Investigations into Audiovestibular Manifestations in Patients with Psoriatic Arthritis

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ABSTRACT. ***Objective.*** Although psoriatic arthritis (PsA) is a common chronic inflammatory rheumatic disease, little is known about audiovestibular impairment in this condition. We aimed to establish whether audiovestibular manifestations were present in patients with PsA.

Methods. A set of 60 consecutive patients who fulfilled the Moll and Wright criteria for PsA and 60 matched controls were studied. During the period of recruitment, individuals were excluded who had a history of cardiovascular disease, cerebrovascular complications, peripheral artery disease, renal insufficiency, syphilis, Meniere disease and other vestibular syndromes, infections involving the inner ear, barotrauma, or were in treatment with ototoxic drugs.

Results. Most patients with PsA were men (63%). The mean age at the time of our study was 52.9 years and the mean age at the onset of symptoms was 33 years. Thirty-six (60%) of the 60 patients showed abnormal hearing loss in the audiogram compared to only 5 (8.3%) of the 60 controls ($p < 0.001$). Values of audiometric tests (pure-tone average and speech reception threshold) yielded significant differences between patients and controls ($p < 0.001$). The audiogram disclosed a bilateral and symmetrical sensorineural hearing loss (SNHL) in PsA with predominant pattern of high frequency SNHL in patients with PsA (46.7%) compared to controls (8.3%, $p < 0.001$). Patients with PsA exhibited abnormal vestibular tests more commonly than controls. A significantly increased frequency of abnormal computerized dynamic posturography with a predominant vestibular loss pattern was also observed in patients (23.3%) compared to controls (0%, $p < 0.001$).

Conclusion. Our current study demonstrates strong evidence for inner ear damage in patients with PsA. (First Release Sept 1 2014; J Rheumatol 2014;41:2018–26; doi:10.3899/jrheum.140559)

Key Indexing Terms:
PSORIATIC ARTHRITIS HEARING LOSS VESTIBULAR DYSFUNCTION

Psoriatic arthritis (PsA) is a type of chronic inflammatory rheumatic disease[1,2]. Its recognition as an inflammatory disease distinct from rheumatoid arthritis (RA) raises several questions regarding its specific comorbidity[1].

Sensorineural hearing loss (SNHL) and acute audiovestibular dysfunction have been found in individuals with rheumatic diseases including RA[3,4]. Subclinical sensorineural dysfunction has also been observed in patients with systemic lupus erythematosus (SLE) and Sjögren syndrome (SS)[5,6]. Both auditory and vestibular dysfunction were also found in patients with biopsy-proven giant cell arteritis (GCA)[7,8] and in patients with systemic sclerosis (SSc)[9,10], even in the limited form of this connective tissue disease[10].

PsA belongs to a group of rheumatic diseases called the spondyloarthropathies. A previous study demonstrated strong evidence for inner ear compromise in patients with ankylosing spondylitis (AS), a condition included within this group of spondyloarthropathies[11]. However, little is known about auditory manifestation in patients with PsA[12,13].

In our present study, we sought to determine whether the frequency of SNHL was increased in a cohort of patients with PsA treated in a community hospital. We also aimed to establish whether vestibular abnormalities were also more common in patients with PsA than in matched controls. In addition, we analyzed whether an association of audiovestibular manifestations with demographic and clinical variables of the disease might exist.

MATERIALS AND METHODS

Patients. The participants in our study were consecutive patients attending hospital rheumatology outpatient clinics over a period of 6 months (July to December 2012) who fulfilled the Moll and Wright criteria for PsA: (1) presence of an inflammatory arthritis-peripheral arthritis, and/or sacroiliitis

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or spondylitis, (2) presence of psoriasis, and (3) absence of serological tests for rheumatoid factor[2]. They were treated by the same group of rheumatologists and were recruited from the Hospital Lucus Augusti, formerly called Xeral-Calde, Lugo, Spain. This hospital is the single referral center for rheumatic diseases for a well-defined, stable, and ethnically homogeneous, mixed rural and urban, white population living in the region of Lugo, central Galicia (northwestern Spain)[14]. The main characteristics of the Lugo population have been reported[15,16].

For the purpose of our present study, only patients with PsA who had been treated for at least 1 year at the outpatient rheumatology clinic at the time of our study were included. The same procedure was followed when we assessed audiovestibular manifestations in patients with AS[11]. Because degeneration of the cochlea has been found to be apparent in young adults with generalized arteriosclerosis[17], to minimize the potential influence of atherosclerosis in the development of SNHL and/or vestibular abnormalities, as previously reported[18], we excluded all patients with PsA seen during the period of recruitment who had various cardiovascular diseases (CVD). These included ischemic heart disease (angina or myocardial infarction electrocardiographically confirmed), heart failure, cerebrovascular events [transient ischemic attacks or strokes confirmed by magnetic resonance imaging (MRI) and/or computerized tomography brain scan], and peripheral arterial disease (confirmed by Doppler and/or arteriography). Renal insufficiency was also an exclusion criterion (serum creatinine values in all included patients had to be < 1.3 mg/dl, the upper normal range in our laboratory).

Patients with PsA and controls were questioned about any history of previous audiovestibular disturbances, cranial trauma, exposure to noise, ear infection, metabolic disease, renal failure, ototoxic drug use, and familial history of hearing impairment. Those with a known cause, such as trauma, Meniere disease, other audiovestibular disorders, ear surgery, previous history of cerebrovascular complications, infections involving the inner ear, syphilis, barotrauma, acoustic schwannoma, or those in treatment with ototoxic drugs were excluded.

None of the patients included in this series were taking salicylates at the time of our study, which are known to have ototoxic properties. Also, none of the patients were taking other analgesics (such as hydrocodone) that may induce sensorineural hearing loss.

Because the vestibular assessment required neck motion, we also excluded patients with severe cervical involvement or neck pain that yielded severe limitation in the range of movements of the neck.

Patients with PsA included in our study had been treated with or were receiving nonsteroidal antiinflammatory drugs (NSAID). Fifty percent of them had also received or were in treatment with prednisone (10 mg/day or less) because of disease severity. At the time of our study, two-thirds of the patients were receiving methotrexate therapy, in most cases alone or in combination with tumor necrosis factor-α antagonists. The mean ± SD duration of treatment with disease-modifying antirheumatic drugs (DMARD) was 73.6 ± 50.1 months, median 60 months (interquartile range 36–94 mos). Additional information on conventional or biologic DMARD is shown in Table 1.

Based on these inclusion and exclusion criteria, 60 patients with PsA were assessed in our present study. During the period of recruitment, 3 patients with PsA, who had been followed for at least 1 year at the rheumatology outpatient clinics of our center, were excluded because of audiovestibular disturbances (2 because of a history of noise-induced hearing loss and 1 because of a previous history of ear surgery-tympanoplasty). Another 2 were excluded because of a history of CVD.

Disease patterns. Patients were divided into different disease groups according to the Moll and Wright classification criteria[2]. Peripheral arthritis was defined as previously reported by the history or presence of 1 or more swollen joints for at least 3 months[19]. Patients were included into 1 of the following categories according to the predominant rheumatic manifestation: (1) distal joint disease affecting the distal interphalangeal joints only, (2) oligoarthritis involving 4 or fewer joints, (3) polyarthritis affecting 5 or more joints, (4) arthritis mutilans, a severely deforming form of arthritis manifesting with either joint lysis or ankylosis, and (5) spondyloarthritis (SpA), an inflammatory arthritis of the back.

As previously reported[18,20,21] and in keeping with a former study[22], PsA may evolve from oligoarticular to polyarticular over time[23]. For the purpose of our study, patients with an oligoarticular presentation that evolved into polyarticular distribution over the course of the disease and displayed this polyarticular pattern at the time of assessment were included in the category of polyarticular. Patients with inflammatory arthritis of the back who presented a predominant polyarticular pattern were included in the category of polyarthritis.

Besides demographic and clinical characteristics, C-reactive protein (CRP; by a latex immunoturbidity method) and erythrocyte sedimentation rate (ESR; Westergren) were assessed in all the patients at the time of our study. Information about CRP (by nephelometry) and ESR at the time of disease diagnosis was also reviewed.

Control group. A list of potential controls was obtained from the cooperating health centers. Once a case was recruited, we randomly selected his/her control from the patients included in that list who also met the age and sex criteria.

Controls (n = 60) were community based. They were recruited from family physician health centers in the Lugo region. They were age ± 2 years, and matched by sex and ethnic group without a family history of SpA, psoriasis, PsA, RA, or any other inflammatory rheumatic diseases. As requested for the inclusion of patients with PsA, none of the controls included in our study had a history of CVD or renal insufficiency.

Informed consent was obtained from all cases and controls. The local institutional committee approved our study.

Clinical definitions of otolaryngology data are included in the supplementary material available online at jrheum.org.

Audiologic and vestibular assessment. Patients and controls were asked whether they had hearing loss, vertigo, tinnitus, dizziness, or disequilibrium symptoms at the time of our study.

All patients and controls underwent a complete ear, nose, and throat examination, including pneumatic otoscopy and otomicroscopic examinations, and the following audiologic tests: pure-tone audiometric test (0.5, 1, 2, 3, 4, 6, and 8 kHz), both aerial and bone conduction stimulus[24], and speech reception threshold (SRT) in decibels hearing level. Speech discrimination test[25], tympanometry, and stapedius reflex threshold were also performed[26].

MRI of the posterior fossa and brainstem was performed to those individuals with asymmetric sensory-neural hypoacusia to exclude central nervous system involvement.

Functional evaluation of the eye movements during the oculographic and vestibular tests were recorded by a videonystagmography (VNG) testing device with specific oculographic software (VN 415 Videonystagmography Interacoustics A/S). This device consisted of an infrared camera positioned to detect movement of 1 eye while the other is occluded. Chart VNG for Windows software was used to process the signals in each patient. Calibration was performed at the beginning of each VNG testing. Facing a wall, patients were seated 100 cm away and a projector was mounted on top of the patient chair. Patients were asked to keep their head and eyelids stationary while visually tracking a target[27].

In all patients and controls, spontaneous nystagmus[28], gaze-evoked nystagmus, oculocephalic response (OCR)[29,30], head-shaking nystagmus[31], oculographic tests (saccades; slow, smooth pursuit evaluation; and optokinetic stimulus) were completed[32], and positional nystagmus in supine, lying on the right, lying on the left, and cervical hyperextension positions (head hanging) were performed[33,34]. Then, the cephalic rotational test in the supine position[7,35] and the Dix-Hallpike test were done[36]. Later, a quantitative postural function test was conducted[37]. Finally, a bithermal water caloric test was also performed[38].

Statistical analysis. Continuous data were expressed as mean ± SD and categorical variables as percentages. Continuous variables were compared using the Student t test or the Mann-Whitney U test. Categorical variables

Table 1. Demographic, clinical, and laboratory findings of 60 patients with psoriatic arthritis (PsA).

Variables	Patients, n = 60	Controls, n = 60	p
Mean age, yrs, ± SD			
At the time of study	52.9 ± 10.7	53.0 ± 10.7	0.97
At the time of psoriasis onset	33.0 ± 14.5		
At the time of PsA diagnosis	42.5 ± 12.2		
Men/women	38/22	38/22	1.00
Mean disease duration, yrs, ± SD at the time of study	9.5 ± 4.8		
Patients presenting with arthritis before cutaneous manifestations	13 (21.7%)		
Patterns of PsA			
Polyarticular	30 (50.0%)		
Oligoarticular	24 (40.0%)		
Mutilans	1 (1.7%)		
Distal interphalangeal joints only	2 (3.3%)		
Spondylitis	6 (10.0%)		
Hypertension	8 (13.3%)		
Dyslipidemia	4 (6.7%)		
Diabetes	7 (11.7%)		
Obesity	10 (16.7%)		
Smoking (current or former)	4 (6.7%)		
Mean blood pressure, mm Hg, ± SD at the time of study			
Systolic	119.7 ± 16.7		
Diastolic	74.3 ± 8.7		
Mean heart rate, bpm, ± SD at the time of study	69.5 ± 7.0		
Body mass index, kg/m^2	24.8 ± 2.6		
Mean serum creatinine, mg/dl, ± SD at the time of study	0.89 ± 0.17		
Mean CRP, mg/l, ± SD			
At the time of disease diagnosis	13.8 ± 14.2		
At the time of study	6.2 ± 6.5		
Mean ESR, mm/1 h, ± SD			
At the time of disease diagnosis	23.0 ± 19.9		
At the time of study	13.8 ± 10.3		
Mean cholesterol or triglycerides at the time of study, mg/dl, ± SD			
Total cholesterol	193.8 ± 28.0		
HDL cholesterol	51.7 ± 11.5		
LDL cholesterol	116.4 ± 28.5		
Triglycerides	120.4 ± 72.9		
Mean fasting serum glucose, mg/dl, ± SD at the time of study	97.5 ± 19.9		
Patients treated with MTX alone	22 (36.7%)		
Initially treated with MTX and then with other DMARD+	32 (53.3%)		
Patients treated with anti-TNF-α therapy*	15 (25.0%)		

+Conventional DMARD (generally leflunomide and less commonly sulfasalazine) or biologic DMARD–anti-TNF-α therapy (adalimumab, infliximab, or etanercept) alone or in combination with MTX. *In most cases in combination with MTX. HDL: high-density lipoprotein; LDL: low-density lipoprotein; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; MTX: methotrexate; DMARD: disease-modifying antirheumatic drug; TNF-α: tumor necrosis factor-α.

were compared using the Fisher's exact test. Association between audiovestibular tests and epidemiological and clinical features in patients with PsA was measured as OR and 95% CI, adjusting for age at the time of our study through multiple logistic regressions. Two-sided $p < 0.05$ were considered statistically significant.

Analyses were performed with the package Stata 8/SE (Stata Corp.).

RESULTS

Main clinical features of patients with PsA. Men (63.3%) outnumbered women. The mean age at the time of our study was 52.9 years and the mean age at the onset of psoriasis was 33 years. In most cases, cutaneous manifestations preceded the development of PsA. Patients included in our study had a long disease duration of PsA (mean 9.5 yrs). Polyarticular and oligoarticular were the most common PsA patterns (Table 1).

Audiovestibular symptoms and auditory differences between patients with PsA and controls. Besides subjective hearing loss (31.7% of PsA vs 6.7% of controls, $p = 0.001$), the

frequency of other symptoms such as tinnitus, vertigo dizziness, and disequilibrium was significantly increased in patients with PsA when compared to matched controls ($p < 0.001$ for all comparisons; Table 2).

Audiometric tests were more sensitive than clinical symptoms to disclose subclinical hearing loss. Thirty-six (60%) of the 60 patients with PsA showed abnormal hearing loss in the audiogram compared to only 5 (8.3%) of the 60 controls ($p < 0.001$). Values of audiometric tests [pure tone average (PTA)] also yielded significant differences between patients and controls ($p < 0.01$; Table 2).

A bilateral SNHL was registered in 28 of the 36 patients with PsA with hearing impairment. It was asymmetrical in 6 and symmetrical in the other 22 patients. In contrast, SNHL was bilateral in all controls (n = 5) with hearing impairment. The audiogram shape disclosed a predominant pattern of high frequency SNHL in patients with PsA (46.7%) compared to controls (8.3%, $p < 0.001$). Other differences are shown in Table 2.

MRI excluded the presence of degenerative and tumoral lesions of the central nervous system in all patients who presented asymmetrical or unilateral SNHL.

Oculographic, vestibular, and postural differences between patients with PsA and controls. Patients with PsA experienced abnormal OCR more commonly than did controls (13.3% in patients vs 0% in controls, $p = 0.006$). They also showed a significantly increased frequency of abnormal caloric test (26.7%) when compared to controls (0%, $p < 0.001$). A significantly increased frequency of abnormal computerized dynamic posturography (CDP) was also observed in patients with PsA [14 (23.3%) of the patients vs 0 (0%) of controls, $p < 0.001$]. Vestibular loss was the most common CDP pattern in patients with PsA; it was observed in 9 of the 14 patients with abnormal CDP (Table 3).

Association of abnormal audiovestibular symptoms with demographic and clinical features of PsA. A trend for association between the presence of audiovestibular symptoms and age at the time of the study was observed

Table 2. Auditory differences between patients with psoriatic arthritis and controls.

Variables	Patients, n = 60 (%)	Controls, n = 60 (%)	p
Individuals with abnormal audiovestibular symptoms			
Hearing loss	19 (31.7)	4 (6.7)	0.001
Tinnitus	17 (28.3)	2 (3.3)	< 0.001
Vertigo	12 (20.0)	0 (0.0)	< 0.001
Dizziness	15 (25.0)	1 (1.7)	< 0.001
Dysequilibrium	17 (28.3)	0 (0.0)	< 0.001
Individuals with abnormal hearing loss in the audiogram[#]	36 (60.0)	5 (8.3)	< 0.001
Bilateral	28 (46.7)	5 (8.3)	
Symmetrical	22 (36.7)	5 (8.3)	
Asymmetrical[##]	6 (10.0)	0 (0.0)	
Unilateral			
Asymmetrical[##]	8 (13.3)	0 (0.0)	0.006
Audiograms shape			
High frequency SNHL	28 (46.7)	5 (8.3)	< 0.001
Flat pattern SNHL	4 (6.7)	0 (0.0)	0.12
Low frequencies SNHL	1 (1.7)	0 (0.0)	1.00
Cookie–bite loss	3 (5.0)	0 (0.0)	0.24
Abnormal tympanogram	1 (1.7)	0 (0.0)	1.00
Absence of stapedial reflex	12 (20.0)	3 (5.0)	0.03
PTA at 0.5–3 kHz[###]			
Right ear	15.5 ± 11.9	10.1 ± 4.7	0.002
Left ear	15.8 ± 13.6	10.9 ± 3.6	0.008
PTA at 4–8 kHz[####]			
Right ear	28.2 ± 20.8	13.5 ± 6.9	< 0.001
Left ear	28.5 ± 21.2	16.8 ± 5.8	< 0.001
SRT in dB HL			
Right ear	18.7 ± 11.5	13.6 ± 4.3	0.002
Left ear	19.2 ± 13.5	13.6 ± 4.3	0.003
Abnormal SRT and PTA correlation	0 (0.0)	0 (0.0)	
Abnormal SDT[+]	0 (0.0)	0 (0.0)	

[#]At least 1 frequency in the audiogram (0.5–3 kHz) with thresholds at 25 dB HL or greater. [##]A hearing loss difference greater than 15 dB HL between each ear at least in 1 frequency (0.5–3 kHz). [###]Arithmetic mean of 0.5, 1, 2, and 3 kHz. [####]Arithmetic mean of 4, 6, and 8 kHz. [+]SDT was at least 85% or greater in all patients and controls. SNHL: sensorineural hearing loss; SRT: speech reception threshold; PTA: pure tone average; SDT: speech discrimination test.

Table 3. Oculographic, vestibular, and postural differences between patients with psoriatic arthritis and controls.

Variables	Patients, n = 60 (%)	Controls, n = 60 (%)	p
Individuals with abnormal vestibular tests			
Spontaneous nystagmus	0 (0.0)	0 (0.0)	
Evoked nystagmus	0 (0.0)	0 (0.0)	
Abnormal OCR[+]	8 (13.3)	0 (0.0)	0.006
Head-shaking nystagmus	2 (3.3)	0 (0.0)	0.50
Patients with positional nystagmus with ≥ 1 abnormal position	4 (6.7)	0 (0.0)	0.36
Dix–Hallpike test	1 (1.7)	0 (0.0)	1.00
Abnormal cephalic rotation test	1 (1.7)	0 (0.0)	1.00
Abnormal caloric test	16 (26.7)	0 (0.0)	< 0.001
Individuals with abnormal CDP*	14 (23.3)	0 (0.0)	< 0.001
Patterns in individuals with abnormal CDP			
Vestibular loss	9 (15.0)		
Visually dependent	2 (3.3)		
Somatosensory dependent	0 (0.0)		
Visually preference	3 (5.0)		
Individuals with abnormal oculographic tests[#]			
Smooth pursuit test	5 (8.3)	2 (3.3)	0.44
Saccade test	1 (1.7)	1 (1.7)	1.00
Optokinetic test	3 (5.0)	0 (0.0)	0.24

[+]Abnormal OCR was considered present when the eyes drifted in the same direction as the head and clinically evident compensatory refixation saccades were necessary to reset gaze on the stationary target. *CDP was considered abnormal when individuals showed a composite lesser than 50%. [#]Tracking test (smooth pursuit) and saccades. OCR: oculocephalic response; CDP: computerized dynamic posturography.

(OR 1.05, 95% CI 1.00–1.11, p = 0.07). However, no significant association between the presence of audiovestibular symptoms in patients with PsA and the age at the time of the disease diagnosis or the duration of the disease was found (Table 4). A marginally significant association with laboratory markers of inflammation (CRP and ESR) at the time of our study and abnormal audiovestibular symptoms was also disclosed (Table 4).

Association of hypoacusia in audiometric tests with demographic and clinical variables in patients with PsA. As expected, a significant association between hypoacusia in audiometric tests and the age at the time of our study was found (OR 1.16, 95% CI 1.06–1.26, p = 0.001). A marginally significant association between the CRP at the time of our study and hypoacusia was also observed (OR 1.12, 95% CI 1.00–1.26, p = 0.04; Table 5).

Association of abnormal vestibular tests, excluding CDP, with demographic and clinical variables in patients with PsA. No association of age at the time of our study, age at the time of disease diagnosis, or disease duration with abnormal vestibular tests were observed (Table 6). Likewise, no associations between abnormality of these tests and specific patterns of PsA were found (Table 6).

Association of abnormal CDP with demographic and clinical variables in patients with PsA. Apart from an association with age at the time of our study and abnormal CDP (OR 1.11, 95% CI 1.03–1.20, p = 0.007), no other associations between specific clinical patterns of PsA,

Table 4. Association of abnormal audiovestibular symptoms with demographic and clinical variables in 60 patients with psoriatic arthritis (PsA).

Variables	OR (95% CI)	p
Age, yrs, at the time of study, by yr	1.05 (1.00–1.11)	0.07
Age, yrs, at the time of disease diagnosis, by yr	1.02 (0.98–1.05)	0.37
Disease duration, mo	1.00 (0.99–1.01)	0.77
Patterns of PsA		
Polyarticular	1.51 (0.53–4.24)	0.43
Oligoarticular	0.57 (0.20–1.62)	0.29
Mutilans	N/A	
Distal interphalangeal joints only	0.71 (0.04–11.8)	0.81
Spondylitis	0.69 (0.13–3.73)	0.66
Presence of classic cardiovascular risk factors*	0.51 (0.17–1.50)	0.22
CRP (mg/l) at disease diagnosis	1.02 (0.98–1.06)	0.36
ESR (mm/first h) at disease diagnosis	1.02 (0.99–1.06)	0.13
CRP (mg/l) at the time of the study	1.11 (1.00–1.23)	0.06
ESR (mm/first h) at the time of the study	1.06 (1.00–1.12)	0.05
Patients treated with MTX alone	0.42 (0.06–2.77)	0.37
Initially treated with MTX and then with other DMARD[+]	0.95 (0.15–6.06)	0.96
Patients treated with anti-TNF-α therapy[#]	2.41 (0.67–8.70)	0.18

*One or more of the following: hypertension, dyslipidemia, diabetes, obesity, and smoking history. [+]Conventional DMARD (generally leflunomide and less commonly sulfasalazine) or biologic DMARD–anti-TNF-α therapy (adalimumab, infliximab, or etanercept) alone or in combination with MTX. [#]In most cases in combination with MTX. CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; MTX: methotrexate; DMARD: disease-modifying antirheumatic drug; TNF-α: tumor necrosis factor-α; N/A: not available.

Table 5. Association of hypoacusia in audiometric tests with demographic and clinical variables in 60 patients with psoriatic arthritis (PsA).

Variables	OR (95% CI)	p
Age, yrs, at the time of study, by yr	1.16 (1.06–1.26)	0.001
Age, yrs, at the time of disease diagnosis, by yr	1.08 (1.03–1.13)	0.002
Disease duration, mo	1.00 (0.99–1.00)	0.38
Patterns of PsA		
Polyarticular	0.66 (0.24–1.86)	0.43
Oligoarticular	1.33 (0.46–3.83)	0.59
Mutilans	N/A	
Distal interphalangeal joints only	0.71 (0.04–11.8)	0.81
Spondylitis	0.69 (0.13–3.73)	0.66
Presence of classic cardiovascular risk factors*	1.26 (0.42–3.71)	0.68
CRP (mg/l) at disease diagnosis	1.02 (0.98–1.06)	0.45
ESR (mm/first h) at disease diagnosis	1.02 (0.99–1.05)	0.29
CRP (mg/l) at the time of the study	1.12 (1.00–1.26)	0.04
ESR (mm/first h) at the time of the study	1.02 (0.97–1.08)	0.36
Patients treated with MTX alone	1.44 (0.24–8.84)	0.69
Initially treated with MTX and then with other DMARD+	1.46 (0.25–8.40)	0.67
Patients treated with anti-TNF-α therapy#	1.10 (0.33–3.60)	0.88

*One or more of the following: hypertension, dyslipidemia, diabetes, obesity, and smoking history. +Conventional DMARD (generally leflunomide and less commonly sulfasalazine) or biologic DMARD–anti-TNF-α therapy (adalimumab, infliximab, or etanercept) alone or in combination with MTX. #In most cases in combination with MTX. CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; MTX: methotrexate; DMARD: disease-modifying antirheumatic drug; TNF-α: tumor necrosis factor-α; N/A: not available.

Table 6. Association of abnormal vestibular tests, excluding CDP, with demographic and clinical variables in 60 patients with psoriatic arthritis (PsA). The p values for equal odds in those who never received MTX/treated with MTX alone/initially treated with MTX and then with other DMARD alone or in combination with MTX = 0.06.

Variables	OR (95% CI)	p
Age, yrs, at the time of study, by yr	1.06 (1.00–1.12)	0.06
Age, yrs, at the time of disease diagnosis, by yr	1.00 (0.96–1.04)	0.93
Disease duration, mo	1.01 (1.00–1.02)	0.21
Patterns of PsA		
Polyarticular	2.87 (0.95–8.72)	0.06
Oligoarticular	0.47 (0.15–1.45)	0.19
Mutilans	N/A	
Distal interphalangeal joints only	N/A	
Spondylitis	0.34 (0.04–3.12)	0.34
Presence of classic cardiovascular risk factors*	1.23 (0.41–3.71)	0.71
CRP (mg/l) at the time of disease diagnosis	0.99 (0.95–1.03)	0.66
ESR (mm/first h) at the time of disease diagnosis	1.01 (0.98–1.03)	0.64
CRP (mg/l) at the time of the study	1.03 (0.95–1.12)	0.42
ESR (mm/first h) at the time of the study	1.01 (0.96–1.06)	0.71
Patients treated with MTX alone	N/A**	
Initially treated with MTX and then with other DMARD+	N/A**	
Patients treated with anti-TNF-α therapy#	0.91 (0.26–3.12)	0.88

*One or more of the following: hypertension, dyslipidemia, diabetes, obesity, and smoking history. **Patients who never received MTX had normal vestibular tests, so OR could not be estimated. +Conventional DMARD (generally leflunomide and less commonly sulfasalazine) or biologic DMARD–anti-TNF-α therapy (adalimumab, infliximab, or etanercept) alone or in combination with MTX. #In most cases in combination with MTX. CDP: computerized dynamic posturography; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; MTX: methotrexate; DMARD: disease-modifying antirheumatic drug; TNF-α: tumor necrosis factor-α; N/A: not applicable.

classic CV risk factors or laboratory markers, and the presence of CDP abnormalities were observed (data included in the supplementary material available online at jrheum.org).

DISCUSSION

Our present study demonstrates the presence of auditory impairment in patients with PsA. Our results disclosed a high number of patients with bilateral and symmetrical hearing loss in the audiogram. Patients with PsA exhibited significantly higher values of PTA and SRT than controls. The shape of audiometry predominantly observed in these patients was a pattern of SNHL in the high frequencies of the audiogram.

Another relevant result was the presence of vestibular dysfunction in patients with PsA. To our knowledge, ours is the first study that specifically assessed the presence of oculographic, vestibular, and postural abnormalities in a series of patients with PsA. We observed abnormal head thrust test (OCR) and caloric test in our patients. OCR, a simple clinical test that can be performed at the physician's office, has high correlation with abnormal caloric test. These closely related tests are associated with the presence of hypofunction (canal paresis) of the inner ear. Therefore, these findings support a peripheral etiology for the audiovestibular impairment observed in patients with PsA. In addition, posturography studies (CDP) confirmed the presence of a high degree of balance disorder in PsA. Although CDP is not a reliable diagnostic tool to determine the site of damage, it appears to be useful for the diagnosis of hypofunction of each of the sensory systems involved in balance. Specifically in our series, CDP showed a predominantly vestibular pattern that was closely related to the abnormal caloric test and OCR. Altogether, these findings suggest that the injury of the inner ear is located at the cochleovestibular peripheral level.

Patients with autoimmune disorders often exhibit a syndrome characterized by SNHL that is associated with vertigo and tinnitus[39,40]. Audiovestibular dysfunction was reported in primary systemic necrotizing vasculitides[41,42,43] and in patients with vasculitis secondary to other underlying conditions such as Behçet disease[44]. We also described audiovestibular dysfunction and benign paroxysmal positional vertigo in patients with biopsy-proven GCA[7,8]. Vasculitic and autoimmune mechanisms may be responsible for the subclinical sensorineural dysfunction observed in patients with SLE[5], SS[6], relapsing polychondritis[45], and SSc[9,10]. However, an underlying vasculitis does not appear to be the cause of the audiovestibular manifestations in patients with spondyloarthritides. Interestingly, inflammation has been associated with pathophysiological processes of aging, including vascular damage and neurodegeneration. There are some reports relating hearing loss with chronic inflammation. A recent study found that individuals younger than 60 years with CRP levels > 3 mg/l or increasing levels of serum CRP over 10 years were nearly twice as likely to develop hearing impairment over the subsequent 10-year period. This was not observed in individuals included in the study who were 60 years and older[46]. In keeping with these observations, in our series of patients with PsA who had a mean age of 52.9 years, we also observed a marginally significant association of abnormal audiovestibular symptoms and hypoacusia with laboratory markers of inflammation at the time of assessment. Therefore, chronic inflammation may be a plausible explanation for the audiovestibular findings in patients with PsA.

There is little information concerning audiovestibular findings in PsA. To our knowledge, only 2 case reports highlighting the presence of hypoacusia in PsA have previously been done[12,13]. As observed in PsA, we and others described SNHL in patients with AS that was predominantly bilateral[11,47,48]. It may be the result of an underlying autoimmune etiology. However, an ischemic vascular etiology cannot be completely excluded.

We disclosed a predominant pattern of high frequency SNHL in PsA. This finding was also observed in patients with AS[11,47]. Interestingly, Dagli, *et al* observed significant differences in pure-tone thresholds levels for hearing levels at low (0.25–0.5 kHz) and high (4–8 kHz) frequencies, but not at middle (1–2 kHz) frequencies of the audiogram between patients with AS and controls[48].

As previously reported in patients with AS[11], in our series of patients with PsA, SRT was in keeping with PTA results (within a range of difference between SRT and PTA ≤ 5 decibels hearing level). This result reinforces the relevance of our data, as a significant difference between these 2 thresholds would have raised doubts about the validity of the pure tone thresholds. In addition, SRT yielded good discrimination scores and correlation between the type and degree of hearing loss, suggesting the presence of a cochlear impairment.

The absence of a stapedius reflex in 12 of 60 patients from our series of PsA may indicate that abnormalities in these patients may be attributable to a cochlear lesion in the inner ear. However, information on cochleovestibular dysfunction in patients with spondyloarthropathies is scarce and limited to a few series of patients with AS[11,49,50].

Patients with AS from northwestern Spain had peripheral vestibular lesion[11]. In line with these findings, we also observed data supporting the presence of vestibular damage in PsA. Besides increased frequency of abnormal OCR and abnormal caloric tests, we disclosed increased frequency of CDP abnormality in patients with PsA when compared to controls. In addition, as observed in AS, a vestibular loss was the predominant pattern of abnormal posturography.

In our present study, we also aimed to determine whether audiovestibular dysfunction might be associated with a

specific PsA pattern. However, no differences according to the type of joint involvement were observed.

A potential limitation of our present study was the use of NSAID in patients with PsA. The mean age at the time of our study in the patients with PsA was 52.9 years. Therefore, most healthy matched controls included in our study were not taking NSAID. To minimize the potential effect of these drugs on audiovestibular manifestations, we could have included patients with osteoarthritis (OA) taking NSAID. However, the use of controls with OA might have strongly biased the control sample toward older age, which was confirmed to be associated with audiovestibular symptoms in our study. Another potential controversial issue might be that the prevalence of audiovestibular manifestations in the control group used for comparison with patients with PsA was lower than that found in the controls assessed in our former studies on GCA, limited SSc, and AS[8,10,11]. Nevertheless, the ages of the controls were not similar in these studies. An analysis of the age of the controls from our previous studies revealed that when we assessed the audiovestibular manifestations in biopsy-proven GCA in our population, matched controls were older than those included in our present study because GCA generally affects elderly people in their 70s and 80s[8]. In our study on audiovestibular manifestations in limited SSc, the mean ages of patients and controls were 64 and 62 years, respectively[10]. Controls were older than in our present study. On the other hand, in our study on audiovestibular manifestations in patients with AS[11], the mean age of the controls was 51 years (very close to that of current work), but the SD of controls was much higher than in the controls of our present study on PsA (16.3 vs 10.7). In this regard, in the former study on AS, 9 out of 44 controls were older than 70 years. In contrast, in our present study on PsA, only 4 out of 60 patients and matched controls were older than 70. This fact can justify the difference in prevalence of hearing loss in the controls used in these studies because the frequency of hearing loss increases with age.

Our current study demonstrates strong evidence for inner ear compromise in patients with spondyloarthritides, including PsA. It provides justification to screen for inner ear compromise in these patients.

ONLINE SUPPLEMENT

Supplementary data for this article are available at jrheum.org.

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