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Audio-vestibular evaluation in patients with Behçet's syndrome

Cem Evereklioglu, M.D., Yasar Cokkeser, M.D., Selim Doganay, M.D., Hamdi Er, M.D., Ahmet Kizilay, M.D.*

Abstract

A prospective controlled clinical study was carried out at the Department of Ophthalmology and ENT, Inönü University Medical Faculty, Turgut Ozal Medical Center, Research Hospital, to evaluate the audio-vestibular involvement in patients with Behçet's syndrome compared with controls.

Twenty-five consecutive patients with Behçet's syndrome (mean age ± SD, 34.96 ± 8.50) and 20 age- and sex-matched healthy volunteers (hospital staff) as control subjects (mean age ± SD, 34.45 ± 9.16) were included in this study. Behçet's patients were divided into two groups according to the number of criteria, complete (all four major criteria) and incomplete (three major criteria without ocular involvement). The groups were compared with each other or controls regarding inner ear involvement. Audiometric pure-tone thresholds at 125 to 8000 Hz were obtained in all subjects in both groups, and pure tone average (PTA) hearing thresholds were calculated for the middle, high and low frequencies. In addition, short increment sensitivity index (SISI), tone decay and BERA examinations were performed in all Behçet's patients.

Sensorineural hearing loss (SNHL) was present in six of 25 patients with Behçet's syndrome. Two Behçet's patients had unilateral total SNHL, two had bilateral moderate level SNHL, one had bilateral low-frequency SNHL and one bilateral high frequency SNHL. In two, BERA, and in five SISI, examination disclosed inner ear involvement. In control subjects, the past medical history was normal and there was no consistent audio-vestibular complaint. Their PTA thresholds were all in the normal range. Otoscopic examination findings were normal, with intact, mobile tympanic membranes in both groups.

The present study showed that audio-vestibular involvement is not infrequent in Behçet's syndrome compared with age- and sex-matched healthy controls, and it is under-estimated. All Behçet's patients should regularly be followed by an otolaryngologists and be given information about the possibility of inner ear involvement. According to our results, hearing loss occurs more often in older patients and also in the complete form of Behçet's syndrome.

Key words: Behçet's Syndrome; Vestibulocochlear Nerve Diseases

Introduction

Behçet's syndrome, originally described by Professor Dr Hulusi Behçet in 1937[1], is a chronic systemic relapsing disorder of young adults with a generalized vasculitis of small vessels with unknown aetiology.[2] After its description as recurrent oral and genital ulceration with hypopyon uveitis, the multisystem character of the disease has been established. Although the aetiopathogenesis of the disease has not been clarified, it is now considered to be an autoimmune disease with a genetic basis.[2,3] The intermittent nature and the lack of consistent response to therapy makes the underlying aetiology difficult to define.

Since Behçet's syndrome is a generalized systemic vasculitis of arteries and veins, it has been demonstrated that central nervous system, cardiovascular system, pulmonary and gastrointestinal tract involvement are present.[4] In addition, ear and vestibular involvement are reported to be present from 27 to 80 per cent of cases.[5–12]

The present study investigated the frequency, degree and type of hearing loss, and vestibular symptoms in patients with Behçet's syndrome compared with age- and sex-matched healthy controls. We also investigated if the ocular involvement, the age of Behçet's patients or the duration of the disease has correlation with the incidence of hearing loss in Behçet's syndrome.

From the Departments of Ophthalmology and Otolaryngology* Inönü University Medical Faculty, Turgut Ozal Medical Center, Research Hospital, Malatya, Turkey.
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Patients and methods

Twenty-five consecutive patients with Behçet's syndrome (11 male and 14 female) who were regularly followed by the Department of Ophthalmology (Behçet's clinic) and ENT were included in this study. All Behçet's patients in the present study fulfilled the diagnostic criteria of the Behçet's disease Research Committee of Japan (BDRCJ).[13] The four major criteria consist of the classic triad of recurrent aphthous oral ulceration, recurrent hypopyon iritis or iridocyclitis, and genital ulceration, initially described by Behçet, with the addition of cutaneous lesions (erythema nodosum-like eruptions, subcutaneous thrombophlebitis) afterwards. In addition *minor criteria* included arthritic symptoms and signs (arthralgia, swelling, redness), gastrointestinal lesions (appendicitis-like pains, melaena), epididymitis, vascular occlusions, and CNS involvement. All four major symptoms are needed for the diagnosis of *complete* Behçet's syndrome. The syndrome is termed *incomplete* if only three major symptoms

TABLE I
CLINICAL FINDINGS OF BEHÇET'S PATIENTS WITH OR WITHOUT EAR INVOLVEMENT

Pt. No	Age	Sex M/F	Dis Dur	OA GU	Skin lesions	Eye lesions	MC	SNHL	SISI	BERA	OD OV	Other findings
1*	42	M	5	+/+	Folliculitis, pyoderma	–	1	Bilateral (Moderate)	↑↑	–	OD	Left facial paralysis
2	26	M	3	+/+	Folliculitis	Chorioretinitis, iridocyclitis	1	–	N	–	OD	–
3	36	M	5	+/+	Folliculitis, pyoderma	–	1	–	N	–	–	Varicocele
4*	41	F	2	+/+	Folliculitis, erythema nodosum	Chorioretinitis, iridocyclitis	2	Bilateral (LF)	N	–	–	–
5*	43	M	8	+/+	Folliculitis, erythema nodosum	–	2	Right (total)	↑↑	–	OD	Left nephrectomy
6	30	F	1	+/+	Folliculitis, subcutaneous thrombophlebitis	Chorioretinitis, iridocyclitis	1	–	N	–	OD	–
7*	34	F	8	+/−	Folliculitis, subcutaneous thrombophlebitis	Chorioretinitis, iridocyclitis	1	Bilateral (Moderate)	N	–	–	Right enucleation
8	49	F	18	+/+	Folliculitis, erythema nodosum	–	2	–	N	–	OD	Spastic Colon
9	48	F	9	+/+	Folliculitis, pyoderma, erythema nodosum, Subcutaneous thrombophlebitis	–	–	–	N	–	OV	–
10*	43	M	10	+/−	Folliculitis	Chorioretinitis, iridocyclitis	1	Bilateral (HF)	↑↑	Bilateral increase in I. Wave	OV	–
11	34	F	10	+/+	Folliculitis	–	1	–	N	–	OD	–
12*	44	M	10	+/+	Folliculitis, pyoderma, Subcutaneous thrombophlebitis	Hypopyon uveitis	1	Left (total)	↑↑↑	–	V	–
13	29	F	1	+/+	Folliculitis	–	1	–	N	–	OD	–
14	27	M	2	+/+	Folliculitis, erythema nodosum	Chorioretinitis, irodocyclitis	1	–	N	–	OD	–
15	36	F	9	+/+	Folliculitis, pyoderma,	–	–	–	N	–	–	–
16	33	M	9	+/+	Folliculitis	–	2	–	↑	Bilateral increase in I. Wave	–	–
17	37	M	17	+/+	Folliculitis, erythema nodosum, Subcutaneous thrombophlebitis	–	–	–	N	–	OD	–
18	39	F	1	+/+	Folliculitis	–	1	–	↑↑	–	OD;V SN	–
19	17	F	2	+/+	Folliculitis, Subcutaneous thrombophlebitis	–	2	–	N	–	OD;V	–
20	21	M	1	+/+	–	Chorioretinitis, iridocyclitis	1	–	N	–	–	–
21	41	F	5	+/+	Folliculitis, pyoderma	–	1	–	↑	–	V	–
22	41	M	15	+/+	Folliculitis, pyoderma, Erythema nodosum, Subcutaneous thrombophlebitis	–	2	–	N	–	SN OV	Intestinal colon resection
23	35	F	11	+/+	Folliculitis, pyoderma	–	2	–	N	–	–	–
24	22	F	5	+/+	Folliculitis, pyoderma	–	2	–	N	–	–	–
25	26	F	8	+/+	Folliculitis, pyoderma, Erythema nodosum	–	1	–	N	–	–	–

Pt. No = patient number; M = male; F = female; Dis. Dur. = disease duration; OA = oral aphthae, GU = genital ulceration; MC = minor criteria; SNHL = sensorineural hearing loss; OD = orthostatic disequilibrium; V = vertigo; OV = objective vertigo.
N = normal; LF = low frequency; HF = high frequency; SN = spontaneous nystagmus; ↑↑↑; very severe; ↑↑ = mild, ↑ = very little.
Patients with SNHL.

TABLE II
THE FREQUENCY OF SYMPTOMS IN BEHÇET'S PATIENTS ACCORDING TO THE DIAGNOSTIC CRITERIA OF BEHÇET'S DISEASE RESEARCH COMMITTEE OF JAPAN[13]

Symptom	Frequency	n =	%
Oral aphthae (at least 5 times in a one-year period)	1st	25	100
Skin lesions	2nd	24	96
Articular symptoms	3rd	24	96
Recurrent genital ulceration	4th	23	92
Vestibular complaints	5th	16	64
Ocular involvement	6th	8	32
Ear involvement	7th	6	24
GIS	8th	3	12

GIS = gastrointestinal system.

are present or if uveitis occurs with one of the other major symptoms.

Past medical and family histories were obtained regarding trauma, ear infection, and audio-vestibular diseases, and drug use or exposure to noise was questioned. Those with a known cause, such as trauma, Ménière disease, or surgery, were not included in the study. The Behçet's patients were divided into two groups according to BDRCJ, incomplete (three major criteria without ocular involvement) and complete (all four major criteria).

After informed consent was obtained from all Behçet's patients and healthy volunteers, the audiological evaluation including pure tone audiogram, SISI, tone decay and BERA examinations was performed in all patients with Behçet's syndrome but only pure tone audiograms for the asymptomatic control subjects. In evaluation of the vestibular system, the subjects were asked whether they had any vertigo, light-headedness, or orthostatic disequilibrium symptoms and were evaluated for the presence of spontaneous nystagmus using Frenzel glasses.

Statistics: The correlation between the audio-vestibular symptoms and the duration of the disease and age were investigated by the Mann-Whitney U test.

Results

Twenty-five patients (11 male and 14 female) with Behçet's syndrome and 20 healthy normal control subjects from our hospital volunteers (nine male and 11 female) were included in this study. The mean age ± SD between two groups (34.96 ± 8.50 *vs.* 34.45 ± 9.16 years, respectively) was comparable.

The clinical findings and the diagnostic criteria of Behçet's patients included in this study are presented in Table I. Oral lesions were present in all cases (100 per cent). Twenty-four patients (96 per cent) had various cutaneous lesions. Recurrent genital ulceration was found in 23 patients (92 per cent). In addition, articular symptoms were present in 24 patients (96 per cent) and gastrointestinal system symptoms and signs in three patients (12 per cent) Table II).

In both groups, past medical and family histories were non-contributory. There was no ototoxic drug or noise exposure on history in either the Behçet's group or the control group except one case of noise exposure with Behçet's syndrome. There was no history of inner or middle-ear disease, hearing loss, or auditory complaints in the healthy volunteers. None of the Behçet's patients with hearing loss complained of any kind of tinnitus, nausea, or vomiting. None of the patients nor the control group complained of abrupt hearing loss. On the contrary, subjective unilateral or bilateral hearing decrease or loss was acquired with gradual onset. The progression was slow over months to years. Otoscopic examination findings were normal, with intact, mobile tympanic membranes in both groups.

Pure-tone audiogram revealed SNHL in six of 25 patients (24 per cent) with Behçet's syndrome. One of the six patients had right-sided total SNHL, one had left-sided total SNHL, two had bilateral moderate level SNHL, one had bilateral low-frequency SNHL and one had bilateral high-frequency SNHL. Seventeen out of 25 patients with Behçet's syndrome had three major criteria (incomplete form), two of whom (11.7 per cent) showed SNHL. On the other hand, four of eight Behçet's patients (50 per cent) with all four major criteria (complete form) showed SNHL. Duration of the disease in patients with, or without, hearing loss was 5.67 ± 3.61 and 6.95 ± 5.50 years respectively and the difference was not significant ($p>0.05$). The mean age of these groups were 41.16 ± 3.65 and 33.00 ± 8.70 years respectively and the difference was significant ($p<0.05$). None of the healthy controls had any kind of hearing decrease or loss and their pure tone audiogram revealed normal thresholds in all subjects bilaterally.

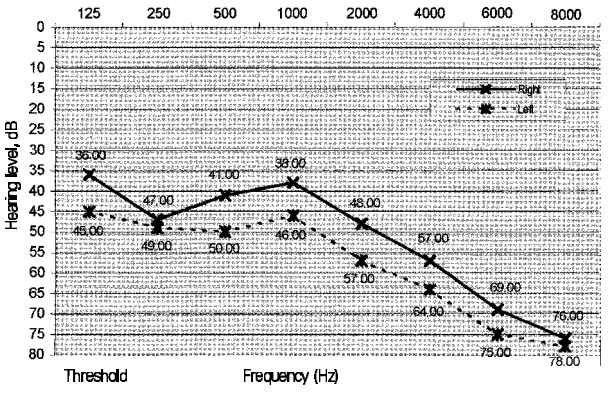

FIG. 1
Mean audiogram of Behçet's patients with SNHL.

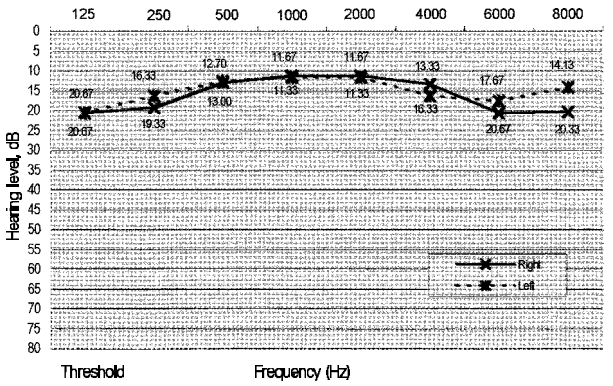

FIG. 2
Mean audiogram of Behçet's patients within normal range.

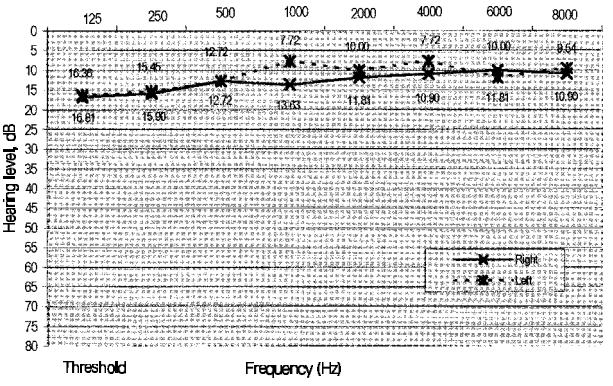

FIG. 3
Mean audiogram of control subjects.

The pure-tone audiograms of these affected and non-affected Behçet's patients and the healthy controls are shown in Figures 1, 2 and 3, respectively.

Vestibular system evaluation showed that nine patients did not have disequilibrium. Eleven patients with Behçet's syndrome complained of orthostatic disequilibrium and three patients complained of objective vertigo. Two of the others had a pull-push thrust and flying sensation. No subject in the control group complained of consistent vertigo. No abnormality was found in tone decay testing except a small increment in two cases (below five in high frequencies) in Behçet's patients. One very severe, four mild and two very little increment in SISI scores were also observed. In BERA examinations, two cases showed only first wave abnormality, one was from the SNHL group and the other one was from the normal hearing group.

Discussion

Behçet's syndrome is a chronic, multisystem generalized vasculitis with perivascular infiltration that may involve many organs.[1,3,4] Since the first description by Alajouanine *et al.*,[8] hearing loss in Behçet's syndrome have been reported to be between 12 and 80 per cent of cases in several studies.[5–12] A significant percentage of audiovestibular involvement in Behçet's group, especially in complete Behçet's patients was also observed in this study when compared with control subjects.

Six out of 25 patients with Behçet's syndrome had unilateral or bilateral SNHL from partial to total. Although no typical audiogram was observed in Behçet's patients with severe hearing loss, the Behçet's patients with an audiogram within the normal range showed a downward sloping of the audiogram in the low and high frequencies, but there was only a little shallow downward sloping of the low frequencies in the controls, which was in the normal range. Regarding other tests such as BERA, SISI, tone decay as well as tympanometry and reflex testing, they did not show any correlation or specificity to Behçet's disease in our series. In two, BERA examinations and in five SISI examination showed peripheral involvement, which may suggest fine vascular involvement.

Brama and Fainaru[5] reported that 10 of 16 patients without central nervous system involvement showed inner ear involvement and stated that inner ear involvement occurred more in older Behçet's patients with a longer duration of the disease, four showed progressive hearing loss. In a neurologically involved group, Belkahia *et al.*[7] reported that eight of the 16 Behçet's patients showed vestibular involvement. Soylu *et al.*[14] and Gemignani *et al.*[11] did not find any relation between the age or the disease duration and inner ear involvement, nor that audio-vestibular damage was progressive as it was in our study. In our series, the mean age of the Behçet's group with inner ear involvement was higher than the patients without hearing loss and the difference was significant. On the other hand, the duration of the disease and the hearing loss or vestibular involvement did not show any correlation. The same was found by Soylu *et al.*[14] Belkahia *et al.*[7] found a correlation between inner ear involvement and neurological involvement. Soylu *et al.*[14] could not find any correlation between the hearing loss and other system involvement in Behçet's group.

In the present study, inner ear involvement (significant hearing loss) is the seventh most frequent symptom and vestibular findings the fifth (Table II). Most of the vertiginous complaints are orthostatic, and it is not clear whether this comes from the inner ear or if this imbalance results from the involvement of the fine vessels of the vasa nervorum. Some of the series[7,11] showed more frequent inner ear involvement, probably resulting from a selected case presentation to a specific clinic instead of representing the general Behçet's population.

Regarding treatment for newly diagnosed hearing loss and vestibular involvement, Elidan[12] reported significant hearing improvement with cyclosporine A. But Soylu *et al.*[14] did not observe any improvement in four patients treated with cyclosporine A. We did not attempt to treat any of the established patients with previous hearing loss, but we suggested to prevent volume loss to patients in order to relieve the orthostatic disequilibrium from getting up especially from bed.

Peripheral vestibular syndrome, cochlear and vestibular abnormalities were the main types of involvement.[5] A significant vestibular symptomatology was observed in our series compared with control group. Gemignani *et al*.[11] found five of the eight patients complaining of vestibular symptoms showed altered vestibular test values. In our cases, nearly half of the patients had orthostatic disequilibrium and seven other cases had shown orthostatic disequilibrium mixed with an objective turning sensation, varying for frequency or seriousness from patient to patient, even in the same patient from time to time. Regarding the origin of this symptomatology the authors think that general microneurovascular involvement of the patients would lead to peripheral end organ hearing loss and vestibular complaints; obviously this needs to be worked further and clarified.

In conclusion, this study showed that audio-vestibular involvement is not infrequent in Behçet's patients and underestimated. All Behçet's patients should regularly be followed by an otolaryngologist and be given information to be aware of the possibility of inner ear involvement that could be treated by immunosuppressive agents. Hearing loss occurs more often in older Behçet's patients. Older Behçet's patients with the complete form of the syndrome were observed to show ear involvement more frequently during the course of the disease.

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Address for correspondence:
Dr. Cem Evereklioglu,
Sivas Cad. Cebeci Apt. A-Blok, 175/15,
38020, Kayseri, Turkey.

Fax: +90 422 341 0619
E-mail: evereklioglu@hotmail.com

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