Hearing loss in Sjögren’s syndrome patients. A comparative study

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ABSTRACT

Objective
In an attempt to investigate the presence of hearing loss in primary Sjögren’s syndrome (SS) patients and to determine the factors that might be involved in its pathogenesis, we prospectively evaluated 45 female SS patients with a mean age of 56.8 ± 9.23 years and a mean disease duration of 8.32 ± 5.39 years.

Methods
Forty patients underwent a complete ear-nose-throat physical examination and audiological evaluation with: (a) pure tone audiometry thresholds at octave frequencies of 250 to 8000 Hz; (b) impedance audiometry ( tympanogram, static compliance, acoustic reflexes, reflex decay; and (c) speech audiometry and auditory brainstem response where indicated. In addition, glandular and extraglandular manifestations of the disease and drug therapy were recorded. Finally, all patients were tested for the presence of autoantibodies, including: rheumatoid factor, antinuclear antibodies, antibodies to Ro(SSA), La(SSB) nuclear antigens, anticytotoxic lymphocytes, and antineutrophil cytoplasmatic antibodies. The results were compared with those of 40 healthy, age-matched women.

Results
We found sensorineural hearing loss (SNHL) in 9 patients (22.5%): 4 patients bilaterally, 4 patients in the left ear only and one in the right ear only. In all cases the site of the ear damage was cochlear. A correlation between SNHL and the duration of the disease was found, while there was no correlation with age, systemic manifestations of the disease or the presence of autoantibodies. In addition, no correlation was found between SNHL and drug therapy.

Conclusion
Approximately one-fourth of our SS patients presented SNHL of cochlear origin affecting mainly the high frequencies. This prevalence was lower than that reported by other investigators. SNHL was associated only with disease duration. Further investigation is needed to attain a better understanding of the mechanism of inner ear involvement in SS patients.

Introduction
Inner ear involvement has been reported in many autoimmune connective tissue diseases (ACD) including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and Wegener’s granulomatosis (1-6). Sjögren’s syndrome (SS) is a cell-mediated immune disorder of unknown etiology affecting primarily the exocrine glands. Essential features of SS include focal lymphocytic infiltrates in the lacrimal and salivary glands and the presence of many autoantibodies that participate to cause immunological cell-mediated tissue injury (7, 8). The deposition of immune complexes (IC) leads to vasculitic lesions and systemic manifestations with a high prevalence of cranial neuropathies. Inner ear autoantibodies and IC-mediated hearing loss have been suggested by a number of clinical and experimental studies (9, 10). However, the involvement of the VIII cranial nerve in patients with primary SS has not been studied efficiently (11, 12). This prompted us to investigate the presence of hearing loss in primary SS patients and to determine the factors that might be implicated in its pathogenesis.

Patients and methods
Forty-five unselected, consecutive female patients who fulfilled the preliminary European criteria for SS (13) and who were followed up in our outpatient rheumatology clinic were evaluated for hearing loss. The patients entered in the study had a complete physical and laboratory evaluation. All the glandular and extraglandular manifestations, as well as the current treatment were recorded. In addition, all patients had an immunological evaluation including: rheumatoid factor (RF) (latex test), antinuclear antibodies (ANA) (indirect immunofluorescence), antibodies to Ro(SSA) and La(SSB) using immunodiffusion, anticytotoxic lymphocytes, and antineutrophil cytoplasmatic antibodies (ANCA) (indirect immunofluorescence). In addition, all patients had a complete ear-nose-throat (ENT) evaluation which included: 1) a specific medical questionnaire for ear involvement; 2) ENT examination; and 3) audiological examination. These evaluations were carried out by the same investigators (IK, NZ) in all patients and included:
A) Pure tone audiometry: (i) air conduc-
tory of ear disease or SS, were selected
and other parameters, with no his-
addition, 40 healthy women matched for
were taking drugs known to cause oto-
because of acoustic trauma, 2 because
for hearing loss and 5 were excluded, 2
normalities of the head and neck, skull
A total of 45 SS patients were screened
Results
hearing loss, congenital anatomical ab-
test and the Mann-Whitney test where
ber (type Amplaid); and (d) Biologic
Statistical analysis was performed using
Amplaid 720); and (c) soundproof cham-
individuals of various ages (14).
450); (b) impedance audiometer (type
curves of hearing thresholds for normal
rived from the international standard
tion score. For the audiological eval-
the following devices were used: (a)
two-channel audiometer (type Amplaid
Since age can influence the results, for
more reliable comparisons we divided
our patients and controls into four groups
by age: group A (30-44 years), group B
(45-54 years), group C (55-64 years) and
group D (65-74 years). A patient was
considered to have abnormal hearing if
at any frequency her hearing threshold
was 20 dB HL or more above the mean
for the control individuals from the same
age group. It should be noted that the
latter conformed to the mean values de-
rived from the international standard
curves of hearing thresholds for normal
individuals of various ages (14).
Statistical analysis was performed using
contingency tables with Fisher’s exact
test and the Mann-Whitney test where
indicated.

Results
A total of 45 SS patients were screened
for hearing loss and 5 were excluded, 2
because of acoustic trauma, 2 because
of chronic use of salicylates and one due
to the use of streptomycin injections for
chest tuberculosis. The demographic,
clinical, immunological and therapeutic
findings of our patients are shown in
Table I. Based on age, 4 patients were
placed in group A, 11 in group B, 15 in
group C and 10 in group D.
Extraglandular manifestations were
found in 9 patients. Seven had Raynaud’s
phenomenon and 2 had peripheral sen-
sory neuropathy. Antinuclear antibodies
were found in 92.5% of our patients,
Ro(SSA) in 62.5%, and La(SSB) in 35%,
while aCL antibodies were found only
in 10%. None of our patients had ANCA
antibodies.
Pure tone audiometry revealed sensori-
near hearing loss (SNHL) of the coch-
lar type in 9 patients (22.5%). The distri-
bution according to age group was as
follows: one patient in group B, 5 pa-
tients in group C, and 3 patients in group
D. None of the subjects in the control
groups presented findings of SNHL.
There were no differences between the
patients with and those without SNHL
as far as their mean age, glandular and
extraglandular manifestations, autoanti-
body profile, and drug therapy were con-
cerned. SS patients with SNHL had a
longer disease duration compared to
those without SNHL (Table I). Among
these 9 patients, 4 had bilateral symmetric
SNHL (10%). In 3 of these patients
the audiometric configuration sloped at
high frequencies (3000 to 8000 Hz) and
the degree of SNHL was severe (60 to
80 dB HL), while the configuration of
the fourth patient was essentially flat and
the degree of SNHL was moderate (40
to 60 dB HL). The other 5 patients had
unilateral SNHL at high frequencies (one
in the right ear only and 4 in the left ear
only). In 2 of them the hearing loss was
moderate (40 to 60 dB HL) while in
the remaining 3 the hearing loss was severe
(60 to 80 dB HL). The absolute values of the mean ± SDs of the hearing thresholds of patients and
controls in dB HL at the serial frequen-
cies are presented in Table II. No patient
had conductive or mixed type hearing
loss. Middle ear pressure was normal in

| Table I. Clinical, immunological and drug therapy data on Sjögren’s syndrome patients with and without sensorineural hearing loss (SNHL). |
|-----------------|-----------------|-----------------|
| Variables       | All patients    | Patients with SNHL | Patients without SNHL |
| Mean age (x ± SD) (years) | 56.9 ± 9.2    | 60 ± 8.7          | 55.9 ± 9.5             |
| Mean disease duration (x ± SD) | 8.3 ± 5.4    | 12.1 ± 6.8*       | 7.4 ± 4.4*             |
| Clinical        |                |                  |                      |
| Dry eyes        | 37             | 8                | 29                    |
| Dry mouth       | 36             | 8                | 28                    |
| Parotid gland enlargement | 7        | 2                | 5                     |
| Raynaud’s phenomenon | 7          | 1                | 6                     |
| Peripheral neuropathy | 2          | 1                | 1                     |
| Immunological   |                |                  |                      |
| Antinuclear antibodies | 37          | 9                | 28                    |
| Rheumatoid factor | 16           | 2                | 14                    |
| Ro(SSA)         | 25             | 7                | 18                    |
| La(SSB)         | 14             | 3                | 11                    |
| aCL (IgG)       | 4              | 1                | 3                     |
| aCL (IgM)       | 4              | 1                | 3                     |
| Drug therapy    |                |                  |                      |
| Methotrexate    | 5              | 1                | 4                     |
| Hydroxychloroquine | 11        | 2                | 9                     |
| NSAIDs          | 6              | 1                | 5                     |
| Steroids        | 3              | 1                | 2                     |
| Buflomedil      | 4              | 1                | 3                     |

*p: 0.0148; aCL: anticardiolipin antibodies; NSAIDs: non steroid antiinflammatory drugs.
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Table II. Hearing thresholds in dB HL (air conduction) of the patients and controls at serial frequencies (right ears only) (mean ± SD).

<table>
<thead>
<tr>
<th>Age group</th>
<th>250 Hz</th>
<th>500 Hz</th>
<th>1 KHz</th>
<th>2 KHz</th>
<th>4 KHz</th>
<th>8 KHz</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Patients</td>
<td>15 ± 7.1</td>
<td>10 ± 5.8</td>
<td>8.7 ± 2.5</td>
<td>7.5 ± 5</td>
<td>7.5 ± 2.9</td>
<td>13.7 ± 7.5</td>
</tr>
<tr>
<td>B Patients</td>
<td>24.5 ± 7.6</td>
<td>20.5 ± 10.1</td>
<td>7.5 ± 2.9</td>
<td>13.7 ± 7.5</td>
<td>20.5 ± 10.1</td>
<td>24 ± 8.7</td>
</tr>
<tr>
<td>C Patients</td>
<td>23.3 ± 9.4</td>
<td>18.7 ± 9.1</td>
<td>19.7 ± 10.4</td>
<td>22 ± 12.1</td>
<td>28.7 ± 15.3</td>
<td>37.7 ± 17</td>
</tr>
<tr>
<td>D Patients</td>
<td>24.5 ± 7.6</td>
<td>20.5 ± 10.1</td>
<td>24 ± 8.7</td>
<td>23 ± 12.5</td>
<td>40 ± 19</td>
<td>53 ± 19.3</td>
</tr>
<tr>
<td>Controls</td>
<td>10 ± 3.5</td>
<td>10 ± 3.5</td>
<td>11 ± 4.2</td>
<td>8 ± 6.7</td>
<td>11 ± 2.2</td>
<td>15 ± 3.5</td>
</tr>
</tbody>
</table>

Discussion

Sjögren’s syndrome is a systemic autoimmune disease whose extraglandular manifestations may include focal or diffuse lymphocytic and plasma cell infiltrates of almost any organ. Extraglandular manifestations may involve the skin, lungs, kidneys neuromuscular system, etc. (7, 8). Cranial nerve involvement is observed in patients with SS and may be peripheral or central. The most well recognized cranial nerve syndrome is a trigeminal sensory neuropathy (11), although other cranial nerve deficits, with or without trigeminal neuropathy, may occur.

The middle and inner ear involvement in SS patients has not been studied sufficiently (11, 12, 15-17). A series of studies has been published concerning hearing damage in patients with RA, SEL and vasculitis (1-6). The mechanism of inner ear involvement in most CTDs has not been clarified. Vascular inflammation of small vessels on the epineurium or vasa vasorum has been reported (7).

In RA patients, a prevalence of SNHL of the cochlear type has been reported in a percentage ranging from 29.4% to 55% by different investigators (1, 2, 4). The sensorineural damage is attributed to vasculitis or neuritis, or may represent an ototoxic effect of the drugs used in the treatment of the disease.

In a control study of patients with SLE, 57% of them had SNHL which was not correlated with the severity of the underlying disease or the presence of vasculitis (5). The pathogenesis of SNHL in SEL may be due to cochlear hydrops (hearing loss affecting mainly the low frequencies), but an early degeneration of the hair cells of Corti’s organ has also been reported (5). In our study, SNHL was observed in 22.5% of the patients. The acoustic reflex thresholds were within normal limits in all patients and the reflex decay was normal. Furthermore, speech audiometry showed discrimination scores compatible with cochlear disease.

The configuration of the audiograms in our SS patients revealed one case with SNHL affecting all frequencies to the same degree (flat audiogram) and 8 cases with SNHL affecting mainly the high frequencies. SNHL affecting the low frequencies is usually observed in vestibular hydrops syndromes and is associated with tinnitus and vertigo, but 10% of hydrops patients present with only cochlear symptoms (18).

In our study the patient with the flat audiogram did not have a history of concomitant tinnitus and vertigo. Thus, the possibility of a subclinical hydrops in our SS patients is not verified. However, several recent studies suggest that the deposition of IC in the stria vascularis or the endolympathic sac via complement activation can interfere with the production or absorption of the endolymph, resulting in endolympathic hydrops (19).

None of the differences were found concerning the immunological profile between the 2 groups of patients. Thus, the possibility of inner ear damage due to aCL and other autoantibody activities has not been demonstrated in our study and our results are not in agreement with those of Tumiati et al. who found a correlation between SNHL and aCL in SS patients (12). However, our observations concerning aCL are in agreement with those of Manousakis et al. who did not find a significant correlation between the presence of aCL and clinical manifestations in unselected autoimmune patients (20).

In the present study, no evidence of damage to the central auditory pathways was found in SS patients with SNHL; there were also no lesions in the area of the brainstem affecting the cochlear nerve. On the other hand, the majority of our SS patients with SNHL (8/9) had a hearing impairment of cochlear origin affecting mainly the high frequencies. However, we found a statistically significant difference with disease duration between SS patients with SNHL and those without.

In conclusion SNHL was found in 22.5% of our patients with primary SS. The damage is of the cochlear type, affecting mainly the high frequencies, and is correlated with disease duration. Further investigation is needed for a better understanding of the mechanism of SNHL in SS patients.

Acknowledgements

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References