How Significant Is Sensorineural Hearing Loss in Primary Sjögren’s Syndrome? An Individually Matched Case-Control Study

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ABSTRACT. Objective. We evaluated whether sensorineural loss and vestibular abnormalities are common in patients with primary Sjögren’s syndrome (pSS) and whether such abnormalities are clinically significant.

Methods. In an individually matched case-control design, 48 patients with pSS underwent complete audiovestibular evaluation along with 48 age and sex matched individuals without otologic problems. Differences of > 20 dB between patient and control ears at any frequency tested were considered to be significant.

Results. Significant differences in hearing loss were seen at 4000 Hz (6 vs 0 ears; p = 0.03) and at 8000 Hz (9 vs 0 ears; p = 0.003). Small differences in hearing acuity were also observed in the lower frequencies, but the absolute mean difference was < 3 dB. A decrease of at least 60 dB in hearing acuity at any frequency up to 4000 Hz was seen only in 3 elderly pSS patients. Abnormal brainstem auditory evoked responses were recorded in 7 patients and 5 controls, but no patient had retrocochlear lesions identified on magnetic resonance imaging. Four patients in each group had abnormalities on electronystagmography.

Conclusion. pSS is associated with sensorineural hearing loss affecting preferentially the high frequencies, but clinically significant defects are not common. There is no evidence of retrocochlear disease or increased vestibular involvement in pSS. (J Rheumatol 2001;28:798–801)

Key Indexing Terms:
SENSORENIAL HEARING LOSS SJOËGRÈN’S SYNDROME
VESTIBULAR ABNORMALITIES BRAINSTEM AUDITORY EVOKED RESPONSES

The presence and extent of hearing and vestibular abnormalities in primary Sjögren’s syndrome (pSS), a disease characterized by autoimmune epithelitis1,2, are controversial3,4. One recent study of limited sample size suggested that hearing loss may be a major manifestation of pSS and that it is associated with antinuclear antibody, an otherwise uncommon finding in this syndrome4. Important questions remain: is hearing loss common in pSS and, if so, what are the characteristic patterns observed? Most importantly, are these abnormalities clinically important? We evaluated 48 patients with pSS for evidence of hearing and vestibular abnormalities compared with age and sex matched controls.

MATERIALS AND METHODS

Study population. Forty-nine patients with pSS were randomly selected from the pool of 300 pSS patients followed at the Department of Pathophysiology, University of Athens, and underwent audiovestibular examination. Primary SS was defined on the basis of the validated European consensus criteria5. The patients also fulfilled the suggested revised European criteria6. One patient with bilateral conductive hearing loss due to chronic otitis media was excluded. Similarly, in 4 pSS patients conductive hearing loss of various etiology affecting one ear only was documented. These 4 affected ears were not included in the analyses. The 48 patients were individually matched for age and sex with a control group selected from subjects visiting the outpatient clinic of the Department of Otolaryngology. The control subjects complained of various head and neck area problems excluding otological problems.

Clinical and laboratory data. From the patients’ medical records the following data were collected: age, sex, disease duration, arthralgias or arthritis or arthralgias, Raynaud’s phenomenon, purpura, leg ulcers, lymphadenopathy and/or splenomegaly (by physical examination), lung disease (carbon monoxide diffusing capacity < 70% of predicted, and/or ground glass appearance in computed tomography scan)7, interstitial nephritis (persistently alkaline urine with pH ≥ 7 and serum bicarbonate < 19 mEq/dl and/or characteristic histology in renal biopsy)8, glomerulonephritis (proteinuria > 500 mg/day or cellular casts and documentation by renal biopsy)8, and
peripheral neuropathy (defined by examination and nerve conduction studies in symptomatic patients).

Additionally, we collected information on the following laboratory variables; rheumatoid factor (IgM latex fixation, positive titer ≥ 40), anti-nuclear antibodies (immunoﬂuorescence using Hep2 cells as substrate), antibodies to extractable nuclear antigens Ro/SSA and La/SSB (counterimmunoﬂuorescence), C3 and C4 components of complement (nephelometry), and serum cryoglobulins.

**Audiologic and vestibular evaluation.** The evaluation included: a speciﬁc medical questionnaire for ear involvement; otological examination with the use of microscope; and audiologic evaluation. All subjects were questioned about any history of other audiovestibular disturbances, metabolic conditions, congenital anatomical abnormalities of the head and neck, Meniere’s disease, and the use of drugs known to cause ototoxicity. Subjects with a history of other diseases or toxic exposures that might have caused ear damage and subjects with diseases of the external ear, otitis media, perforated tympanic membrane, or cholesteatoma were not included in the study. Patients and candidate controls were screened for a history of signiﬁcant noise exposure. All subjects with potentially signiﬁcant noise exposure due to occupation or other reasons were not eligible for the study.

Audiologic evaluation was performed in both groups by 2 investigators. It included impedance audiometry with tympanograms and acoustic reﬂexes in order to exclude conductive hearing loss; assessment of hearing with pure tone audiometry for both ears for the frequencies of 250 to 8000 Hz; and brainstem evoked responses (BSER). BSER were assessed when the difference of audiometric threshold between the 2 ears was ≥ 10 dB for 2 frequencies or > 15 dB for one frequency; and in patients with vertigo, tinnitus, and aural fullness. When the interwave latency of waves I–V was > 0.2 ms and the endaural difference of wave V latency was > 0.3 ms, magnetic resonance image (MRI) scan with gadolinium enhancement was recommended. Modest aberrations in BSER are not uncommon even in the normal population and typically they need corroboration with neuroimaging studies to assess their importance.

Electronystagmographic (ENG) evaluation of spontaneous, positional, and caloric stimulation induced nystagmus was performed in all subjects complaining of a history of dizziness or vertigo. As for BSER, induced abnormalities in one of the ENG evaluations are not very uncommon even in otherwise normal subjects and therefore a comparison of patients with healthy controls is important.

**Statistical analysis.** The hearing loss (in dB) at each frequency was compared between patients with pSS and controls using paired observations and using data from each ear as separate measurements. Four patients with pSS had chronic otitis media in one ear and data for these ears (and the respective control ears) were excluded from analysis. The comparison between pSS and control ears was done with Wilcoxon’s test at each frequency. Frequencies were treated independently rather than in a repeated measures approach, because each frequency testing may suggest abnormalities of a different pattern (high frequency hearing loss is pathophysiologically different from low frequency hearing loss). Measurements from the 2 ears of each subject were treated as independent observations and the results were similar when analyses were performed considering them as repeated measurements of each individual (data not shown).

Hearing loss for a given frequency was deﬁned as a difference of > 20 dB between the compared ears. The numbers of subjects with hearing loss at each frequency were compared between pSS patients and controls with McNemar’s test. At frequencies where differences were observed between the 2 groups, we explored whether clinical and laboratory characteristics of pSS were associated with hearing loss. Comparisons involved the Mann-Whitney U test and chi-square test for continuous and discrete variables, respectively.

We also evaluated the total area under the audiogram curve (AUC) for the exception of the 8000 Hz (average difference 6 dB) (Table 2). By deﬁning hearing loss as a difference of > 20 dB between compared ears, there was a statistically signiﬁcant difference at 4000 Hz and at 8000 Hz.

An auditory threshold of ≥ 60 dB at any frequency tested was recorded in 7 pSS patients (14.6%) and in 3 (6.3%) control subjects. Excluding the frequency of 8000 Hz, all 3 subjects with at least 60 dB auditory threshold at some other frequency were elderly pSS patients (68, 72, and 78 yrs old).

**Regression analyses.** No clinical or laboratory variable was a strong predictor of hearing loss for any of the tested frequencies. There was only a trend for patients with lung involvement to have more frequent hearing loss at 8000 Hz than those without lung involvement (odds ratio, OR 3.9, p = 0.11). Patients with hearing loss at 4000 Hz had modestly longer disease duration (mean 9.5 vs 6.9 yrs), but the difference was not statistically signiﬁcant (p = 0.4). The difference in disease duration was even smaller for hearing loss at 8000 Hz (mean 8.0 vs 6.8 yrs; p = 0.6).

There were 9 pairs where the AUC was worse by > 60 dB in the pSS case versus the respective control. The opposite occurred in only one pair. Raynaud’s phenomenon (OR 3.2, p = 0.12) and lung involvement (OR 3.7, p = 0.18) showed trends for associations with hearing loss according to this deﬁnition, but neither association reached statistical signiﬁcance.

<table>
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<th>Table 1. Patient characteristics.</th>
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<tr>
<td>Age, mean (SD), yrs</td>
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<td>Duration of disease, mean (SD) yrs</td>
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<td>Xerostomia</td>
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<td>Rheumatoid factor</td>
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<td>Low levels of C4 complement</td>
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**RESULTS**

**Hearing loss.** Patient characteristics are shown in Table 1. The pSS group had more pronounced hearing loss, but the mean absolute difference from controls was very small, with the exception of the 8000 Hz (average difference 6 dB) (Table 2). By deﬁning hearing loss as a difference of > 20 dB between compared ears, there was a statistically signiﬁcant difference at 4000 Hz and at 8000 Hz.

Additionally, we collected information on the following laboratory variables: rheumatoid factor (IgM latex fixation, positive titer ≥ 40), anti-nuclear antibodies (immunoﬂuorescence using Hep2 cells as substrate), antibodies to extractable nuclear antigens Ro/SSA and La/SSB (counterimmunoﬂuorescence), C3 and C4 components of complement (nephelometry), and serum cryoglobulins.
Retrocochlear damage. Seven pSS patients and 5 controls showed abnormalities of brain stem evoked responses. Examination was repeated and MRI was recommended for 4 patients and 3 controls. No retrocochlear lesions were identified.

Vestibular impairment. ENG was performed in 10 pSS patients with complaints of dizziness and vertigo in the past. The examination revealed abnormalities for 4 of them: caloric responses were bilaterally reduced in 2 patients and unilaterally reduced in one patient, while positional nystagmus was documented in one patient. Nine control subjects had similar complaints and 4 of them had an abnormal ENG evaluation. Two subjects had unilaterally reduced caloric responses and 2 other subjects had positional nystagmus.

DISCUSSION

Although hearing loss has previously been observed in patients with pSS, the exact effect and clinical significance of this potential association is unclear. In a study of 14 patients, 3 had sensorineural hearing loss9 and in another report of 22 patients, sensorineural hearing loss was identified in only one patient1. A controlled study of 30 patients presented a very high prevalence of significant sensorineural hearing loss (46%)4. Using a controlled design and a larger number of subjects, we clearly show that hearing loss is not a major problem in patients with pSS. Nevertheless, mild to moderate sensorineural hearing impairment involving preferentially the high frequencies is not uncommon. Exploratory analyses found no strong and consistent associations between hearing loss and disease severity, the presence of extraglandular manifestations, or autoantibodies. On the basis of the current evidence, we cannot recommend special audiovestibular screening to be directed to specific subgroups of patients with pSS.

In autoimmune diseases immune complexes may cause hearing loss by blocking blood vessels (capillaries) and causing ischemia or local inflammation in the inner ear. The site of the lesion is the stria vascularis, where dense packing of red blood corpuscles and slow blood flow may occur. The resulting sensorineural hearing loss is typically most prominent for the higher frequencies, representing damage to the basal turn of the cochlea. This pattern is consistent with what we observed in patients with pSS.

Finally, our study shows that there is no evidence to suggest retrocochlear damage or an excess of vestibular damage in patients with pSS. There has been a lot of debate on the presence and extent of central nervous system involvement in pSS10. While peripheral neuropathies, in particular sensory or autonomic, are a common feature of both pSS10-13 and isolated sicca syndrome14, central nervous system involvement is less clear-cut13. In our study we found no patient with retrocochlear pathology. Similarly, our sample size was adequate to rule out the possibility of a significant effect on vestibular function. Modest sensorineural hearing loss is thus likely to be the only audiovestibular abnormality associated with pSS.

REFERENCES

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