as pain, swelling or stiffness and sausage digits (dactylitis) in one or more joints, Achilles tendinitis or plantar fasciitis. Psoriasis and PsA have been considered by some clinicians as different diseases due to various diagnostic criteria and different clinical courses, but the relationship between both diseases cannot be ignored [5–7]. It is well known that psoriatic disease with or without arthritis can occur at any age and negatively affects the quality of life by disrupting lifelong physical and psychosocial health [8, 9].

External ear involvement is also common in psoriasis [10]. Approximately two-thirds of patients have typical psoriatic lesions characterized by itchy, well-demarcated, erythemato-squamous plaques on the earlobe and conchal bowl. Although non-specific erythematous, scaly and dry lesions are sometimes seen in the ear, the precise diagnosis of ear psoriasis can be made easily by detecting typical psoriatic lesions in other areas of the body [2, 11]. Despite the high prevalence of clinical lesions affecting the auricle and the external auditory canal in psoriasis, there are not many studies evaluating the possible effect of psoriatic disease on the auditory system [12–25]. The auricle and outer one-third of the external auditory canal contain elastic cartilage covered with skin and its appendages, including mainly hair cells, and sebaceous and apocrine glands. It has been reported that chronic cutaneous inflammation and keratinocyte hyperproliferation induce progressive skin thickening with the tendency of substenosis and serum accumulation in the external auditory canal and stenosis of the tympanic membrane, causing disruption in sound transmission to the middle ear [22]. It is also well known that otitis externa is frequently seen in infection-prone conditions such as psoriasis [10]. Moreover, the rare ototoxic effect of topical salicylic acid, which is among the antipsoriatic topical treatments, was reported in a few cases. Maune et al. observed recurrent, symmetrical, pancochlear, reversible inner ear failure in a psoriasis patient using topical salicylate [26]. However, for the first time in 2004, sudden-onset autoimmune sensorineural hearing loss (SNHL) was reported in two cases with PsA [27, 28]. Yen et al. evaluated the risk of sudden SNHL in patients with psoriasis in a retrospective cohort study involving 28.817 patients and gender-, age-, and comorbidities-matched controls. The incidence of sudden SNHL was found about 1.51 times higher in the psoriasis cohort after 6 years of follow-up than in the control cohort [12].

In previous studies, it has been mentioned that the inner ear is sensitive to local or systemic autoimmune attacks and SNHL can occur as a complication of non-organ-specific autoimmune diseases [29–32]. The hypothesis that SNHL may develop as a result of an autoimmune process against the inner ear was first introduced by Lehnhardt in 1958 [33]. 20 years later (1979), McCabe was the first to describe SNHL that may occur in the autoimmune diseases. The idea was suggested by the author that an autoimmune pathogenesis may be present in the etiology upon improvement of hearing after corticosteroid therapy in a patient with progressive bilateral idiopathic SNHL [34]. Since then, several cases of SNHL and acute/subclinical audiovestibular dysfunction accompanied by various autoimmune and autoinflammatory diseases including vitiligo, inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis), Behçet's disease, Wegener's granulomatosis, rheumatoid arthritis, systemic lupus erythematosus, Sjogren's syndrome, relapsing polychondritis, giant cell arteritis, ankylosing spondylitis, Vogt-Koyanagi-Harada syndrome, Cogan's syndrome and Susac's syndrome, have been reported in the literature [29, 35, 36]. Current literature information shows that SNHL is the most common auditory symptom of systemic autoimmune diseases, but due to the

different presentations (sudden or progressive) and severity (mild or severe) of SNHL, early correlation between symptom and systemic autoimmune disease may be difficult [29]. Additionally, audiovestibular symptoms found in autoimmune conditions are also common in other disorders, such as diabetes and hypertension. For these reasons, the correct differential diagnosis of the cause of audiovestibular involvement is very important [30, 31].

Although autoimmunity has been accused of sudden hearing loss for many years, interest in studies related to the inner ear involvement secondary to systemic autoimmune diseases has been gradually increasing in recent years [30, 35]. In the literature about psoriatic disease-related hearing loss, firstly, Srikumar et al. reported a 62-year-old male patient with PsA, who had been under methotrexate therapy, developed sudden onset of SNHL and recovered with oral corticosteroids. So that, it was suggested by the author that PsA should have added to autoimmune diseases that can cause SNHL [27]. Subsequently, Giani et al. reported the development of bilateral asymmetric sensorineural deafness, which improved with oral prednisolone without interruption of previous etanercept therapy, in a 13-year-old girl with juvenile PsA [28]. However, after these case reports, a limited number of studies evaluating hearing and/or the audiovestibular system were conducted to determine whether the chronic inflammatory process and/or autoimmunity affect the inner ear in psoriasis patients with or without joint involvement [12–25].

In this chapter, case reports, clinical trials, cohort studies, systematic reviews and meta-analyses associated with hearing impairment and audiovestibular dysfunction in patients with psoriasis and PsA published up until now were comprehensively reviewed and discussed. The Medline literature database was searched through PubMed using the keywords, individually and in combination: 'psoriasis', 'psoriatic arthritis', 'hearing loss', 'sensorineural hearing loss', 'deafness', 'hearing impairment' and 'audiovestibular dysfunction'. Only articles available in original or translated English were evaluated.

2. Audiological/audiovestibular evaluations in patients with psoriasis/psoriatic arthritis

When all clinical studies are reviewed, it has been observed that psoriasis/PsA patients and the control group consisting of volunteer healthy subjects were compared with each other in terms of audiological changes [12–25]. In just a few studies, these groups were also evaluated in terms of the accompanying vestibular system involvement [15, 20, 21, 25]. Comprehensive ear, nose and throat examinations were performed by otorhinolaryngologists in all cases before audiological evaluations. Subsequently, pure tone audiometric and otoacoustic emission (distortion product or transient evoked) tests, as well vestibular tests in some studies were applied by audiometrists (**Table 1**). Generally, cases with the current and/or past history of chronic otitis externa, recurrent otitis media, inner ear infections, otosclerosis, suppurative labyrinthitis, Meniere disease and other vestibular syndromes, congenital ear disease, ear membrane perforation, ear surgery, head and neck trauma, exposure to high-decibel levels, cardiovascular disease (ischemic heart disease including angina, myocardial infarction, heart failure), cerebrovascular events (transient ischemic attacks/strokes confirmed by MRI/CT brain scan), peripheral arterial disease confirmed by Doppler ultrasound and/or arteriography, renal insufficiency, vertigo, any ototoxic drug use (e.g., quinolones, macrolides, aminoglycosides, antidepressants, beta blockers, hormone antagonists, antiglaucoma preparations, antimalarials), flat tympanogram and hearing aid use were not included in these studies. It was observed that current and/or past use of

References	Study cases	Audiological/audiovestibular diagnostic tests
[13]	42 PSO patients, 60 healthy controls	Pure tone audiometry (0.25, 0.5, 1, 2, 4, 6 kHz) Tympanometry, Acoustic reflex Distortion product otoacoustic emission testing
[14]	51 PSO patients, 51 healthy controls	Pure tone audiometry
[15]	60 PsA patients, 60 matched controls	Pure tone audiometry (0.5, 1, 2, 3, 4, 6, 8 kHz) Speech discrimination test, tympanometry, stapedius reflex threshold MRI of the posterior fossa and brainstem Videonystagmography testing device Spontaneous nystagmus, gaze-evoked nystagmus, oculocephalic response, head-shaking nystagmus Oculographic tests (saccades; slow, smooth pursuit evaluation; and optokinetic stimulus) Positional nystagmus in supine, lying on the right, lying on the left, and cervical hyperextension positions (head hanging) Cephalic rotational test in the supine position; Dix-Hallpike test Quantitative postural function test Bithermal water caloric test
[16]	31 PsA patients, 31 healthy controls	Pure tone audiometry (0.25, 0.5, 1, 2, 4, 6 kHz) Speech discrimination score, tympanometry Transient evoked otoacoustic emissions
[17]	41 PSO patients, 41 healthy controls	Pure tone audiometry (air-conduction at 0.25, 0.5, 1, 2, 4, 8 kHz; bone-conduction at 0.5, 1, 2, 4 kHz) Transient evoked otoacoustic emissions
[18]	24 PsA patients, 38 healthy controls	Distortion product otoacoustic emissions (1–4 kHz) Tympanometric examination Stapes reflex values, speech reception threshold Speech discrimination values Pure tone values (0.25 kHz – 8 kHz) High-frequency values (10, 12.5, 16 kHz)
[19]	50 PSO patients, 45 healthy controls	Pure tone audiogram (0.5 kHz –16 kHz) Speech audiometry
[20]	60 PsA patients, 60 matched controls	Clinical test of sensory integration and balance Computerized dynamic posturography
[21]	61 PSO patients, 61 healthy controls	Pure tone audiometry (0.25–1 kHz, 2–6 kHz), autoacoustic emission, stapes reflex, detection threshold of speech - discrimination Electronystagmography tests; spontaneous nystagmus, gaze-evoked nystagmus, oculographic tests (saccades; slow, smooth pursuit evaluation; optokinetic stimulus) Positional nystagmus in supine, lying on the right, lying on the left, cervical hyperextension positions (head hanging) Cephalic rotational test in the supine position Dix-Hallpike test, Bi-thermal water caloric test
[22]	77 PSO patients, 77 healthy controls	Tympanometry Audiometric tests
[23]	29 PSO patients, 30 healthy controls	Tympanography Pure tone audiometry (0.25, 0.5, 1, 2, 4, 8, 10, 12, 14, 16 kHz) Speech audiometry, impedance audiometry Transient evoked otoacoustic emissions Distortion product otoacoustic emissions
[24]	50 PSO patients, 50 healthy controls	Pure tone audiometry (0.25, 0.5, 1, 2, 4, 8 kHz)

References	Study cases	Audiological/audiovestibular diagnostic tests
[25]	32 PSO patients (−) arthritis, 35 healthy controls	Pure tone audiometry (0.25, 0.5, 1, 2, 4, 6, 8 kHz) Distortion product otoacoustic emission (2,3,4,5 kHz) Spontaneous and gaze-evoked nystagmus Head shake test, tandem stance test, Unterberger test, Romberg test, Dix-Hallpike test, supine roll test, head hanging test Oculomotor and caloric tests

PSO (Psoriasis); PsA (Psoriatic Arthritis).

Table 1.
Audiological/audiovestibular diagnostic tests in patients with psoriasis/psoriatic arthritis.

non-steroidal anti-inflammatory drugs, prednisone, methotrexate and/or tumor necrosis factor-α (TNF-α) antagonists were present in all patients with PsA and in some psoriasis patients. To evaluate the clinical severity of psoriatic disease, mostly Psoriasis Area and Severity Index (PASI) was used. In addition to PASI, body surface area, investigator's global assessment and dermatology life quality index were applied in a few studies [13–25]. The results of these studies are summarized below in chronological order.

Firstly, Karabulut et al. (2010) did not find a statistically significant difference between each groups for either pure tone audiometric hearing thresholds or distortion product autoacustic emissions in a case-control study involving 42 patients with psoriasis. In addition, neither SNHL nor any damage of outer hair cells of cochlea was detected. The authors suggested that the increase in the frequency of hearing loss and vestibular disorders in chronic inflammatory and autoimmune diseases may be due to the more prominent role of CD4 T cells rather than the predominant CD8 T cells in psoriasis [13].

In 2012, Guvenc et al.'s study (involving 51 psoriasis patients, 51 controls) demonstrated that the hearing threshold values at all frequencies for air conduction and bone conduction in psoriasis patients were significantly higher than in the control group with the pure tone audiometry measurements. Statistical significance was achieved in all frequencies (more pronounced at higher frequencies) except to right ear air conduction 1000 Hz, bone conduction 500 and 1000 Hz, as well left ear air conduction 500 Hz and bone conduction 500 Hz measurements. No significant relationship was found in the correlation analysis between age and psoriasis duration and hearing loss. When the PASI score adjusted for age and disease duration and threshold values matching the frequencies were compared with the correlation analysis, a significant correlation was found between the PASI score and hearing loss at medium and high frequencies. The fact that the hearing loss detected was independent of age and disease duration suggested to the authors that hearing loss in psoriasis is not an age-related degeneration and is not due to the long-term low-level effect of inflammatory mediators. Due to the statistically significant and moderately correlation between hearing loss at medium and high frequencies (bone conduction 2000, 4000 Hz; air conduction 1000, 2000, 4000, 8000 Hz) and high PASI scores, the authors considered that hearing loss is occurred as a consequence of increasing proinflammatory cytokines such as TNF-α (which is responsible for the severity of the psoriatic disease) in exacerbation periods of psoriasis and subsequently causing cochlear degeneration [14].

A case-control study of 60 PsA patients by Amor-Dorado et al. (2014) demonstrated that the frequencies of tinnitus, vertigo and disequilibrium as well as the subjective hearing loss (31.7% of PsA vs. 6.7% of controls) were significantly higher in the PsA group. Patients with PsA exhibited significantly higher values of pure tone audiogram and speech reception threshold than controls. Abnormal hearing

loss in the audiogram (60% vs. 8.3%), bilateral and symmetrical SNHL predominant at high frequencies (46.7% vs. 8.3%), abnormal vestibular tests, abnormal oculocephalic response (13.3% vs. 0%), abnormal caloric test (26.7% vs. 0%) and abnormal computerized dynamic posturography with a predominant vestibular loss pattern (23.3% vs. 0%) frequencies were significantly higher in the PsA group than in the control group. No significant relationship was found between the presence of audiovestibular symptoms in patients with PsA and the specific patterns, diagnosis age and disease duration of PsA. This study was the first to show oculographic, vestibular, and postural abnormalities in addition to auditory impairment in psoriatic disease. These tests, which show the presence of hypofunction (canal paresis) of the inner ear, supported that the audiovestibular distortion observed in PsA is at the peripheral etiology and the inner ear damage is at the cochleovestibular peripheral level. It has also been suggested that chronic inflammation may be responsible for audiovestibular findings in patients with PsA [15].

Akdag et al. (2015) investigated hearing changes with audiometric and otoacoustic emission tests in the age-gender matched prospective case-control study involving 31 PsA patients. As a result of the study, statistically significant differences (especially at high frequencies) were observed between pure tone audiometry in all frequencies and right and left emission at the 4.0 and 1.0 Hz in PsA patients versus controls. No significant relationship was found between the duration of PsA and the severity of hearing loss. Except for right ear audio at 2000 Hz, no correlation was found between the PASI measurement of PsA severity and hearing loss. In addition, no significant relationship was found between PASI scores and the degree of hearing changes. These data showed to the authors that the degree of hearing change was not related to the severity of PsA symptoms. Overall, mean hearing thresholds and otoacoustic emissions were detected to be impaired in PsA patients. With these results, it was thought that the inner ear injury is due to cochlear chronic damage caused by disruption of the inner ear microcirculation rather than acute inflammatory reactivation of the disease [16].

Aydın et al.'s study (2015) did not find any hearing loss with pure tone audiometry and transient evoked autoacoustic emission measurements in 41 patients with mild and moderate psoriasis. Hearing thresholds in all frequencies with pure tone audiometry were detected higher in patients with psoriasis than controls. Although the excitability, response values and signal:noise ratios according to frequencies were lower in the transient evoked autoacoustic emission test compared to the controls, these differences were not statistically significant. In addition, a relationship was not demonstrated between PASI score and psoriasis duration and SNHL [17].

In 2016, a case-control study involving 24 PsA patients (younger than 60 years old) conducted by Gunes et al. demonstrated bilateral symmetrical SNHL in 3 patients within the PsA group. When hearing frequencies between 4000 and 6000 Hz and the distortion product otoacoustic emission values at 3000 and 4000 Hz were evaluated in the PsA group, statistically significant differences were found compared to the control group. This study demonstrating that inner ear functions have been affected in patients with PsA provides strong evidence that it is necessary to monitor these patients regarding SNHL, which may cause serious disability, in order to take precautions against the development of sudden deafness [18].

Hapa et al. (2016) found significant differences between patients with psoriasis and controls in terms of median pure tone averages variables in a case-control study involving 50 psoriasis patients. However, no significant differences were observed between median pure tone averages variables according to the distribution of the lesions, previous systemic medications, disease duration and PASI scores. Considering the hearing levels of patients with psoriasis according to certain

hearing frequencies (500, 1000, 2000, 4000, 8000 and 16,000 Hz), a statistically significant difference was detected between patients with psoriasis and the control group. It was determined that all the frequencies which show statistical significance (the median of hearing level at frequencies 500–4000 Hz) were not lower than 20 decibels, but the hearing levels of patients with psoriasis at higher frequencies (such as 8000 and 16,000 Hz) were lower than 20 decibels. This result indicated to the authors that psoriasis patients have hearing loss at high frequencies [19].

Amor-Dorado et al.'s vestibular evaluation study (2017) involving 60 PsA patients observed that the frequencies of abnormal oculocephalic response (13.3% vs. 0%) and abnormal caloric test (26.7% vs. 0%) were found higher than the controls. The frequencies of abnormal clinical test of sensory integration and balance test with vestibular loss pattern (33% vs. 6%) and abnormal computerized dynamic posturography test (23.3% vs. 0%) also increased significantly in PsA patients, indicating that oculographic findings have been frequent in PsA [20].

Temel et al.'s study (2017) including 61 psoriasis patients detected significant differences between the patients and controls in terms of audiovestibular symptoms and the values of the audiometric tests (pure tone average, speech recognition threshold, speech discrimination). While psoriasis patients had higher speech reception threshold than the control group, the speech discrimination test was found to be lower levels. The mean bone conduction and air conduction hearing thresholds were observed to be higher for all frequencies in the patients. These differences were found to be statistically significant at high frequencies (2.4 and 6 kHz). According to audiograms, high frequency bilateral symmetrical SNHL was detected in psoriasis patients compared to the controls. Although the vestibular abnormalities in psoriasis patients were demonstrated to be more common than the control group, only saccadic test values were observed to be statistically significant. No significant relationship was found between the presence of audiovestibular abnormalities and clinical patterns of psoriasis, duration or severity of the disease, concomitant PsA, nail involvement or use of anti-psoriatic drugs [21].

In a case-control study involving 77 psoriatic patients of Borgia et al. (2018), tympanogram abnormalities and hearing loss detected in the psoriasis group were found to be significantly more frequent than the control group (52.6% vs. 14.9%). Most of them were shown to had SNHL (SNHL in 57 ears, conductive hearing loss in 9 ears, and mixed-type hearing loss in the remaining 15 ears). In terms of hearing loss, the difference between both groups was observed to be significant only for SNHL. The frequency of hearing loss, mostly of the sensorineural type, increased with age at a higher rate in the psoriatic patients. Hearing loss frequency was demonstrated to be higher in the patients with psoriasis duration >10 years (mainly of conductive and mixed type), metabolic syndrome, higher body mass index levels (overweight/obesity) or smoking habit. In patients with arthropathic psoriasis, conductive and mixed hearing loss were detected to be more common than non-arthropathic ones. In addition, it was observed that the patients with hearing loss had higher clinical severity of psoriasis determined by PASI and Dermatology Life Quality Index scores [22].

In a case-control study involving 29 psoriasis patients, Vir et al. (2019) found statistically significant differences between patients and controls for pure tone thresholds at high frequencies, and for distortion product otoacoustic emission responses and signal:noise ratio at all frequencies. According to these findings, it was reported that the outer hair cells damage of cochlea causes high-frequency hearing loss in psoriasis patients [23].

In a case-control study including 50 psoriasis patients of Gurel et al. (2019), both the left ear and right ear hearing threshold values at 2000 Hz and the right ear hearing threshold values at 4000 and 8000 Hz were significantly higher in the psoriasis

group than the control group. It was detected that the values of the psoriasis group were statistically significantly higher in terms of both the left ear and right ear mean air conduction and bone conduction hearing thresholds. In the correlation analysis between PASI score or disease duration and hearing loss, no significant relationship was observed [24].

Finally, in a case-control study to evaluate the audiovestibular system in 32 psoriasis patients without joint involvement, Ertugrul et al. (2020) did not find any significant differences between the groups in terms of hearing test results (pure tone audiometry and distortion product otoacoustic emission). However, in balance tests, the abnormal caloric test response was detected to be significantly higher in the psoriatic patients. They also mentioned that the severity of psoriasis rather than its duration is more important for vestibular system. No significant association was found between the Fitzpatrick skin type, medical treatments, the onset age of or clinical pattern of psoriasis and audiovestibular findings [25].

3. Discussion

Since the immunological basis of psoriasis has been understood in recent years, it is emphasized that the disease is not limited to the skin but a T cell-mediated systemic disease with various chronic and progressive comorbidities [37–42]. Like other diseases in this group, many IMIDs can appear in association with psoriasis [39–41]. The chronology of IMIDs associated with psoriasis was investigated by Andersen et al. in a large-scale study (psoriasis patients = 10.923; general population controls = 109.230). It was observed that approximately 20% of the patients with psoriasis developed ≥1 IMID, this risk was about five times higher than the general population, and most IMIDs had been diagnosed before psoriasis except PsA [43]. Many studies have demonstrated that some major comorbidities including PsA (mainly associated), metabolic syndrome, diabetes mellitus, coronary heart disease, hyperlipidemia, hypertension, obesity, inflammatory bowel disease, uveitis, obstructive sleep apnea, non-alcoholic fatty liver disease and psychiatric disturbances are more frequent than the normal population as a result of chronic inflammation in patients with psoriasis. These observations indicate the necessity to investigate for possible morbidities that may accompany psoriasis [39–42]. In the IMPROVE (incentives for health care management based on patient-related outcomes and value) study conducted in Denmark, it was observed that psoriasis has had a significant impact on health care costs, income and employment. In addition, psoriasis was also associated with a range of comorbidities (with higher incidence of cardiovascular and psychiatric conditions) compared to controls [8]. In another study of Baviere et al., it was shown that 30.6% of patients with PsA had ≥3 comorbidities but the type of comorbidity had more effects than the number of comorbidities [9].

Immune-mediated or autoimmune SNHL may be a primary localized disease caused by region-specific immune-mediated damage in the inner ear or may be a secondary expression of a systemic autoimmune disease. It is characterized by bilateral, asymmetrical, often asynchronous and fluctuant deafness, which clinically worsens in weeks or months [29–31]. Tinnitus, dizziness and imbalance can also be accompanied [30]. Clinical diagnosis of autoimmune SNHL, mostly seen in women and middle age, can be confirmed with a positive response to steroid therapy following exclusion of other possible causes [31]. In SNHL accompanying autoimmune diseases, inner ear involvement has been observed to be more pronounced at high frequency hearing thresholds. Therefore, evaluating the high frequencies of the hearing values along with the conventional frequencies in patients who do not

identify the clinical symptoms of hearing loss can help detect the presence of early hearing impairment and measures against sudden hearing loss can be taken [29–31, 44]. Extended high-frequency audiometry, expressing sounds above 8000 Hz, has been proven as a promising tool for the early detection of hearing disorders [18, 31]. In a population-based study using a National Health Insurance Service National Sample Cohort data from Korea, Jeong et al. investigated the risk of sudden SNHL (commonly known as sudden deafness; a SNHL of 30 dB or more over at least three contiguous audiometric frequencies occurring over less than 3 days) in patients with autoimmune diseases and compared these findings to a control group. As a result of this study, the risk of sudden SNHL was found significantly higher in the autoimmune-disease group than in the controls (autoimmune-disease group: 145/13.250 = 1.09%; control group: 484/6.250 = 0.73%) [45]. Due to unilateral involvement in most of the sudden SNHL cases, it may be difficult to demonstrate the relationship of this condition with an autoimmune disease. Therefore, it should not be ignored that immune-mediated SNHL can rarely occur with unilateral involvement in the initial period, similar to sudden SNHL [35, 36].

T lymphocyte-mediated cytotoxicity, vasculitis and immune complex accumulation have been generally accepted as the main causal mechanisms in development of SNHL accompanying immune-mediated diseases [29, 32]. Kumar et al. proposed a different theory like that "In autoimmune and chronic inflammatory diseases, prolonged serum levels of peripherally active T lymphocytes and proinflammatory cytokines (e.g., IL-1, IL-6, TNF-α) may cause degeneration in the cochlea, so hearing loss is a result of the harmful and unexpected effects of circulating inflammatory mediators". This model was recommended firstly based on patients with ulcerative colitis and was argued to be applicable for other chronic inflammatory and autoimmune diseases [46]. Although the cause of psoriasis disease is precisely unknown, recent genetic and immunological studies have shown that it is also a chronic IMID [38, 39]. Considering that the deteriorations in the structure and functions of the skin, nails and joints in psoriasis are primarily related to systemic chronic inflammation, it has been suggested that the same pathological process may have similar effects on the cochlea and play a role in the development of immune-mediated hearing loss [37, 47, 48]. T helper (Th) 1, Th17 and Th22 lymphocytes, which play a role in the pathogenesis of psoriasis, are active in psoriatic skin and circulation. The levels of proinflammatory cytokines (IL-1, IL-6, TNF-α, etc.) have also increased. It is well-known that TNF-α is an important mediator that also enhances the synthesis of other proinflammatory cytokines such as IL-1, IL-6, and IL-8 [3, 37]. The excellent response of psoriasis to TNF-α inhibitors has been emphasized that the role of TNF-α is indisputable in the pathogenesis of psoriasis [49]. Another situation demonstrating the effects of current cytokines on hearing loss is that TNF-α inhibitor drugs have been used successfully in the treatment of SNHL [50, 51]. Ertugrul et al. suggested that the immune response of the inner ear in psoriasis is likely to be impaired by antibody response in the endolymphatic sac, which has a central role in immunological activity within the inner ear and has capable of both processing antigen and producing antibodies [25]. In the case of inflammation in the body, accumulation of leukocytes entering the cochlea from the peripheral circulation and local immunoglobulin production cause an inflammatory reaction. This local inflammation leads to the degeneration of organ of corti, stria vascularis and spiral ganglion, which ultimately causes SNHL [32].

High frequency hearing loss in patients with psoriasis and PsA may be associated with chronic inflammation and autoimmune etiology [14, 15, 19, 21, 23]. It has been postulated that comorbidities such as metabolic syndrome and high body mass index values, which are frequently accompanied by psoriasis, may also contribute to hearing impairment [22]. Comorbid hypertension was determined as independent

risk factor for sudden SNHL in psoriasis patients by Yen et al. [12]. In addition, it has been suggested that the correlation between high PASI scores and hearing loss at medium and high frequencies may be related to the increase of the mediators responsible for psoriatic disease to high levels in exacerbation periods [14, 22, 25]. However, in most studies, no relationship was found between the duration of psoriatic disease, clinical patterns of psoriasis, medical treatments and patient age, and hearing loss and/or audiovestibular dysfunction [14–17, 19, 21, 24, 25]. In studies demonstrating significant hearing loss in psoriasis patients, accompanying joint involvement was observed in 5.8% to 51.9% of them [14, 21, 22]. It has been mentioned that the presence of joint involvement in patients with psoriasis may lead to a more chronic inflammatory process and so adversely affect hearing [25]. Indeed, studies evaluating the hearing of psoriasis patients have different results, but it has been reported that hearing was adversely affected in all studies examining patients with PsA [15, 16, 18, 20]. It has been stated that PsA, which condition facilitates additional bone formation, can disrupt outer hair cell integrity through the formation of autoimmune-mediated fibro-osseous deposits in the cochlea [16].

The main treatment for autoimmune inner ear disease is by corticosteroids, and significant improvement of hearing impairment has also been reported in previous PsA cases following steroid administration [27–29]. Moreover, promising advances have been performed in the treatment of immune-mediated inner ear disease with various TNF-α inhibitors (etanercept, infliximab, golimumab; as used in other underlying autoimmune diseases or as form of local intratimpanic infusion), demonstrating them to be effective in reducing inflammation and hearing loss in cochlear diseases [44, 51]. Nonetheless, if hearing loss still occurs, cochlear implantation is a safe and effective method for the auditory rehabilitation of severe SNHL [44, 52]. However, flap complications are more common in cases such as psoriasis, where the risk of surgical site infection is higher than normal patients. It has been beneficial to add perioperative antipsoriatic topical agents and/or UVB phototherapy to standard infection prophylaxis in terms of reducing postoperative infection and sequelae [52].

4. Conclusion

The relationship between psoriasis/PsA and audiovestibular dysfunction supports the need for further studies aimed at better identification of the underlying pathogenic mechanisms, and accordingly to update diagnostic and even treatment approaches. It is well known by most dermatologists that psoriasis is a lifelong multisystemic chronic inflammatory disease rather than just a skin and/or joint condition. It should also be remembered that psoriatic disease, which has become the target of modern biological treatments today, is often accompanied by certain comorbidities such as metabolic syndrome, cardiovascular disease and obesity. For this reason, psoriasis and its associations should be approached in an integrated manner as well as related physicians should be in regular coordination with specialists in a special multidisciplinary team. However, it is obvious that physicians, especially dermatologists and rheumatologists, need to be more aware of the prevalence of hearing loss in psoriasis patients. It should be kept in mind that subclinical SNHL is a neglected but an important comorbidity in patients with psoriasis and PsA. Psoriatic patients, particularly with severe clinical symptoms, arthropathy, obesity, hypertension and metabolic syndrome, should be followed up with regular audiometric tests even if there is no subjective hearing complaint. In fact, regardless of clinical severity or type of psoriasis, evaluation of all psoriatic patients for the audiovestibular perspective would be more useful for the future quality of life

of patients. If patients with psoriasis have any hearing problem, they should be addressed to otorhinolaryngologists and audiometrists in terms of the follow-up to possible development of audiovestibular dysfunction and sudden SNHL.

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