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Labyrinthine involvement in Behçet's syndrome

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Abstract

We report the neuro-otological findings in 26 consecutive patients with definite and probable Behçet's syndrome unselected for audiovestibular complaints. Auditory and/or vestibular abnormalities were found in 19 (73 per cent) patients, with auditory involvement in 14 (54 per cent) and vestibular in 10 (38.5 per cent) of patients. Peripheral involvement was more common than central involvement for both auditory and vestibular lesions. Bilateral cochlear hearing impairment was the most common audiological finding, whereas unilateral peripheral dysfunction was the prevailing vestibular abnormality. No correlation has been found between audiovestibular lesions and other organ lesions, disease duration or age or sex of the patients. Moreover, there was a lack of interdependence between cochlear and vestibular labyrinthine lesions. We conclude that a full neuro-otological assessment in patients under investigation for Behçet's syndrome may reveal labyrinth involvement in a substantial proportion of patients. In view of the absence of a specific diagnostic test for Behçet's syndrome, audiovestibular lesions may provide further diagnostic support for this disorder.

Key words: Behçet's Syndrome; Abnormalities; Audiology; Vestibular Diseases

Introduction

Behçet's syndrome is a systemic relapsing inflammatory disease of unknown aetiology. It is common in the Far East and eastern Mediterranean (prevalence 1:1000), but less common in Northern Europe and the United States.[1–6] The disease affects both males and females, usually in their third or fourth decade.[3]

The clinical presentation of Behçet's syndrome is heterogeneous, with variable involvement of many organs. Since there is no accepted diagnostic test, recognition of the disease relies on identification of its characteristic clinical features. The International Study Group[1,2] have recommended that recurrent oral ulceration be required for definite diagnosis, together with two of the four following features – genital ulcers, eye lesions, skin lesions and skin hypersensitivity reaction (pathergy). The presence of other signs such as arthritis, gastrointestinal, vascular or central nervous system involvement ('minor criteria') may support the diagnosis, but they do not occur with sufficient frequency to be included in a set of diagnostic criteria.[1,2]

Inner ear involvement in patients with Behçet's syndrome has been reported, but while extensive audiological studies have been performed, vestibular function has not been studied in detail.[7–13] We report the clinical and neuro-otological findings in a series of 26 consecutive patients with Behçet's syndrome and the relationship of these findings to other clinical manifestations.

Methods

Patients

Twenty-six consecutive patients with Behçet's syndrome, unselected for audiovestibular complaints, were referred from the Rheumatology Unit of Hammersmith Hospital, London, for neuro-otological assessment. Detailed information was obtained regarding present complaints, past medical history (with particular reference to ear, eye and neurological disease), family and drug history. Patients with a history of cranial trauma, use of ototoxic drugs, otological or neurological disease unrelated to Behçet's syndrome, or patients with metabolic conditions associated with inner ear damage, were excluded from the study.

All patients underwent a clinical neuro-otological examination, which included a Romberg test, gait testing with and without eye closure, and an eye movement examination (assessment of convergence, smooth pursuit, saccades, doll's head manoeuvre and optokinetic nystagmus in response to a small motorized drum which we use for clinical examination and an evaluation of spontaneous nystagmus in primary gaze and during gaze deviation to 30° in

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each direction in the horizontal and vertical planes, as well as positional nystagmus during the Hallpike positional test.[14]

Detailed audiometric and vestibular testing were conducted.

Audiometric methods

Pure-tone audiometry. Pure-tone audiometry (PTA) was carried out at 0.25, 0.5, 1, 2, 4 and 8 kHz using a GSI 16 diagnostic audiometer. Asymmetry was defined by a difference of >15 dB on at least two frequencies, or >20 dB on a single frequency. A hearing loss of 21–40 dB was defined as mild, 41–80 dB as moderate and above 80 dB as severe.[16]

Acoustic reflex thresholds. Ipsilateral and contralateral acoustic reflex thresholds (ARTs) were obtained using a GSI 33 oto-admittance-meter in 5-dB steps up to a maximum output of 110 dB HL at 0.5 and 1 kHz, 105 dB at 2 kHz and 100 dB at 4 kHz ipsilaterally, and up to 120 dB HL at 0.5, 1 and 2 kHz and 115 dB at 4 kHz contralaterally. ART upper limits not exceeding 105 dB HL at up to two adjacent frequencies and/or an interaural difference not exceeding 10 dB at no more than two adjacent frequencies were considered normal in patients with cochlear hearing loss less than 60 dB.[17]

Brainstem auditory evoked potentials. Brainstem auditory evoked potentials (BAEPs) were performed on Medelec MSL 10 Sensor, using 100-μs click stimuli of up to 100 dB HL stimulus intensity delivered through TDH 49 headphones. Two averages of 1024 sweeps were recorded and the reproducible components of each trace were identified.[18] The normal values in our laboratory are: I–III<2.4 msec, III–V<2.2 msec and I–V<4.4 msec, asymmetry <0.2 msec.

Transient evoked otoacoustic emissions. Transient evoked otoacoustic emissions (TOAEs) were recorded using the Otodynamics ILO 88 analyser with a 'non-linear' click stimulus of 80 μsec electrical duration, presented at a repetition rate of 50 Hz and an intensity of 80 ± 4 dB SPL. A foam tip was used to seal the probe in the external canal and recordings were taken only if a stable stimulus was present. Each response consisted of an average of 260 sweeps obtained with a preset artefact rejection facility. Spectral analysis and amplitude measurements were calculated automatically by the system. Three TOAE parameters (total response energy, total noise energy and interwave correlation) were analysed. A response was considered normal or present if the total response energy was significantly greater (3 dB) than the noise level, and if the correlation (reproducibility) was greater than 50 per cent.[19]

Vestibular assessment

Eye movements were recorded by direct current electronystagmography using a standard test battery.[20] Surface electrodes were attached at the inner and outer canthi to record horizontal eye movements. Calibration was performed at the beginning and at the end of the testing. The eye movements were recorded on polygraph paper.

Horizontal saccades were tested by asking the patient to look between two fixation points, positioned straight ahead and at 30° to the right and left, while sitting with the head fixed. A consistent amplitude step of <80 per cent of the target step or velocity of <300°/sec was deemed abnormal.

Smooth pursuit was generated by a smoothly moving sinusoidal laser target, while the patient was asked to track it. The amplitude of the target was set at 30° to right and left of centre and the frequency of the target oscillation was 0.2, 0.3 and 0.4 Hz. A gain of <70 per cent was considered abnormal.

Optokinetic nystagmus (OKN) was induced by rotating a large curtain with white vertical stripes spaced at 15.6° intervals. The curtain was rotated at constant velocity of 40°/sec for 20 sec, alternately to right and left around the patient. A gain of <60 per cent was considered abnormal. The full field large curtain is part of the vestibular investigation which allows for quantitative optokinetic stimulation and EOG recording.

The vestibuloocular reflex (VOR) was tested by both sinusoidal oscillation (0.2 Hz, peak velocity 30°/sec) and by step acceleration stimulus to right and left (<1 sec to a constant velocity of 60°/sec), while the subject was sitting in the dark with eyes open. The peak velocity of the slow component of the induced nystagmus was measured and a gain of <40 per cent or an asymmetry of >25 per cent were deemed abnormal.

Vestibuloocular reflex suppression (VORS) was tested during sinusoidal rotation, as above, while the patient fixated at a small light attached to the chair directly in front of him. Break through nystagmus, with a slow component velocity to stimulus velocity ratio exceeding 0.05, was deemed abnormal.

Spontaneous or gaze evoked nystagmus, in the presence and absence of optic fixation, was recorded by asking the patient to fixate on LEDs directly ahead and 30° to the right and left, respectively, and maintain their direction of gaze, after the light was turned off. More than 5 beats of nystagmus of 4°/sec was deemed abnormal.

The bithermal caloric testing was performed by direct observation of the induced nystagmus response.[21] The duration of the nystagmus was measured with visual fixation in the light and without fixation in a dark room using Frenzel's glasses. Canal paresis or directional preponderance were calculated according to Jongkees formula.[22] Values greater than eight per cent for canal paresis and 12 per cent for directional preponderance were deemed abnormal.[23] Either of these patterns, in the absence of any central oculomotor abnormality and with a normal vestibular suppression, was considered to indicate peripheral vestibular pathology.

Unidirectional horizontal nystagmus, obeying Alexander's law and suppressed by optic fixation, was defined as nystagmus of the peripheral type.

Direction changing vertical or horizontal nystagmus, uninhibited by vision, was defined as nystagmus of central type. Central oculomotor abnormalities comprised unilateral or bilateral abnormalities of OKN, smooth pursuit or VORS.[20]

Data analysis

The eye movement records were analysed for peak velocities of OKN, VOR and smooth pursuit to both right and left. The gain of each of these parameters was calculated. Normal values in our laboratory can be seen at the bottom of Table III.

Statistical analysis

A chi-squared test was performed to check whether the occurrence of audiovestibular involvement was associated with individual organ involvement. In addition, the method of linear regression was applied to look for correlation between the patients' age, disease duration and audiovestibular involvement.[24]

Results

Clinical characteristics

The clinical characteristics of the patients with Behçet's syndrome are summarized in Table I. There were nine men and 17 women of mean age 38.2 years (SD 11.5, range 16–62). the mean disease duration was 13.8 years (SD 8.9, range 3–36). The diagnosis of Behçet's syndrome was considered 'definite' in 20 (77 per cent) of patients, based on the ISG criteria. In the remaining six patients the diagnosis was considered 'probable', based upon the presence of two of the manifestations listed under the ISG criteria and a consistent overall clinical picture.

Oral ulcers were present in all patients. Present or past genital ulcers were noted in 21 (81 per cent) of patients. Sixteen (61.5 per cent) of patients had eye involvement (iridocyclitis, hypopyon or chorioretinitis) at some stage of the disease. Of the 18 (69 per cent) of patients with skin lesions (erythema nodosum, pustules), five had demonstrated a positive pathergy test. Central nervous system involvement, in the form of meningoencephalitis, brainstem syndrome, pseudotumour cerebri and/or white matter lesions on brain MRI, was present in 11 (42 per cent). There was a history of vascular occlusion and/or thrombophlebitis in seven (27 per cent) patients, arthritis in six (23 per cent), and gastrointestinal involvement in three (11 per cent) patients. Patient 19 had also a history of epididymitis. Headaches were common (27 per cent) even in the absence of objective CNS involvement.

TABLE I
CLINICAL MANIFESTATIONS OF PATIENTS WITH BEHÇET'S SYNDROME IN OUR SERIES

				'Major signs'					'Minor signs'					
Patient No.	Age (years)	Sex	Disease Duration (years)	Oral Ulcers	Genital Ulcers	*a Eye lesions	*b Skin lesions	Pathergy	Arthritis	*c GIT inv.	*d Vascular Inv.	*e CNS Inv.	Audio and/or vestibular Inv.	Behçet's diagnosis
1	46	M	15	+	+	−	−	−	−	−	+	+	+	Probable
2	36	F	11	+	+	+	+	−	−	−	+	−	−	Definite
3	51	F	4	+	−	+	+	−	+	−	−	+	+	Definite
4	35	F	20	+	+	−	−	−	−	−	−	+	+	Probable
5	38	M	30	+	+	+	+	+	+	+	−	−	+	Definite
6	41	F	11	+	+	+	+	−	−	−	−	−	+	Definite
7	47	F	30	+	+	+	−	−	−	−	−	−	+	Definite
8	16	M	4	+	+	+	+	−	+	−	−	+	+	Definite
9	37	M	10	+	−	−	+	−	−	−	−	−	−	Probable
10	56	M	14	+	+	−	+	−	−	−	−	−	−	Definite
11	28	F	18	+	−	+	−	−	−	−	−	−	+	Probable
12	46	F	9	+	+	+	+	−	+	−	−	+	+	Definite
13	62	M	13	+	+	+	−	−	−	−	−	+	+	Definite
14	58	F	36	+	+	−	+	−	−	−	+	+	+	Definite
15	32	F	14	+	+	+	+	+	−	−	+	+	+	Definite
16	34	F	5	+	+	−	+	−	−	−	−	−	+	Definite
17	23	M	15	+	+	−	−	−	+	−	−	+	−	Probable
18	29	F	3	+	+	+	+	−	−	−	−	−	−	Definite
19	36	F	23	+	+	+	+	+	−	+	−	−	−	Definite
20	33	M	4	+	+	−	+	+	−	−	−	−	−	Definite
21	22	F	3	+	+	−	+	+	−	+	−	−	+	Definite
22	30	F	14	+	+	+	+	−	−	−	−	−	+	Definite
23	33	M	10	+	−	+	+	−	−	−	+	−	+	Definite
24	46	F	5	+	+	+	−	−	−	−	+	−	+	Definite
25	28	F	20	+	+	−	−	−	−	−	−	+	+	Probable
26	49	F	18	+	−	+	+	−	+	−	+	+	+	Definite
			Total	26	21	16	18	5	6	3	7	11	19	Definite = 20
			%	100	81	61.5	69	19	23	11	27	42	73	77

inv; involvement; +, present; −, absent; F, female; M, male. *a Iridocyclitis, hypopyon or chorioretinitis; *b Erythema nodosum, pustular lesions; *c Gastrointestinal symptoms and/or ulcerative colitis; *d Vascular occlusions or thrombophlebitis; *e Meningoencephalitis, brainstem syndrome, pseudotumour cerebri and/or presence of white matter lesions on MRI.

Nineteen (73 per cent) patients had detectable auditory and/or vestibular involvement. No statistical relationship was found between any other system involvement and audiovestibular involvement, nor between the auditory and vestibular lesions ($p>0.097$). In addition, there was no correlation between the patients' age, disease duration and audiovestibular involvement.

Audiological findings

The audiological findings are summarized in Table II. Sixteen (61.5 per cent) patients reported auditory symptoms, such as hearing impairment, tinnitus, aural fullness or hearing distortion, and in three the auditory symptom was a major complaint. In 12 of these 16 patients and in a further two asymptomatic patients, abnormalities were found on audiological testing.

Audiometric evaluation showed sensorineural hearing loss (SNHL) in 11 patients: in three patients the SNHL was mild, in six moderate and two patients severe. In three patients, the hearing loss was asymmetric. No typical audiometric configuration was detected; low frequency, high frequency, and plateau configuration were all observed, but bilateral involvement was more commonly observed than unilateral involvement.

The ART measurements were elevated or absent in five cases and in two cases, in conjunction with other audiological tests, suggested the presence of a retrocochlear lesion (patients 7 and 8).

BAEP recordings revealed a central auditory lesion in two patients, with a history of CNS involvement (focal neurological signs in patient 3 and aseptic encephalitis in patient 8). Prolonged latencies or absent waves V were recorded. Patient 8

TABLE II
AUDIOLOGICAL ASSESSMENT OF PATIENTS WITH BEHÇET'S SYNDROME

Patient No.	Symptoms *a	PTA *b	ART *c	BAEP *d	OAE *e	Conclusions
1	+	mild BiSNHL (hf a)	N	N		Bilateral cochlear lesion
2	−	N	N	N		Normal
3	−	N	N	_V lt	N	Central auditory involvement
4	+	N	N	N		Normal
5	−	N	N	N	N	Normal
6	+++	severe BiSNHL	absent	bilat absent I		Bilateral cochlear lesion
7	−	N	all elevated	N	absent rt	Right cochlear and retrocochlear lesion
8	+++	mild/mod BiSNHL (hf a) (poor speech discrimination)	absent or elevated	bilat absent V		Bilateral asymmetric retrocochlear lesions
9	+	N	na	N		Normal
10	−	N	N	N		Normal
11	−	N	N	N		Normal
12	+	bilat mild SNHL a	N	N		Bilateral asymmetric cochlear lesion
13	++	bilat moderate SNHL (hf)	N	N		Bilateral cochlear lesion
14	+	moderate lt SNHL (lf)	N	N		Unilateral cochlear lesion
15	+	N	N	N		Normal
16	+	moderate lt CHL	absent or elevated	N		Unilateral conductive hearing impairment
17	−	N	N	N	N	Normal
18	−	N	N	N		Normal
19	−	N	N	N		Normal
20	−	N	N	N	N	Normal
21	+++	bilat moderate SNHL lf, bilat severe SNHL hf a	N	N	absent lt	Asymmetric cochlear lesion
22	+	N	N	N	abnormal bilat	Bilateral cochlear lesion
23	++	bilat moderate SNHL	N	N	absent	Bilateral cochlear lesion
24	++	bilat moderate SNHL hf & mild lt CHL	absent or elevated	na		Bilateral cochlear lesion, unilateral conductive hearing loss
25	+	N	N	N	N	Normal
26	+	bilat mild SNHL	N	N	absent	Bilateral cochlear lesion

*a + mild, ++ moderate, +++ severe, − absent.
*b PTA = pure tone audiometry, SNHL = sensorineural hearing loss, CHL = conductive hearing loss, mild = 21–40 dB, moderate = 41–80 dB, severe = >80 dB, a = asymmetric (⩾10 dB difference between ears at least 2 frequencies), hf = high frequencies (3000–8000 Hz), lf = low frequencies (250, 500 Hz).
*c ART = acoustic reflex thresholds, N = normal (for cochlear HL < 60 dB SRT ⩽ 105 dB at 2 adjacent frequencies)
*d BAEP = brainstem auditory evoked potentials, N = normal (wave latencies and interpeak latencies within normal limits), _ = prolonged wave or interpeak latencies.
*e OAE = otoacoustic emissions.
na not available.
bilat bilateral.
lt left.
rt right.

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also had central eye movement dysfunction and multiple white matter lesions on MRI. Absent waves I in patient 6 were in keeping with severe cochlear lesions.

TOAE were tested in 10 patients and five had abnormal findings. This was the only abnormal finding in patient 22, who complained of tinnitus.

In summary, 16 patients complained of auditory symptoms, but in only 12 of these were audiological abnormalities demonstrated. An additional two asymptomatic patients also showed audiological abnormalities. Ten patients revealed a bilateral sensorineural hearing loss and further two patients demonstrated a unilateral sensorineural hearing loss. Ten patients had evidence of a cochlear lesion, one patient had retrocochlear pathology and a further patient demonstrated findings compatible with a mixed cochlear and retrocochlear lesion. Two patients, with no previous history of middle ear disease, had an unilateral conductive hearing loss (patients 16 and 24) and were referred for further otological investigation.

Vestibular testing

The results of vestibular testing are summarized in Table III. Of the 26 patients with Behçet's syndrome, who underwent a quantitative vestibular assessment, 17 had symptoms which were suggestive of vestibular dysfunction, such as dizziness, vertigo, disequilibrium or oscillopsia, and in seven these symptoms were a major complaint. Vestibular testing, however, revealed abnormalities in only 10 patients. Smooth pursuit gain was within normal limits in all patients. Two patients (4 and 8) were deemed to demonstrate

TABLE III
QUANTITATIVE VESTIBULAR AND OCULOMOTOR ASSESSMENT IN PATIENTS WITH BEHÇET'S SYNDROME

Patient No.	Symptoms *a	Nystagmus *b	Pursuit *c	OKN *d	VOR *e	VORS *f	Caloric Testing *g	Conclusions
1	++	−	0.85	1.10	0.41	<0.05	N	Normal
2	−	−	0.96	0.99	0.76	<0.05	N	Normal
3	++	−	1.04	0.94	0.58	<0.05	N	Normal
4	++	p	1.15 **saccadic**	**lt 0.51** **rt 0.29**	0.50 **lt 1.16**	<0.05	**lt CP 13%**	Central and peripheral vestibular dysfunction
5	+++	p	0.73	0.85	**rt 0.86**	<0.05	N	Mild peripheral vestibular dysfunction
6	+++	p	0.74	0.63	0.60	<0.05	na	Mild peripheral vestibular dysfunction
7	++	−	0.76	1.02	0.54	<0.05	N	Normal
8	++	−	0.71 **saccadic**	**dysrhythmic 0.48**	0.58	**0.07**	N	Central eye movement dysfunction
9	+++	−	0.6	0.72	0.66	<0.05	N	Normal
10	++	−	na	na	na	na	N	Normal
11	−	−	0.85	0.63	lt 0.61 **rt 0.32**	<0.05	**lt CP 13%**	Mild peripheral vestibular dysfunction
12	+	−	na	na	na	na	N	Normal
13	+++	−	0.69	0.81	**0**	<0.05	**Bilateral CP 100%**	Bilateral vestibular failure and mild central oculomotor dysfunction
14	++	−	0.74	0.71	0.60	<0.05	**rt CP 10%**	Mild peripheral vestibular dysfunction
15	−	−	1.02	1.01	0.64	<0.05	**lt CP 100%**	Peripheral vestibular dysfunction
16	−	−	0.75	0.73	0.41	<0.05	N	Normal
17	−	−	0.80	na	0.44	<0.05	N	Normal
18	+	−	1.17	0.84	1.11	<0.05	N	Normal
19	−	−	na	na	na	na	N	Normal
20	−	−	0.76	0.81	0.56	<0.05	N	Normal
21	+++	p	0.93	0.65	**0.16**	<0.05	**lt CP 100%** **rt CP partial**	Bilateral asymmetric vestibular lesion
22	+	−	0.73	0.82	0.42	<0.05	N	Normal
23	−	−	0.72	0.68	0.80	<0.05	N	Normal
24	+++	−	0.74	0.61	0.64	<0.05	N	Normal
25	+++	−	0.71	0.68	0.44	<0.05	**rt CP 10%**	Peripheral vestibular dysfunction
26	−	−	na	na	na	na	N	Normal
Normal:			>0.60	>0.60	>0.40	<0.05	CP<8% DP<12%	

*a + mild, ++ moderate, +++ severe, − absent.
*b p = nystagmus of peripheral type, c = nystagmus of central type, − = absent.
*c Gain of smooth pursuit, peak eye velocity/peak stimulus velocity at 0.2 Hz 30 deg.
*d Gain of optokinetic nystagmus: peak eye velocity/peak stimulus velocity at 40 deg/sec.
*e Gain of vestibuloocular reflex: peak eye velocity/peak stimulus velocity of sinusoidal rotation at 0.2 Hz 30 deg/sec (patients 1, 28, 30 at 60 deg/sec).
*f Vestibuloocular nystagmus suppression by visual fixation: peak eye velocity/peak stimulus velocity at sinusoidal rotation at 0.2 Hz 30 deg/sec.
*g Bithermal caloric testing by Fitzgerald-Hallpike method measuring duration f nystagmus. CP = canal paresis, DP = directional preponderance.
na Not available
Numbers in **bold** indicate abnormal findings.
lt left.
rt right.

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central visuo-vestibular dysfunction with saccadic pursuit, low gain of OKN and a VORS abnormality (patient 8). Patient 4 also demonstrated a peripheral spontaneous nystagmus and a unilateral canal paresis on caloric testing. This patient was therefore considered to demonstrate both peripheral and central vestibular dysfunction. Three further patients (5, 6 and 21) showed peripheral vestibular dysfunction, as judged by unidirectional, horizontal spontaneous nystagmus, with enhancement in the absence of optic fixation. Patients 5 and 21 also demonstrated VOR abnormalities.

Five patients had a unilateral canal paresis on caloric testing (patients 4, 11, 14, 15, and 25) and two patients demonstrated bilateral vestibular dysfunction on caloric testing (patients 13 and 21). Patient 13 showed complete vestibular failure on both caloric testing and sinusoidal VOR oscillation, while patient 21 had a subtotal loss on both tests.

In summary, nine patients with vestibular abnormalities showed evidence of a peripheral vestibular involvement, one of whom demonstrated additional central vestibular dysfunction. One further patient showed a mild central oculomotor abnormality. In five patients, the peripheral vestibular lesion was unilateral and in two it was bilateral. Two additional patients demonstrated spontaneous nystagmus of the peripheral type and one of them showed also directional preponderance on rotatory testing. In the absence of any central oculomotor sings, these findings were interpreted to indicate a peripheral vestibular lesion.

Discussion

In this study we have documented the type and frequency of auditory and vestibular abnormalities in Behçet's syndrome. The lack of correlation between other organ and audiovestibular involvement is in keeping with the multifocal nature of the disease process.[1–3] A lack of correlation was also found between the auditory and vestibular lesions, but this may be explained by an understanding of the vascular supply. The common cochlear artery and the anterior vestibular artery are the main branches of the labyrinthine artery and can be selectively involved by immunologically mediated inflammation. The cochlea, saccule and posterior canal are supplied by the common cochlear artery, whereas the utricle, together with the anterior and horizontal canals, are supplied by the anterior vestibular artery.[20] Routine clinical vestibular tests allow evaluation of only the horizontal semicircular canal and, thus, a lesion of the anterior vestibular artery will manifest as an isolated vestibular abnormality, while involvement of the common cochlear artery will give abnormalities on audiological testing.[20]

Although the aetiology and pathogenesis of Behçet's syndrome are unknown, there is evidence supporting an important role for immunological mechanisms. These include an association with class I HLA B51 antigen, the presence of raised circulating levels of cytokines, and the presence of γδ T lymphocytes reactive with peptides derived from heat shock proteins.[25–27] These findings support the hypothesis of an immunologically mediated vasculitis in Behçet's syndrome. Improvement of hearing impairment in patients with this condition, in response to immunomodulatory therapy has been reported,[28,29] and this provides additional evidence that the inner ear lesions are immunologically mediated.

An earlier report described 16 patients with Behçet's syndrome, 10 of whom demonstrated inner ear involvement: five of them with cochlear, one with vestibular and four with auditory and vestibular peripheral deficits.[7] Belkahia (1982), reporting 16 patients with neuro-Behçet's, found eight with central vestibular damage, five with peripheral vestibular damage and two with hearing loss.[8] The 1991 study of Gemignani *et al*. revealed cochlear hearing impairment in 12 patients out of 20 patients with Behçet's syndrome. Five patients had evidence of altered vestibular dysfunction, four of the peripheral type. The authors concluded that audiovestibular involvement in Behçet's syndrome is frequent and generally underestimated, the cochlea being more frequently involved than the vestibular labyrinth.[9]

The data obtained in our series are consistent with these reports, although differences in patient selection hinder exact comparisons. Our series contains a relatively large proportion (42 per cent) of patients with neurological abnormalities and this may represent more aggressive or advanced pathology and, thus, an increased prevalence of audiovestibular involvement. Despite the high percentage of patients with neurological involvement in this study, it is interesting to note that almost all audiovestibular abnormalities were of peripheral labyrinthine type, indicating specific involvement of the labyrinth in this condition and the relatively uncommon involvement of the brainstem or cerebellum. However, the slightly higher frequency of vestibular abnormalities in our patients may reflect the full battery of vestibular investigations applied.

BAEPs were studied in 44 Behçet's patients by Stigby *et al*. Abnormalities were found in 52 per cent of patients with neurological manifestations and in 31 per cent without. The abnormalities found consisted of decreased amplitude of wave V, or prolonged I–III or III–V interpeak latencies.[30] Rizzo *et al*. reported a longitudinal multimodal evoked potentials study in two patients with neuro-Behçet. In one patient the BAEPs remained normal throughout, while the other had absent BAEPs attributed to a sensorineural hearing loss.[31] Our study showed BAEP abnormalities only in three patients, in one of whom there was a severe cochlear lesion and in another there was clear evidence of widespread neurological involvement including central eye movement dysfunction. The third patient demonstrated no other audiovestibular abnormality. Thus, BAEP alone would be an inappropriate test to detect subclinical auditory lesions in Behçet patients, particularly as the majority of patients in this study

had cochlear hearing loss. Characteristically, unless the loss is profound, BAEPs are normal in cochlear lesions.

Mild subclinical cochlear loss may be revealed using TOAEs. In this study, five out of 10 tested patients showed abnormalities on TOAEs, and in one patient this was the only abnormal audiological finding. Moreover, four patients, who had been evaluated prior to the introduction of routine TOAE testing, had auditory complaints, but no audiological deficit was revealed. It is in this group that OAE testing may be of greatest value for detecting auditory abnormalities.

Overall, this study identifies that auditory and/or vestibular abnormalities were found in 73 per cent of unselected group of Behçet's syndrome, a prevalence equalling that of common symptoms in this condition, including arthritis, gastrointestinal complaints and neurological involvement.[1,2] While we not have an age-matched control population in this study, we considered the control population of 40 normal subjects with an average age of 37.35 years (SD 11.4) used in an earlier community study within this unit.[32] In this control group of similar age distribution, the same audio-vestibular tests were applied and we identified auditory abnormalities in 32.5 per cent and vestibular abnormalities in 20 per cent. In view of similar demographics and identical assessment methodology, we assume that the neuro-otological abnormalities found in this group can be used as a control for our study. Significant difference was found between the prevalence of audio-vestibular abnormalities in Behçet's patients versus control ($p = 0.003$).

Little is known about inner ear involvement in other systemic autoimmune disorders. Bowman reported an eight per cent incidence of SNHL in 30 patients with systemic lupus erythematosus,[33] while, in a controlled study by Andonopoulos, 57.5 per cent of 40 lupus erythematosus patients had SNHL, without any correlation to disease activity or system involvement.[34] Similarly, in our study of Behçet's patients, the disease activity was not correlated to audio-vestibular involvement. We would, therefore, propose that the decision to treat audio-vestibular symptoms in patients with otherwise quiescent auto-immune disease should be taken on clinical grounds. For example, rapidly worsening cochlear symptoms would be treated aggressively, whereas unilateral vestibular symptoms, which may be expected to undergo central compensation, would allow a more conservative approach.

SNHL has also been reported in rheumatoid arthritis with a prevalence between 29 per cent to 48 per cent.[35] In Wegener's granulomatosis, hearing loss has been reported to occur in 20–45 per cent of patients, but the most common otological abnormality was conductive hearing loss.[36,37] While the above studies concentrate on audiological findings, details of vestibular assessment in autoimmune diseases are sparse or absent.

This study represents the largest study of audio-vestibular investigations in unselected patients with Behçet's syndrome and the most detailed in terms of neuro-otological investigation. Audiovestibular dysfunction is defined in approximately three-quarters of patients with this disorder.

Since the diagnosis of Behçet's syndrome is based on the presence of the typical organ involvement, identification of dysfunction in the auditory or vestibular system, in the absence of any other satisfactory explanation, may provide an additional valuable clue in support of the diagnosis, particularly in patients who do not fully meet the ISG criteria.

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