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BRIEF PAPER

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, anticardiolipin antibodies 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, anticardiolipin antibodies (aCL) (Elisa) 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-

tion thresholds at octave frequencies from 250 to 8000 Hz; and (ii) bone conduction thresholds at octave frequencies from 250 to 4000 Hz.

B) Impedance audiometry: (i) tympanogram, according to Jerger's types; and (ii) acoustic reflexes as follows: (a) measurement of the acoustic reflex threshold at octave frequencies from 500 to 4000 Hz ipsilaterally and contralaterally, (b) measurement of reflex decay for the frequencies 500 and 1000 Hz contralaterally.

C) Speech audiometry: (i) speech reception threshold; and (ii) speech recognition score. For the audiological evaluation the following devices were used: (a) two-channel audiometer (type Amplaid 450); (b) impedance audiometer (type Amplaid 720); and (c) soundproof chamber (type Amplaid); and (d) Biologic traveler ABRs. Patients with congenital hearing loss, congenital anatomical abnormalities of the head and neck, skull or neck trauma, ottorhea, or those who were taking drugs known to cause ototoxicity (such as salicylates and streptomycin) were excluded from the study. In addition, 40 healthy women matched for age and other parameters, with no history of ear disease or SS, were selected from hospital personnel and healthy blood donors and used as the control group.

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 derived 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 sensory 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 sensorineural hearing loss (SNHL) of the cochlear type in 9 patients (22.5%). The distribution according to age group was as follows: one patient in group B, 5 patients 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, autoantibody profile, and drug therapy were concerned. 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 frequencies 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 (n=40)	Patients with SNHL (n=9)	Patients without SNHL (n=31)
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.

Table II. Hearing thresholds in dB HL (air conduction) of the patients and controls at serial frequencies (right ears only) (mean ± SD).

Age group	250 Hz	500 Hz	1 KHz	2 KHz	4 KHz	8 KHz
A Patients	15 ± 7.1	10 ± 5.8	8.7 ± 2.5	7.5 ± 5	7.5 ± 2.9	13.7 ± 7.5
Controls	10 ± 3.5	10 ± 3.5	11 ± 4.2	8 ± 6.7	11 ± 2.2	15 ± 3.5
B Patients	20 ± 11.4	15 ± 12.2	14.5 ± 7.2	12.3 ± 6.1	26.4 ± 19.6	37.3 ± 21.9
Controls	18.5 ± 5.9	17.3 ± 6.6	16.9 ± 5.6	15.4 ± 5.6	19.2 ± 7	28.8 ± 8.7
C Patients	23.3 ± 9.4	18.7 ± 9.1	19.7 ± 10.4	22 ± 12.1	28.7 ± 15.3	37.7 ± 17
Controls	19.1 ± 5.8	19.5 ± 5.7	21.4 ± 5.5	19.5 ± 5.7	25.9 ± 5.8	38.2 ± 11
D Patients	24.5 ± 7.6	20.5 ± 10.1	24 ± 8.7	23 ± 12.5	40 ± 19	53 ± 19.3
Controls	26.4 ± 7.4	27.3 ± 7.5	20.9 ± 4.9	27.3 ± 9.6	36.4 ± 9.5	47.7 ± 8.5

all patients and all controls. Tympanograms were type A according to Jerger's classification. No significant difference in the mean static compliance value was found between the patients with SS and the controls. In all patients acoustic reflexes presented within normal limits contralaterally and ipsilaterally. No positive reflex decay was found.

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 epineurum 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 SLE 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 endolymphatic sac via complement activation can interfere with the production or absorption of the endolymph, resulting in endolymphatic hydrops (19). No 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.

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