Vestibular evaluation in Behçet's disease. Personal experience

La valutazione vestibolare nella malattia di Behçet. Nostra esperienza

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Key words

Vestibular abnormalities • Behçet's disease • Diagnosis • Otoneurological tests

Parole chiave

Vestibulopatia • Malattia di Behçet • Diagnosi • Valutazione vestibolare

Summary

Few reports have appeared in the literature concerning vestibular findings in Behçet's disease. In the present study, extensive vestibular testing, performed in 14 patients (8 male, 6 female; mean age: 32 years; range: 12-51) presenting definite Behçet's disease, revealed a high prevalence of central vestibular dysfunctions (78%). Data reported here suggest that an otoneurological evaluation of Behçet's disease patients may be helpful in identifying unexpected vestibular dysfunctions and central nervous system involvement different from the classical manifestations of the neuro-Behçet's syndrome.

Riassunto

In letteratura esistono pochi dati a riguardo delle alterazioni del sistema vestibolare nella malattia di Behçet. 14 pazienti (8 di sesso maschile e 6 di sesso femminile, età media 32 anni, range compreso tra 12 e 51 anni) con diagnosi di malattia di Behçet, sono stati sottoposti a valutazione vestibolare mediante registrazione dell'oculomotricità, del riflesso vestibulooculare con stimolazione rotoacceleratoria e calorica bitermica e studio delle componenti somatosensoriali del mantenimento dell'equilibrio con posturografia dinamica computerizzata. In questi pazienti è stata evidenziata una elevata prevalenza di disfunzioni vestibolari centrali (78%). I dati da noi riportati suggeriscono che una valutazione otoneurologica nei pazienti con malattia di Behçet può rilevare alterazioni dell'apparato vestibolare usualmente non considerate tra le classiche manifestazioni cliniche della malattia ed un coinvolgimento del sistema nervoso centrale quale iniziale evento della sindrome di neuro-Behçet.

Introduction

Behçet's disease (BD) is a rare systemic vasculitis of young adults consisting of recurrent attacks of acute inflammation. It occurs endemically in the Middle East and Mediterranean regions but is also present in Central and Far Eastern Asia including Korea, Japan and China. Turkey has the highest prevalence: 80-370 cases per 100,000 population. The incidence of this disease in Europe is very low at 1:500,000 [1].
The aetiology of BD is unknown. Susceptibility to BD is strongly associated with the HLA-B51 allele [2]. Environmental, viral, bacterial and immunological factors have been suggested as causative agents [3 4]. Although the pathogenesis of BD has not yet been fully elucidated, the condition is considered to be triggered, at least in part, by autoimmune mechanisms even if it remains to be determined whether the autoimmune mechanism is a primary or a secondary event in the development of BD [1].

The common symptoms of BD are: recurrent oral aphthous ulcers, genital ulceration, uveitis, iritis and hypopyon, retinal vasculitis, arthritis/arthralgia, folliculitis, neurological lesions, gastrointestinal lesions, venous thrombosis and cardiovascular lesions, and pleuropulmonary lesions and epididymitis. Ocular involvement occurs in approximately 70% of cases and can cause blindness despite vigorous treatment. The diagnosis of definite BD is made on the basis of the criteria proposed by the International Study Group for Behçet's Disease in 1990 [5 6]. Recurrent oral ulceration must be present as well as two of the following: recurrent genital ulceration, eye lesions, skin lesions and a positive pathergy test.
There are few papers reporting on the vestibular findings in BD. Aim of the present investigation was to evaluate the prevalence and the features of vestibular dysfunctions in definite BD and to assess the role of otoneurological tests in this disease.

Material and methods

Patients

A total of 14 consecutive patients (6 female, 8 male, aged between 12 and 53 years, mean age: 32), presenting definite BD were enrolled in the study during the period 1998-2002 (Table I). The diagnosis of definite BD was performed on the basis of the criteria proposed by the International Study Group for Behçet's Disease in 1990 [6]. Duration of the disease ranged between 2 and 20 years. All patients had a negative family history of deafness, showed no evidence of ear infections, use of ototoxic drugs or exposure to noise. All patients underwent immunosuppressive treatment with cyclosporine A or cyclosporine A and steroids, at the time of diagnosis. The standard dosage of cyclosporine A was 5 mg/kg/day, the concomitant oral prednisone dose was 0.4 mg/kg/day and therapy was adjusted according to the clinical picture and response to treatment.

Vestibular testing

The clinical test protocol comprised an extensive vestibular examination with positional, oculomotor, rotatory chair, caloric stimulation and computed dynamic posturography tests.

Rotatory chair stimulation and oculomotor tests

Horizontal eye movements were recorded by bitemporal DC-coupled silver-silver chloride electrodes (impedance < 20 kΩ) connected to a Nystagliner Toennies 1996 (Toennies, Germany) electronystagmograph. The electronystagmography (ENG) signal was filtered with a 4-pole, high-pass filter with a bandwidth of 25 Hz. The signal was then digitally sampled at 200 Hz before being stored for subsequent computer analysis. ENG calibration was achieved by measuring the digitized change in ENG potential for saccades to illuminated targets from centre to 15° left and from centre to 15° right. Horizontal saccades were tested by asking the subject to look at a small visual target that moved abruptly 10° left to 10° right of the centre (normal value of latency, i.e., the time between the stimulus onset and the response = 129-255 msec). Smooth pursuit was generated by a smoothly moving target, while the patient was asked to track it. The target moved sinusoidally at a rate of 0.29°/sec and amplitudes of 15° right and 15° left (normal value of gain i.e., the relationship between the visual stimulus and the eye movement velocity = 0.65-1.07). Oculomotor tests were recorded before rotatory chair stimulation. ENG recordings were obtained during a torsion test in complete darkness with the subject wearing Frenzel's glasses. The chair performed pendular sinusoidal movements, with a frequency of 0.1 Hz. Speed was set at 90°/s. Rise and fall times were both set at 5 s and the plateau was 65 s. The subject's head was bent by 30°. Subjects were instructed to look straight ahead and alertness was maintained using mental arithmetic and alphabetical listing tasks. The VOR gain, i.e., the ratio between the response amplitude (slow-phase eye velocity) and the stimulus amplitude (head rotation velocity) was automatically calculated by Fourier

Table I. Clinical manifestations of patients with definite Behçet's syndrome.

Patients	Age	Sex	Disease duration (yrs)	Oral ulcers	Genital ulcers	Eye lesions	Skin lesions	*Arthritis*	NB	Vestibular symptoms
1	34	F	7	+	+	R	+		+	
2	12	M	2	+		AU				
3	13	M	3	+		AU				
4	35	F	7	+		AU				Instability
5	53	F	16	+	+	R	+			Instability
6	47	F	9	+		AU		+		Instability
7	33	F	11	+	+	R	+		+	Instability
8	29	M	4	+		P	+		+	
9	51	M	10	+	+	R	+	+		
10	30	M	12	+		R	+		+	
11	26	M	6	+		P	+			
12	30	F	15	+	+	AU		+		Instability
13	26	M	7	+		P	+		+	Deafness
14	40	M	20	+	+	R	+	+		

NB: neuro-Behçet; R: retinitis; AU: anterior uveitis; P: papillitis

analysis to avoid bias from human intervention. The normal value range of VOR gain, at our laboratory, is considered as 0.40-0.85.

Bithermal caloric testing was performed using the method of Fitzgerald and Hallpike [7]. The visual suppressioin test was performed.

Computed dynamic posturography (CDP) with the analysis of Sensory Organization Tests (SOTs) and composite equilibrium score: CDP was performed with the subject standing on a dual forceplate enclosed by a visual surrounding. The dual forceplate records the vertical forces between the feet and ground, as well as horizontal shear forces, thereby allowing an estimation to be made of the position of the swaying body. The SOT consists of six different conditions, each lasting for 20 sec, which were repeated three times in order to obtain more stable values. The conditions were as follows: 1) The eyes were open, and platform surface and visual surroundings fixed. 2) As condition 1, but the subject's eyes were closed. 3) The platform was fixed while the visual surroundings kept moving around an axis collinear with the patient's ankle joint, in direct proportion to the antero-posterior sway of the patient's centre of gravity. In this way, the patient could not perceive changes in the body sway orientation with respect to the visual surrounding. 4) The visual surrounding was fixed, the eyes were open and the platform was kept moving in direct proportion to the patient's sway so that changes in the patient's orientation with respect to the platform were cancelled. 5) The visual surrounding was fixed, the eyes were closed and the platform was kept moving as in condition 4. 6) The eyes were open, and the platform and visual surrounding were rotated proportionally to the anteroposterior body sway. The composite equilibrium score (ES) indicating the range of sway angle with respect to the earth vertical was computed for each condition. The following formula was used:

$$ES = 12.5° - (\theta_{max} - \theta_{min}) \times 100/12.5°$$

where θ is the angle between a line extending vertically from the centre of the foot support and a line extending from the centre of gravity. Sensory analysis calculating the relationships between the equilibrium scores in the 6 conditions identified the sensory dysfunction and individual preference for different inputs: somatosensory (test condition 2/1), visual (4/1), vestibular (5/1) and vision preference (3+6/2+5).

Results

Clinical manifestations

The clinical manifestations in 14 patients with definite BD are outlined in Table I. All patients showed oral ulcers and clinical evidence of posterior or anterior uveitis. Retinal vasculitis was present in 6 cases (bilateral in 5 patients and unilateral in one case): the picture was characterised by vascular occlusion and areas of haemorrhage and oedema with an inflammatory response in the vitreous. Optic nerve vasculitis leading to ischaemic papillitis was observed in 3 patients with bilateral non-simultaneous involvement. An anterior uveitis (non-granulomatous iridocyclitis) was present in 5 cases. Five patients showed ocular signs of neuro-BD: diplopia due to extra-ocular muscle paralysis from central involvement was present in one patient, ptosis in 2, dysarthria and transient coma in 2. Genital ulcers, skin lesions and arthritis were present in 6, 9 and 4 patients, respectively. Only one patient complained of deafness. Of the 14 patients, 5 complained of instability.

No association between time of disease and vestibular findings was observed.

Vestibular abnormalities (Table II)

Even though only 5 patients complained of instability, 11 out of 14 (78.6%) cases showed vestibular test abnormalities. Vestibular and positional examination showed the absence of spontaneous and positional nystagmus in all cases. Bithermal caloric tests showed no labyrinthic preponderance in any of the cases. At the rotary chair test using electronystagmography, the nystagmus response was symmetrical in all 14 patients, but 9 out of these 14 patients had an increased gain of the VOR suggesting impaired central processing of signals coming from both labyrinths.

All patients were able to perform eye movements in both directions but the oculomotor tests revealed a low gain at smooth pursuit (SP) in 3 cases (patients 5, 9, 10) and a high latency value at saccades in one case (patient 7): these results could be explained as a detection of abnormalities in the efferent part of the VOR even though only one patient (n. 7) had diplopia as an ocular sign of neuro-BD.

The Sensory Organization Test (SOT) revealed that 6 patients showed abnormal findings following the CDP examination with a reduction of the composite equilibrium score. In these 6 patients, SOT results were altered in one or more test conditions. Patients 3 and 7 presented abnormal SOT 4, 5, 6 interpreted as a sign of CNS disorders. The other 4 patients presented neuro-BD with a combination pattern seldom observed in vestibular pathology. In particular, 2 patients had abnormal SOTs 2, 3, 4, 5, 6 with somatic, visual, vestibular dysfunction; 1 patient had abnormal SOT 5 with vestibular dysfunction; 1 patient had abnormal SOT 4 with visual dysfunction: these findings are difficult to interpret since one or more abnormal test conditions suggest both central and peripheral problems at vestibular level.

Table II. Vestibular testing in patients with definite Behçet's disease.

Patient No.	Spontaneous and positional nystagmus	Bithermal caloric stimulation	VOR gain	Ocular motor studies Saccades latency	Ocular motor studies Pursuit gain	SOT
1	- Absent	Normal	2.69	140	0.85	5
2	- Absent	Normal	1.99	215	0.95	Normal
3	- Absent	Normal	0.91	210	1.18	4, 5, 6
4	- Absent	Normal	0.45	185	0.87	Normal
5	- Absent	Normal	1.26	165	0.56	Normal
6	- Absent	Normal	0.45	200	0.69	Normal
7	- Absent	Normal	1.03	350	1.08	4, 5, 6
8	- Absent	Normal	1.86	190	1.01	2, 3, 4, 5, 6
9	- Absent	Normal	0.63	200	0.51	Normal
10	- Absent	Normal	0.71	200	0.51	2, 3, 4, 5, 6
11	- Absent	Normal	0.62	190	0.69	Normal
12	- Absent	Normal	1.02	160	0.89	Normal
13	- Absent	Normal	1.10	175	0.80	4
14	- Absent	Normal	1.05	190	1.07	Normal

VOR: Vestibulo-Ocular Reflex (Gain normal value = 0.24-0.85); Saccades latency: N: normal (normal value:129-255 ms); Pursuit gain (normal value = 0.65-1.07); SOT = sensory organization test in computed dynamic posturography

Discussion

Vestibular abnormalities have not been included among BD symptoms. However, some Authors have reported a common vestibular involvement in BD [8-11]. The present data show a high prevalence (78%) of vestibular disturbances in definite BD.

Vestibular function studies, in the literature, have more frequently reported peripheral lesions than central vestibular damage in BD patients [8 11 12]. Results emerging from the present study, on the contrary, show the absence of vestibular labyrinth dysfunctions in BD. In our series, the association of increased gain of the VOR, abnormalities in the efferent part of the VOR, a combination pattern seldom observed in peripheral vestibular pathology, at sensory organization tests of computed dynamic posturography, seems to reveal CNS disorders [13 14] more frequently than peripheral vestibular lesions in BD.

Indeed, at the rotatory chair test using electronystagmography, the nystagmus response was symmetrical in all 14 patients, but 9 out of the 14 cases had an increased gain of the VOR. The gain of the VOR expresses the relationship between the stimulus (the rotation speed of the patient on a rotatory chair) and the response (the compensatory eye movement velocity). An increased gain of the VOR reveals additional information coming from both labyrinths and may detect a central vestibular dysfunction.

Furthermore, upon screening of visual-ocular control, a low gain, at smooth pursuit, in 3 cases and a high latency, at saccades, in one, suggested abnormalities in the efferent part of the VOR. Even if the interpretation of the smooth pursuit and saccades is mainly morphological, these findings are compatible with a diagnosis of central visuo-vestibular dysfunction.

Last but not lease, SOT results, at computed dynamic posturography, were extremely abnormal in 6 cases: 2 patients showed abnormal SOTs 4, 5, 6 that are rarely seen in the vestibular population and indicate the presence of a central vestibular disorder; 4 patients with neuro-BD had at least one abnormal test condition, both in central and peripheral vestibular function.

Although the finding of central vestibular tract dysfunction might be expected in patients with a diagnosis of neuro-BD, we can only surmise that, in the others, the detection of central vestibular impairment was an initial symptom of CNS involvement in the absence of the classical neurological and radiological CNS manifestations.

Our results support the clinical usefulness of vestibular evaluation in the diagnosis of uncommon symptoms in BD.

Although the measurement of brainstem auditory evoked potentials has been reported to be helpful in the diagnosis of neurological complications [3], our data suggest that the rotatory chair and computed dynamic posturography tests could play a useful role in the detection of CNS involvement.

Further studies are needed to elucidate and to define the features of vestibular system abnormalities in order to provide further information concerning this rare and, as yet, not completely well-known disease.

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